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HIV Drug Therapy 2012 GLASGOW

Abstract supplement

Eleventh International Congress on Drug Therapy in HIV Infection

11–15 November 2012, Glasgow, UK

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KEYNOTE LECTURES

KL1

Prevention of HIV-1 infection 2013: glimmers of hope

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The efficiency of transmission of HIV depends on the infectiousness of the index case and the susceptibility of those exposed. Infectiousness is dictated by the concentration of HIV-1 in relevant fluids (regardless of route of transmission) and the viral genotype and phenotype. People newly infected with HIV-1 (i.e. acute infection) and those with STI co-infections excrete such a large concentration of virus as to be ''hyperinfectious.'' The actual transmission of HIV likely occurs in the first few hours after exposure. The probability of transmission may be as low as 1/10,000 episodes of intercourse or 1/10 sexual exposures when anal intercourse is practiced. The transmission of HIV is generally limited to one or a small number of founder variants which themselves may be ''hyperinfectious.'' Synergistic behavioural and biologic HIV prevention strategies have been developed and implemented. Safer sex includes limiting the number of sexual partners, use of male latex condoms, and structural interventions to reduce exposure. These strategies appear to have contributed to reduced HIV incidence in many countries. Biological interventions have proved catalytic: these include treatment of inflammatory cofactors, voluntary male circumcision and use of antiviral agents either for infected people (who can be rendered remarkably less contagious) or as pre- and post-exposure prophylaxis (PrEP and PEP). Ecologic evidence suggests that broader, earlier antiviral treatment of HIV may be reducing incidence in some (but not all) populations. However, maximal benefit of HIV ''treatment for prevention'' and application of PrEP will likely require a program of universal ''test and treat,'' where many more infected patients are identified, linked to care, and treated very early in disease and for life. Community randomized trials designed to support this approach are under way in Africa. The ''test and treat'' prevention strategy is resource-intensive and serves to emphasize research that searches for a cure for HIV infection so that people living with HIV can eventually reduce or stop treatment. Likewise, success in HIV prevention emphasizes the importance zof development of an HIV vaccine, which remains focused on agents that may evoke CTL responses, antibody dependent cytotoxicity, and (perhaps most important) broad neutralizing antibodies. A human clinical trial (RV144) and animal experiments have provided hope, excitement and a roadmap for development of an HIV vaccine.

http://dx.doi.org/10.7448/IAS.15.6.18066

KL2

HIV eradication: virological chances and clinical perspectives

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Once a retrovirus infects a eukaryotic cell and integrates within chromosomal DNA, it becomes part of its genome and can be activated/transcribed/translated to produce viral proteins and/or new viral particles. Over the years, some of these retroviruses may lose their pathogenicity and become adapted to the new host. Under these conditions, retroviruses can paradoxically ameliorate the functional portfolio of the infected cell, thus potentially increasing its functionality and/or chances of survival in a difficult environment. Individuals whose cells are infected by retroviruses have acquired, in the last millions of years, innovative functions that, once transmitted to the new generation through germinal cells, have become essential for their homeostasis, or even for their survival. This is the case of some endogenous retroviruses, whose products are mandatory for the proper vascularization of human placenta. To our knowledge, there are no natural means able to selectively eliminate retroviral genes from an infected cell or an individual. Therefore, the chances of getting naturally cured by retroviruses, once infection is set and viral genomes are spread into the body, are minimal or absent. HIV is a retrovirus that behaves as all other retroviruses that interacted with humans in the past millennia. Its fate is to remain forever within the infected body. For these reasons, the chances of getting rid of HIV infection and being biologically cured (that is, eliminating all viral genomes from the body) are very limited if we consider current knowledge, biotechnology and available medical tools (yet it cannot be fully excluded in very peculiar cases). The option offered by the so-called ''functional cure'' is different. In this case, medical manipulation may create conditions whereby viral genomes, decreased in number and function by proper therapies/vaccines, are no longer able to harm the host for an indefinite period of time. Patients do remain infected, but viral replicative cycles are absent, and progression of the disease is interrupted. This latter clinical approach may be suitable, and this is where clinical research is directing its efforts. If achievable, infected persons should cope with the virus and keep it under control for decades, without support of chronic antiviral therapy. In conclusion, the proper knowledge of the biological characteristics of HIV helps in selecting the best strategies aimed at obtaining the maximum achievable clinical result.

http://dx.doi.org/10.7448/IAS.15.6.18067

KL3

From HIV to global health: opportunities and challenges

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Remarkable advances have been achieved over the past decade in confronting the global HIV epidemic. By the end of 2010, 6.5 million persons living with HIV had initiated antiretroviral therapy in low and middle-income countries, the majority in sub Saharan Africa. Of the total of 2.5 new HIV infections that occurred in 2010, 1.9 million occurred in sub Saharan Africa. Nonetheless, 22 countries in sub Saharan Africa have experienced a decrease in HIV incidence. These remarkable achievements have involved a transformation of fragile health system. Examples include new models of care, task shifting, infrastructure enhancement, establishment of new data systems and mobilization of communities.
However, many of the same countries where HIV is prevalent also confront other health threats including high maternal and child mortality, high rates of tuberculosis and malaria as well as a burgeoning non-communicable chronic disease threat. Addressing these health threats requires taking the lessons learned from the HIV response and adapting them to confront these threats. Through building on the foundation established, similar progress may be achieved in addressing these health threats while maintaining the momentum of the HIV response.

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ORAL ABSTRACTS

O11 - ART FOR PREVENTION AND TREATMENT

O111

Pre-exposure prophylaxis: where are we in Europe?

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Despite major advances in HIV therapy, the number of new HIV infections remains very high, even in high-income countries where resurgence among men who have sex with men (MSM) has been witnessed. New prevention strategies have therefore to be assessed in order to curb the incidence of HIV infection. Recent studies have explored the effectiveness of antiretroviral therapy (ART) for HIV prevention and have generally yielded encouraging results. ART has been used successfully to prevent mother-to-child transmission of HIV, HIV acquisition following occupational or sexual exposure to HIV (post-exposure prophylaxis), and more recently, to reduce the risk of HIV transmission within a serodiscordant couple by treating the HIV-positive partner (HPTN 052 study). Another possible use of ART in prevention is pre-exposure prophylaxis, where ART is taken by an HIV-seronegative individual before HIV exposure. This PrEP strategy has been validated in animal models and more recently assessed in clinical trials in humans. The results of six large efficacy trials of PrEP are now available, but results have been inconsistent. The use of tenofovir gel in women at higher risk in Sub-Saharan Africa has shown efficacy when given before and after sex in the Caprisa 004 study (reduction of 39% of the incidence of HIV), whereas no efficacy was shown with daily use in the VOICE trial. Similarly, daily oral PrEP with tenofovir or tenofovir and emtricitabine has proved effective in the Iprex trial in MSM (reduction of 42% of HIV incidence), in the Partners PrEP study (reduction of 67 to 75% in HIV incidence) and in the TDF-2 trial (reduction of 63% in HIV incidence), but not in the Fem-PrEP or the VOICE trials in women. There are many potential explanations for these apparently conflicting results, such as the populations in which these strategies have been assessed, the differential pharmacokinetics of ART in the male and female genital tracts and most likely the high level of adherence which is required to confer protection against HIV acquisition. These results have also generated a lot of controversy about the implementation of PrEP. Some think that the data are good enough to rollout PrEP in key populations at higher risk. Others think more research is needed before PrEP is implemented because of concerns around safety, emerging resistance, cost and change in sexual behaviour that might offset the benefit of PrEP. Safety is indeed a major concern in healthy individuals. New studies are underway to address these issues and are assessing PrEP regimens in open-label studies (Iprex-OLE in MSM), intermittent PrEP regimens to try to improve adherence, new ART classes and new modalities of drug delivery. PrEP is therefore a promising biomedical intervention that might be used in the near future in addition to current prevention methods to prevent HIV infection and help control the spread of this infection.

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O112

When to start: as soon as possible

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Debate regarding ''When to start'' antiretroviral (ARV) therapy has raged since the introduction of zidovudine in 1987. Based on the entry criteria for the original Burroughs Wellcome (002) study, the field has been anchored to ''CD4 counts'' as the prime metric to indicate ARV treatment initiation for asymptomatic HIV-positive individuals. The pendulum has swung back and forth, based mostly on the efficacy and toxicity of available regimens. In today's world, several factors have converged that compel us to initiate therapy as soon as possible: (i) The biology of viral replication (1 to 10 billion viruses/day) screams that we should be starting early. (ii) Resultant inflammation from unchecked replication is associated with earlier onset of multiple co-morbid conditions. (iii) The medications available today are more efficacious and less toxic than in years past. (iv) Clinical trials have demonstrated benefit for all but the highest CD4 strata ($>$450 to 500 cells/μL). (v) Some cohort studies have demonstrated clear benefit of ARV therapy at any CD4 count, and almost all cohort studies have demonstrated no detrimental effects of early treatment. (vi) In addition to the demonstrated and inferred benefits to the individual patient, we now have a public health benefit of earlier intervention: treatment is prevention. Finally, from a practical/common sense perspective, we are talking about life-long therapy. Whether we start at a CD4 count of 732 or 493/μL, the patient will be on therapy for over 40 to 50 years! There does not seem to be much benefit in waiting, and there is likely to be significant long-term harm. Treat early!

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O113

When to start: not so fast

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It remains controversial whether and, if so, the extent to which antiretroviral therapy (ART) results in net benefit if used by HIV-positive persons with a high CD4 count, particularly those with early HIV infection. This controversy is primarily reflecting lack of solid evidence from randomized controlled trials. Currently published trials have compared early ART with initiation of ART below currently globally accepted thresholds for initiation (i.e. CD4 count at 350 cells/μL) and, hence, are unable to inform this discussion. Analyses on large observational studies that have attempted to address this question have shown inconsistent results; therefore, those results are considered low-quality evidence, as per the GRADE criteria used by, for example, WHO when formulating guidelines. In resource-constrained regions, not even observational data are available to inform this question. The START study is underway to answer this question. Data remain blinded, but START may show net harm from early use of ART; such a result would severely undermine use of ART as prevention in early HIV infection. Prescription of any type of medicine is guided by the principle of ''do no harm'' – that is, ''the doctor should not prescribe medications unless s/he knows that the treatment is unlikely to be harmful.'' Hence, the balance of risk/benefit to individuals versus prevention benefit is important to accurately determine, and current guidelines of generally initiating ART once the patient develops HIV-related symptoms or the CD4 count drops to levels around 350 cells/μL should be adhered to until further evidence has emerged.

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O114

Late presenters: what can we do?

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Late presentation represents a major problem for patients with HIV infection. Actually, it should be made a distinction between late testers and late presenters since the strategies to reduce the percentage of these two groups of subjects could be different. Indeed, the first population is represented by individuals unaware of their serological status, while in the second case the problem is related to engagement and retention in care. Concerning the first population, it has been shown that most of the patients had been seen by their family doctor or admitted to hospital during the year before HIV diagnosis. Indeed, this is a relevant problem, and new strategies to increase the level of suspicion of HIV infection among doctors who are non-HIV specialists are needed, as testing in presence of indicator diseases, should be applied. Concerning the population of late presenters, American data showed a percentage of engagement in care ranging between 50 and 59%. These low percentages could be due to the American Health System, while in a public health system setting, the percentage of patients not engaged in care or lost to follow-up could be lower, even if still relevant. Another important factor that should be considered in both populations is stigma. Indeed, many patients that present late, either late testers or late presenters, are immigrants and have important cultural barriers to disclose their HIV serostatus to family members and friends. Obviously, all subjects unaware or refusing their HIV infection could potentially infect their partners. In conclusion, all efforts should be made to reduce the phenomenon of late presentation since these two populations represent an epidemiological problem not only for the prognosis of the single patient but also for the treatment as prevention strategy.

http://dx.doi.org/10.7448/IAS.15.6.18072

O12 - CLINICAL CHALLENGES

O121

HIV, co-morbidity and ageing

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As treatment for HIV infection needs to be used continuously and lifelong, issues concerning long-term outcomes, including those involving tolerability and safety of treatment, are gaining increasing importance. Although current combination antiretroviral therapy (cART) regimens are generally better tolerated than those in the early days of cART, treatment toxicity remains an important cause for discontinuation of (components) of treatment. Moreover, several of the potential toxicities of cART (including cardiovascular, metabolic, renal and bone toxicity) overlap with known ageing-associated co-morbidities. Given that our patient population with HIV is increasingly getting older as a result of the success of cART in reducing traditional HIV-associated morbidity and mortality, these co-morbidities are increasingly being seen and importantly influence patient management. Moreover, persons with HIV, in spite of having suppressed viraemia on cART seem to be at increased risk of the premature development of age-associated non-communicable co-morbidities, including cardiovascular, chronic kidney, liver and pulmonary disease, diabetes mellitus, osteoporosis, non-AIDS associated malignancies, and neurocognitive impairment. It has therefore been hypothesised that such individuals, despite effective cART, may be prone to accelerated ageing. The underlying pathogenesis is likely to be multifactorial and, apart from include sustained immune activation, both systemically and within the central nervous system. The presentation will review the current state of knowledge and investigation in this area.

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O122

TB and HIV: how can we reduce mortality?

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Despite ART scale-up, tuberculosis (TB) remains a leading cause of HIV-related deaths worldwide and much of this disease may remain unascertained. In patients receiving ART, TB incidence is highest during the first few months of treatment (many cases of which were prevalent disease missed by baseline screening) and long-term rates remain several-fold higher than background. We identify three groups of patients starting ART for which different interventions are required to reduce TB-related deaths. First, diagnostic screening is needed in patients who have undiagnosed active TB so that timely anti-tuberculosis treatment can be started. This may be greatly facilitated by new diagnostic assays such as the Xpert MTB/RIF assay and a novel point-of-care urine test for lipoarabinomannan (LAM). Second, patients with a diagnosis of active TB need optimised case management, which includes early initiation of ART (with early timing now defined by randomised controlled trials), trimethoprim-sulphamethoxazole prophylaxis and treatment of co-morbidity. Third, in high TB burden settings, all remaining patients who are TB-free at enrolment have high ongoing risk of developing TB and require optimised immune recovery (with ART ideally started early in the course of HIV infection), isoniazid preventive therapy and infection control to reduce infection risk. Further specific measures are needed to address multi-drug resistant TB (MDR-TB) and there are now new promising developments in antimycobacterial agents. Finally, in high burden settings, scale-up of all these interventions requires nationally and locally tailored models of care that are patient-centred and provide integrated health care delivery for TB, HIV and other co-morbidities.

http://dx.doi.org/10.7448/IAS.15.6.18074

O123

HIV in women

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Globally over 50% of HIV-infected individuals are women. With the widespread use of HAART, we can expect women to have mortality rates approaching normal. Indeed, studies have shown that women may expect a slower disease progression than men following seroconversion; furthermore, it appears that female who injects drugs can live longer than their male counterparts. However, other studies from cohort analysis have reported worse outcomes in women. In essence, many studies are consistently underpowered to adequately address these questions. The proportion of women in clinical trials remains at 20 to 30%, with pregnancy potential being a major exclusion factor. Hence, many questions remain unanswered. Recent data suggest women are more likely to present late with a new AIDS diagnosis. Why this should be the case is not well understood. In addition, HIV-positive women should have the same access to reproduction health as their negative counterparts, but unfortunately

many inequalities remain. Advise on contraception and fertility services are very variable across both the developed and developing world. Data are limited on the most appropriate use of contraceptives in the presence of HAART, the possible drug interactions and possible increased risk of HIV transmission. There remain significant differences in guidelines regarding prevention of mother-to-child transmission (MTCT) across Europe, and implications of stopping and starting HAART for MTCT have not been adequately addressed. The mode of timing of delivery, and the effect of length of time of ruptured membranes on this decision is also contentious. Further issues relate to the desire for HIV-positive women to breastfeed in the setting of HIV viral suppression, where some guidelines now support women in this situation and others categorically would inform child protection authorities. Finally as women age it is more difficult to separate the effect of the menopause and its symptoms from the increased HIV-related cardiovascular and bone fracture risk. This presentation aims to discuss key issues which conflicting or inadequate data fail to resolve.

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O13 - LIVING LONGER WITH ART

O131

Review of life expectancy in people with HIV in settings with optimal ART access: what we know and what we don't

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Life expectancy (LE) is an important indicator of health used widely by government and healthcare agencies to monitor trends over time and to determine resource allocation, as well as by insurance companies and pension providers. LE of the HIV-positive population has increased dramatically since the introduction of combination antiretroviral therapy (cART); indeed, it is now believed that LE may be similar to that of the general population in some subgroups. There are, however, specific subgroups in which LE remains substantially impaired. The impact of HIV and of cART on mortality may be expressed in several ways. LE itself provides an estimate of the average additional number of years that an individual would be expected to live beyond a particular age. However, the detrimental impact of HIV may also be described in terms of the number of years of life lost or the gains in LE if HIV were to be eliminated as a cause of morbidity in the population. My presentation will start with a description of the different methods that researchers have used to describe the mortality outcomes of those with HIV, and the impact of cART on these. I will then consider how LE in the HIV-positive population has changed over time and will describe the impact of demographic factors (e.g. gender, age, ethnic group) on LE. To investigate the circumstances under which LE may return to normal levels, I will also consider the potential impact of timely diagnosis and linkage into care, continued engagement with care, optimal initiation of cART and maintenance of viral suppression on LE. Finally, I will discuss some of the limitations of the approaches used to estimate LE, with particular emphasis on the confounding effects of lifestyle and behavioural factors when making any comparison with LE in the general population.

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O132

Currently available medications may not be sufficient for lifelong treatment of HIV

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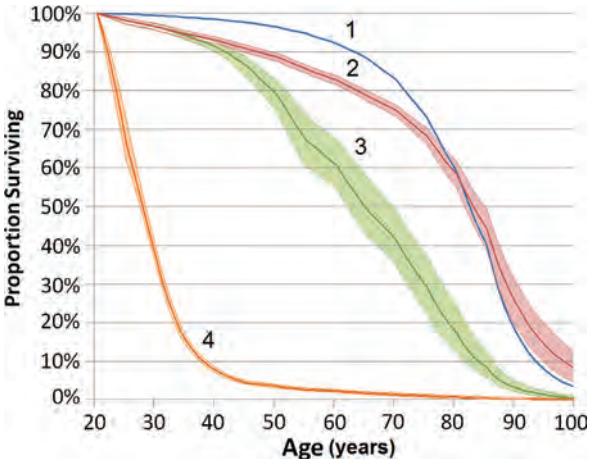
Purpose of the study: Combination antiretroviral therapy (cART) has greatly improved the life expectancy of people living with HIV (PLHIV). A series of cohort studies have predicted near-to-normal life expectancies for PLHIV receiving cART but have not considered the impact of multi-class resistance on long-term survival. Our study aims to project the future life expectancy of PLHIV in a resource-rich setting in the context of the currently available antiretroviral treatments.
Methods: Patient antiretroviral treatment data, including time on each regimen until treatment failure, were sourced from an observational cohort of 3434 predominantly male (94.2%) PLHIV in Australia over the period 1997 to 2010. These data were analyzed in an individual-based mathematical model to calculate the time until exhaustion of all treatment options and the expected impact on HIV-associated mortality. Standardized mortality ratios were used to simulate expected survival before and after treatment exhaustion.
Summary of results: The model estimated that the median time until exhaustion of currently available treatment options is 43.4 years (interquartile range =31.4 to 58.6 years). However, the model predicts that 10% of PLHIV will use up all currently available cART options after just 22.6 years. The figure shows the survival proportions of males from age 20 years in four mortality scenarios: (1) the general population mortality rate; (2) the mortality rate in PLHIV as currently measured (without considering exhaustion of currently available treatments); (3) mortality rate in PLHIV considering additional mortality due to limited cART options; and (4) mortality rate if no cART is available. PLHIV who start currently available cART regimens at age 20 years are expected to live to a median of 64.7 (95% uncertainty bound (UB) =61.8 to 69.3) years of age, when adjusting for treatment option exhaustion. This is a substantial improvement on no cART (median survival to 27.6 [95% UB =27.2 to 28.1] years of age) but is lower than the expected life expectancy (82.2 years of age) of an HIV-negative male in the general population. The gap between life expectancy among PLHIV and the general population is greater for those infected at younger ages.



Conclusions: As treatment options are exhausted in the coming years, a substantial difference in life expectancy between PLHIV and the general population is expected, particularly for people who acquire HIV at a younger age or who are currently highly treatment-experienced.

http://dx.doi.org/10.7448/IAS.15.6.18077

O133

Life expectancy of HIV-1-positive individuals approaches normal conditional on response to antiretroviral therapy: UK Collaborative HIV Cohort Study

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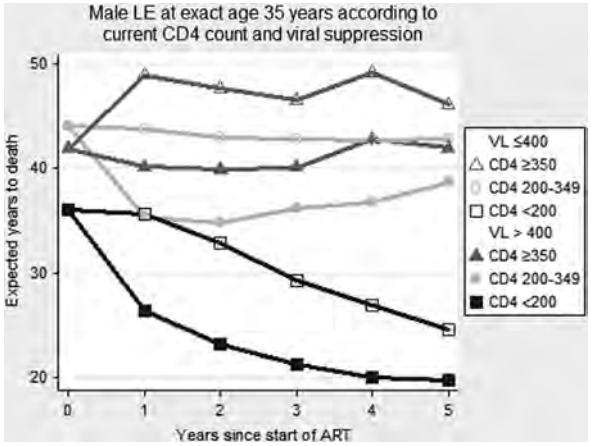
Life expectancies (LEs) of patients in UK Collaborative HIV Cohort (UK CHIC) stratified by CD4 count at start of antiretroviral therapy (ART) have been estimated [1] but not gains in years of life in response to ART. We estimated LE associated with attained CD4 count and viral suppression at different durations of ART. Patients in UK CHIC aged >20 years who started ART in 2000 to 2008 (excluding person who injects drugs) were followed to end of 2010. All-cause mortality was ascertained from clinic notes and by linkage to national records. We used the nearest CD4 count before ART and the last in each of years 1 to 5 of ART and determined whether patients were virally suppressed (HIV-1 RNA <400 copies/mL) in the past year for those remaining under follow-up. Poisson models were used to estimate mortality rates by sex, age, latest CD4 count (<200, 200 to 349, ≥350) and viral suppression for each duration of ART. Abridged life tables were constructed from age-specific mortality rates to estimate LE for ages 20 to 85 years. Results are presented as the average number of years that will be lived after exact age 35 years. A total of 17,021 patients started ART from 2000 to 2008 of whom 708 (4.2%) died; 3956 (23%) were lost to study follow-up. There was no difference in mortality between those with attained CD4 350 to 499 and ≥500. On starting ART, male LE at exact age 35 was 36, 44 and 42 (female LE 38, 46 and 44) years for attained CD4 <200, 200 to 349, ≥350, respectively; after 5 years on ART, it was 22, 42 and 46 (female LE 27, 46 and 51) years, respectively. Only 17% of patients had CD4 ≥350 at ART start, compared with 78% of patients on ART for >5 years. The difference in LE between suppressed versus unsuppressed patients was around 11 years. The figure shows that both CD4 count and viral suppression contribute to changes in LE. Male patients that increased their CD4 in the 1st year of ART from <200 to 200–349 or ≥350 gained 6 and 11 years of LE to 42 and 48 years, respectively, with similar rises for women. Overall, LE was 4 years greater for those on ART for >5 years compared with those starting ART. Individuals that attain viral suppression and a CD4 count >350 within 1 year of ART start have a normal LE with 35-year olds estimated to live to over 80 years on average. LE in patients with CD4 count <200 beyond 5 years on ART drops by 15 years. Estimated LE may be biased by under-ascertainment of deaths, missing CD4 measurements and extrapolation beyond available data.



Reference

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O14 - THE HIV RESEARCH TRUST

O141

Clinical pharmacokinetics of antiretroviral drugs in Ugandan patients

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Clinical pharmacokinetic data on antiretroviral drugs are scarce in African HIV-1-positive patients. Most available pharmacokinetic data are derived from ethnically distinct Caucasian research volunteers. This presentation will focus on the clinical pharmacokinetics training and research outputs of an HIV Research Trust scholarship recipient in Uganda. The work highlights the need for post-marketing pharmacokinetic studies in the target populations in order to optimize therapy for patients in resource-limited settings.

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O21 - ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF GLASGOW LOCK LECTURE

O211

Treatment optimization in low- and middle-income countries

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The unprecedented, successful collaborative international effort to provide universal access to HIV care, including effective antiretroviral therapy (ART), has reached a critical time point. The global economic downturn, changing donor priorities and competing priorities in the health sector threaten the capacity of various agencies to maintain support for the continued scale-up of access toward the UN General Assembly-agreed target of 15 million people with HIV/AIDS receiving ART by 2015. This aspiration has recently received added impetus as we have come to understand that treatment acts as prevention by reducing the infectiousness of treated individuals. It is now necessary to review the elements of the success to date, in order to be able to do more with less. These elements include efforts to optimize delivery of HIV care, including ART, in low- and middle-income countries (LMIC); the emergence of new agents and drug classes which have simplified HIV treatment and made broader successful management more achievable; and changes to commencement protocols. Recent studies have indicated that earlier commencement of HIV therapy is beneficial, leading to changes in the recommended ART initiation threshold in LMIC to <350 CD4 T cells/μL. Studies currently underway are investigating approaches to second-line ART in LMIC. The results from these studies will better inform the rollout of effective second-line therapy. In addition, the financial cost of ART makes

optimization of dosing an important consideration in LMIC, in order to maximize effectiveness while limiting costs. ART monitoring is also an important priority in LMIC. Efforts to develop simple and reliable technologies that can provide rapid results in the field are underway. The final priority is operational optimization, to ensure service delivery through initiatives such as exploiting economies of scale and the training and retention of health professionals. Although the challenges in LMIC are substantial and evolving, considerable inroads have been and are being made into optimizing HIV treatment in this area, which is crucial in reducing the global impact of the disease.

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O22 - ART DILEMMAS IN RESOURCE-LIMITED SETTINGS

O221

HAART rollout in the new fiscal and economic environment

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The trend towards universal access for HIV prevention and treatment that was initiated at the beginning of the 21st century (international donor funding has been multiplied by 3 to reach 27 billion US$ in 2010) has been threatened by the 2008–9 economic crisis which currently translates in a fiscal crisis for most developed countries (including the US, France and the UK – the main donors for HIV/AIDS). Other advances such as the drastic drop in ARV drug prices are also threatened (generic first line drugs close to marginal cost, insufficient drop in second line drug prices, etc.). The presentation will discuss the negative consequences of slowing down and delaying universal access on macro-economic growth in the most affected countries and suggest alternative sources of funding such as the financial transaction tax recently introduced by the French Parliament.

http://dx.doi.org/10.7448/IAS.15.6.18081

O222

Eliminating paediatric infections and keeping mothers alive

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The global plan of reducing the number of new child HIV infections and a reduction in the number of HIV-related maternal deaths by 2015 will require inordinate political commitment and strengthening of health systems in Sub-Saharan Africa where the burden of HIV infections in pregnant women is the highest. Preventing HIV infection in women of child-bearing age and unwanted pregnancies in HIV-positive women forms the cornerstone of long-term control of paediatric HIV infections. To achieve the goal of eliminating paediatric HIV infection by 2015, health systems strengthening to address prevention of mother-to-child HIV transmission cascade attrition and focusing on the elimination of breastmilk transmission is critical. Understanding the pathogenesis of breastmilk transmission and the mechanisms by which antiretroviral therapy impacts on transmission through this compartment will drive future interventions. Identifying and retaining HIV-positive pregnant women in care and committed to long-term antiretroviral therapy will improve maternal outcomes and concomitant reductions in maternal mortality. Research assessing the natural history of HIV infection and long-term outcomes in women who interrupt antiretroviral therapy post-weaning is urgently required. Data on the outcome of women who opt to continue the long-term use of antiretroviral therapy after initiating therapy during pregnancy will determine future policy in countries considering option B+. The prevalence of antiretroviral resistance and impact on survival in infants who sero-convert whilst receiving neonatal prophylaxis, or are exposed to maternal HAART through breastmilk at a population level, are currently unknown. In addition to the provision of biomedical interventions, healthcare workers and policy makers must address the structural, cultural and community issues that impact on treatment uptake, adherence to medication and retention in care.

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O223

HIV drug resistance surveillance in low- and middle-income countries: 2004 to 2010

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Background: At the end of 2011, over 8 million people were receiving antiretroviral therapy (ART) in low- and middle-income countries (LMIC), a 26-fold increase from 2003. Some degree of HIV drug resistance (HIVDR) will emerge among populations on combination ART even when high levels of adherence are achieved. In 2004, the World Health Organization (WHO) initiated global HIVDR surveillance to monitor emergence and transmission of HIVDR in countries scaling-up ART.

Methods: WHO HIVDR surveillance strategy was designed to inform public health decision-making regarding choice of ART and to identify ART programme factors which could be adjusted to minimize HIVDR emergence. The strategy includes (1) surveillance of transmitted HIVDR (TDR) in recently infected populations, (2) surveillance of acquired HIVDR (ADR) in populations on ART and (3) monitoring of early warning indicators (EWI) of HIVDR which are ART programme factors favouring HIVDR emergence. Surveys used standardized protocols. Epidemiological and sequence data were quality assured.

Results: *TDR*: Eighty-two surveys were conducted in 30 countries in 2004 to 2010, assessing 3588 recently infected individuals. Pooled analysis indicates an overall prevalence of 3.1% TDR to at least one drug class, 1.6% to non-nucleoside reverse transcriptase inhibitor (NNRTI), 1.3% to nucleoside reverse transcriptase inhibitor (NRTI) and 0.7% to protease inhibitor (PI). Levels of NNRTI resistance, particularly in the areas surveyed in Africa, increased over time, reaching 3.4% (95% CI = 1.8 to 5.2%) in 2009. Greater ART coverage was associated, though modestly, with increased prevalence of TDR to NNRTI (*P*-value adjusted for region = 0.039). *ADR*: Thirty-six ADR surveys assessing 6370 people in 12 LMIC were conducted in 2007 to 2010. HIVDR prevalence to any drug among those initiating ART ranged from 4.8% (95% CI = 3.8 to 6.0%) in 2007 to 6.8% (95% CI = 4.8 to 9.0%) in 2010. Ninety per cent of patients alive and on therapy at 12 months achieved viral load <1000 c/mL. Among people with virological failure, 72% had HIVDR to at least one drug. *EWI*: EWIs were monitored at 2017 clinics in 50 countries assessing 131,686 people since 2004. Overall, 75% of clinics met the target of 100% of patients receiving appropriate ART; 69% of clinics met the $<20\%$ target for lost to follow-up at 12 months; and only 65% of clinics provided a continuous supply of ART during a 12-month period.

Conclusion: Expansion of ART in LMIC has resulted in an overall increase in HIVDR, particularly to NNRTI in Africa. EWIs reveal important gaps in service delivery and programme performance.

While these data call for continued and improved scale up of surveillance, they also suggest that resistance is under control in the areas surveyed, and the majority of patients initiating or switching therapy are likely to respond to currently available first- and second-line therapy.

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O224

Does early initiation of ART in infants affect virological and resistance outcomes? Data from the CHER trial after 6 years of follow-up

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Purpose of the study: Virological outcomes and resistance patterns in children initiating protease inhibitor (PI)-based antiretroviral therapy (ART) immediately following HIV-1 diagnosis are not well described. Challenges include maintaining adherence in asymptomatic patients with very high pre-ART viral loads. The CHER trial compared deferred but continuous ART (arm 1) with early limited ART (arms 2 and 3).

Methods: LPV/r + ZDV + 3TC was commenced either immediately (in 250 of 252 children randomized in arms 2 and 3) or at clinical/immunological progression (103 of 125 children in arm 1). Interruption of ART occurred after 40 (arm 2) or 96 weeks (arm 3) and re-initiation with LPV/r + ZDV + 3TC was based on immunologic/clinical criteria. Viral load was measured on all children with a stored specimen at their last visit, having been on initial or restarted ART following interruption (arms 2 and 3) for at least 24 weeks. Children in arms 1, 2 and 3 not initiating ART due to death (16, 0, 0), LTFU (2, 2, 0) or other reason (4, 0, 0) are excluded. Resistance testing was performed on samples with a viral load (VL) $\geq$1000 c/mL together with the matched baseline sample, if available. Reverse transcriptase (NRTI and NNRTI) and PI inhibitor mutations were analyzed using a validated in-house population-based sequencing assay and the IAS 2011 mutation list.

Summary of results: A total of 377 infants were enrolled; median was age 7.4 (interquartile range (IQR) 6.7 to 8.9) weeks and median baseline viral load was $\log_{10}$ 5.7. By end of study (June 2011), 353/377 children had started LPV/r + ZDV + 3TC. Median (IQR) age at ART initiation in arms 1, 2 and 3 was 26.1 (19.9 to 40), 7.4 (6.6 to 8.7) and 7.5 (6.6 to 9.0) weeks. Median (IQR) duration on ART was 240 (216 to 252), 243 (200 to 260) and 240 (194 to 257) weeks in arms 1, 2 and 3, respectively. HIV-1 RNA was $<$400 c/mL in 88/101 (87%), 95/113 (84%) and 97/117 (83%) ($P = 0.96$). Twenty-two of thirty-two children with VL $>$1000 c/mL (2/5, 8/14, 12/13 in arms 1, 2 and 3) have had resistance tests to date; nine (41%) had mutations. There were seven with M184V mutations (1, 4, 2 in arms 1, 2 and 3); two with major PI mutations (V82A/L76V) (one in each of arms 1 and 2); and two with major NNRTI mutations (K103N/M230L) (one in each of arms 2 and 3). Two of ten children tested to date had NNRTI mutations prior to starting PI-based triple therapy.

Conclusions: Virological response on ART was excellent in this large cohort of infants initiating LPV/r + ZDV + 3TC at a very young age, with no differences between randomized strategies, suggesting that planned interruption after early limited ART does not adversely affect virological outcomes. Overall, approximately 40% of those on ART with VL $>$1000 c/mL had a resistance mutation; PI mutations were infrequent, despite around 5 years on therapy. Ongoing work will investigate impact of length of time with detectable viral load on risk of developing resistance.

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O225

Evolution of resistance in paediatric patients with failure on antiretroviral therapy

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Introduction: HIV-1 resistance data to inform treatment sequencing are limited for children with virological failure on first- and second-line antiretroviral therapy (ART) in Sub-Saharan Africa.

Methods: HIV-1-infected children aged $\leq$15 years were retrospectively identified from an ART cohort in Cape Town, South Africa (2003 to 2010). First-line ART was either non-nucleoside reverse transcriptase inhibitor (NNRTI) or lopinavir/ritonavir-based (with the exception of children $<$6 months old who received full-dose ritonavir as the sole protease inhibitor (PI) from 2004 to 2007). Second-line ART was the alternative regimen. Treatment outcomes, including virological failure, loss to care, death or remaining in care, were determined. Genotypic resistance testing was conducted on stored serum from children at first- or second-line virological failure (two consecutive HIV-1 RNA levels $>$1000 copies/ml). International AIDS Society criteria defined resistance mutations.

Results: Of 472 children starting first-line ART, 352 (75%) remained in care, 45 (9%) were lost and 4 (1%) died on first-line treatment. Seventy-one (15%) had observed virological failure, and 37 of these children had specimens available for genotype testing. Eight children (22%) had wild-type virus, seven (19%) had thymidine analog mutations (TAMs), 24 (65%) had NNRTI resistance and two (5.4%) had multiple protease resistance (PR). Of the 78 children who received second-line ART, 54 (71%) remained in care, 6 (8%) were lost and 1 (1%) died during second-line treatment. Fifteen (20%) had observed virological failure; 13 had samples available for genotype. Three (23%) had wild-type virus, eight (62%) had TAMs, nine (69%) had NNRTI resistance, and five (38%) had multiple PI resistance all of whom had received full-dose ritonavir.

Conclusion: Although virological failure was infrequent in children on first- and second-line ART, rates of observed resistance including multiple PR resistance after failure were high. Reasons for high rates of resistance include use of full-dose ritonavir and continued viremia. Wild-type virus was common, suggesting poor adherence or challenges in correct dosing. Genotype resistance testing in children with virological failure may optimize selection of subsequent regimens and inform recommendations for sequencing of existing ART.

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O23 - DRUG RESISTANCE

O231

Importance of minor variants and their detection (ultra-deep sequencing) in the management of HIV infection

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Sanger genotypic drug resistance assays currently used for routine HIV management often miss low-frequency drug-resistant HIV

variants, potentially posing patients at risk of antiretroviral treatment failure. Next-generation sequencing (NGS) technologies allow detection of such minority variants down to approximately 0.5%–1% frequency. They also facilitate interrogating ''other'' HIV genomic regions like Gag or the RT connection domain, which modulate HIV resistance and are not usually addressed in routine care. Due to the capacity and scalability of NGS platforms, it is even feasible to envision full HIV genome sequencing to inform treatment design at relatively low cost and workload. Although the equipment for NGS remains rather expensive and accurate analysis of NGS still requires comprehensive bioinformatics support, even these barriers are being reduced. The steadfast evolution of NGS platforms is dramatically reducing the cost of genotyping. Open-source and commercial bioinformatic solutions are automatizing and streamlining analyses and NGS drug resistance data interpretation to the extent that lab technicians without bioinformatics knowledge will soon be able to generate reliable estimates of drug resistance from NGS data on their own. However, despite such impressive advances, the main question remains open: do we need NGS for HIV management? In this presentation, we will review the evidence supporting (or not) NGS for HIV clinical management. We will argue that, on one hand, detection of minority variants may further improve the outcomes of first-line efavirenz or nevirapine-based ART, may help design more effective salvage ART regimens, and may improve clinical outcomes to CCR5 antagonists. On the other hand, although well-powered studies are generally lacking, detection of minority variants does not seem to modify the outcomes of first-line ART including higher genetic barrier drugs such as second-generation NNRTIs, protease or integrase inhibitors. We will then discuss the relationship between minority variants and ART adherence and will end by summarizing the main challenges faced by NGS to reach routine HIV clinical management.

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O232

Antiviral activity of dolutegravir in subjects with failure on an integrase inhibitor-based regimen: week 24 phase 3 results from VIKING-3

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Background: VIKING-3 aimed to examine efficacy and safety of dolutegravir (DTG) 50 mg twice daily in patients with resistance to multiple ARV classes, including integrase inhibitors (INI).

Methods: RAL and/or EVG-resistant (current or historical) adult subjects with screening plasma HIV-1 RNA $\geq$500 c/mL and resistance to $\geq$2 other ART classes received open-label DTG 50 mg BID while continuing their failing regimen (without RAL/EVG). At Day 8 the background regimen was optimised and DTG continued. Activity of the optimized background regimen (OBR) was determined by Monogram Net Assessment. Primary endpoints were antiviral efficacy at Day 8 and Week 24.

Results: 183 subjects enrolled, 124 with INI-resistance at screening and 59 with historical (but no screening) resistance. Population was advanced: at BL, median CD4 140, prior ART 13 yrs, 56% CDC Class C; 79% had $>$2 NRTI, 75% $>$1 NNRTI, and 70% $>$2 PI resistance-associated mutations, and 61% had non-R5 HIV detected. Of the 114 subjects who had the opportunity to complete 24 weeks on study before data cutoff, 72 (63%) had $<$50 c/mL RNA at Week 24 (SNAPSHOT algorithm). Mean HIV RNA declined by 1.4 $\log_{10}$ c/mL (95% CI: 1.3, 1.5; p $<$0.001) at Day 8; response differed by genotype pathway (Table).

Primary INI mutations at BL	N	Mean HIV RNA ($\log_{10}$) Change from BL (SD) at Day 8	% $>$1 log HIV RNA decline of $<$50 c/mL at Day 8
TOTAL	183	−1.4 (0.61)	82%
T66	1	−1.9	100%
Y143	28	−1.7 (0.42)	96%
N155	33	−1.4 (0.51)	82%
Q148+ $\leq$1 secondary mutation[#]	32	−1.1 (0.51)	69%
Q148+ $\geq$2 secondary mutations[#]	20	−1.0 (0.81)	48%
$\geq$2 primary mutations	8	−1.4 (0.76)	75%
No primary mutations	60	−1.6 (0.55)	95%

[#]Key secondary mutations comprised G140_ACS, L741, E138_AKT.

In subjects with Q148 pathway mutations, virologic response decreased with increasing number of secondary mutations. Background overall susceptibility score (OSS) was not associated with Wk 24 response: % $<$50 c/mL were 83%, 63%, 59% and 69% for OSS 0, 1, 2 and $>$2, respectively. Discontinuations due to adverse events were uncommon (6/183, 3%); the most common drug-related AEs were diarrhoea, nausea and headache, each reported in only 5% of subjects.

Conclusion: A majority of the highly treatment-experienced subjects in VIKING-3 achieved suppression with DTG-based therapy. Responses were associated with Baseline IN genotype but not OSS, highlighting the importance and independence of DTG antiviral activity. DTG had a low rate of discontinuation due to adverse events at 50 mg BID in this advanced patient population.

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O233

Selection in culture of HIV resistance to dolutegravir by mutations at integrase positions R263K and H51Y that diminish viral replication fitness

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Purpose of the study: We selected for resistance in tissue culture against dolutegravir (DTG), a second-generation HIV integrase strand transfer inhibitor, which is now in phase 2/3 clinical trials, in order to try to characterize the resistance profile of this compound.

Methods: HIV-1 of different subtypes was grown in both MT-2 cells and peripheral blood mononuclear cells over protracted periods, with the concentration of DTG being incrementally increased from an initial concentration of 0.05 nM, i.e. 4 times less than the EC_{50}. After a total of 6 months of growth, a final drug concentration of 50–100 nM was achieved, beyond which virus could no longer be grown. Viral DNA was then sequenced to reveal the presence of mutations that might confer resistance to DTG. The biological relevance of these mutations was confirmed through site-directed mutagenesis

experiments in which individual mutations or combinations of mutations were studied in comparison with wild-type (wt) virus in tissue culture and with recombinant HIV integrase enzyme in biochemical assays.

Summary of results: The most common integrase resistance mutation to arise in subtype B and recombinant A/G viruses was R263K followed by H51Y. In the case of subtype C viruses, the most common mutation was G118R followed by H51Y. The presence of R263K alone conferred an approximate 3–6-fold level of resistance to DTG in culture, a 30% drop in levels of recombinant integrase strand transfer activity, as well as an approximate 20–30% loss in viral replicative capacity. Biochemical experiments indicated that the t residency times of DTG for subtype B and C viruses for wt integrase were 26 h and 38 h, respectively, and for R263K, 16 h and 22 h, respectively. In contrast, H51Y by itself did not significantly affect either strand transfer activity or resistance to DTG. However, the combination of R263K together with H51Y led to an increase in levels of DTG resistance to about 15-fold accompanied by an ~50% loss in both viral replication capacity and integrase strand transfer activity.

Conclusions: R263K and H51Y can combine to augment levels of resistance to DTG yet result in a more severe attenuation of viral replication capacity and integrase strand transfer activity than R263K alone. These data suggest that viruses containing both mutations may be at a severe replicative disadvantage and help to explain why primary resistance to DTG is so rare to arise in clinical studies performed to date.

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O234

Computational models that predict response to HIV therapy can reduce virological failure and therapy costs in resource-limited settings

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The results of genotypic HIV drug-resistance testing are, typically, 60–65% predictive of response to combination antiretroviral therapy (ART) and have proven valuable for guiding treatment changes. However, genotyping is not available in many resource-limited settings (RLS). The purpose of this study was to develop computational models that can predict response to ART without a genotype and evaluate their potential as a treatment support tool in RLS. Random forest models were trained to predict the probability of response to ART ($<$400 copies HIV RNA/ml) using the following data from 14,891 cases of ART change following virological failure in well-resourced countries: viral load and CD4 count prior to treatment change, treatment history, drugs in the new regimen, time to follow-up and follow-up viral load. The models were assessed during cross-validation, with an independent set of 800 cases, with 231 cases from RLS in Southern Africa, 206 from India and 375 from Romania. The area under the ROC curve (AUC) was the main outcome measure of the accuracy of the model's predictions. The models were used to identify alternative regimens for those cases where the salvage regimen initiated in the clinic failed. Finally, annual therapy costs were used to determine the potential cost effectiveness of this strategy for the Indian cases. The models achieved an AUC of 0.74–0.81 during cross validation and 0.76–0.77 with the 800 test TCEs. They achieved an AUC of 0.59–0.65 with cases from Southern Africa, 0.64 for India and 0.73 for Romania. The models identified alternative, locally available drug regimens that were predicted to result in virological response for 97% of cases where the salvage regimen failed in Southern Africa, 98% of those in Romania and 100% in India. Cost-neutral or cost-saving regimens that were predicted to be effective were identified for 88% of the Indian salvage failures with a mean saving of $638 per year. We developed computational models that predict virological response to ART without a genotype with comparable accuracy to genotyping with rules-based interpretation. The models were able to identify alternative regimens that were predicted to be effective for the great majority of cases where the new regimen prescribed in the clinic failed. The models were also able to identify cost-saving alternatives for most cases of failure in India. These models are now freely available over the internet as part of the HIV Treatment Response Predictions System (HIV-TRePS), which has the potential to help optimise antiretroviral therapy in countries with limited resources where genotyping is not generally available.

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O24 - HIV HCV CO-INFECTION

O241

New agents for hepatitis C and the challenges in treating co-infected patients

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More recently, the improved understanding of the hepatitis C viral life cycle has led to the identification of numerous potential targets for novel, direct-acting antiviral compounds. Two NS3/4A protease inhibitors, telaprevir and boceprevir, were the first oral HCV protease inhibitors which were approved in Europe and the United States in 2011 in combination with pegylated interferon (IFN)-α and ribavirin for the treatment of chronic hepatitis C related to HCV genotype 1, in both treatment-naïve and treatment-experienced patients. Sustained virological response rates in the range of 66–75% and 59–66% have been achieved in these two patient populations, respectively, with treatment durations of 24 to 48 weeks. Despite these significant advances the high rate of adverse events and the high costs of these regimens have limited the uptake of these new regimens. In particular, the quest for removal of interferon from HCV therapy remains one of the great unmet medical needs in HCV therapy development. With an increasing number of other DAAs in clinical development including second-wave, first-generation, and second-generation NS3/4A protease inhibitors, nucleoside/nucleotide analogue inhibitors and non-nucleoside inhibitors of HCV-RNA-dependent RNA polymerase, inhibitors of nonstructural protein 5A (NS5A) and host-targeted compounds such as cyclophilin inhibitors and silibinin, the hope for better tolerated HCV therapies and potentially interferon-free HCV combination therapies has grown considerably. The proof of concept that IFN-free regimens may lead

to HCV eradication has recently been brought in GT2/3 patients treated with PSI-7977 and ribavirin for 12 weeks as well as in GT1b patients treated with BMS-790052 + BMS-650032 for 24 weeks. Although some patients with GT1a infection were also cured under this regimen, the majority of patients relapsed after treatment discontinuation, suggesting that at least for the 1a HCV genotype more effective interferon-free regimens still need to be developed. Interestingly, also GT1 non-responders treated with GS-7977 + ribavirin showed a high relapse rate, again underlining that more challenging patient populations will still exist which either need broader oral combinations or longer treatment durations. Overall, the dramatic increase in efficacy has also been seen in DAA-based HCV therapy in HIV/HCV-coinfected patients. However, complex drug-drug interactions and tolerability issues remain a concern for all HCV patients, but particularly for HIV patients receiving antiretroviral therapy with a high potential for drug interactions.

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O242

Increases in acute hepatitis C (HCV) incidence across Europe: which regions and patient groups are affected?

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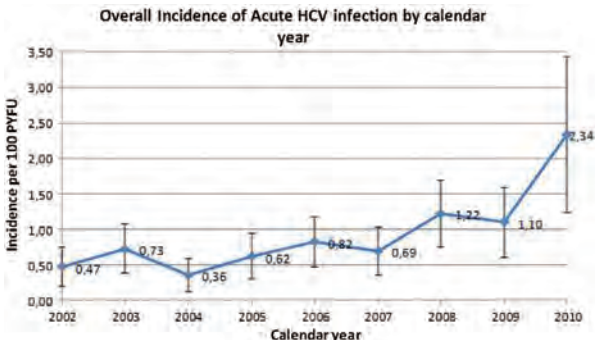
Background: In the last decade, several outbreaks of sexually acquired acute HCV have been described in men who have sex with men (MSM) infected with HIV in Australia, Europe, and North America. The aims of this study were to determine the incidence of acute HCV within the large EuroSIDA cohort and to explore possible regional differences throughout Europe and in different HIV transmission risk groups.

Methods: Baseline was defined as 1st Jan of 2002 or entry into EuroSIDA, whichever comes later. All patients from EuroSIDA who were HCV antibody-negative at baseline and had at least 2 HCV antibody test results available were included into the study. HCV seroconversion was defined as change from negative to positive HCV-antibody test within the observation period from 2002 onwards. Follow-up was counted from baseline to HCV antibody positivity for seroconverters and to the last HCV antibody-negative test result for those that did not seroconvert for HCV. Poisson regression analyses were performed to identify predictive factors for HCV seroconversion.



Results: A total of 150 HCV seroconversions (95 [63.3%] in MSM) occurred in 4295 patients during 18,928 person years of follow-up (PYFU), overall incidence of 0.79 acute infections per 100 PYFU (95% CI: 0.67–0.92) (see figure). The incidence of HCV seroconversions increased from 0.47 (CI: 0.19–0.74) in 2002 to 2.34 (CI: 1.24–3.44) in 2010. Similar patterns were observed across all European regions ($p = 0.89$, test for interaction). In multivariate analysis, IDU was associated with a higher incidence rate ratio (IRR) than MSM: 4.59 (2.40–8.80; $p < 0.0001$), South and East Europe both had higher IRR compared to Western Europe, respectively (1.98 [1.12–3.49]; $p = 0.018$ and 2.41 [1.41–4.12]; $p = 0.0014$). Calendar year per 2 years was also associated with a higher IRR (1.29 [1.19–1.39]; $p < 0.0001$).

Conclusion: The incidence of acute HCV within EuroSIDA increased over time. Although, the incidence of seroconversion was 54% higher in MSM than in heterosexuals, IDUs had the highest incidence of HCV seroconversion. Rising incidences can be found in all European regions highlighting the need for increased prevention efforts in all European countries.

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O243

Temporal changes and regional differences in treatment uptake of hepatitis C therapy in EuroSIDA

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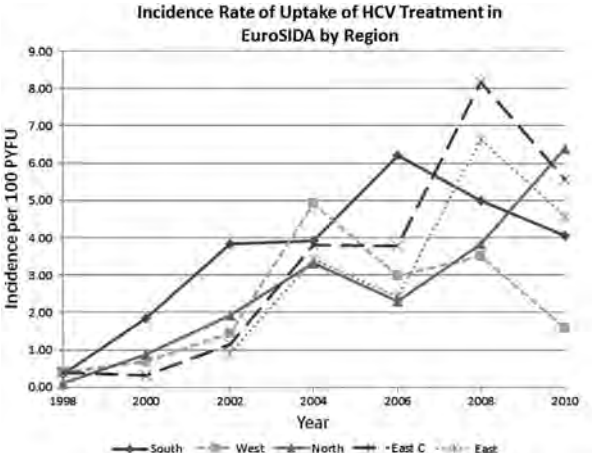
Up to 30% of European HIV-positive patients tested for hepatitis C virus (HCV) are seropositive. All co-infected patients with chronic HCV and ≥F2 fibrosis should be considered for HCV therapy given their increased risk of death from liver disease. Despite this the extent to which co-infected patients initiate HCV treatment is not well described. The aims of this study were to determine the rate of HCV treatment uptake among co-infected patients and to estimate the effect of treatment on all-cause and liver-related death. EuroSIDA patients positive for HCV antibody and HCV-RNA were included in the study. Baseline was defined as the date of recruitment or HCV seroconversion, whichever occurred later. Poisson regression was



used to identify temporal changes and regional differences in HCV treatment uptake (use of at least interferon-α [peg-IFN] ± ribavirin) and to study the association between HCV treatment and progression to all-cause and liver-related death. 1947 patients were included, with a median follow-up time of 107 months (IQR: 57–156). Overall 456 (23.4%) of HIV/HCV co-infected patients have received HCV therapy so far. The incidence of HCV treatment rose from 0.29 (95% CI: 0.13–0.45) per 100 person-years follow-up in 1998 to 5.26 (95% CI: 3.87–65) in 2007, before falling to 3.73 (95% CI: 2.40–5.06) in 2009. There were considerable regional differences (Figure). In a multivariable model treatment incidence increased 11.0% (95% CI: 4.0–18.4; $p = 0.0016$) per 2 calendar years. Patients with CD4 cell counts greater than 350 cell/mm^3 (incidence rate ratio [IRR]: 1.75 [1.37–2.23; $p < 0.0001$]), HIV-RNA less than 500 copies/ml (IRR: 1.58 [1.18–2.12; $p = 0.0023$]), with HCV genotype 3 (IRR: 1.55 [1.21–1.98; $p = 0.0006$]) compared to genotype 1) and those from south (IRR: 1.99 (1.45–2.72; $p < 0.0001$) and east central Europe (IRR: 1.61 [1.11–2.34; $p = 0.011$]) compared to west Europe, were more likely to initiate treatment. In a multivariable model treatment for HCV was not significantly associated with all-cause death (355 deaths, IRR: 0.81 [95% CI: 0.54–1.19; $p = 0.28$]) or liver-related death (95 deaths, IRR: 1.0 [95% CI: 0.50–2.02; $p = 0.99$]). The incidence of treatment for HCV among co-infected patients increased from 1998 until 2007 and was common in those with higher CD4 cell counts and lower HIV-RNA, consistent with HCV treatment guidelines. HCV treatment was not associated with all-cause or liver-related death in this population.

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O31 - ARVS UPS AND DOWNS

O311

Abacavir and the altered peptide repertoire model: clinical implications

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Structural and biochemical studies showing that abacavir binds non-covalently to the floor of the peptide binding groove of HLA-B*5701 with exquisite specificity to alter the self-peptides that load on the molecule to be presented to the immune system have recently been published [1–4]. This precise mechanistic explanation of why abacavir binds to HLA-B*5701 and no other allele accounts for the 100% negative predictive value of HLA-B*5701 testing for hypersensitivity which underpins its utility as a screening test. The specificity of the interaction between abacavir, peptide and HLA-B*5701 provides strong evidence that abacavir will not cause any off-target, HLA restricted immune-mediated side effects in HLA-B*5701 negative individuals. The rapid and direct non-covalent binding of abacavir to HLA-B*5701 without the requirement for metabolism of the drug explain the clinical symptoms of hypersensitivity including dose-related escalation of symptoms and rapid offset of symptoms following drug cessation. Importantly, if abacavir were being developed today its propensity to bind HLA-B*5701, alter the peptide repertoire presented, and the functional consequences of this interaction between HLA-B*5701 and abacavir could be determined in vitro and before use in man. This provides an important pre-clinical screening strategy to identify compounds in development that bind HLA and alter peptide presentation which could then be structurally modified to abrogate this property to avert hypersensitivity while retaining on-target effects.

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O312

An investigation into frequency and reasons why patients switch antiretroviral therapy and which antiretrovirals are commonly implicated in toxicity

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Purpose of the study: Previous investigation into antiretroviral (ARV) therapy switches in our HIV cohort suggested an annual switch rate of 20% in 2006 with 60% of switches being secondary to toxicity [1]. The purpose of this study was to investigate whether this switch rate has changed in recent years, determine reasons why patients change regimens, and identify which ARVs are most likely to be switched for toxicity concerns.
Methods: The electronic patient database was reviewed to identify all patients within our HIV cohort who switched ARV therapy between 1st December 2009 and 31st May 2011. Details of which ARVs were switched and the reasons why were recorded. Any switches due to toxicity were investigated further to identify the actual or perceived adverse effect.
Summary of results: Nine hundred and twenty-three regimens were switched over 18 months affecting 12% ($n = 722$) of patients on treatment during this time. The most common reason for switching medication was due to toxicity, occurring in 452 (49%) cases. Other reasons included simplification (15%), clinical trials (8%), virological failure (8%) and drug interactions (4%). The remaining 16% switched for various reasons including pregnancy and co-morbidities. Of 452 switches for toxicity (or perceived toxicity), 122 (27%) were due to CNS side effects (89 out of a total of 122 were related to efavirenz), 64 (14%) gastrointestinal disturbances (38/64 related to protease inhibitors), 54 (12%) actual/perceived cardiovascular risk (21/54 related to abacavir and 21/54 related to saquinavir), 54 (12%) hepatotoxicity (21/54 related to atazanavir and 14/54 related to efavirenz), 42 (9%) metabolic concerns (24/42 related to protease inhibitors) and 38 (8%) renal toxicity (28/38 related to tenofovir). Other toxicities accounted for 78 (18%) switches. An observed toxicity switch rate (OTSR) per 1000 patient years (95% CI) was calculated for each ARV.

NRTIs	OTSR (95% CI)	PIs	OTSR (95% CI)
Zidovudine	43.5 (27.0–66.6)	Saquinavir	96.1 (62.2–141.8)
Abacavir	18.6 (12.3–26.9)	Lopinavir	69.1 (50.6–92.2)
Tenofovir	6.4 (4.7–8.5)	Atazanavir	27.2 (19.8–36.5)
Lamivudine	1.4 (0.3–4.2)	Darunavir	15.0 (9.7–22.2)
Emtricitabine	1.2 (0.5–2.3)		
INI		NNRTIs	
Raltegravir	15.0 (6.0–30.9)	Efavirenz	27.8 (22.9–33.5)
CCR5		Etravirine	25.7 (15.3–40.7)
Maraviroc	5.2 (0.1–29.2)	Nevirapine	3.1 (0.6–9.1)

Conclusions: 12% of patients switched therapy in 18 months, predicting an annual switch rate of 8%. Toxicity remained an important reason for switching. Saquinavir and lopinavir have a significantly higher OTSR than other PIs as does zidovudine compared with other NRTIs. Nevirapine has a significantly lower OTSR than other NNRTIs.

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O313

Durability of FTC/TDF-containing cART regimens in a large cohort of HIV-infected patients seen for care in Italy

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Atripla is a fixed-dose drug combining FTC/TDF/EFV into a single pill and may increase adherence. To our knowledge, there is little data comparing the durability of Atripla vs. other regimens. Our first aim was to compare the durability of Truvada (TVD)/EFV or TVD/PIr or Atripla started when ART-naïve, in terms of time to virological failure (VF first of 2 consecutive values >50 and >200 copies/mL), time to discontinuation of any drug in the regimens, or both. Then, we aimed to compare the incidence of virological rebound (VR) >200 copies/mL in patients (pts) currently receiving these same regimens after achieving a viral load (VL) ≤ 80 copies/mL. Pts in the Icona Foundation Study who started for the first time a cART regimen with TVD/EFV or TVD/PIr or Atripla, either while ART-naïve (analysis 1) or while with a VL ≤ 80 (analysis 2) were included. In analysis 1, pts' follow-up accrued from cART initiation to the date of the event (VF or discontinuation of any drug in the regimen) or to the date of last available visit/VL. In the TVD/EFV group a switch to Atripla was not counted as an event. Survival analysis employing KM curves and Cox regression model was used. In analysis 2, follow-up accrued from the date of first VL ≤ 80 (which could be achieved with any cART) to VR or last VL and only person years (PY) on the regimens of interest were considered. Rates were calculated as number of VR per 1000 PY and relative rates (RR) compared using a Poisson regression model. In analysis 1, 515 pts starting TVD/EFV, 1001 TVD/PIr and 160 Atripla when ART-naïve on average in 2010 (IQR: 2008–2011) were included. PI/r were LPV (33%), ATV (38%) fos-APV (4%) and DRV (24%). Median age was 38 years, 19% females, 40% heterosexuals. Pts starting Atripla were younger, less likely to be female, IDU, HCV co-infected, to have AIDS and they had higher CD4 count (334 vs. 280). By 2 years, 48% (95% CI: 43–53) of those initiating TVD/PIr experienced the composite endpoint of VF or drug discontinuation vs. 20% in the other groups ($p = 0.0001$). Median time to switch from TVD to Atripla in the EFV group was 17 months (95% CI: 12–23). The table shows the results of the Cox regression analysis. In analysis 2 ($n = 1{,}425$), the rates of VR were 16.8 per 1000 PY for TVD/PIr, 11.17 for TVD/EFV and 5.3 for Atripla (adjusted RR vs. TVD/PIr $= 0.51$, 95% CI: 0.19–1.34). Durability of Atripla was comparable to that of TVD/EFV and potentially longer than that of TVD/PIr. Unmeasured confounding cannot be ruled out.

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O314

Advanced renal disease, end-stage renal disease and renal death among HIV-positive individuals in Europe

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Abstract O313

	Crude and adjusted relative hazards from fitting a Cox regression				
Outcomes	**No. with event (%)**	**Crude RH (95% CI)**	**p-value**	**Adjusted* RH (95% CI)**	**p-value**
VL >50 copies/mL					
Truvada + PI/r	131 (13%)	1.00		1.00	
Truvada + EFV	54 (10%)	0.60 (0.43,0.83)	0.002	0.61 (0.42,0.89)	0.009
Atripla	8 (5%)	0.66 (0.32,1.37)	0.265	1.15 (0.54,2.48)	0.716
Stop of any drug					
Truvada + PI/r	322 (32%)	1.00		1.00	
Truvada + EFV	79 (15%)	0.37 (0.29, 0.47)	<.001	0.33 (0.25,0.44)	<.001
Atripla	23 (14%)	0.50 (0.32,0.77)	0.002	0.50 (0.31,0.80)	0.004
VL >200 copies / mL or stop of any drug					
Truvada + PI/r	314 (31%)	1.00		1.00	
Truvada + EFV	84 (16%)	0.39 (0.31,0.50)	<.001	0.37 (0.28,0.49)	<.001
Atripla	23 (14%)	0.52 (0.33,0.80)	0.003	0.57 (0.35,0.91)	0.017

*adjusted for age, gender, nation of birth, mode of HIV tranmission, hepatitis co-infection status, AIDS diagnosis, baseline CD4 count and viral load an year of starting cART and stratified by clinical centre.

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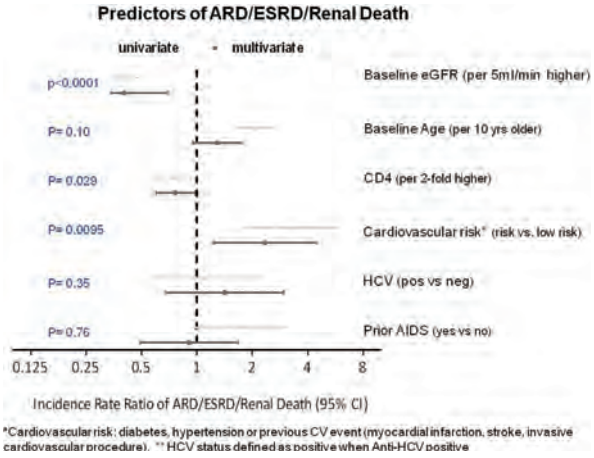
Many studies have focused on chronic kidney disease in HIV-positive individuals, but few have studied the less frequent events, advanced renal disease (ARD) and end-stage renal disease (ESRD). The aim of this study was to investigate incidence, predictors and outcomes for ARD/ESRD and renal death in EuroSIDA. ARD was defined as confirmed eGFR <30 ml/min per 1.73 m^2 (>3 months apart) using Cockcroft-Gault. ESRD was defined as hemo- or peritoneal dialysis >1 month/renal transplant. Renal deaths were defined as renal failure as the underlying cause of death, using CoDe methodology. Patients were followed from baseline (first eGFR after 1/1/2004) until last eGFR, ARD/ESRD/renal death; whichever occurred first.



Poisson regression was used to identify predictors. 8817 persons were included, the majority were white (87.3%), males (73.9%) infected though homosexual contact (41.5%) and with a median age of 42 years (IQR 36–49). 45 persons (0.5%) developed the composite endpoint; ARD (24), ESRD (19) and renal death (2) during a median follow up (FU) of 4.5 years (IQR 2.7–5.8), incidence rate (IR) 1.21/1000 PYFU (95% CI 0.86–1.57). Of 312 persons (3.5%) with baseline eGFR <60 ml/min/1.73 m^2, 13.3% (7.5–18.9) are estimated to develop ARD/ESRD/renal death within 6 years after baseline compared to 0.86% (0.58–1.1) of all patients, using Kaplan-Meier methods. Predictors in multivariate analysis were older age (IRR 1.29 per 10 years [0.95–1.75]) any cardiovascular risk (IRR 2.34 [1.23–4.45]), CD4 count (IRR 0.76 per 2-fold higher [0.60–0.97]) and eGFR (IRR 0.63 per 5 ml/min/1.73 m^2 higher [0.58–0.69]).
Ethnicity, gender, nadir CD4, VL, HBV and using potential nephrotoxic antiretrovirals were insignificant in uni- and multivariate analysis. At 1 year after ARD/ESRD, 23.3% (CI 9.8–36.8) were estimated to have died using Kaplan-Meier methods. The 11 deaths were from renal causes (2), non-AIDS-defining malignancies (2), hepatitis-associated liver failure (1), respiratory failure (1), cardiovascular disease (1), pancreatitis (1) and unknown causes (3). The ARD/ESRD/renal death incidence was low in this population with the available FU, and was associated with traditional and HIV-related risk factors. Most persons with ARD/ESRD/renal death had pre-existing renal impairment, but some experienced a rapid progression from initial normal levels. Prognosis after ARD/ESRD was poor. Larger studies are required to address the possible contribution of specific antiretrovirals.

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O315

Recovery of eGFR in patients who develop renal complications on tenofovir

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Purpose: Tenofovir (TDF) use has been linked to chronic kidney disease (CKD) and rapid decline in kidney function; the potential reversibility of these complications remains poorly studied. We compared changes in estimated glomerular filtration rate (eGFR) before, during and after TDF use.
Methods: Patients in the UK Collaborative HIV Cohort (CHIC) Study who discontinued a TDF-containing regimen after >3 months were included. Incident CKD on TDF was defined as an eGFR <60 for >3 months (eGFR units = ml/min/1.73 m^2) and rapid eGFR decline as a negative eGFR slope >3 on TDF (eGFR slopes measured in ml/min/1.73 m^2/year). Linear piecewise regression was used to estimate each person's eGFR slope before, during and after TDF, excluding the initial 4 weeks on TDF and the first 3 months post-entry and post-discontinuation. These slopes were compared in those with/without CKD or rapid eGFR decline using t-tests. A piecewise linear random effects model compared the average slopes before and during TDF, and during and post TDF. Maximum eGFR after discontinuation was compared with eGFR at TDF start to determine the extent of recovery.
Results: 935 subjects were included, of whom 80% were male, 70.5% of white ethnicity, 66.2% MSM. Median age at TDF start was 41. Patients with incident CKD tended to have lower eGFR at TDF

Abstract O315–Table. eGFR slopes before, during and after TDF exposure in those with and without renal complications

eGFR slope	Pre-TDF	On-TDF	Post-TDF	Pre-TDF vs. on-TDF	On-TDF vs. post-TDF
CKD	−2.7	−7.3	+5.2	$p<0.0001$	$p<0.0001$
No CKD	−1.1	−4.4	+2.6	$p<0.0001$	$p<0.0001$
	$p=0.10$	$p=0.003$	0.001		
Rapid eGFR decline	−0.5	−10.1	+5.1	$p<0.0001$	$p<0.0001$
No rapid eGFR decline	−1.8	+0.2	+1.1	$p=0.28$	$p<0.0001$
	$p=0.07$	$p<0.0001$	$p<0.0001$		

start than those without (median 75 and 93 respectively), while baseline eGFR in those with/without rapid eGFR decline were similar (median 90 and 91 respectively). Small eGFR declines pre-TDF were observed in all patients, with significantly more rapid eGFR decline observed during TDF exposure in those with renal complications (Table).
Although eGFR recovery was observed in the majority of patients without renal complications following TDF discontinuation (70.5% of those without CKD, 76.3% of those without rapid eGFR decline), only 43.7% of patients with CKD and 56.4% of those with rapid eGFR decline reached a maximum eGFR that was at least as high as their eGFR at TDF start.
Conclusions: Improvements in eGFR were observed in patients who discontinued TDF. However, incomplete eGFR recovery was frequent in those with renal complications.

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O32 - A YEAR IN REVIEW AND TREATMENT AS PREVENTION

O321

My favourite 10 publications of 2011–2012

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As the published literature on HIV therapy continues to grow, it becomes increasing difficult for treating physicians to keep up to date with the latest developments. For example, several thousands of papers have been published since HIV10 in the HIV literature. Websites such as HIV Drug Therapy, which includes a section on new HIV publications, can be a great help, providing a brief summary of interesting papers that have been recently published. In my presentation, I will review what I believe to be some of the most useful and key papers that have been published in the last 2 years.

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O322

Pregnant women with HIV on ART in Europe: how many achieve the aim of undetectable viral load at term and are able to deliver vaginally?

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Purpose of the study: Mother-to-child transmission rates in Europe are below 1% in HIV-infected women on successful combined antiretroviral therapy (cART) irrespective of mode of delivery. Consequently, most national guidelines updated between 2001 and 2009 recommended vaginal deliveries for women with undetectable or very low viral load (VL). The aim of this study was to explore the impact of these new guidelines on the rates of vaginal deliveries following complete viral suppression on cART.
Methods: A pooled analysis of data on HIV-1-positive women enrolled in the Swiss Mother & Child HIV Cohort Study and the European Collaborative Study with a live birth between 2000 and 2010 was carried out. Deliveries were classified as occurring pre- or post-publication of national guidelines recommending vaginal delivery in women with low/ undetectable VL for each country.
Summary of results: Overall, 2527 mothers, 2848 deliveries and 2903 births were included from 10 countries. The women were mostly Caucasian (44%) or black (47%) and had a median age of 31 at the time of delivery. They were diagnosed with HIV a median of 3.3 years before pregnancy and 84% were CDC stage A with a median CD4 cell count of 450 cells/mm^3. 17% reported a history of injecting-drug use (IDU) and 3% current IDU. 29% of women conceived on cART, 63% started in pregnancy and 8% received no antenatal ART. The most common regimen used was PI based cART (50%). Of the deliveries, elective caesarean section (CS) was carried out in 58%, emergency CS in 17% and vaginal delivery in 23%. Of 1869 women with a VL measure within the last trimester of pregnancy, only 65% had undetectable HIV-RNA. Overall, 21% of all deliveries occurring before the guideline change were vaginal, increasing to 48% subsequently. The proportion of women with undetectable VL having a CS decreased from 29% before to 13% after the guidelines update.
Conclusions: Nearly half of all deliveries subsequent to European guideline changes were vaginal. Nevertheless, there are missed opportunities to achieve fully suppressed viral load at time of delivery and to deliver vaginally in HIV infected women. Further evaluation of treatment regimens, adherence data and barriers to treatment is planned within these cohorts.

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O323

ART use, viral suppression, and sexual behaviour among HIV-diagnosed MSM in the UK: results from the Antiretrovirals, Sexual Transmission Risk and Attitudes (ASTRA) Study

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Objective: To assess the associations of ART use, viral load (VL) suppression and transmission risk beliefs with sexual behaviour among HIV-diagnosed men who have sex with men (MSM) in the UK.
Methods: ASTRA is a multicentre UK study of >3000 HIV outpatients in 2011/12. A self-completed questionnaire defined 'unprotected sex with an HIV-discordant partner' (USD) as anal or vaginal sex without a condom in the past 3 months with a partner of negative or unknown HIV status. Transmission risk belief score (TRBS) was classified as 0–2 [2: agree 'when VL is undetectable, a condom is

not needed to prevent HIV transmission'; 1: agree 'undetectable VL makes someone less infectious to a sexual partner' 0: do not agree with either statement]. Associations of USD with TRBS, self-reported ART and VL status, and other factors were assessed using Chi-squared tests and logistic regression.

Results: Data are available for 2086 MSM [88% white; mean age: 45 years]. 1767 (84.7%) were on ART; of whom 1470 (83.2%) reported VL $\leq$ 50 c/mL, 148 (8.4%) reported VL $>$ 50 c/mL and 149 (8.4%) did not know VL status. TRBS was 0, 1 and 2 for 48.0%, 47.7% and 4.3% of MSM. Prevalence of USD was 14.8% (n = 308) overall; 123 of 308 reported receptive anal sex only. USD prevalence increased with higher TRBS [8.2%, 19.4%, 35.2% for TRBS 0,1,2 respectively; $p < 0.001$]. ART use and VL status were also associated with USD. USD prevalence was lower among MSM taking ART compared to those not on ART [13.8% vs 20.1%; $p = 0.004$]. However, among MSM on ART, USD prevalence was higher among those reporting VL $\leq$ 50 c/mL compared to reporting VL $>$ 50 c/mL/unknown (14.7% vs 9.4%; $p = 0.016$). This pattern of association between ART/VL status and USD was similar after adjustment for demographic, lifestyle, and HIV-related factors: compared to MSM on ART with VL $<$ 50 c/mL, adjusted odds ratios (95% CI) were: 0.58 (0.38, 0.89) for MSM on ART with VL $>$ 50 c/mL/unknown, and 1.25 (0.87, 1.79) for MSM not on ART, global $p = 0.006$. Absence of an HIV-positive stable partner, more recent HIV diagnosis and recreational drug use were also independently associated with USD (all $p < 0.05$).

Conclusions: Approximately 15% of HIV-diagnosed MSM report recent USD. Among MSM on ART, self-reported undetectable VL is associated with USD, suggesting that perceived VL status may influence sexual behaviour and condom use. However, prevalence of USD is also high among MSM not taking ART. These findings have implications for prevention strategies among MSM in the UK.

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O324

Increased HIV incidence in men who have sex with men despite high levels of ART use: analysis of an extensively documented epidemic

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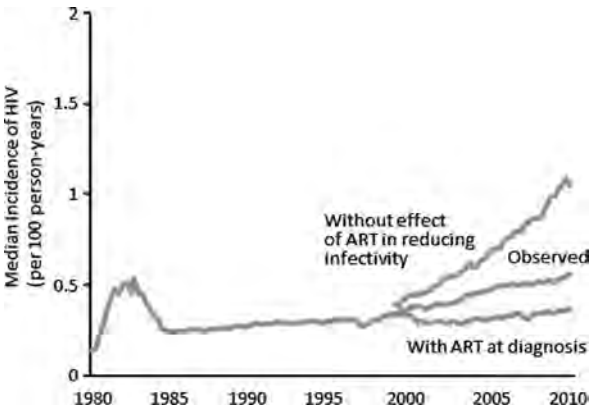
There is interest in expanding ART to prevent HIV transmission, but in the group with the highest levels of ART use, men who have sex with men (MSM), numbers of new infections have not decreased as coverage has increased for reasons which remain unclear. We analysed data on the HIV epidemic in MSM in the UK from a range of surveillance sources using a individual-based simulation model, allowing us to reconstruct the epidemic's main features. Model runs using parameter sets found to result in good model fit were used to infer changes in HIV-incidence and risk behaviour. Our results indicate that HIV incidence has increased (estimated mean incidence 0.30/100 person-years 1990–1997, 0.45/100 py 1998–2010), associated with a modest (26%) rise in condomless sex. Our model allows us to explore counter-factual scenarios: had ART not been introduced, but the rise in condomless sex had still occurred, then incidence 2006–2010 would have been 68% higher (95% CI 62% to 74%); a policy of ART initiation in all diagnosed with HIV from 2001 would have resulted in 32% lower incidence (95% CI 27% to 37%); had levels of HIV testing been higher (68% tested/year instead of 25%) incidence would have been an estimated 25% lower; a combination of higher testing and ART at diagnosis would have resulted in 62% lower incidence; cessation of all condom use in 2000 was predicted to result in a 424% increase in incidence. We conclude that a rise in HIV-incidence has occurred in MSM in the UK despite an only modest increase in levels of condomless sex in the era of ART. ART has almost certainly exerted a limiting effect on incidence. Much higher rates of HIV testing combined with initiation of ART at diagnosis would be likely to lead to substantial reductions in HIV. However, before advocating such a policy for all MSM we await data from well-powered randomized trials of the individual health risk of ART initiation at CD4 $>$ 350 cells/mm^3, and from studies of the effect of ART on infectivity through anal sex. Increased condom use should be promoted to avoid the erosion of the benefits of ART and to prevent other serious sexually transmitted infections.



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O33 - HIV, ARVS AND THE BRAIN

O331

The brain and potent ART: the final frontier?

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The current era of potent antiretroviral therapy, with the resultant dramatic improval in survival of HIV-infected patients, has focussed much attention on non-infectious complications of HIV infection. It has been recognized since the early days of the epidemic that the brain is an important target of viral infection, with both direct and indirect effects leading to brain disease, especially the most severe form, progressive HIV-associated dementia. Potent antiretroviral therapy has clearly decreased the incidence and prevalence of dementia, and even with an ageing population there is little evidence of a significant return of severe HIV-associated neurological disease. There has been some recent attention to the concept of a milder form of HIV-associated neurocognitive disease (HAND), with some cohorts reporting prevalence rates of 30% or more, even in patients with otherwise well-controlled infection. However, diagnosis of HAND is methodologically difficult and debatable, with confounders such as mood, mental health, age and lack of standards in testing technique complicating the issue. Co-infection with hepatitis C is an additional complicating factor. It is important that we do not overdiagnosis or misclassify patients as having a potentially progressive complication of HIV infection. Equally, it is premature to alter therapeutic decision-making on this basis; in particular there are insufficient data to

support a conclusion that specific antiviral agents are more likely to prevent or slow the progression of HAND.

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O332

Baseline data from the MSM Neurocog study

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We present baseline data (follow up due w24–48) from MSM Neurocog - prospective cohort study describing neurocognitive (NC) function in men who have sex with men (MSM) 18–50y.

Objectives: Describe prevalence of positive screen for NC impairment (NCI) using Brief Neurocognitive Screen (BNCS); follow NC function over time.

Data collected: Demographics, medical history, current/nadir CD4, current/peak viral load, antiretroviral (ART) use, recreational drug/tobacco/alcohol use. Subjects screen for depression (PHQ9), anxiety (GAD7), subjective memory problems (Everyday Memory Questionnaire [EMQ]). PHQ9, GAD7, EMQ, IHDS have fixed numerical cut-offs. BNCS interpreted by calculating composite z score for each subject based on distance from mean in three component tests. Comparing to population norms may overcall NCI. We used participants to construct HIV+ normal ranges after exclusion of anxiety/depression, comparing individuals to this range. 235 screened (205 HIV+, 30 HIV−). In HIV+group 59 (28.8%) excluded as GAD7 > 10, PHQ9 > 15 or both (2 no data). 144 HIV+ analysed. 124 (86.1%) had normal z score (within 1 SD of mean). 20 (13.9%) had abnormal z: 7 (35%) asymptomatic, 13 (65%) symptomatic (analysed together). Not enough cognitive domains assessed by BNCS to formally diagnose HIV-related NCI. BNCS abnormals less likely to be educated at university level/beyond (40% vs. 62.1%, p = 0.02) or in skilled work (45% vs. 81.5%, p < 0.0001). Current/ex-recreational drug use similar (~80%); no significant association to score. All patients with abnormal z receiving ART; individual agents not associated with abnormality. IHDS correlated with abnormal BNCS (60% abnormal z had abnormal IHDS vs. 15.3% of normal, p < 0.0001). No CD4 association with abnormal z (median nadir 244 in both, p = 0.38). Of note, group median age was statistically different but actual difference small (normal 41y vs. abnormal 44y p < 0.0001; HIV− 33y). BNCS outcome is age-related but stratification of results would make abnormal numbers too low for interpretation. In any case, no NCI seen following referral. No-one referred for formal psychometric testing after screening shown to have NCI. We show high anxiety, depression and current/previous recreational drug use in HIV+MSM 18–50y. Subjective concerns do not translate into confirmed NCI. Patient pathways should include screening for anxiety/depression and substance use, but in this young MSM group concerns regarding memory/functional impairment seem unfounded.

Reference

1. Winston A, Arenas-Pinto A, Stöhr W, Fisher M, Orkin C, Aderogba K, et al. Factors influencing neurocognitive function in a large cohort of HIV infected patients on effective antiretroviral therapy. Presented at the 13th European AIDS Conference, Belgrade, 2011. Abstract PS2/4.

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O333

Prolonged treatment with boosted protease inhibitor monotherapy is not associated with a higher rate of neurocognitive impairment than triple drug ART

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	Triple therapy (n = 95)	Monotherapy (n = 96)	p value
Male. n (%)	70 (73.7)	70 (72.9)	0.91
Former IVDU. n (%)	30 (31.6)	34 (35.4)	0.85
MSM. n (%)	29 (30.5)	30 (31.3)	0.85
Age. Median (IQR)	44.7 (40.6–48.4)	47.4 (44.8–51.4)	< 0.01
Years of education. Mean (SD)	11.3 (4.1)	10.4 (4.4)	0.13
Prior neurologic disease. N (%)	12 (12.6)	10 (10.4)	0.63
Prior psychiatric disease. n (%)	19 (20.0)	24 (25.0)	0.44
Current or past use of illicit drugs. n (%)	49 (53.6)	46 (47.9)	0.66
HCV coinfection (past or active)	43 (47.3)	43 (45.3)	0.54
Years of ART. Median (IQR)	10.7 (4.8–15.7)	14.1 (10.7–15.9)	0.01
Years of monotherapy. Median (IQR)	Not applicable	2.3 (1.7–3.2)	Not applicable
Years suppressed (< 50 c/mL). Median (IQR)	4.8 (2.9–8.9)	7.5 (4.5–10.0)	< 0.01
No prior blip	63 (66.3)	61 (63.5)	0.17
Currently on LPV. n (%)	70 (73.7)	53 (55.2)	< 0.01
Currently on DRV. n (%)	25 (26.3)	43 (44.8)	< 0.01
CPE score (2010). Median (IQR)	7 (7–7)	3 (3–3)	Not applicable
CD4 cell nadir. Median (IQR)	153 (49–255)	182 (76–288)	0.11
CD4 cell current. Median (IQR)	560 (440–754)	629.5 (476–845.5)	< 0.05

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Purpose of the study: To investigate if boosted protease inhibitor monotherapy is associated with a higher risk of neurocognitive impairment (NCI).
Methods: HIV-infected patients from two hospitals in Madrid (Spain) without concomitant major neurocognitive confounders, currently receiving for ≥1 year lopinavir/ritonavir (LPV) or darunavir/ritonavir (DRV) as monotherapy or with two N(t)RTIs were included if they had prolonged (≥1 year) plasma viral suppression (<50 c/mL, single blip allowed). Patients underwent full neurocognitive assessment (7 domains) by two psychologists blinded to the treatment group. NCI was defined as per 2007 Frascati criteria using demographically adjusted normative scores. Rates of NCI and the association between NCI and boosted protease inhibitor monotherapy, adjusted by significant confounders, were analyzed. Two categories of monotherapy duration were considered: short-term (1–2 years) and long-term (2–9 years). We evaluated as potential confounding variables: demographics, HIV risk factor, AIDS, CD4 (nadir/current), smoking, alcohol/illicit drug use, prior medical, neurological and psychiatric disease, HCV coinfection, years of ART, prior blips, time with HIV viral suppression, type of protease inhibitor, lipids and HOMA index.
Summary of results: 191 patients (89.5% Caucasian) were included (Table 1).
Proportion (95% CI) with NCI: Overall: 27.2% (20.9–33.6, all asymptomatic or mild). Triple therapy: 31.6 (22.1–41.0). 1–2 years of monotherapy (n = 40): 25.0 (11.3–38.7). 2–9 years of monotherapy (n = 56): 21.4 (10.5–32.3) No differences in rates of NCI were found by treatment group (p = 0.38). In our regression model confounding variables for NCI were years on ART, ethnicity, years of education, transmission category and the HOMA index. Adjusted by those variables the odds ratio (95% CI) for NCI of patients receiving boosted protease inhibitor monotherapy monotherapy during 1–2 years was 0.85 (0.29–2.50) and for 2–9 years was 0.40 (0.14–1.15).
Conclusions: Boosted protease inhibitor monotherapy, regardless of duration, was not associated with a higher rate of neurocognitive impairment than triple drug ART. These results call into question the ability of neuropenetrance scores to predict the neuroefficacy of antiretroviral regimens in HIV-infected patients with adequate blood viral suppression.

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O334

Prevalence and risk factors for HIV CSF Viral Escape: Results from the CHARTER and HNRP cohorts

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Background: During HAART, HIV RNA can be detectable (>50 cop/mL) in CSF when it is undetectable in plasma, a condition termed CSF viral escape (CVE). The aim of the current analysis was to determine the prevalence and risk factors for CVE in two large US cohorts.
Methods: 1,264 volunteers enrolled in CHARTER or HNRP at their most recent visit between 2003 and 2011 were included in this cross-sectional analysis if their HIV RNA level in plasma was undetectable while on stable HAART (>6 months) and if they had CSF collected. Potential risk factors were identified using univariable and multivariable analysis. Odds ratios for detected risk factors were calculated.
Results: Mean age was 46 years, 82% were men, 70% had AIDS, 22% were HCV+, 49% were Caucasians, median CD4 nadir was 129, and 38% were cognitively impaired. CVE was present in 55 (4.35%) with a median HIV RNA in CSF of 155 (IQR 80-283). The table summarizes the main analysis results. CVE was associated with longer durations of HIV disease, higher platelet count, higher total serum protein, and higher CSF white blood cells (WBCs). CVE was also associated with treatment-associated factors, including use of boosted PIs and unboosted atazanavir.
Conclusions: In this large, cross-sectional analysis, CVE was uncommon in subjects on effective HAART. A combination of disease and treatment factors were associated with CVE. The associations with higher levels of CSF WBCs, blood platelets, and serum total protein may reflect greater immune activation. Treatment with PI-based HAART was particularly associated with CVE, especially if unboosted atazanavir was part of the regimen. CVE was not associated with neurocognitive impairment. Prospective analyses are needed for better characterization of CVE.

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O41 - VACCINES, AIDS AND NON-AIDS EVENTS

O411

Progress in HIV vaccine research: an outsider's view

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Despite the potential for pre-exposure prophylaxis (PrEP) and treatment as prevention (TasP) to have a significant impact on HIV transmission, there is broad agreement that a safe and effective preventive vaccine remains an essential tool for ending the AIDS epidemic. To date, progress towards a vaccine has been painstaking. Nevertheless, recent progress has opened up promising new leads. Results of the STEP and RV-144 trials provide novel insights that may lead to improved design of candidate vaccines. In addition, the identification of highly potent, broadly neutralizing monoclonal antibodies from some infected patients suggests novel approaches to generating protective immunity. Refinements in our understanding of the gp120 structure and its interaction with CD4 also provide opportunities for improving immunogen design. Although the challenges remain daunting, these advances have instilled a renewed sense of optimism into the field.

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O412

CD4 count and viral load specific rates of AIDS, non-AIDS and deaths according to current antiretroviral use

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Variable	Measure	CSF viral load >50 (n = 55)	CSF viral load <50 (n = 1209)	Univariable analysis	Multivariable analysis	Odds ratio	Odds ratio info
Age (years)	Mean ± SD	45.3 ± 7.48	46 ± 9.50	p = 0.663			
Gender (male)	n (%)	43 (78.18)	978 (81.98)	p = 0.486			
Ethnicity (white)	n (%)	25 (45.45)	590 (49.50)	p = 0.692			
Years since first HIV+	Median [IQR]	16.02 [11.55–19.9]	12.72 [6.79–18.24]	p = 0.018	p = 0.016	1.367 [1.058–1.785]	(each 5 years)
HCV (positive)	n (%)	10 (22.22)	219 (22.42)	p = 0.976			
CD4 nadir (cells/mL)	Median [IQR]	71 [8.75–188.5]	133 [27.5–240]	p = 0.025			
AIDS (CDC)	n (%)	41 (83.67)	775 (69.07)	p = 0.021			
Cognitively impair (Yes)	n (%)	21 (38.18)	447 (37.69)	p = 0.914			
Global Deficit Score	Median [IQR]	0.4 [0.11–0.87]	0.33 [0.11–0.72]	p = 0.943			
CD4 in blood (cells/mL)	Median [IQR]	506 [268–711]	508.5 [340.25–710]	p = 0.678			
Hb in blood (mg/dL)	Median [IQR]	14 [12.9–15.1]	14.4 [13.4–15.3]	p = 0.104			
Platelets in blood ($x10^3$/mL)	Median [IQR]	232 [202–283]	230 [189–273]	p = 0.056	p = 0.022	1.314 [1.041–1.645]	(each 50,000)
Protein in serum (g/dL)	Median [IQR]	7.7 [6.90–8.30]	7.4 [7–7.9]	p = 0.013	p = 0.035	1.649 [1.036–2.614]	(each 1 g/dL)
WBC in CSF (cells/mL)	Median [IQR]	4 [2.5–16.5]	2 [1–3]	p ≤ 0.001	p ≤ 0.001	3.416 [2.204–5.582]	(each 10 cells)
Protein in CSF (mg/dL)	Median [IQR]	47 [31.5–55.5]	38 [30–48]	p = 0.002			
Glucose in CSF (mg/dL)	Median [IQR]	62 [57.5–68.5]	63 [58–68]	p = 0.740			
Previous blips (Y/N)	n (%)	6 (10.91)	111 (9.2)	p = 0.677			
Months VL <50 in plasma	Median [IQR	13.07 [6.04–37.66]	18.63 [7.51–40.8]	p = 0.543			
Months on current HAART	Median [IQR]	13.07 [6.05–29.78]	18.32 [6.7–35.89]	p = 0.18			
Months on HAART ever	Median [IQR]	77.55 [39.65–124.15]	72.87 [34.94–117.07]	p = 0.419			
CPE score	Median [IQR]	7 [6–8]	7 [7–9]	p = 0.625			
NNRTI + NRTIs	n (%)	8 (14.55)	438 (36.23)	p < 0.001			
PI/r + NRTIs	n (%)	31 (56.36)	501 (41.47)	p = 0.03	p = 0.006	2.749 [1.340–5.976]	(Yes vs No)
ATV + NRTIs	n (%)	4 (7.27)	27 (2.23)	p = 0.052	p = 0.024	6.006 [1.302–21.57]	(Yes vs No)
Other HAART regimens	n (%)	12 (21.82)	243 (20.07)	p = 0.747			

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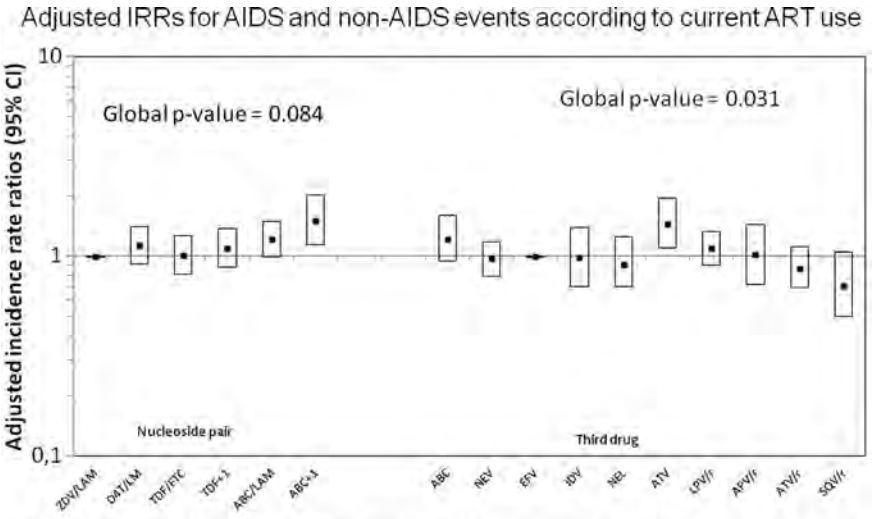

Multivariate models also adjusted for gender, ethnic origin, risk group, region, prior AIDS, prior non-AIDS, age and CD4 nadir, time since starting third drug, plus year of follow-up, hepatitis B/C status, development of CKD, anaemia, diabetes, hypertension and smoking status, current CD4 and viral load as time-updated variables

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Background: CD4 and viral loads are used in clinical trials as surrogate endpoints for assessing efficacy of newly available antiretrovirals. If antiretrovirals act through other pathways or negatively affect the risk of disease this would not be identified prior to licensing. The aims of this study were to investigate the CD4 and viral load specific rates of fatal and non-fatal AIDS and non-AIDS events according to current antiretrovirals.

Methods: Poisson regression was used to compare overall events (fatal or non-fatal AIDS, non-AIDS or death), AIDS events (fatal and non-fatal) or non-AIDS events (fatal or non-fatal) for specific nucleoside pairs and third drugs used with >1000 person-years of follow-up (PYFU) after January 1st 2001.

Results: 9801 patients were included. The median baseline date was January 2004 (interquartile range [IQR] January 2001–February 2007), age was 40.4 (IQR 34.6–47.3 years), and time since starting cART was 3.3 (IQR 0.9–5.1 years). At baseline, the median nadir CD4 was 162 (IQR 71–257/mm^3), baseline CD4 was 390 (IQR 249–571/mm^3), viral load was 1.9 (IQR 1.7–3.3 $\log_{10}$copies/ml) and 2961 (30.2%) had a prior AIDS diagnosis and 6.4 years) prior to baseline. During 42372.5 PYFU, 1203 (437 AIDS and 766 non-AIDS) events occurred. The overall event rate was 2.8 per 100 PYFU (95% confidence interval [CI] 2.7–3.0), of AIDS events was 1.0 (95% CI 0.9–1.1) and of non-AIDS events was 1.8 (95% CI 1.7–1.9). Of the AIDS events, 53 (12.1%) were fatal as were 239 (31.2%) of the non-AIDS events. After adjustment, there was weak evidence of a difference in the overall events rates between nucleoside pairs (global p-value $=0.084$), and third drugs (global p-value $=0.031$). Compared to zidovudine/lamivudine, patients taking abacavir/ lamivudine (adjusted incidence rate ratio [aIRR] 1.22; 95% CI 0.99–1.49) and abacavir plus one other nucleoside (aIRR 1.51; 95% CI 1.14–2.02) had an increased incidence of overall events. Comparing the third drugs, those taking unboosted atazanavir had an increased incidence of overall events compared to those taking efavirenz (aIRR 1.46; 95% CI 1.09–1.95) (Figure).

Conclusions: There was little evidence of substantial differences between antiretrovirals in the incidence of fatal and non-fatal AIDS and non-AIDS events for a given CD4 or viral load, suggesting there are unlikely to be major unidentified adverse effects of specific antiretrovirals, although confounding by indication cannot be ruled out.

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O413

Immuno-virological discordance is associated with a higher frequency of AIDS, severe non-AIDS, and death

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Persistent immunosuppression despite viral suppression (immunovirological discordance, ID) has been associated with higher risk of AIDS and death, although the risk for AIDS seems to decrease with longer time of suppressed viral load (sVL). The impact of ID on a composite endpoint of AIDS/serious non-AIDS/death has not been thoroughly investigated. Patients in EuroSIDA starting ≥ 1 new antiretroviral drugs after January 2001, when CD4 was <200 cells/mm^3 and VL >500 copies/mL, and who achieved a sVL ≤ 50 copies/mL within 1 year were included. Person-years of follow-up (PYFU) accrued from the date of sVL until the first of a new AIDS or severe non-AIDS (SNA) event or death, viral rebound >50 copies/mL (first of 2 consecutive values) or last visit. Rate ratios (RR) were calculated using Poisson regression according to whether or not patient's current CD4 count was still below 200 cells/mm^3 (ID). Models were stratified according to whether or not persons were ART-naïve at baseline. Multivariable models included age, HBV/HCV status, mode of HIV transmission, race, cohort, anemia, diabetes, hypertension or current eGFR, current cART, number of previous antiretrovirals, and time to viral suppression. 994 patients satisfied the inclusion criteria and contributed 4520 PYFU. Median age was 41 (IQR 34–47) years and 72.8% were male. 36.5% of patients were ART-naïve and started a median of 3 (IQR 2–3) new drugs. 31 AIDS and 58 non-AIDS events occurred, and 31 patients died (7 due to AIDS, 24 due to SNA). The rate of the combined

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Exposure	No. events	PYFU	Rate (95% CI)	Crude RR (95% CI)	Adjusted**RR (95% CI)
			All patients		
No Discordance	84	3805	22.1 (17.6–27.3)	1	1
Discordance	36	716	50.3 (35.2–69.6)	2.28 (1.54–3.38)	2.08 (1.32–3.28)
			ART-naïve* patients		
No Discordance	29	1324	21.9 (14.7–31.5)	1	1
Discordance	9	228	39.5 (18.1–74.9)	1.80 (0.84–3.85)	1.87 (0.81–4.33)
			ART-treated* patients		
No Discordance	55	2481	22.2 (16.7–28.9)	1	1
Discordance	27	488	55.4 (36.5–80.6)	2.50 (1.67–3.97)	1.89 (1.08–3.32)

*before starting a new antiretroviral drug according to the inclusion criteria, p(test for interaction):0.47
**adjusted for smoking, HBV/HCV coinfection, transmission risk, race, cohort, current cART, change of ART before viral suppression, time to viral suppression, presence of diabetes, hypertension, anemia, current eGFR <90, CD4 nadir, CD4 count and viral load at baseline.

endpoint in patients with ID (50.3 per 1000 PYFU [95% CI 35.2–69.9]) was higher than in patients recovered from ID (22.1 [17.6–27.3], adjusted RR 2.08 [1.32–3.28]; table). This was similar regardless of whether or not people were ART-naïve before starting a new drug (interaction test $p = 0.47$). In ID, rate was highest in the first 6 months of sVL (63.1 [33.6–107.9]) and declined thereafter (month 6–12: 60.5 [26.1–119.2], >12 months: 39.8 [22.2–65.6], adjusted RR compared to month 0–6 0.52 [0.24–1.13]). In analyses with endpoints AIDS/death due to AIDS and SNA/death due to SNA separately, the adjusted RR of ID vs. non ID was 4.11 ([1.76–9.60]; $p = 0.001$) and 1.46 ([0.81–2.61]; $p = 0.207$), respectively.
ID is a risk factor for clinical disease progression particularly related to AIDS events. In patients with ID, we found a trend for a declining incidence of events with longer periods of sVL, suggesting that sustained viral suppression might be of benefit.

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O414

Risk of AIDS-defining cancers in HIV-1-infected patients (1992–2009): results from FHDH-ANRS CO4

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Purpose of the study: To describe long-term incidence trends and median age at diagnosis for the three AIDS-defining cancers (ADC) in HIV-1- infected (HIV1+) patients compared to general population. To study the risk of ADC in HIV1+ patients with good immune status (CD4 $\geq 500/mm^3$ for at least 2 years).
Methods: Incident ADC (Kaposi's sarcoma [KS], non-Hodgkin's lymphomas [NHL] and cervix uteri cancer [CUC]) were retrieved in HIV1+ adults followed in the French hospital database on HIV (FHDH) cohort between 1992 and 2009. Cancer incidence rates (IR) in general population were calculated using data from the French cancer registries (Francim network). IR among the HIV1+ and the general population were standardized using the 5 years age and sex groups structure of the HIV1+ population (1997–2009) and standardized incidence ratios (SIR) were estimated in HIV1+ patients vs. general population in 4 calendar periods (1992–1996, 1997–2000, 2001–2004, and 2005–2009). Median age at diagnosis was estimated after adjusting for the difference in age structure between HIV1+ and general population.
Summary of results: 5,935 incident ADC were diagnosed among 100,536 HIV1+ patients followed between 1992 and 2009. All ADC IRs were significantly reduced between pre- and post-cART eras and continue to decline in the cART period ($p < 10^{-4}$). SIR are presented in the table.

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	Pre-cART (1992–1996)		Early-cART (1997–2000)		Intermediate-cART (2001–2004)		Lte-cART (2005–2009)	
	O/E	SIR (95% CI)	O/E	SIR (95% CI)	O/E	SIR (95% CI)	O/E	SIR (95% CI)
Kaposi's sarcoma	2177/0.9	2299.7 (2204.1–2398.4)	462/0.4	1080.1 (983.87–1183.3)	403/0.4	1130.1 (1022.5–1246.1)	354/0.4	817.7 (734.8–907.52)
Non-Hodgkins's lymphoma	1111/4.0	278.7 (262.5–295.6)	515/6.2	83.8 (76.7–91.4)	370/8.8	42.1 (37.9–46.6)	372/14.8	25.1 (22.6–27.8)
Cervix uteri	38/3.2	12.0 (8.5–16.5)	48/5.3	9.1 (6.7–12.1)	37/7.0	5.3 (3.7–7.3)	48/10.4	4.6 (3.4–6.1)

O/E: Observed cases / Expected cases.

Median age at diagnosis was significantly younger among HIV1+ patients than the general population for KS (40.4 vs. 42.5; $p < 10^{-4}$), NHL (41.4 vs. 52.5; $p < 10^{-4}$) and CUC (39.3 vs. 42.5; $p < 10^{-4}$). For HIV1+ patients under treatment who maintained controlled viral load (<500 copies/μL) and CD4 ≥500/mm^3 for at least 2 years, the risk for KS, NHL and CUC were respectively SIR = 71.6 (28.7–147.5), 2.4 (0.9–4.8) and 1.6 (0.3–4.7) vs. general population.

Conclusions: The incidence rates of KS, NHL and CUC continued to decline through 2009 but the risk remained elevated as compared to general population in the most recent cART period. Despite the great reduction when compared to general population, the risk is still very high for KS in HIV1+ patients who maintained CD4 ≥500/mm^3 for at least 2 years. The risk was not significant for CUC and NHL.

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O415

CMV co-infection and risk of AIDS and non-AIDS events in a large cohort of HIV-infected patients

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In HIV-positive patients (pts), CMV co-infection has been proposed as a key factor in sustaining immune activation, which in turn could play a role in determining immune senescence. We evaluated the prevalence and predictors of CMV co-infection in a cohort of HIV+pts and assessed the impact of CMV co-infection on the risk of AIDS and non-AIDS events. We included pts in the ICONA study with <1 month follow-up and <1 CMVIgG (CMV) test available without active CMV disease. Pts' characteristics at time of the first CMV test (baseline) were compared in those tested positive (CMV+) and negative (CMV-) using X2/Wilcoxon tests. Factors associated with CMV+ were identified by logistic regression. A prospective analysis was also performed with endpoints AIDS/AIDS-related death and severe non-AIDS (SNA: cardio-cerebrovascular, neurologic disease, renal failure, non-AIDS tumours)/death due to SNA. Time to event was estimated by Kaplan-Meier curves and Cox regression (multivariable model included: age, gender, ethnicity, risk factor for HIV, HCVAb and HBsAg, AIDS and CD4 at baseline, initiation of ART prior to baseline). 6,053 pts were included; 83.7% were tested CMV+ a median of 17 (IQR 6–45) months after enrolment. As compared to CMV-, CMV+ were older (adjusted odds ratio (AOR) 1.03 per 1 year older [95% CI 1.02–1.04]), HIV infected by homosexual route (MSM) (AOR 1.39 [95% CI 1.06–1.82]), less frequently Caucasian (AOR 0.56 [95% CI 0.42–0.76]), with higher CD4 count at baseline (AOR per 1 cell higher 1.035 [95% CI 1.00–1.06] By 10 years from first CMV test, 402 (12.6% [95% CI 11.1–13.6]) CMV+ and 74 (10.1% [95% CI 7.7–12.5]) CMV- pts developed AIDS/AIDS-related death (log-rank p = 0.43). After adjustment for potential confounders, CMV+was still not associated with the risk of AIDS/AIDS-related death (adjusted hazard ratio (AHR) 1.23 [95% CI 0.96–1.60]). By 10 years, 339 (10.6% [95% CI 9.4–11.9]) CMV+ and 41 (6.4% [95% CI 6.1–6.6]) CMV- pts experienced a non-AIDS event/non-AIDS death (log-rank p = 0.0006): 151 cancers, 128 CVD, 33 neurological, 1 renal. The association was still significant after controlling for a number of potential confounders: AHR 1.77 [95% CI 1.25–2.51] p = 0.001; Table). In our study population, CMV/HIV co-infection was associated with the risk of non-AIDS events/deaths independently of other prognostic factors, supporting a potential role of CMV infection in vascular/ degenerative organ disorders commonly associated with chronic immune activation and aging.

Characteristic	AHR	95% CI	p-value
CMVIgg+vs. CMVIgg —	1.77	1.25–2.51	0.001
Age, per 10 years older	1.64	1.46–1.84	0.0001
Female vs. male	1.43	1.12–1.83	0.004
Caucasian vs. Other	0.64	0.40–1.02	0.06
Homosexuals vs. IVDU	0.84	0.55–1.28	0.42
Heterosexuals vs. IVDU	0.87	0.60–1.26	0.47
HCVAb+vs. HCVAb —	1.28	0.92–1.78	0.13
HBsAg+vs HBsAg —	1.05	0.67–1.62	0.83
AIDS at baseline	0.94	0.67–1.32	0.75
CD4/μL at baseline per 100 cells/μL higher	0.97	0.93–1.01	0.16
HIV-RNA at baseline per $\log_{10}$ cp/mL higher	1.05	0.96–1.16	0.26
Years from HIV diagnosis per 5 years longer	1.02	0.90–1.17	0.69
ART experienced vs. naïve at baseline	0.94	0.66–1.36	0.77

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O42 - ART STRATEGIES

O421

HAART roll-out in the new fiscal and economic environment

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There are 27 approved antiretroviral drugs and combinations of these drugs clearly change the natural history of HIV infection, dramatically decreasing HIV-related morbidity and mortality and promoting healthy survival. Despite the proven benefits, we continue to consider basic strategic questions about antiretroviral therapy: When should we start ART? What regimen to start? When should we change ART? What ART regimen should we change to?

Also, despite the benefits of treatment, some antiretroviral regimens may be inconvenient, toxic, and/or have suboptimal antiretroviral activity, particularly against drug-resistant viruses. Thus, newer compounds are needed that continue to improve convenience and tolerability, reduce toxicity, and improve antiretroviral activity, particularly against drug-resistant viruses. Additionally, new drugs may better penetrate tissue reservoirs (e.g. genital tract, central nervous system) or exploit new targets with new mechanisms of action.

There are a number of HIV drugs in development currently. These include a new pharmacokinetic ''boosting'' agent and newer antiretroviral agents in a number of existing classes, including new nucleoside reverse transcriptase inhibitors, non-nucleoside reverse transcriptase inhibitors, protease inhibitors, entry inhibitors, and integrase inhibitors. In addition there are drugs with new mechanisms of action in development, including the CD4 attachment inhibitors. The clinical use of the newer agents will depend on the results of clinical trials, and the timeline for development and availability.

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O422

Timing of cART initiation after a first AIDS-defining event (ADE): temporal changes in clinical attitudes in a large cohort of HIV-infected patients

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Criteria of cART initiation after a first ADE have been modified over time based on evidence suggesting that treatment should be initiated earlier. The impact of these changes on clinical practice is unknown. Objective of this analysis was to evaluate temporal changes of time of starting cART after a first diagnosis of ADE in ART-naïve patients (pts).

Methods: All HIV+ enrolled in ICONA Foundation Study who presented with a diagnosis of ADE while cART-naïve regardless of CD4 cell count were included. Pts were grouped according to have ADE for which additional medications that may have interactions with cART are required (Tb, atypical mycobacteriosis, non-Hodgkin lymphoma) [group A], ADE treatable only by cART (PML, isosporidiasis/cryptosporidiasis, KS, wasting syndrome) [group B] and ADE treatable with specific drugs (PCP, toxoplasmic encephalitis, CMV disease, esoph candidiasis, bacterial pneumonia, cervical cancer, cryptococcosis) [group C]. Standard survival analysis by KM was used to estimate the cumulative percentage of pts starting cART, overall and after stratification for calendar period of diagnosis (1996–2000, 2001–2008, 2009–2011) and type of ADE (groups A, B, C). Multivariable Cox regression was used to investigate association between calendar year of ADE and time to cART initiation after controlling for demographics.

Calendar Period	Crude RH (95% CI)	p-value	Adjusted RH (95% CI)	p-value
1996–1999	1.00		1.00	
2000–2008	1.19 (0.95, 1.50)	0.132	1.18 (0.88, 1.57)	0.272
2009+	1.51 (1.16, 1.96)	0.002	1.36 (0.89, 2.08)	0.151
Type of ADE	**Crude RH (95%)**	**p-value**	**Adjusted RH (95% CI)**	**p-value**
A	1.00		1.00	
B	2.59 (1.90, 3.53)	<.001	2.24 (1.44, 3.48)	<.001
C	2.09 (1.65, 2.67)	<.001	1.14 (0.99, 2.00)	0.058

Summary of results: A total of 715 pts with a first ADE were observed over 1996-2011 (group A, n = 187; B, n = 123; C, n = 405). 519 (73%) male, median age 38 (IQR:33–45), median CD4+64 (23–187)/mm^3 and HIV/RNA 5.25 (4.57–5.70) $\log_{10}$ cps/mL, with no differences by calendar period. By 30 days from ADE, 23% (95% CI: 19–27) of those diagnosed in 1996–2000 have started cART vs. 32% (95% CI: 25–39) in 2001–2008 and 36% (28–44) after 2009 (log-rank p = 0.001). After stratifying by CD4 at ADE, 45% of pts with CD4 <50/mm^3, 30% of those with 51–200/mm^3 and 16% of those >201/mm^3 had started cART by 30 days (p <0.0001). Restricting the analysis to pts diagnosed after 2009, the percentages of cART initiation were 9% for group A, 52% for group B and 39% for group C (p = 0.05). The table shows the relative hazards of starting cART from fitting a multivariable Cox regression model.

Conclusions: In our 'real-life' setting, time from AIDS diagnosis to cART was significantly shorter in pts diagnosed in more recent years, although for most ADE cART initiation was less prompt than expected, even in pts with severe immunodeficiency.

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O423

Metabolic effects of atazanavir/ritonavir vs darunavir/ritonavir in combination with tenofovir/emtricitabine in antiretroviral-na ve patients (ATADAR Study)

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Purpose of the study: ATV/r or DRV/r plus TDF/FTC are recommended for first-line therapy due at least in part to their clinical tolerability and scarce metabolic effects. We investigated whether both regimens might differ regarding plasma lipids, insulin resistance (HOMA-IR), and estimated glomerular filtration rate (MDRD).

Methods: Multicentre, randomized, clinical trial (ATADAR Study, NCT01274780). Primary end-point: 24-week change in total cholesterol. Secondary end-points: changes in lipids other than total cholesterol, HOMA-IR, and MDRD; clinical tolerability; and efficacy. We assumed that patients assigned to DRV/r would have an increase in plasma total cholesterol <21 mg/dL, which was the difference between lopinavir/r and ATV/r in CASTLE study. Fasting plasma lipids, glucose, insulin, and creatinine were measured at baseline, and 4, 12, and 24 weeks. Analyses were by intent-to-treat.

Summary of results: 180 patients were randomized (ATV/r = 91, DRV/r = 89), 95% Caucasian, and 8% co-infected with hepatitis C virus. At baseline (mean, SD): age 36 (9) years; plasma log HIV RNA 4.8 (0.7); CD4 334 (189) cells/mm^3; triglycerides 107 (62), total cholesterol 158 (32), LDL cholesterol 97 (28), HDL cholesterol 39 (11) mg/dL, and glucose 84 (13) mg/dL; HOMA-IR 2.47 (3.46); and MDRD 108 (21) mL/min/1.73 m^2. At 24 weeks, total cholesterol (mean, SD) changed +7.26 (26.76) mg/dL with ATV/r and +11.47 (25.85) mg/dL with DRV/r (estimated difference ATV/r minus DRV/r −4.21 (95% CI −12.11 to +3.69), P = 0.2944), thus confirming our primary hypothesis. Changes (mean, SD) in triglycerides were roughly similar: +16.29 (61.76) mg/dL with ATV/r and +18.40 (64.24) mg/dL with

DRV/r (P = 0.8261), but there were trends to more favourable changes in LDL (−2.14 [21.45] vs +3.14 [21.97] mg/dL, P = 0.1160) and HDL cholesterol (+5.50 [10.36] vs +3.88 [8.42] mg/dL, P = 0.2625), and total-to-HDL cholesterol ratio (−1.16 [6.38] vs −0.14 [0.86], P = 0.0652) with ATV/r than with DRV/r. There were small, non-significant decreases in HOMA-IR (ATV/r −0.17 [2.48] vs DRV/r −0.70 [3.38], P = 0.3785) and MDRD (ATV/r −7 [22] vs DRV/r −6 [15] mL/min/1.73 m^2, P = 0.6652). 6 ATV/r and 3 DRV/r patients had their study drugs discontinued because of adverse effects (P = 0.4967). 7 additional patients in each arm had confirmed HIV RNA >50 copies.

Conclusions: There were trends to more favourable changes in LDL and HDL cholesterol and particularly total-to-HDL cholesterol ratio at 24 weeks with ATV/r than with DRV/r.

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O424A

Elvitegravir/cobicistat/emtricitabine/tenofovir DF (Quad) has durable efficacy and differentiated safety compared to efavirenz/emtricitabine/tenofovir DF at week 96 in treatment-na ve HIV-1-infected patients

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Purpose of the study: The primary Week 48 analysis of this ongoing, randomized, double-blind, double-dummy, active-controlled Phase 3 trial of elvitegravir/cobicistat/emtricitabine/tenofovir DF (Quad) in treatment-naïve patients demonstrated that Quad was non-inferior to efavirenz/emtricitabine/tenofovir DF (EFV/FTC/TDF) with a differentiated safety profile. We report the Week 96 interim data.

Methods: Key eligibility criteria included HIV-1 RNA ≥5,000 c/mL and eGFR ≥70 mL/min. Virologic success (HIV-1 RNA <50 c/mL) at Week 96 was assessed per snapshot algorithm. Adverse events and laboratory data were collected prospectively.

Results: 700 patients (89% male, 63% white, 33% with HIV-1 RNA >100,000 c/mL) were randomized and treated. At Week 48, Quad was non-inferior to EFV/FTC/TDF (88% vs 84%, difference +3.6%, 95% CI -1.6% to 8.8%). High rates of virologic success were maintained at Week 96 (84% vs 82%, difference 2.7%, 95% CI -2.9% to 8.3%). Subgroup analysis revealed similar rates of virologic success in patients with baseline HIV-1 RNA >100,000 c/mL (81% vs 83%). Mean CD4 cell increase (cells/mm^3) was 295 vs 273. Emergent resistance was infrequent (3% vs 3%). Rates of study drug discontinuation due to adverse events (AEs) were low and comparable (5% vs 7%). Rates of neuropsychiatric AEs were lower in Quad than in EFV/FTC/TDF (47% vs 66%, P <0.001), as were rates of rash (21% vs 31%, P = 0.006). Drug discontinuation due to renal reasons occurred in 7 (2%) vs 0 patients through Week 96; only two patients discontinued Quad since Week 48 due to serum creatinine (Cr) increase without features of proximal renal tubulopathy. Median changes in serum Cr (μmol/L [mg/dL]) at Week 96 in Quad vs EFV/FTC/TDF (11.5 vs 0.9 [0.13 vs 0.01]) were similar to those at Week 48 (12.4 vs 0.9 [0.14 vs 0.01]). Quad had smaller median increases (mmol/L [mg/dL]) in total (0.23 vs 0.47 [9 vs 18], P <0.001) and LDL cholesterol (0.23 vs 0.41 [9 vs16], P = 0.011), and similar increase in triglycerides (0.05 vs 0.09 [4 vs 8], P = 0.41).

Conclusions: At Week 96, Quad demonstrated high rates of virologic suppression with low rates of resistance and a differentiated safety and tolerability profile relative to EFV/FTC/TDF. These results support the durable efficacy and long-term safety of Quad in HIV-1 infected patients.

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O424B

Elvitegravir/cobicistat/emtricitabine/tenofovir DF (Quad) has durable efficacy and differentiated safety compared to atazanavir boosted by ritonavir plus emtricitabine/tenofovir DF at week 96 in treatment-na ve HIV-1-infected patients

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Purpose of the study: The primary Week 48 analysis of this ongoing, randomized, double-blind, double-dummy, active-controlled Phase 3 international trial of elvitegravir/cobicistat/emtricitabine/tenofovir DF (Quad) in treatment-naïve patients demonstrated that Quad was non-inferior to atazanavir boosted by ritonavir (ATV/r) + FTC/TDF with a differentiated safety profile. We report the Week 96 interim data.

Methods: Key eligibility criteria included HIV-1 RNA ≥5,000 c/mL and eGFR ≥70 mL/min. Virologic success (HIV-1 RNA <50 c/mL) at Week 96 was assessed per snapshot algorithm. Adverse events and laboratory data were collected prospectively. Bone mineral density (BMD) was assessed by DEXA scan in a subgroup of patients.

Results: 708 patients (90% male, 74% white, 41% with HIV-1 RNA >100,000 c/mL) were randomized and treated. At Week 48, Quad was non-inferior to ATV/r + FTC/TDF (90% vs 87%, difference 3.0%, 95% CI −1.9% to 7.8%). High rates of virologic success were maintained at Week 96 (83% vs 82%, difference 1.1%, 95% CI −4.5% to 6.7%). Subgroup analysis revealed similar rates of virologic success in patients with baseline HIV-1 RNA >100,000 c/mL (82% vs 80%). Mean CD4 cell increases (cells/mm^3) were 256 vs 261 at Week 96. Emergent resistance was infrequent (2% vs <1%). Rates of study drug discontinuation due to adverse events (AEs) were low and comparable (4% vs 6%). Rates of study drug discontinuation due to renal reasons remained low and similar through Week 96 (3 [0.8%] vs 2 [0.6%]); since Week 48, 1 patient in each group discontinued study drug due to serum creatinine (Cr) increase without features of proximal renal tubulopathy. Median increases from baseline in serum Cr (μmol/L [mg/dL]) in Quad vs ATV/r + FTC/TDF at Week 96 (10.6 vs 7.1 [0.12 vs 0.08]) were similar to those at Week 48 (10.6 vs 7.1 [0.12 vs 0.08]). Quad continued to have smaller increases (mmol/L [mg/dL]) in triglycerides (0.06 vs 0.18 [5 vs 16], P = 0.012); Quad had greater increases in total cholesterol (0.36 vs 0.21 [14 vs 8], P = 0.046) at Week 96 only; changes in LDL and HDL cholesterol were similar. Quad had smaller mean decreases (%) in BMD (hip: −3.16 vs -4.19, P = 0.069, spine: −1.96 vs −3.54, P = 0.049).

Conclusions: At Week 96, Quad demonstrated high rates of virologic suppression with low rates of resistance and a differentiated safety and tolerability profile relative to ATV/r + FTC/TDF. These results support the durable efficacy and long-term safety of Quad in HIV-1 infected patients.

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O425

STAR Study: single tablet regimen emtricitabine/rilpivirine/tenofovir DF is non-inferior to efavirenz/emtricitabine/tenofovir DF in ART-na ve adults

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Simplified antiretroviral treatment (ART) regimens improve quality of life and long-term medication adherence. Emtricitabine/rilpivirine/tenofovir DF (FTC/RPV/TDF) is a well-tolerated, once daily single tablet regimen (STR) treatment option. This is the first study to directly compare the safety and efficacy of the two STRs FTC/RPV/TDF and efavirenz/emtricitabine/tenofovir DF (EFV/FTC/TDF) in treatment-naïve adults. STaR is a randomized, open-label, multicenter, international, 96-week study to evaluate the safety and efficacy of the STR FTC/RPV/TDF compared to the STR EFV/FTC/TDF in treatment-naïve HIV-1-infected subjects. Subjects were randomized 1:1 to FTC/RPV/TDF or EFV/FTC/TDF. Eligibility criteria included screening HIV-1 RNA $\geq$2,500 c/mL, genotypic sensitivity to EFV, FTC, TDF, and RPV, and no prior ARV therapy. Randomization was stratified by HIV-1 RNA level ($\leq$100,000 c/mL or $>$100,000 c/mL) at screening. The primary endpoint was the proportion of subjects with HIV-1 RNA $<$50 c/mL at Week 48 as determined by the FDA snapshot algorithm (12% pre-specified non-inferiority margin). A total of 784 subjects were randomized and received at least one dose of study drug (392 FTC/RPV/TDF; 392 EFV/FTC/TDF). Baseline characteristics were similar in both treatment arms, with a baseline mean CD4 count of 390 cells/mm^3. and HIV-1 RNA of 4.8 $\log_{10}$ c/mL. FTC/RPV/TDF was non-inferior to EFV/FTC/TDF (86% vs 81%) at Week 48 for HIV RNA $<$50 c/mL (difference 4.0%, 95% CI [-1.2%, 9.2%]) per FDA snapshot analysis. Superior efficacy was demonstrated for baseline HIV-1 RNA $\leq$100,000 c/mL (n = 508), 88% FTC/RPV/TDF vs 81% EFV/FTC/TDF (difference 7.2%, 95% CI [0.9%, 13.4%]), and non-inferior for $>$100,000 c/mL (n = 276), 80% FTC/RPV/TDF vs 82% EFV/FTC/TDF (difference $-$1.8%, 95% CI [$-$11.2%, 7.5%]). Overall, virologic failure, defined as HIV RNA $\geq$50 c/mL at Week 48, discontinuation due to lack of efficacy per investigator or discontinuation of study drug for reasons other than an adverse event (AE) with HIV RNA $\geq$50 copies/mL was 8% for FTC/RPV/TDF vs 6% for EFV/FTC/TDF (difference 2.7%, 95% CI [$-$0.9%, 6.3%]). There were fewer study drug discontinuations due to AEs in the FDA snapshot analysis in FTC/RPV/TDF (2%) compared to EFV/FTC/TDF (8%). The STR FTC/RPV/TDF demonstrated overall non-inferior efficacy and improved tolerability compared to the STR EFV/FTC/TDF as well as superior efficacy for subjects with a baseline viral load $\leq$100,000 c/mL in treatment-naïve HIV-1-infected subjects.

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POSTER ABSTRACTS

ADHERENCE

P1

Association of partial adherence (PA) to antiretroviral therapy with hospitalizations and healthcare costs in an HIV population

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Purpose: One intrinsic feature of once daily single tablet regimens (STR) in HIV treatment is to prevent missing part of a multi-drug regimen (i.e., partial adherence [PA]). We explored the frequency of PA among HIV patients (pts) treated with multi-pill protease inhibitor (PI), raltegravir (RAL), and non-nucleoside reverse transcriptase inhibitor (NNRTI) regimens and associations with hospitalizations and costs.
Methods: We analyzed healthcare claims from a US Medicaid population. Patients with an HIV diagnosis from 1/09 to 12/11 receiving complete ART (2 NRTIs plus a NNRTI, PI, or RAL) for $\geq$90 days as a STR or 2+ tablets daily were selected. Adherence and costs were observed from initiation until discontinuation of the entire regimen, switching third component classes, or database end. Adherence was reported as the percent of days (from pharmacy refill data) having a complete regimen, PA, or no medication. A logistic model assessed predictors of hospitalizations and a generalized linear model assessed healthcare costs with covariates for PA and complete non-adherence (CNA), third component, demographics, and prior ART use.
Results: N = 1,878 STR, 729 RAL, 3,556 PI, and 775 NNRTI pts. CNA was similar across cohorts: 14.3% (46.4 days[d]) for STR, 14.0% (40.8 d) for RAL, 15.5% (53.0 d) for PI, and 13.5% (51.7 d) for multi pill NNRTI regimens. PA was seen in 12.1% (39.7 d) for RAL, 6.9% (31.7 d) for NNRTI, and 6.6% (26.7 d) for PI regimens. Thus, pts on STR had the highest percent of days (85.7%) with complete adherence to their regimen, vs. pts on multi pill RAL (73.9%), PI (77.9%), and NNRTI (79.6%) regimens. Likelihood of hospitalization significantly increased with both PA and CNA. Compared to $<$10 days of PA, the risk of hospitalization significantly increased (all $p<0.05$) with degree of incomplete adherence. For 20–30 days, the odds ratio [OR] was 1.34 for PA, and 1.45 for CNA. The OR was 1.74 for PA and 2.00 for $>$50 days CNA. Adjusted monthly healthcare costs were significantly greater for patients who were partially adherent for $>$5% of days (mean [SD] $5,108 [$1,315]) vs. $\leq$5% of days ($3,602[$894]).
Conclusions: Patients on multi pill PI, RAL, and NNRTI regimens had significantly lower complete adherence vs. STR users, mainly due to PA to a multi-pill regimens. PA and CNA to multi-pill PI, RAL, and NNRTI regimens are independently associated with a significant increase in hospitalizations and healthcare cost.

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P2

Facilitators and barriers to cotrimoxazole and nevirapine prophylaxis among HIV exposed babies: a qualitative study from Harare, Zimbabwe

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Implementation of cotrimoxazole prophylaxis (CTX-p) among HIV-exposed children is poor in southern Africa. We conducted a multi-methods study to investigate the barriers to delivery of CTX-p to HIV exposed infants in Zimbabwe at each step of the care cascade. Here we report findings of the qualitative component designed to investigate issues related to adherence conducted among women identified as HIV positive whose babies were started on CTX-p postnatally. Between Feb–Dec 2011, the first 19 HIV infected mothers identified were invited for in-depth interview 4–5 months postnatally. Interviews were recorded, transcribed, translated and analysed thematically. Of note, Zimbabwe also provides nevirapine prophylaxis for HIV-exposed babies, so the majority were giving nevirapine and CTX-p to their babies. All women desired their baby's health above all else, and were determined to do all they could to ensure their wellbeing. They did not report problems remembering to give drugs. The baby's apparent good health was a huge motivator for continued adherence. Testimonies from women whose babies had tested HIV negative strengthened the resolve to adhere. However, most women reported that their husbands were less engaged in HIV care, refusing to be HIV tested and in some cases stealing drugs prescribed for their wives for themselves. In two instances the man stopped the woman from giving CTX-p to the baby either because of fear of side effects or not appreciating its importance: ''he said if I kept giving CTX-p he would take the baby away from me and give him to his mother.'' Stigma continues to be an important issue. Mothers reported being reluctant to disclose their HIV status to other people so found it difficult to collect prescription refills from the HIV clinic for fear of being seen by friends/relatives. Some women reported that it was hard to administer the drugs if there were people around at home. Other challenges faced were stock-outs of CTX-p at the clinic, which occurred four times during the study. The baby would then go without CTX-p if the woman could not afford buying at a private pharmacy. The study highlights that adherence knowledge and desire alone is insufficient to overcome the familial and structural barriers to maintaining CTX-p. Improving adherence to CTX-p among HIV exposed infants will require interventions to improve male involvement, reduce HIV stigma at facilities and ensure adequate supply of drugs.

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P3

MEMRI study - feedback of MEMS dosing history improves adherence to long-term HAART: adherence is associated with incidence of 'blips' in viral load

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In routine clinical care we investigated the effect on adherence to HAART of feedback to each patient of graphical plots highlighting recent errors in their dosing history, as compiled electronically using MEMS®. Patients established on HAART were randomised to receive either active feedback of recent dosing errors (Group A) at clinic visits, or to serve as controls (no feedback) (Group B). After 12 months the control group were un-blinded and given feedback for a further 6 months. Questionnaires were completed in the waiting

room for adherence (GEEMA), Necessity/Concerns, Intrusiveness, Self-efficacy and Conscientiousness (baseline only). Those declining/excluded from using MEMS were invited to complete baseline questionnaires (Group C). Adherence was estimated from MEMS data as the average proportion of days with at least the prescribed number of doses taken between successive appointments. Drug Holidays (DH) were defined as 3 or more consecutive days without dosing. Of a cohort of 727 ~270 were approached. 180 were randomised. 147 had evaluable MEMS data (68 Group B: 79 Group A). 85 were in Group C (questionnaires only). Baseline characteristics were similar between Group A and B. Group C had a less common past history of AIDS. There was no significant difference in baseline conscientiousness between Groups A and B. Missed doses were much more likely at weekends than weekdays (OR = 1.25; [1.15–1.35]). Those taking <95% of prescribed doses during the first interval between visits were defined as poor adherers, which included 69 patients (49%). Their average baseline adherence was 78%. In Group A, average adherence increased ($p = 0.001$) to 90% after the first feedback session, while in Group B average adherence remained stable ($p = 0.405$). In Group B, after unblinding and start of feedback, adherence increased to 93%. Patients in Group B were significantly less likely to bring back their MEMS for reading at each appointment ($p = 0.031$). The incidence of viral load 'blips' (>50 copies/ml) was significantly increased by DH ($p = 0.007$), frequency of DH ($p = 0.016$), length of DH ($p = 0.005$), and missed doses during the 4 weeks before attendance ($p = 0.001$). Feedback of electronically compiled dosing history data improves adherence to HAART treatment and appears to be an effective intervention for reducing the incidence of viral load 'blips'. Further results including analysis of the questionnaires will be presented.

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P4

Impact of comorbidities on HIV medication persistence: a retrospective database study using US claims data

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Medication persistence (MP) is important in HIV management as lifelong HIV therapy is needed and discontinuation of HIV therapy could represent a permanent loss of therapeutic options. Many factors have been shown to decrease HIV treatment persistence; however, the evidence for comorbidities has been conflicting [1,2]. This study was conducted to further explore the impact of comorbidities on HIV MP. Data from the IMS PharMetrics claims database was used. To be included, patients had to 1) be 18 years of age or older; 2) have a diagnosis code for HIV during the study period (Jan 2006–Sep 2011); 3) have a claim for at least one HIV medication during the index period (Jan 2007–Sep 2010); and 4) have continuous enrollment 12 months before and after the index date. Patients could not have a diagnosis code for pregnancy during the study period or a claim for an HIV medication during the 12 months prior to the index date. The index date was the date of the first claim of an HIV medication during the index period and all HIV medications recorded on the index date were included as the HIV index regimen. MP was defined as time to discontinuation of the HIV index therapy using a 90-day grace period. Variables statistically significant ($p < 0.05$) in bivariate testing were included in a Cox proportional hazard model to adjust for confounding. Gender, index year, insurance provider type, number of HIV pills/day, and number of comorbidities were included in the final Cox model. A total of 3,057 patients were included in the analysis. The mean age was 43.9 yrs and 76.3% were male. The average MP was 315 days (min 92–max 365). In the Cox model, patients with 1, 2 and ≥3 comorbidities had a 6% ($p = 0.528$), 28% ($p = 0.014$) and 31% ($p = 0.002$), respectively, higher risk of discontinuing HIV index regimens than patients with no comorbidities. Additionally, females had a 29% ($p < 0.001$) higher risk of discontinuing HIV index regimens than males. The analysis supports prior evidence that comorbidities decrease HIV MP. This observation may be the result of patients switching HIV medications due to drug-drug interactions from polypharmacy for managing HIV and comorbidities or due to HIV medication adverse effects. Further research should address the impact of specific HIV regimens on HIV MP among patients with comorbidities and potential differences between genders.

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P5

Benefits of ART simplification on adherence, clinical and economic outcomes

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Purpose of the study: Fixed-dose combinations (FDCs) and single-tablet regimens (STRs) may reduce complete non-adherence (CNA) but also have the potential additional benefit of avoiding partial non-adherence (PNA) (some but not all drugs taken). We test this hypothesis and then estimate the impact of PNA-free regimen (STRs) on clinical and economic outcomes.
Methods: The unit analysis was a person-regimen of 2 NRTI+(NNR-(NNRTI, PI/r) lasting ≥90 days. Adherence was measured by the proportion of days covered using pharmacy refill data. The Wilcoxon rank-sum test was used to compare CNA, PNA and total non-adherence (TNA) in the following groups: STR vs its components (EFV+TDF/FTC) and non-FDC vs FDC vs STR. The level of adherence per group and the impact of PNA and CNA on virological failure (VF) were estimated using multivariate regression panel data models (MVRPDM). Control variables included age, gender, hepatitis co-infection, cumulative comorbidity score, CD4, viral load, regimen duration and calendar year. MVRPDM we also used to access the impact of PNA-free regimens on the probability of at least one hospitalization and on annualized hospitalization+ART costs. The analysis was performed in Stata 11®.
Summary of results: The retrospective analysis was performed on 2,449 person-regimens from a cohort of 1,435 HIV-infected individuals followed in one HIV unit in Portugal, between 2001 and 2011. Median age was 38 years old and median regimen duration was 1.9 years. CNA was higher (23%) in the non-FDC ($p < 0.001$ vs other groups) and similar in FDC vs STR (15% vs 11%, $p = 0.951$). PNA was higher in non-FDC than FDC (4.2% vs 3.4%; $p = 0.020$) and obviously null with STR ($p < 0.001$ vs other groups). In the subgroup analysis of EFV+FTC/TDF vs STR, TNA was 16% and 11% ($p = 0.0025$). In MVRPDM, STRs are estimated to result in a decrease of 11% ($p < 0.001$) and 5.3% ($p < 0.001$) in TNA relatively to non-FDC and

FDC, respectively. Both CNA and PNA were found to be predictors of VF ($p < 0.001$ and $p = 0.020$, respectively). The odds ratio of hospitalization with STRs vs other regimens was 0.33 ($p = 0.019$). STRs were associated with lower sum of ART + hospitalization annualized costs ($-1{,}330$€; $p < 0.001$) when compared to other regimens.

Conclusions: This study suggests that FDC and STRs are of value in avoiding PNA and TNA, thereby reducing the probability of virological failure, and that PNA-free regimens are associated with clinical and economic benefits.

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P6

Causes of virological failure in a population of 1895 HIV-infected patients: the experience of an infectious diseases service in Lisbon, Portugal

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Despite the increasing optimization of combined antiretroviral therapy (cART) regimens in the last decades, a significant percentage of patients still do not achieve viral replication control. We present a retrospective analysis focusing on human immunodeficiency virus (HIV)-infected population on cART, followed at our ambulatory care clinic between 1st January and 31st December 2011, in order to identify the causes of virological failure. From the 1895 patients in our population we included 1854 in the study. Ten percent (187) of the included patients had detectable HIV RNA (≥ 40 cp/mL) at the time of last laboratory evaluation: 70,1% were males, mean age was 46 years and 72,7% were Portuguese. Patients with detectable HIV RNA were divided into group A (HIV RNA < 200 cp/mL) - 78 (41,7%) patients and group B (HIV RNA ≥ 200 cp/mL) 109 (58,3%) patients. The comparison of both groups revealed an higher mean count of TCD4+ (568 vs 334 cells/mm^3; $p < 0{,}001$) in group A, although similar mean TCD4+ count at time of cART initiation (276 vs 262 cells/mm^3; $p = 0{,}412$). Group A patients experienced longer exposure to cART (10 vs 8 years; $p < 0{,}05$) and have undergone, on average, 3 previous regimens ($p < 0{,}05$). With regard to cARV current regimen: 32,1% patients in group A and 30,3% in group B were prescribed non-nucleoside reverse transcriptase inhibitors based regimes and 51,3% patients in Group A and 59,6% in group B were under cARV based on Protease inhibitors. The identified causes of virologic failure for patients with detectable HIV RNA were: poor adherence (54%); unsuccessful retention in care (14,4%); sporadic detectable HIV RNA ($40 \leq$ viral load < 200), ''blips'' (14,4%); mutations of resistance to ARVs (13,4%); intolerance to the current regimen (2,1%) and pharmacokinetics drug interactions (1,6%). The estimated rate of virological failure was 10,1% in this population. Insufficient adherence and unsuccessful retention in care were identified in 68,4% of treatment failed patients as main causes of virological failure. Failure of therapy due to intolerance or adverse effects was reported in 2,1% of cases, reflecting a better safety profile and tolerability of recent prescribed regimens. Early identification of causes of virologic failure, timely adjustment of therapeutic regimens, and the adoption of measures to promote adherence and retention in care are key factors for successful treatment of HIV-infected patients.

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P7

No significant association between patient self-reported non-adherence to antiretrovirals and HIV-tropism: a preliminary analysis

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Nonadherence to antiretroviral therapy (ART) may cause virologic failure and disease progression has been associated with switch of viral coreceptor usage from CCR5 to CXCR4. We aimed to assess the association between patient-reported non-adherence and HIV tropism. This is a cross-sectional analysis. HIV-tropism was performed within routine clinical practice either at start of ART or at virological failure. Adherence questionnaire includes: how many times ART has been taken during the last month, missed doses in the last week, timing deviation, refill interruption, drug holidays. Demographics, epidemiological data, HIV and ART history, CD4 and HIVRNA were collected. To assess co-receptor tropism, env V3 genotyping from viremic plasma HIVRNA was performed. For the analysis, dual/mixed viruses were considered as X4. We included 102 individuals: 76% males; median age 42 y (IQR, 37–46); transmission was heterosexual 37%, homosexual 31%, intravenous drug use 29%. Median nadir of CD4 154/mmc (IQR, 53–274), median zenith of HIVRNA 5.26 (4.72–5.70), 46% had AIDS. 124 tropism tests were: 78% R5, 17% X4, 5% dual/mixed. In cases with previous ART, mono/dual ART was found in 26%, median number of regimens was 5 (IQR, 2–10), median time on triple-ART was 54 months (IQR, 0–123) with median time of HIVRNA < 50 c/ml of 16 months (IQR, 6.5–34.9). At HIV-tropism, median CD4 and HIV RNA were 321/mmc (IQR, 210–436) and 2.65 (IQR, 2.65–4.91), respectively. Median time between adherence questionnaire and HIV-tropism was 68 days (IQR, 23–116). At adherence questionnaire, median percentage of ART taken during the last month was 100% (IQR, 90–100), 39% reported missed doses in the last week, 40% timing deviation, 7% refill interruption, 17% drug holidays. At univariate analysis, no statistically significant association between non-adherence and dual/mixed-X4 viruses was found ($p > 0.1$). Also gender, age, HIV transmission, AIDS, CD4 nadir, HIVRNA zenith, mono/dual ART, and number of ART regimens were not associated with type of tropism. Only longer time with undetectable HIVRNA before tropism test showed a lower probability of dual/mixed-X4 viruses (OR for each month 0.95; 95% CI 0.90–1.00; $p = 0.06$). No significant association between adherence and HIV-tropism was found in this preliminary analysis. It is possible that patient self-reported adherence is not able to capture nonadherence behaviors that underlie more pronounced viral replication which may be necessary for tropism switch.

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P8

Does a simplified regimen give a better adherence, treatment satisfaction, and quality of life?

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Background: Adherence to treatment is the key to the success of combination antiretroviral therapy (cART) for HIV infection. It is generally assumed that simplification of cART will lead to better adherence, higher treatment satisfaction, and quality of life (QoL),

but randomized studies demonstrating such advantages of simplified regimens are scarce.
Methods: Antiretroviral-naïve patients who achieved viral load <50 c/ml in two consecutive samples between 12–24 weeks after commencing induction therapy with bid lopinavir/ritonavir (LPV/r) and fixed-dose combination AZT/3TC (Combivir®) were randomly assigned to either continue LPV/r/Combivir® or switch to simplified therapy with bid fixed-dose AZT/3TC/abacavir (Trizivir®). Both arms yielded similar antiviral efficacy after 48 weeks as reported previously [1]. Patients completed standardized questionnaires on adherence (Simplified Medication Adherence Questionnaire (SMAQ)), treatment satisfaction (HIVTSQ) and QoL (MOS-HIV) at randomization and at weeks 48, 72 and 96. Adherence data were analyzed using generalized estimating equations, and satisfaction and QoL using mixed linear models.
Results: Patients in the Trizivir®-group (n = 30) tended to skip fewer doses both during the preceding 7 days (p = 0.055) and during the preceding weekend (p = 0.09) than patients in the LPV/r-group (n = 20). Moreover, patients in the Trizivir®-group found their regimen significantly more convenient (p = 0.022) than patients in the LPV/r-group. However, patients in the LPV/r-group reported a better QoL than patients in the Trizivir®-group in the domains measuring cognitive functioning (p = 0.003), energy/fatigue (p = 0.046) and social functioning (p = 0.074).
Conclusions: In this randomized trial simplification of therapy to fixed-dose Trizivir® was perceived to be more convenient, and tended to result in improved adherence, but at the expense of a lower level of QoL. Our findings suggest that the choice for simplified regimens should be individualized and may involve a trade-off between convenience and QoL.

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P9

Adherence and health beliefs in a psychoeducative intervention in na ve HIV-1-infected men: the PROADH study

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Background: Health beliefs are an important factor in the maintenance of an adherent behaviour. However, specific interventions based on the modification of health beliefs to promote adherence have not been applied in naïve HIV-infected subjects.
Methods: Prospective randomized 48-week study to evaluate the efficacy of a psychoeducative intervention based on health beliefs to promote adherence in a sample of naïve HIV-1-infected men who started antiretroviral therapy. Participants were randomized to follow three intervention visits to promote adherence with the use of projective drawing techniques, Life-steps and Motivational interview (Intervention Group; GI) or to continue with the routine care (Control Group; GC). Adherence was assessed through self-report and drug plasma levels. Mann-Whitney nonparametric test, w2 or Fisher exact test were used to compare variables.
Results: Participants were 40 men with a median (IQ) age of 35.2 (30.2–44.8) years, CD4 cell count at the study entry of 316 (229–539) cells/mm^3 and HIV-RNA VL of 65.000 (22.500–250.000) copies. The infection route had been mainly MSM (90%). QD and BID ARV therapy was prescribed in 29 (72.5%) and 11 (27.5%) subjects. Seven patients (2 in GI; 5 in GC) were lost to follow-up. At week 48, 100% of subjects in GI and 60% in GC had 100% adherence (p = 0.01). In GC, 26% and 14% of subjects had ≥95% and <95% adherence, respectively. No differences were found in adherence regarding QD or BID therapy. All subjects except for 3 had VL <25 copies at week 48.
Conclusions: High adherence was observed in the majority of this group of naïve HIV-infected men who initiated their first antiretroviral therapy. However, all subjects following the intervention had 100% adherence after one year of follow-up. A psychoeducative intervention based on the modification of health beliefs may be a useful strategy to promote adherence in naïve HIV-infected patients.

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P10

The role of SEAD project intervention in viral suppression of HIV/AIDS patients with follow-up and adherence barriers

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Purpose of study: Irregular FUP/ADH were associated with virologic failure [1] leading to an increase in mortality [2]. SEAD was a multidimensional intervention project, designed from the patient's perspective, to specifically attend patients with poor FUP/ ADH in an HIV/AIDS outpatient clinic.
Methods: From Jan 2006 to May 2010, patients with poor FUP/ADH were offered SEAD inclusion, all were evaluated by a nurse or a psychologist (adherence collaborators) who assessed all the reasons and barriers precluding a correct FUP/ADH. For each identified problem, different interventions were planned, using our own resources or coordinating others. Follow-up was censored in Nov 2011. Univariate and multivariable models were performed to evaluate the influence of SEAD intervention in virological suppression (HIV-ARN <1.7 log copies/mL) at the end of follow-up.
Summary of results: Overall, 242 patients were assessed: mean age 46 years, 78% men, 69% IDU, 51% AIDS, baseline ADH >90% 29.3%; median CD4 cell count 333 [164–536] cells/mL and HIV-RNA <1.57 45%. Patients were admitted in SEAD due to poor ADH 15%, FUP problems 21%, both FUP/ADH 53% and to prevent poor ADH or FUP 11%. Main reasons driving poor FUP/ADH were severe biopsychosocial problems 26%, severe drug and/or alcohol abuse 23%, logistic problems 21.3%, other psychiatric disorders 14%, oversights 10%, unknown 3% and antiretroviral intolerance 2%. Cocaine/heroin and alcohol abuse was reported by 33% and 16%. Only 57% of patients received >50% of planned interventions. After a median follow-up of 3.9 (3.27–4.43) years 218 patients received 8 (3–12) interventions/year, 95% evaluation interview and 30% psychological counselling (3 sessions/year [2–5]). Virological suppression was achieved by 67% of patients. In logistic regression analysis an intervention higher than 50% of planned HR 0.220 [IC 95% (0.112–0.44)] and receiving psychological counselling HR 0.44 [IC 95% (0.20–0.97)] were

independent predictors of virological suppression whereas alcohol 3.11 (95% CI 1.24–7.80) and severe biopsychosocial problems HR 2.39 (95% CI 1.134–5.040) were associated with worse virological response, after adjusting for age, alcohol or cocaine abuse, degree of adherence, baseline virological suppression, median follow–up, intravenous acquisition of HIV, and family support.
Conclusions: General and psychological SEAD intervention resulted in higher virological suppression in patients with severe follow-up and adherence barriers.

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P11

Single-tablet regimen is associated with reduced efavirenz withdrawal in antiretroviral na ve or switching for simplification HIV-infected patients

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Purpose of the study: Efavirenz (EFV) is still discussed for its high rate of interruption due to adverse event, in particular central nervous system side effects (CNS-SE). Aim of the study was to define if better drug formulations up to single tablet regimen (STR), including (EFV) plus NRTI backbone (tenofovir-emtricitabine), reduced the risk of interruption.
Methods: From the database of two reference centers, patients starting any cART regimen including EFV + 2 NRTI or switching to EFV + 2 NRTI for simplification after virological suppression were selected. Probability of interruption by virological failure, side effects, CNS-SE and any cause were assessed with survival analysis and Cox proportional hazard model.
Summary of results: Overall, 533 patients, starting EFV-containing regimen from May 1998 to March 2012, were included (51.2% naïve, 48.8% switched). Patients characteristics: males 70.7%, median age 39 years, injecting drug use (IDU) 11.2%, median nadir CD4 194/mmc, median CD4 at EFV start 305/mmc: 38.7% started BID regimen, 43.9% OD regimen and 17.4% STR. At survival analysis, the overall proportion of EFV interruption was 19.1% at 1 year and 33.0% at 3 years; interruption for virological failure were 2.8% and 7.4% and for toxicity 10.2% and 15.9%, respectively. CNS-SE accounted for about half of interruptions for toxicity (5.7% and 8.0% at 1 and 3 years, respectively). Naïve patients had a higher risk of interruption as compared to switched patients: 37.7% vs. 28.0% at 3 years ($p = 0.06$). While no significant difference was observed comparing OD vs. B ID regimens, starting with STR was associated with significant lower proportion of overall interruption at 3 years (17.1% vs. 36.6%, $p < 0.01$). No virological failure was observed with STR up to 3 years (0.0% vs. 8.9%, $p = 0.05$); no difference of interruption by overall toxicity and higher, though non-significant, frequency of interruption by CNS-SE (12.8% vs. 6.8%) were also observed. STR also accounted for lower proportion of interruption by patient wish, including low adherence (1.5% vs. 12.3%, $p = 0.01$). At adjusted Cox model, STR (HR: 0.44; 95% CI: 0.26–0.77) and male gender (HR: 0.71; 95% CI: 0.53–0.97) were associated with lower risk of EFV interruption and IDU with higher risk (HR: 1.64; 95% CI: 1.11–2.42).
Conclusions: In our experience, EFV co-formulated in STR was associated with lower virological failure and higher adherence, despite keeping CNS toxicity, thus reducing the risk of treatment interruption.

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P12

Are we conSTRucting the best treatment regimens for all patients with HIV infection?

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The British HIV Association (BHIVA) 2012 guidelines for the treatment of HIV recommend patients start combination antiretroviral therapy (ART) containing tenofovir and emtricitabine as the nucleos(t)ide reverse transcriptase inhibitor (NRTI) backbone. BHIVA third agent preferred choices comprise efavirenz, boosted atazanavir, boosted darunavir and raltegravir, and the guidelines further state that 'fixed dose combinations (FDC) of drugs can increase adherence' [1]. Atripla is currently the only available single-tablet regimen (STR) for the treatment of HIV which contains a combination of BHIVA preferred first-line antiretrovirals (tenofovir, emtricitabine and efavirenz). In addition, studies have shown that Atripla can improve adherence, treatment satisfaction and outcomes for patients infected with HIV [2]. A retrospective case note review was conducted for all HIV-positive patients attending a UK HIV centre and receiving ART. The purpose was to ascertain the proportion of patients receiving BHIVA preferred ART in its simplest dosing format (in this case Atripla) and to investigate whether there were clinically or virologically appropriate reasons why patients not on Atripla were prescribed more complex drug regimens. The total number of patients receiving ART at the time of review was 142, of which 47 (33%) were currently taking Atripla. Of the remaining 95 patients, 30 (32%) had taken Atripla or some of its components in the past and been changed from this for valid clinical or virological reasons. In addition, there were a further 34 cases (36%) where Atripla had never been offered to the patient for appropriate reasons and documentation of 8 instances in which Atripla had been declined by the patient. There remained, however, 28 cases (29%) where there was no documentation of Atripla having been considered or offered, and no apparent contraindications to the STR or its components. This included 4 patients with an elevated cardiovascular risk, all of whom were taking an abacavir-containing ART regimen at the time of review. Despite extensive professional guidance on preferred ART regimens and evidence to suggest that STR can increase adherence and patient satisfaction there remain patients in clinical care taking more complex drug regimens with no clear indication for this. We would encourage physicians to identify such patients and to discuss with them their treatment options in the light of advances in ART combination preparations.

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P13

Adherence and retention on antiretroviral therapy in a public-private partnership program in Nigeria

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Initiation of HIV-positive patients on antiretroviral therapy (ART) in Nigeria was restricted to secondary and tertiary level hospitals due to weak health systems in primary health centres (PHCs). Shell Petroleum Development Company (SDPC) Nigeria and FHI 360 using a systems strengthening approach, piloted ART enrolment in a PHC in south-eastern Nigeria. This study sought to evaluate patients' adherence and mortality on ART, and associated risk factors. We reviewed clinic records of adult patients initiating ART between January 2007 and December 2009. Adherence was calculated as the number of days of medication dispensed as a percentage of total number of days evaluated. Outcome measures were probability of being alive and retained in care at 12 and 24 months on ART. Competing risks regression models were used to assess potential predictors associated with mortality. Total of 196 patients (64.8% males) were initiated on ART. Patients' median age was 35 years (IQR 30–44); median CD4 at initiation was 132 cells/mm^3 (IQR 82–212), Patients in WHO stage III and IV constituted 73 (37.6%) and 83 (42.8%) respectively. Majority (108 [55.1%]) of patients had adherence rates >95%. Adherence levels ranged: 70–85%, 50–65% and <50% in 29 (14.8%), 30 (15.3%) and 29 (14.8%) of patients respectively. Nucleoside backbone use were AZT/3TC (69.4%) d4T/3TC (28.6%) and TDF/FTC (2%). At 12 months of follow up, 80.6% (158) were alive and on ART, mortality accounted for 12.8% (25), 11 (5.6%) were LTFU and 2 (1.1%) transferred out. At 24 months on ART survival decreased to 64.3% (126), 20.4% (40) died, 9.2% (18) were LTFU and 12 (6.1%) transferred out. Competing risks regression models revealed that patients' factors significantly associated with mortality include: bedridden patients (HR = 3.6 [95% CI: 1.11–11.45], p = 0.03, referent: working), <50% adherence levels (HR = 27.7 [95% CI: 8.55–89.47], p < 0.0001, referent: >95% adherence level). In conclusion, majority of attrition was due to mortality. Poor adherence was associated with 27 times higher risk of death compared with patients with >95% adherence. Mortality is likely to reduce by establishing a more robust adherence counselling process.

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P14

Adherence in HIV-positive patients treated with single-tablet regimens and multi-pill regimens: findings from the COMPACT study

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The use of Combination AntiRetroviral Therapy (cART) has decreased the morbidity and mortality of patients infected with HIV. However, adherence to cART remains crucial to prevent virological failure and disease progression. The aim of this study was to assess adherence to treatment among patients treated with Single Tablet Regimen (STR) or with multi-pill regimens based on Protease Inhibitors (PI), Non-Nucleoside Reverse-Transcriptase Inhibitors (NNRTI), or raltegravir (RAL). An observational retrospective cohort analysis based on administrative and clinical databases was conducted at the National Institute for Infectious Diseases (Rome, Italy). HIV-positive patients treated with a cART between Jan 1st, 2008–Dec 31st, 2010 were included. Patients were followed-up for one year since the first prescription during the inclusion period or up to death or switch of at least one drug of the regimen. Adherence and selective non-adherence (days without backbone or 3rd drug) were calculated using pharmacy refill compliance [1]. cART regimens were classified based on number of daily pills (STR vs multi-pill regimen) and on type of third drug. Viral Load (VL) and CD4 cell counts at the end of the follow-up were evaluated. A total of 1,604 patients were analyzed, 70.0% male, age 45.0±8.7, 14.3% newly treated. Patients on STR were 159 (9.9%), PI 878 (54.7%), NNRTI 523 (32.6%), RAL 44 (2.7%). Presence of at least one AIDS-defining conditions (according to Centers for Disease Control classification) was 30% in the STR group, 34% PI, 26% NNRTI, 34% RAL (p = n.s.). Adherence was 80.4±14.7% for STR, 71.8±21.8% PI, 77.1±20.3% NNRTI, 74.0±22.4% RAL. Selective non-adherence was 5.5% (18 days) PI, 2.8% (8 days) NNRTI, 12.5% (43 days) RAL (Figure 1). At the end of the follow-up, VL/CD4 values were available among 709 patients (44%); CD4 count >500 cell/mm3 was observed among 61% of patients on STR, 44% PI, 48% NNRTI, 42% RAL and VL <50 copies/ml was observed among 96% of patients on STR, 78% PI, 88% NNRTI, 87% RAL. Interruptions in cART refill remain a relevant problem across all cART regimens. Patients on STR displayed a higher adherence rate compared to multi-pill regimes (PI, NNRTI, and RAL), primarily due to lack of selective non-adherence. Patients on STR experienced also higher rates of VL <50 and CD4 >500. The use of an STR regimen appears an effective therapeutic option to avoid selective non-adherence and, consequently, to prevent virological failure and disease progression.

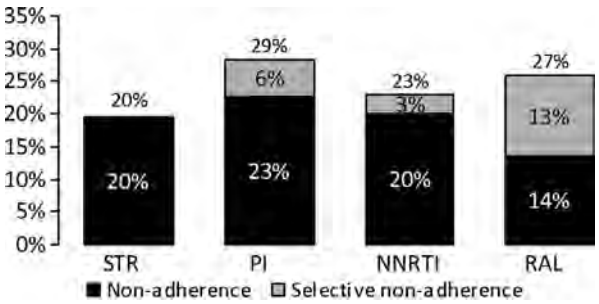

Figure 1. Non-adherence to cART regimens.

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P15

Suppressed or unsuppressed HIV in adults on antiretroviral therapy in Zambia: who is at risk?

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Purpose of the study: To determine factors associated with suppressed or unsuppressed HIV in adults receiving combination antiretroviral therapy (cART) in Zambia.
Methods: This was a cross-sectional study conducted between August 2008 and October 2009 in 16 Zambian communities nested within the ZAMSTAR trial [1]. Adult TB cases identified at a TB clinic of each community and their adult household members were invited to participate in the study. A structured interview was used to obtain information on the participants' social, demographic and clinical characteristics. Socio-economic position (SEP) was measured using household wealth indices used in demographic health surveys. Principal component analysis was used to determine the cut-off for high (wealthy) and low (poor) SEP. Depression symptoms were measured using the Center for Epidemiological Studies Depression scale (CES-D). A cut-off of ≥ 22 on the CES-D was used to define current depression [2]. Participants were included in this analysis if they were found to be receiving cART for >90 days at the time of the interview. The outcome was HIV suppression (viral load ≤ 300 copies/ml). In both univariable and multivariable analyses, log Poisson regression models with robust standard errors adjusted for the 16 communities were used to calculate the risk ratios (RR), 95% confidence intervals (CI) and p-values of factors associated with HIV suppression. In multivariable analysis, each variable was independently assessed for its association with HIV suppression while minimally adjusting for *a priori* confounders (age, gender and education level).
Summary of results: There were 520 patients receiving cART for >90 days. The median age was 35 years (inter-quartile range: 31–41) and 328/520 (63.1%) were married (Table).
Of the 520 patients, 442 (85.0%) had HIV suppression while 78 (15.0%) did not. At univariable analysis, having high SEP was nega-

		HIV suppression		HIV suppression vs. no suppression			
	n = 520	Yes	No	Unadjusted		Adjusted	
	N (column %)	N (row %)	N (row %)	RR (95% CI)	p-value	RR (95% CI)	p-value
Age group, years							
16 to 25	47 (9.0)	39 (83.0)	8 (17.0)	1			
26 to 35	220 (42.3)	183 (83.2)	37 (16.8)	1.00 (0.85–1.18)	0.976		
36 to 45	187 (36.0)	162 (86.6)	25 (13.4)	1.04 (0.91–1.20)	0.541		
Above 45	66 (12.7)	58 (87.9)	8 (12.1)	1.06 (0.90–1.25)	0.503		
Gender							
Men	204 (39.2)	169 (82.8)	35 (17.2)	1			
Women	316 (60.8)	273 (86.4)	43 (13.6)	1.04 (0.97–1.12)	0.261		
Education level							
None/Primary	241 (46.3)	200 (83.0)	41 (17.0)	1			
Secondary	279 (53.7)	242 (86.7)	37 (13.3)	1.05 (0.95–1.15)	0.358		
Socio-economic position (SEP)							
Low	287 (55.2)	252 (87.8)	35 (12.2)	1		1	
High	220 (42.3)	177 (80.5)	43 (19.5)	0.92 (0.86–0.98)	0.009	0.90 (0.84 – 0.96)	0.001
Missing	13 (2.5)	12 (92.3)	1 (7.7)				
Type of cART							
Tenofovir (TDF) + emtricitabine (FTC) + nevirapine (NVP)	61 (11.7)	48 (78.7)	13 (21.3)	1		1	
TDF + FTC + efavirenz (EFV)	182 (35.0)	154 (84.6)	28 (15.4)	1.08 (0.95–1.22)	0.26	1.09 (0.96–1.25)	0.187
Stavudine (d4T) + lamivudine (3TC) + NVP	197 (37.9)	168 (85.3)	29 (14.7)	1.08 (0.97–1.21)	0.158	1.05 (0.94–1.18)	0.379
Zidovudine (ZDV) + 3TC + EFV	78 (15.0)	70 (89.7)	8 (10.3)	1.14 (1.01–1.28)	0.027	1.11 (0.99–1.25)	0.071
Missing	2 (0.4)	2 (100.0)	0 (0.0)				
History of tuberculosis							
No	108 (20.8)	92 (85.2)	16 (14.8)	1		1	
Yes	412 (79.2)	350 (85.0)	62 (15.0)	1.00 (0.89–1.11)	0.961	1.01 (0.91–1.13)	0.818
Current depression							
No	416 (80.0)	355 (85.3)	61 (14.7)	1		1	
Yes	77 (14.8)	63 (81.8)	14 (18.2)	0.96 (0.84–1.09)	0.523	0.96 (0.84–1.09)	0.493
Missing	27 (5.2)	24 (88.9)	3 (11.1)				

tively associated with HIV suppression while receiving ZDV + 3TC + EFV was positively associated with HIV suppression. At multivariable analysis, patients with high SEP were less likely to have HIV suppression than those with low SEP.
Conclusions: Patients with high SEP were found to be at risk of having unsuppressed HIV. There is need for targeted interventions that can improve HIV outcomes in this group of patients receiving cART in Zambia.

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P16

Among once-daily regimens, single tablet regimens (STRs) are associated with better adherence

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Previous published evidences showed that taking HAART once-daily (OD) is associated to better adherence when compared to BID or TID regimens. However, no further studies investigated whether, among OD regimens, adherence levels can be differently influenced. Aim of the study was to evaluate levels of self-reported adherence in HIV + people according to type of HAART dosing (STR, OD with more than one pill or BID). To limit reporting biases, the study was performed in five different non-clinic settings covering North and Central Italy. A total of 230 patients on stable HAART were asked to complete a semi-structured, anonymous questionnaire reporting their attitude toward HAART, their adherence and the acceptability of their regimen. Self-perception of adherence was also investigated with a single item for comparison with real adherence behavior. Most of the subjects were males (66%) with a mean age of 46 years, with higher education level (72%) and a long history of HIV infection (mean 13.6 years). 17% of patients were on a first-line regimen. 21% reported to miss at least one dose during the past week (STR: 6%; OD > 1 pill 23% and BID 21%; $p < 0.05$). People taking STR and BID tend to report less discontinuations (all the drug of the day for at least 3 times in a month) compared to OD > 1 pill (6 and 4% vs 11%). People taking therapies other than HAART reported similar adherence levels of people taking only HAART, even when stratified for dosing groups. Even people judging their adherence as 'optimal' or 'very good', 10 and 17% respectively, reported having missed a dose during the last week. At stepwise regression model, optimal adherence was correlated to being male (OR: 2.38; 95% CI: 1.19–4.74), younger (OR: 3.04; 95% CI: 1.01–9.13) and with a shorter HIV infection (OR: 3.58; 95% CI: 1.04–12.38). People taking simpler once-daily STR tend to report better adherence than people taking OD > 1 pill or BID. Perception of optimal adherence is largely variable among HIV-infected people taking HAART, although only a minority of subjects showing less than perfect adherence do judge their behavior as 'optimal'.

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P17

CD4 count evolution of HIV-infected patients in follow-up as an indicator of quality of care

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Objective: To study the evolution of CD4 count of HIV-infected patients in follow-up as an indicator of quality of care.

Abstract P17–Table 1. Characteristics associated with non optimal CD4 evolution among patients in care

	Optimal CD4 evolution	Non-optimal CD4 evolution	OR (95% CI)	Adjusted OR (95% CI)
Gender (N, %)				
Male	281 (70.1)	51 (63.0)	1	1
Female	120 (29.9)	30 (37.0)	1.38 (0.84–2.27)	0.89 (0.41–1.91)
Age at diagnosis (N, %)				
< 40 yrs	252 (62.8)	51 (63.0)	1	1
≥ 40 yrs	149 (37.2)	30 (37.0)	0.99 (0.61–1.63)	1.06 (0.60–1.98)
Way of transmission (N, %)				
Heterosexual	162 (49.4)	37 (56.1)	1	1
MSM	163 (49.7)	29 (43.9)	0.78 (0.46–1.33)	0.85 (0.40–1.80)
IDU	3 (0.9)	0 (0.0)	/	
Nationality (N, %)				
Belgian	177 (52.8)	32 (46.4)	1	1
SSA	103 (30.8)	27 (39.1)	1.45 (0.82–2.56)	1.37 (0.62–3.01)
European	39 (11.6)	4 (5.8)	0.57 (0.19–1.70)	0.57 (0.19–1.73)
Other	16 (4.8)	6 (8.7)	2.07 (0.75–1.70)	1.74 (0.57–5.30)
Retention in care (N, %)				
≥ 1 consult./period	359 (89.5)	69 (85.2)	1	1
< 1 consult./period	42 (10.5)	12 (14.8)	1.49 (0.74–2.97)	1.45 (0.68–3.12)

Methods: Adult patients newly diagnosed with HIV in 2007 who entered in care in the AIDS Reference Centres (ARC) and remained in care for at least one year were studied until end 2009. Optimal CD4 evolution was defined as having a CD4 count above 350 cells/mm^3 after 1 year in HIV care, or an increasing rate exceeding 50 cells/mm^3 per year, and this regardless of antiviral therapy. The proportion of patients with optimal CD4 evolution was measured and factors associated with outcome were identified by logistic regression.
Results: 482 patients were included. Median age was 37 years, 31.1% were females, 51.7% Belgians, 32.2% from Sub-Saharan Africa, 50.5% heterosexual, 48.7% MSM. 59.5% had a CD4 count above 350 at entry in care, 11.2% did not have a regular retention in care (at least 1 consultation/6-month period). 401 (83.2%) patients had an optimal CD4 evolution after 1 year in care. 60.5% of patients with non-optimal evolution had a CD4 count below 350 at entry in care. Although the proportion of female sex, heterosexual transmission, Sub-Saharan nationality and low retention in care was higher in the non-optimal CD4 evolution group compared to the optimal group, none of these characteristics showed a significant association with non-optimal CD4 count evolution.
Conclusion: 83.2% of patients had an optimal CD4 evolution after at least 1 year in HIV care. This indicator, analysed together with indicators of entry and retention in care, could contribute to a better monitoring of the HIV epidemic and to identify more precisely the steps in care system that could be improved. These indicators should be fully integrated in HIV surveillance.

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P18

Single-tablet regimens (STRs) enhance patients' acceptability of HAART

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Patients' acceptability of HAART is a subjective variable that may deeply influence therapeutic outcome. The feeling of the patient may alter adherence and lead to virologic failure. Acceptability may depend on various variables often difficulty evaluated by the care-giver. In a clinical setting the evaluation of acceptability is difficult, too, as patients may feel a judgement and be less sincere. Aim of this study was to asses adherence and acceptability of HAART. To limit reporting biases, the study was performed in five different non-clinic settings covering North and Central Italy. A total of 230 patients on stable HAART were asked to complete a semi-structured, anonymous questionnaire reporting their attitude toward HAART, their adherence and the acceptability of their regimen. In these notes we focus on this last patient-oriented outcome. Most of the subjects were males (66%) with a mean age of 46 years, with higher education level (72%) and a long history of HIV infection (mean 13.6 years). Consequently only 17% of patients were on a first-line regimen. Patients reporting a high or very high acceptability of HAART were 60% compared to a 31% reporting a fair grade of satisfaction and a 9% indicating low or null acceptability. However the type of the regimen significantly influenced patients' acceptability. Single-tablet regimens (STRs), OD regimens with more than one tablet/day or BID regimens were scored as highly acceptable in 84%; 61%; and 53% of cases, respectively ($P < 0.0001$) (Figure). Statistical significance was retained when the dosing schedule was entered in a multivariate logistic model.

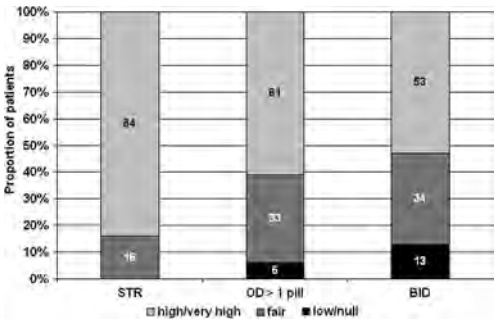

Figure 1. Patient reported acceptability for thier current HAART regimen.

When the analysis was restricted to experienced patients 62% of them were currently on a regimen based on a reduced number of pills compared to the previous one. Patients scored the previous regimen as more difficult to comply with in 72% of cases; as difficult in 22% and less difficult in 6%. The eventuality of AEs (40%); respect of timing of pill intake (39%) and number of pills (27%) were the major reasons of patients' low acceptability of HAART. High acceptability is one of the winning characteristics of a regimen, favoring long-term adherence, durability and efficacy. Although highly subjective, acceptability may be positively influenced by characteristics of the HAART regimen such as simplicity. According to our results, STRs show a higher acceptability compared to more complex regimens.

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P19

Self-reported adherence supports patient preference for the single tablet regimen (STR) in the current cART era

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Objective: To analyze self-reported adherence to antiretroviral regimens containing ritonavir-boosted protease inhibitors, non-nucleoside reverse transcriptase inhibitors (NNRTI), raltegravir, and maraviroc.
Methods: Overall, 372 consecutive subjects attending a reference center for HIV treatment in Florence, Italy, were enrolled in the study, from December 2010 to January 2012 (mean age 48 years). A self-report questionnaire was filled in. Patients were defined as ''non-adherent'' if reporting one of the following criteria: $<90\%$ of pills taken in the last month, ≥ 1 missed dose in the last week, spontaneous treatment interruptions reported, or refill problems in the last 3 months. Gender, age, CD4, HIV-RNA, years of therapy, and type of antiretroviral regimen were analyzed with respect to adherence.
Results: At the time of the questionnaire, 89.8% of patients had <50 copies/mL HIV-RNA and 14.2% were on their first combined antiretroviral therapy. 57% of patients were prescribed a regimen containing ritonavir boosted protease inhibitors (boosted PI), 41.7% NNRTI, 17.2% raltegravir, and 4.8% maraviroc; 49.5% of the subjects were on bis-in-die regimens, while 50.5% were on once-daily regimens, with 23.1% of these on the single tablet regimen (STR): tenofovir/emtricitabine/efavirenz. The non-adherence proportion was lower in NNRTI than in boosted-PI treatments (19.4% vs

30.2%), and even lower in STR patients (17.4%). In multivariable logistic regression, patients with the NNRTI regimen (OR: 0.56, 95% CI: 0.34–0.94) and the STR (OR: 0.45, 95% CI: 0.22–0.92) reported lower non-adherence. Efavirenz regimens were also associated with lower non-adherence (OR: 0.42, 95% CI: 0.21–0.83), while atazanavir/ritonavir regimens were associated with higher non-adherence. No other relation to specific antiretroviral drugs was found. A higher CD4 count, lower HIV-RNA, and older age were also found to be associated with lower non-adherence, while a longer time on combined antiretroviral therapy was related to higher non-adherence.

Conclusion: In conclusion, older age, higher CD4 cell counts, lower HIV-RNA viral loads, and the use of STR are all related to lower non-adherence. In particular, the use of STR maintains an advantage in improving adherence with respect to other cARTs, even with the availability of new, well-tolerated antiretroviral drugs and drug classes in recent years.

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P20

Adherence and neurocognitive screening in Romanian HIV patients

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Background: Adherence is critical for the effectiveness of antiretroviral HIV therapy (ART), accordingly decreasing the opportunistic diseases and increasing the quality of life. Neurocognitive disorders (NCD) are still frequent in ART era and could impair the adherence, but how ethical is to refer ART in patients with NCD?

Objective: To assess the relation between NCD and adherence in HIV Romanian patients.

Material and methods: Cross-sectional screening study on 151 patients under ART, no drug users, from HIV Clinic - Galati, assessed by HIV-Associated Dementia Scale (HDS), Hospital Anxiety and Depression Scale (HADS) [1], ART CNS-effectiveness Letendre scores [2] and adherence assessment questionnaire CNLAS- Romania. Normal values: HDS >10; anxiety/ depression <8. Statistical analysis performed: Chi-square test and Mann-Whitney test, with 5% significance level.

Results: Characteristics of the patients: median age 22 [20; 56] years old; sex ratio F/M 1.17; median educational level 8 [0; >12] years; HBV co-infection 27.8%; AIDS stage 85.3%; current median CD4 526/mm^3 [8; 1605] and 65% undetectable HIV-RNA levels. 49.6% (75/151) patients attain HDS scores <10 and imply probable NCD. Scores below 8 for anxiety are more frequent than for depression: 24% vs 13%. The median ART CNS penetration score is 8 [5; 12]. Adherence is considered for 66% patients and is correlating with CD4 number ($p=0.001$), educational level >4 years ($p=0.001$; OR $=4.2$), HDS >10 ($p=0.01$; OR $=2.4$) and ART-CNS penetration score >7 ($p=0.023$; OR $=2.4$). Low HDS are influenced by old age ($p=0.003$), depression ($p=0.02$) and ART-CNS penetration scores <7 ($p=0.01$). Anxiety is related neither with adherence nor with NCD by HDS, but females are obvious anxious than males ($p<0.001$).

Conclusions: Basic educational level is sufficient for developing ART adherence. High scores of HDS screening should be predictors for ART adherence. Referring ART as well to patients with low HDS scores is rational and ethical, if joint actions of effective ART-CNS regimens and depression improvement strategy are considered.

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http://dx.doi.org/10.7448/IAS.15.6.18144

P21

Impact on adherence of a telephone follow up strategy in HIV-na ve patients who start antiretroviral therapy: cohort study

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Abstract P21

	Non intervention group (n: 50)	Intervention Group (n: 41)	p
Age (mean in years)	36	35	0.58
Women n (%)	17 (34%)	23 (56%)	0.034
Heterosexual n (%)	33 (66%)	28 (68%)	0.81
Education, years (mean)	10.02	10.39	0.58
Preexistent serious disease	6 (12%)	5 (12%)	1
Previous opportunistic events (%)	16 (32%)	10 (24%)	0.28
Baseline CD4 count, median (range)	176 (7–783)	222 (20–868)	0.12
Baseline HIV RNA, log	4.89	4.22	0.001
Abandonment of treatment	9 (18%)	3 (7%)	0.021
Change of treatment	10 (20%)	14 (34%)	0.042
Lost to follow up	23 (46%)	10 (24%)	0.032
Hospitalization after HAART	4 (8%)	3 (7%)	0.3
New opportunistic event	3 (6%)	0 (0%)	N/A
Death	2 (4%)	1 (2.4%)	0.41
CD4/mm^3 at 24 weeks (median)	315	384	0.151
Log HIV RNA at 24 weeks (median)	1.69	1.69	

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Antiretroviral therapy changed the prognosis of people living with HIV/AIDS. However, lack of adherence jeopardizes the success of antiretroviral therapy and enhances the development of treatment-resistant strains, treatment failure, and therefore it stands as a public health problem. The main goal of this study was to measure the impact on treatment discontinuations and lost to follow up, of a telephone follow-up strategy in naïve patients who start antiretroviral therapy. We conducted a single-site, cohort study during a 12-month period (May 2011–May 2012). A prospective cohort of naïve patients received the standard of care plus a specific telephone follow-up strategy. Results were compared with a retrospective cohort of naïve patients followed up at the same site, who started antiretroviral therapy receiving only the standard of care during a similar period (January–December 2009). We used descriptive statistics and Fisher exact test for the comparisons of variables. We enrolled 41 patients in the prospective cohort and 50 in the retrospective one. Both cohorts had similar general characteristics. We found a lower number of patients who were lost to follow up in the prospective cohort (intervention) consistent with lower rates of treatment abandonment, suspensions and a similar tendency for events, including death, even when none of these findings was statistically significant. Baseline characteristics and main results are shown in the table below. Further randomized studies should be conducted applying a telephone follow-up strategy to confirm these findings.

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P22

Characterization of newly diagnosed HIV-infected patients who are lost to follow up

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Purpose of the study: We previously identified that a great amount of newly diagnosed HIV-infected patients were lost to follow up after the diagnosis. The aim of the present study is to describe the characteristics of the newly diagnosed HIV-infected patients who are lost to follow up.
Methods: We reviewed the clinical charts of the adult (>18 y/o) patients who attended for the first time our HIV clinic between 1/Jan/2005 and 31/Dec/2010. Among the patients who were newly diagnosed with HIV infection, we identified those who consulted the clinic only once. We considered patients were lost to follow up if they never came back within 12 months. We compared age, gender, nationality, education level and socioeconomic characteristics between those patients who were lost to follow and those who continue HIV care. We considered the first visit the one in which the patient was informed about his/her HIV seropositive condition.
Summary of results: We included 504 patients, 179 (35.5%) never came back after the first visit. Patients who were lost to follow up (A) were younger (mean age 33.8 vs. 39.07 y/o) than those who continue follow up (B). We identified 11/179 patients older than 50 years in A and 52/325 in B; P = 0.001 (OR 0.34, 95% CI 0.16–0.70). In A 136/179 were male and 232/325 in B. 142/179 were Argentinian in A and 289/325 in B; P = 0.003 (OR 0.48, 95% CI 0.28–0.81). In A 61/179 lived alone and 39/325 in B; P = 0.000 (OR 3.79, 95% CI 0.64–1.37). 41/179 had health insurance in A and 162/325 in B; P = 0.003 (OR 0.30, 95% CI 0.28-0.81). A university or tertiary degree was reached in 33/179 in A and 110/325 in B; P = 0.000 (OR 0.44, 95% CI 0.28–0.70).

	Patients lost to follow up, n = 179	Patients who continue follow up, n = 325	
Male/female	136/43	232/93	P = 1.24 OR 1.27 (95% CI 0.82–1.97)
Mean age (years)	33.8	39.07	
Older than 50 years old	11	62	P = 0.001 OR 0.34 (95% CI 0.16–0.70)
Argentinian	142	289	P = 0.003 OR 0.48 (95% CI 0.28–0.81)
Health insurance	41	162	P = 0.003 OR 0.30 (95% CI 0.28–0.81)
Tertiary/ university degree	33	110	P = 0.000 OR 0.44 (95% CI 0.28–0.70)
Living alone	61	39	P = 0.000 OR 3.79 (95% CI 0.64–1.37)
Employed	83	156	P = 0.72 OR 0.94 (95% CI 0.64–1.37)

Conclusions: We must continue reinforcing need for consistent clinical care in the newly diagnosed HIV patients, especially those who are younger, foreigners and socially excluded.

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P23

Efficacy assessment of the implemented strategies to improve loss to follow-up in recently diagnosed HIV patients

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Purpose of the study: The aim of the present study is to evaluate the strategies performed to decrease the loss to follow up in recently diagnosed HIV patients.
Method: We reviewed the clinical charts of the recently diagnosed adult (>18 y/o) HIV patients who presented for the first time in our HIV clinic between 1/Jan/2009 and 30/Nov/2010. Among the patients who were newly diagnosed with HIV infection, we identified those who attended our clinic only once. Since January 2009, we implemented new strategies: those patients who were diagnosed with HIV infection were assigned an early appointment with an attending; those patients who did not attend the appointment were called to reassign another appointment; clinic hours were increased, another attending joined the team and the matters the patients had to deal with were reduced. The results obtained with regard to loss to follow up in these patients were compared with previous results, before January 2009, to assess the effectiveness of these measures.
Summary of the results: 247 patients attended the clinic for the first time, 43 (17.4%) of them attended the clinic only once. Comparing

with the 45-month period before the implementation of these strategies in which 256 patients attend the clinic and 135 (52.7%) attended the clinic only once, loss to follow up was improved (P = 0.0000 [OR 0.19, 95% CI 0.12–0.29]). No statistically significant differences were found between both groups regarding age, gender, nationality, employment status, presence of family/partner at home or access to health insurance.

	Patients who attended the clinic for the first time between Jan 2005–Sept 2008, n = 256	**Patients who attended the clinic for the first time between Jan 2009–Nov 2010, n = 247**	
Male/ female	186/70	182/65	P = 0.79, OR 1.05 (95% CI 0.70–1.59)
Argentinian	218	199	P = 0.17, OR 0.13 (95% CI 0.84–2.26)
Health insurance	107	94	P = 0.39, OR 0.86 (95% CI 0.59–1.24)
Tertiary/ university degree	74	71	P = 0.96, OR 1.01 (95% CI 0.67–1.15)
Employed	182	192	P = 0.08, OR 1.42 (95% CI 0.93–2.17)
Living alone	52	63	P = 0.16, OR 1.34 (95% CI 0.87–2.08)
Loss to follow up	135/(52.7%)	43/(17.4%)	P = 0.0000, OR 0.19 (95% CI 0.12–0.29)

Conclusions: Although the small sample size, the implemented measures decreased the lost to follow up in our clinic. This study emphasises the need to continue reinforcing engagement with clinical care in the newly diagnosed HIV patients.

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P24

A dynamic assessment of medication-taking behavior during pregnancy and postpartum: should cART adherence be reinforced during postpartum?

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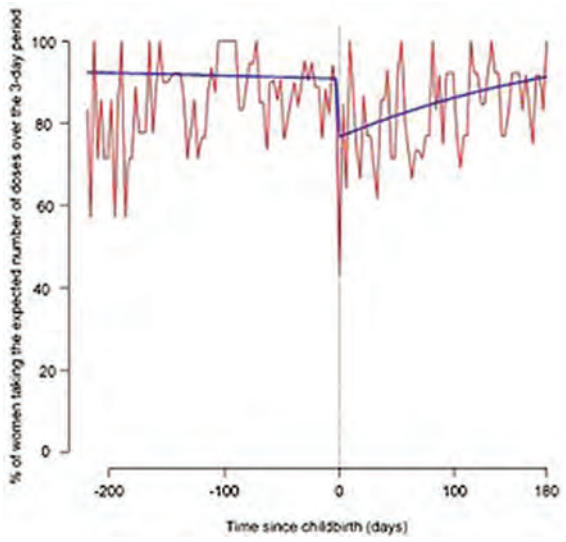
This study compared adherence (persistence and execution) during pregnancy and postpartum in HIV-positive women having taken part in the adherence-enhancing program of the Community Pharmacy of the Department of Ambulatory Care and Community Medicine in Lausanne between 2004 and 2012. This interdisciplinary program combined electronic drug monitoring and semi-structured, repeated motivational interviews. This was a retrospective, observational study. Observation period spread over from first adherence visit after last menstruation until 6 months after childbirth. Medication-taking was recorded by electronic drug monitoring. Socio-demographic and delivery data were collected from Swiss HIV Cohort database. Adherence data, barriers and facilitators were collected from pharmacy database. Electronic data were reconciled with pill-count and interview notes in order to include reported pocket-doses. Execution was analyzed over 3-day periods by a mixed effect logistic model, separating time before and after childbirth. This model allowed us to estimate different time slopes for both periods and to show a sudden fall associated with childbirth. Twenty-five pregnant women were included. Median age was 29 (IQR: 26.5, 32.0), women were in majority black (n = 17,68%) and took a cART combining protease and nucleoside reverse transcriptase inhibitors (n = 24,96%). Eleven women (44%) were ART-naïve at the beginning of pregnancy. Twenty women (80%) were included in the program because of pregnancy. Women were included at all stages of pregnancy. Six women (24%) stopped the program during pregnancy, 3 (12%) at delivery, 4 (16%) during postpartum and 12 (48%) stayed in program at the end of observation time. Median number of visits was 4 (3.0, 6.3) during pregnancy and 3 (0.8, 6.0) during postpartum. Execution was continuously high during pregnancy, low at beginning of postpartum and increased gradually during the 6 months of postpartum.



Major barriers to adherence were medication adverse events and difficulties in daily routine. Facilitators were motivation for promoting child-health and social support. The dramatic drop and very slow increase in cART adherence during postpartum might result in viral rebound and drug resistance. Although much attention is devoted to pregnant women, interdisciplinary care should also be provided to women in the community during first trimester of postpartum to support them in sustaining cART adherence.

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ADVERSE EVENTS

Cardiovascular

P25

Late gadolinium enhancement and subclinical cardiac dysfunction on cardiac MRI in asymptomatic HIV-positive men

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Background: HIV is associated with an increased risk of cardiovascular disease (CVD) and related clinical events. While traditional risk factors play an important role in the pathology of cardiovascular disease, HIV infection and its sequelae of immune activation and inflammation may have significant effects on the myocardium before becoming clinically evident. Cardiac MRI (CMR) can be used to detect the pattern of these subclinical changes. This will lead to a better understanding of risk factors contributing to cardiovascular disease prior to it becoming clinically significant in HIV-positive patients.
Methods: Prospective cohort study of 127 asymptomatic HIV-positive men on ART compared to 35 matched controls. Baseline demographics, HIV parameters, 12-lead ECG, routine biochemistry, and traditional cardiovascular risk factors were recorded. Images were acquired on a 3T Achieva Philips MRI scanner with 5 channel phase array cardiac coil and weight-based IV gadolinium was given at 0.15 mmol/kg dose with post-contrast inversion recovery imaging after 10 minutes.
Results: 6/127 (4.7%) of asymptomatic HIV-positive men had late gadolinium enhancement (LGE) on MRI verses 1/35 (2.9%) in the control group. In 3/6 (50%) of cases this was in a classical infarction pattern with subendocardial involvement. 3/6 (50%) were consistent with prior myocarditis. There was no significant difference in mean LVEF (66.93% vs 65.18%), LVMI (60.05g/m^2 vs 55.94g/m^2) or posterolateral wall thickness (8.28 mm and 8.16 mm) between cases and controls respectively. There was significantly more diastolic dysfunction, E:A ratio <1, found in the HIV-positive group, 18% vs 7% of controls ($p=0.037$). Framingham risk did not predict either of these outcomes.
Conclusions: There is an increased incidence of LGE detected on CMR in this asymptomatic HIV-positive cohort. Two distinct pathological processes were identifed as causing these changes, myocardial infarction and myocarditis. These findings were independent of traditional cardiac risk factors, duration of HIV infection and ART therapy. Sub clinical cardiac dysfunction may be underreported in other cardiac evaluation studies. The true impact of other potential risk factors may also be underestimated, highlighting the need for the development of more complex prediction models.

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P26

Nevirapine vs efavirenz in virologically supressed patients: differences in lipoprotein subclasses and inflammatory biomarkers

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Background: The interaction between lipid disturbances and inflammatory markers is not well known in patients on antiretroviral therapy (ART). As nevirapine (NVP) is associated with a better lipid profile than efavirenz (EFV), we investigated the relationships between lipid profiles, lipoprotein subclasses and inflammatory biomarkers in patients with prolonged viral suppression with either NVP or EFV and no obvious clinical inflammation.
Methods: 122 clinically stable HIV-infected patients with HIV-1 RNA <20 copies longer than 6 months on NNRTI therapy were studied. 72 (59%) were on EFV and 50 (41%) on NVP. Any potentially inflammatory co-morbid diseases (concurrent viral hepatitis, diabetes, hypertension, chronic liver or renal diseases), or statin treatment, were exclusion criteria. Inflammatory biomarkers included hsCRP, LpPLA2, sCD40L, IL-6, IL-8, t-PA, MCP-1, p-selectin and VCAM-1. Lipoprotein subclass measures (VLDL, LDL, IDL and HDL particle number and size) were obtained by the use of proton nuclear magnetic resonance spectroscopy.
Results: 82% were male; median age 45 years. Median CD4 count 550/μL (IQR 324). Median time since HIV diagnosis 96 months (IQR 102) and accumulated time on ART 50 months (IQR 101). Patients on NVP had higher time since HIV diagnosis (126.9 [66.7] vs. 91.3 [6.6] months, $p=0.008$) a prolonged time on ART (89.6 [54.6] vs. 62.3 [52.2] months, $p=0.01$) and were older (47.7 vs. 40.7 years, $p=0.001$) than those on EFV. NVP-treated patients presented increased HDL-c (55.8 [16] vs. 48.8 [10.7] mg/dL, $p=0.007$) and apoA1 levels (153.4 [31.9] vs. 141.5 [20.5] mg/dL, $p=0.02$), and reduced apoB/apoA1 ratio (0.68 [0.1] vs 0.61 [0.1], $p=0.003$) than EFV-treated patients. No differences in inflammatory markers or lipoprotein subclasses were found between NVP and EFV. In patients with extreme lipid values (less favorable: 75th percentiles of LDL, small/dense LDLp and small HDLp, or more favorable: HDL p75 and apoB/apoA1 ratio p25), no consistent differences in inflammatory biomarkers were found.
Conclusions: Patients with prolonged viral suppression on NVP present significantly higher HDL and apoA1 levels and reduced apoB/apoA1 ratios than those on EFV, but no differences were found in lipoprotein particles nor inflammatory biomarkers. Relationships between lipid parameters and inflammatory biomarkers in NNRTI-treated patients are complex and do not show a linear relationship in this study.

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P27

Too old too soon? Heart age compared with actual age in HIV-positive individuals

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Absolute risk of cardiovascular disease (CVD) may be calculated using the Framingham equation. Since risk increases with age, a useful measure of excess risk adjusted for age is 'heart age', the age of a reference person with the same estimated risk, but based on ideal values of risk factors defined as non-smoker, non-diabetic, untreated SBP of 125 mmHg, total cholesterol of 180 mg/dL and HDL cholesterol of 45 mg/dL [1]. Patients attended the Bristol HIV Cohort between 2008–11. HDL and total cholesterol, SBP, CD4 count and viral load measured within a period of 6 months were available for 749/1013 (74%) patients. The median age was 42 years, 33% were female and 82% were on ART. We calculated heart-age deviation (heart age-actual age) by sex and age group. Smoking status was not available and therefore we did all calculations twice assuming all a) non-smokers b) smokers. We used fractional polynomials to model change in heart-age deviation with actual age. We used mutually adjusted multivariable linear regression to determine whether sex, age, CD4, viral load, treatment status and year of starting ART were associated with heart-age deviation. The mean heart-age deviation in males was 3.4 years (females 1.7) for non-smokers, and 14.8 years (females 12.5) for smokers. The figure shows that deviation increased with age; eg for male smokers it was 9.7, 15.0, 20.4 and 23.3 years at ages 16–39, 40–49, 50–59 and ≥ 60 years respectively. On average a 45-year-old male smoker had a heart age of 60 years. Compared with males, deviation was lower in younger females, but became higher after age 48 years. Compared with treated patients (assuming

non-smoker) with viral suppression, untreated patients had similar heart age (0.33 [95% CI 1.67, 2.33]) and treated patients with unsuppressed viral replication had higher heart age (3.01 [0.61, 5.42]). Higher CD4 count was associated with higher heart age: those with CD4 between 500−750 and >750 (v. <500) had an increase of 2.25 (0.61, 3.89) and 4.39 (2.41, 6.36) years respectively.

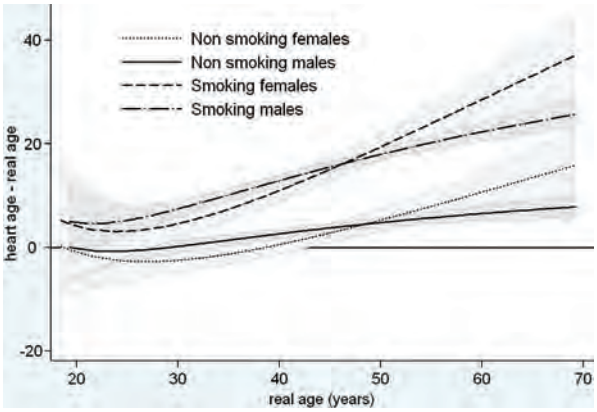

Figure 1. Heart age deviation by actual age by sex and smoking status (95% CI shown shaded).

HIV+ve individuals have a considerably increased risk of CVD compared with the ideal reference values, although we do not know if estimated risk translates to CVD events. Heart-age deviation increases with age and is greater for smokers. Deviation increases more sharply in women, possibly due to lower CVD risk at younger ages or to increased risk postmenopause. Heart age could be a useful communication tool in attempts to reduce CVD risk in HIV+ve individuals.

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P28

Carotid intima media thickness changes, endothelial activation and inflammatory markers in advanced na ve HIV patients starting antiretroviral therapy

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PREVALEAT II (PREmature VAscular LEsions and Antiretroviral Therapy II) is an ongoing multicenter, longitudinal cohort study aimed to the evaluation of cardiovascular risk in advanced naïve HIV-infected patients starting their first HAART. It includes all consecutive naïve pts with <200 CD4 cells/ml who start any PI/r-based or NNRTI-based+2 NRTIs regimen. Pts are subjected to epi-aortic vessels ultrasonography, brachial artery flow mediated dilation (FMD), endothelial cytokine inflammatory markers value at time 0 and after 3, 6 and 12 months. Data about independent risk factors for CV disease are taken at time 0. Viral load, CD4+ counts, serum lipid values, glucose, body mass index (BMI) are recorded at every control. We enrolled 47 pts: 76,6% males, 87,2% caucasians, 40,4% cigarette smokers, 10,6% HCV co-infected, 6,4% had lipodystrophy. 29,8% homosexuals, 12,8% drug addicts, 51,1% heterosexuals. At baseline, 23,4% of pts had pathologic BMI, 31,91% had a epi-aortic vessels lesion (IMT and/or plaque), 27,65% had pathologic FMD; ICAM1 was pathologic in 46,80%, VCAM1 in 53,19%, IL-6 in 51,06%, D-dimers in 29,79%, hsCRP in 23,40%. 27 pts completed stage T1 of the study (after 3 months); percentages and significance level of variations are the following: 44,44% had a lesion of the epi-aortic vessels ($p = 0,28$), 48,14% had a pathologic FMD ($p = 0,08$), ICAM1 was pathologic in 59,26% ($p = 0,30$), VCAM1 in 70,37% ($p = 0,15$), IL-6 in 74,07% ($p = 0,05$), D-dimers in 14,81% ($p = 0,12$), hsCRP in 25,92% ($p = 0,80$). 27 pts completed stage T2 of the study (6 months). Percentages and significance level of variations in regard of baseline are the following: 51,85% had a epi-aortic vessels lesion ($p = 0,462$); 25,92% had pathologic FMD ($p = 0,37$). 10 pts completed stage T3 of the study (12 months): 60% had a epi-aortic vessels lesion ($p = 0,07$); 40% had pathologic FMD ($p = 0,49$). No significant change has been showed in the trend of variation of inflammatory cytokines at T2 and T3. Our data, at baseline, evidence that advanced naïve pts show a relevant deterioration of CV conditions in terms of US data, FMD and cytokine markers. At T1, US and FMD seem to further worsen; cytokines, except D-dimers, show a worsening trend, too. At T1 and T2, prevalence of vessel lesion and pathologic FMD is yet higher, with a p value closer to significance level. Further data deriving from the follow-up of missing pts are warranted to better understand the evolution of the CV risk profile in this setting of pts.

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P29

Role of maraviroc in a dyslipidemic murine model of atherosclerosis RTV-induced

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Purpose: Chemokines and their receptors play a crucial role in the development of atherosclerosis. CCR5 is considered to be crucial to monocyte recruitment during development of atherosclerosis. CCR5, known as a co-receptor of HIV-1, is the target of the approved CCR5 antagonist maraviroc (MVC). Therefore we investigated whether MVC reduces inflammation and atherosclerosis in a rodent model of dyslipidemia (ApoE-/-mice) treated or not with Ritonavir (RTV).
Methods: Two-month-old mice (8 per group): wild type, ApoE-/- plus vehicle; ApoE-/- plus RTV; ApoE-/- plus RTV in combination with MVC. Nine-month-old mice (13 per group): wild type; Apo E-/-+vehicle; and Apo E-/-+MVC. Animals were sacrificed after 3 months treatments and plasma, aortas and epididymal fat were collected. Areas of aortas plaque were measured. Immunohistochemistry was performed to evaluate macrophages infiltration, and protein levels of cytokines/chemokines (i.e. ICAM, PAI, VCAM, IL-10, IL-17, MCP1, Rantes, TNFα, INFγ) were evaluated in aorta lysates.
Summary of results: RTV enhances the plaque areas percentage in two month old ApoE-/- mice and is significantly reduced by MVC.

The ritonavir-enhanced Mac3 expression on plaques is also reduced by MVC. Treatment with MVC lowers aortic concentration of cytokines/chemokines and plasmatic level of CRP that are increased by RTV. Ritonavir, enhancing mRNA expression of IL-6, Rantes and Mip1α, induces lipoatrophy in epididymal fat; MVC revertes this lipoatrophy and reduces mRNA levels of these cytokines-chemokines. Moreover, in ApoE-/- mice 9 months old, MVC significantly reduces the percentage of plaque areas (from 16.6 ± 3.35% to 7.13 ± 1.44%) (en-face coloration), lowers aortic MAC3 staining and reduces the aortic concentration of cytokines/chemokines.
Conclusions: In a dyslipidemic rodent model the CCR5 inhibitor Maraviroc significantly reduces the percentage of aortic plaque areas, aortic inflammation and lipoatrophy of the epididymal fat. Therefore, the current use of CCR5 antagonists to treat HIV infection, a condition associated with an increased occurrence of cardiovascular disease, should also be exploited to determine any beneficial cardiovascular effects [1,2].

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P30

HIV-infected patients show functionally defective high-density lipoprotein (HDL) paralleled with changes in HDL-associated proteins

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Purpose of the study: Epidemiological studies have consistently demonstrated an inverse association between plasma HDL concentrations and cardiovascular risk. Although this cardioprotective role has been mainly attributed to its role in promoting cellular cholesterol efflux, there is an emerging interest in the anti-inflammatory and antioxidant properties of HDL. The aim of the study is to investigate the anti-inflammatory properties of HDL isolated from HIV-infected patients.
Methods: Cross-sectional study of 113 HIV-infected patients and 70 non-infected control subjects without evident CVD. From each subject, HDL was isolated by ultracentrifugation and its anti-inflammatory status was tested as its ability to inhibit MCP-1-induced migration of the monocytic cell line THP-1 using transwell cell culture chamber inserts with micropore filters of 5 microns pore size. HDL-associated proteins were measured by commercial ELISAs.
Results: Twenty-three HIV-infected patients were ART-naïve (32 ± 15 years, 66.7% male) and ninety were currently on ART (46 ± 11 years, 78.9 % male). Most patients on ART (91.1%) had undetectable viral load (< 50 copies/mL). When compared to healthy subjects, both naïve and treated HIV-infected patients had lower plasma HDL-cholesterol levels (naïve: 45 ± 12, ART: 50 ± 10, controls: 55 ± 10 mg/dL, $p < 0.05$). HDL isolated from HIV naïve patients showed a significantly reduced anti-inflammatory activity (THP-1 monocyte migration capacity was 203% times higher in HIV patients than in control subjects). The anti-inflammatory activity of HDL from ART-treated HIV-infected patients was significantly improved when compared to naïve patients, although it remained significantly lower than controls (130% THP-1 monocyte migration vs controls). HDL from HIV-infected patients had a decreased concentration of the anti-inflammatory proteins Apo A1 (controls: 2.1 ± 0.3, naïve: 1.4 ± 0.2, ART: 1.6 ± 0.1 mg/ml) and LCAT (controls: 0.53 ± 0.09, naïve: 0.34 ± 0.06, ART: 0.48 ± 0.05 μg/ml), and increased of the pro-inflammatory protein serum amiloid (controls: 1.42 ± 0.53, naïve: 3.23 ± 1.29, ART: 2.72 ± 0.70 μg/ml) than healthy controls.
Conclusions: Our data demonstrate HIV-infected patients, even with effective therapy, showed a marked reduction of HDL anti-inflammatory properties. This dysfunctional HDL seems to be associated with changes HDL composition and may contribute to the increased CVD risk observed in HIV infection.

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P31

Incidence and risk factors of major cardiovascular events in a multicentre HIV cohort

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Cardiovascular (CV) [1] and cerebrovascular [2] events threaten HIV+ subjects, affecting them earlier as compared to the general population and the current algorithms seem inadequate to estimate the CV risk, in particular concerning the weight of drugs, immunity and virus-related inflammation as risk factors. We analysed three Italian HIV cohorts from January 2005 to August 2011, extracting cases of acute myocardial infarction (AMI) or stroke. We analysed at the time of the event the subjects' age, the risk factors, the Framingham score, the antiviral regimen and the time spent on each drug, the CDC stage, the nadir CD4+ T cells and the outcome. Out of 4893 patients 92 experienced major CV events (76 AMI and 19 stroke, 2 subjects having both) and 10 died, at a median age of 50 years (range 33–77). Classical risk factors were widely represented, mainly smoke (72.8%) and dyslipidemia (53.3%). Three young subjects had no risk factors and dramatic coronary patterns, leading in one case to transplantation. No one ever had pathological bone fractures, and only 4/81 had GFR < 60 mL/min (range 33.6–57.4). The median 10 years' Framingham score was 10.5 (range 1–31). Abacavir had been taken by 19 subjects, equal to tenofovir and less than zidovudine (n = 55), and lopinavir/ritonavir by 20, and no single drug emerged as risk. The median time spent on abacavir and/or on lopinavir/ritonavir was 48 weeks (range 1–552) and 106 weeks (range 8–256), respectively. One patient was antiretroviral–naïve. The CD4 nadir was 183/mm^3 and 41.3% were CDC stage C. Although infrequent (1.8%), major CV events affect HIV people at younger age. Classical risk factors are common, while no drug effect emerged clearly. HIV infection was managed late in most of the patients. Early initiation of HAART [3] and reduction of risk factors seem the key points for preventing the occurrence of CV disease.

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P32

SCORE underestimates cardiovascular risk (CVR) of HIV+ patients

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The new European Guidelines of Dislipidemia Management of the European Societies of Cardiology and Arteriosclerosis consider HIV+ as patients at high risk of developing cardiovascular events and deaths. The objective of the study was to evaluate cardiovascular events and deaths in a series of HIV+ patients. Observational, cross-sectional study, including a cohort of HIV+ and HIV − patients from 2008. CVR was calculated using the SCORE-CVR chart. Variation on lipid profile and incidence of cardiovascular events, cardiovascular death or death related to any cause were recorded. Data was analyzed using SPSS version 20.0 for MAC. 154 HIV+ and 155 HIV − patients were included. Mean age: 44.8 ± 9.5 vs 55.2 ± 14.3 y and 69.5% vs 49% males respectively ($p < 0.01$). Mean time since HIV+ diagnosis was 11 ± 6.2 y. Mean BMI and systolic blood pressure were lower in HIV+ (25.1 ± 6.7 kg/m^2 vs 28.7 ± 5.1 kg/m^2, ($p < 0.01$) and 119.6 ± 19.4 vs 124.7 ± 14.7 mmHg, ($p = 0.044$; respectively)). A lower proportion of hypertense, diabetic and obese patients was observed in HIV+ (25.5% vs 6.5%; 20.6% vs 3.9% and 36.8% vs 12.3%) but a larger proportion of smokers (68.8% vs 29.7%) was observed ($p < 0.01$ in all cases). Mean cholesterol and LDLc were lower in HIV+ (191.2 ± 41.4 vs 218.5 ± 44.6 mg/dl and 109.5 ± 33.9 vs 134.6 ± 37.7 mg/dl; $p < 0.01$; respectively) but with a lower mean HDLc and higher TG (50.3 ± 19 mg/dl vs 55.2 ± 14.9 mg/dl; $p = 0.013$ and 156.7 ± 85.7 vs 135.8 ± 66.2 mg/dl; $p = 0.017$; respectively). There was no significant difference in mean CVR-SCORE (3.5 ± 3.6% vs 4.4 ± 3.8%; $p = 0.091$). With this SCORE, 5.2 ± 5.3 and 6.7 ± 5.8 cardiovascular events or deaths should be expected in HIV+ and HIV − respectively at 10 y. Four years later cholesterol, LDLc, HDLc, TG in HIV+ and HIV − patients did not vary compared with those obtained 4 y before. 5 events and 1 death were seen at 4 y follow-up in HIV+, and in HIV − patients. The incidence of events in HIV+ patients is similar to the expected according to their SCORE at 10 y. We could suppose that once the 10 y follow-up is reached, this incidence would be higher. On the other side, in HIV − at 4 y just 3 events ocurred, far from the 6.7 events expected. There were no significant differences between lipid profiles in any of the cohorts. Lipid profile with low HDLc and high TG is persistent in HIV+ patients at 4 y follow-up. Understimation of CVR in HIV+ patients by SCORE charts could be present as soon as 4 y after the first assesment. This supports the stratification of HIV+ patients as high-risk patients in new guidelines.

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P33

Effectiveness of antihypertensive therapy in HIV-positive patients: evaluation to 144 weeks

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Hypertension is more prevalent among HIV-infected subjects than in the general population, contributing to increased cardiovascular risk in HIV+ patients. The angiotensin II receptor blocker telmisartan is also a partial peroxisome proliferator activated receptor (PPAR)-γ agonist, with documented effects on improving hypertension, lipid metabolism and renal function. Therefore telmisartan was found to be the first choice for treatment of HIV+ hypertensive patients. Aim of this study was to evaluate the durability on 144 weeks of treatment with telmisartan in HIV+ patients. 13 HIV+ Caucasian male patients treated with combined antiretroviral therapy (cART) and discovered to be naïve hypertensive, were given 80 mg telmisartan daily. Systolic (SBP) and diastolic (DBP) blood pressure, viro-immunological, lipid and metabolic parameters, including triglycerides, cholesterol, insulin resistance (HOMA-IR), inflammatory markers, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), indexes of renal function and cardiovascular risk, microalbuminuria, cystatin C, were measured at baseline (T0), and after 24 (T24), 48 (T48), 72 (T72), 96 (T96), 120 (T120) and 144 (T144) weeks. Treatment with telmisartan decreased SBP and DBP levels during the 144 weeks of observation. We also observed improved HDL-cholesterol, HOMA-IR, microalbuminuria and cystatin C at the end of study. Triglycerides and total cholesterol significantly decreased and HDL-cholesterol significantly increased. Total cholesterol/HDL cholesterol ratio improved significantly. Throughout in the course of the trial our patients showed a significant improvement of the percentage of CD4+ and CD8+. Eventually in all 144 weeks of therapy with telmisartan 80 mg/day have not observed adverse events or dropouts. Telmisartan was effective in improving hypertension, lipid metabolism and renal function in 144 weeks of evaluation. It determines the improvement of cystatin C and microalbuminuria, markers of renal function and cardiovascular risk. Telmisartan doesn't interfere with cART, not interfering with the recovery of immunological HIV patients. Telmisartan has confirmed durability and effectiveness, excellent tolerability and an high persistance with a good blood pressure control. Therefore telmisartan reveals the first choice in the treatment of hypertension in HIV+ because of significant morbidity in this group of patients.

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Metabolic

P34

Impact of antiretroviral therapy (ART), immunosuppression and viraemia on lipid levels: the D:A:D study

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Purpose of the study: To investigate the impact of ART, HIV viremia and immunosuppression on triglyceride (TG), total cholesterol (TC) and high density lipoprotein cholesterol (HDL-C) levels.

Abstract P34–Table 1. Impact of ART, immunosuppression and viraemia, on TG, TC and HDL-C (mmol/l)

	Average impact on log_{10}TG*†		Average inpact on TC*		Average impact on HDL-C*	
ART and VL						
Off ART & VL ≥100000	−0.09 (−0.10, −0.08)	<0.001	−0.55 (−0.60, −0.51)	<0.001	−0.14 (−0.16, −0.13)	<0.001
Off ART & VL <100000	−0.04 (−0.06, −0.03)	<0.001	−0.85 (−0.91, −0.78)	<0.001	−0.31 (−0.33, −0.29)	<0.001
On ART & VL <500	Ref		Ref		Ref	
On ART & VL ≥500	0.00 (−0.01, 0.00)	0.38	−0.40 (−0.44, −0.36)	<0.001	−0.16 (−0.17, −0.15)	<0.001
CD4 count						
<200	−0.03 (−0.04, −0.02)	<0.001	−0.33 (−0.39, −0.28)	<0.001	−0.04 (−0.06, −0.02)	<0.001
200–349	−0.02 (−0.03, −0.01)	<0.001	−0.11 (−0.15, −0.06)	<0.001	0.00 (−0.01, 0.02)	0.72
350–499	Ref		Ref		Ref	
500+	0.04 (0.03, 0.04)	<0.001	0.12 (0.08, 0.16)	<0.001	−0.02 (−0.03, −0.00)	0.02
Nadir CD4 Count						
<200	0.07 (0.06, 0.08)	<0.001	0.19 (0.14, 0.24)	<0.001	−0.05 (−0.06, −0.03)	<0.001
200–349	0.02 (0.01, 0.03)	<0.001	0.01 (−0.03, 0.06)	0.57	−0.03 (−0.05, −0.02)	<0.001
350–499	Ref		Ref		Ref	
500 +	0.00 (−0.02, 0.01)	0.33	0.03 (−0.02, 0.09)	0.23	0.04 (0.02, 0.06)	<0.001
Prior AIDS	0.05 (0.05, 0.06)	<0.001	0.11 (0.08, 0.15)	<0.001	−0.03 (−0.04, −0.01)	<0.001

*estimates included are mutually adjusted for each other and for the following demographic variables: age; gender; mode of infection; ethnicity; body mass index; smoking; family history of CVD; diabetes; use of lipid lowering drugs; co-infection with hepatitis C; participating cohort; and year of entry into study.
†TG is log_{10} transformed. Thus, the results presented for TG reflect relative rather than absolute effects. For example, lipid levels for those off ART & VL ≥100000 are 9% lower than those on ART & VL < 500.

Methods: We considered the cross-sectional associations between TG, TC and HDL-C (mmol/l; first available measurement on/after enrolment in the D:A:D study) and use of ART, HIV viral load (VL; copies/ml), and CD4 count (cells/mm^3) measured at the same time. TG was log_{10} transformed to ensure normality. Analyses were performed using linear regression and adjusted for other factors known to impact lipid levels (table footnote). ART and VL status were combined (off ART&VL >100,000, off ART&VL <100,000, on ART&VL <500, on ART&VL >500), current and nadir CD4 count were categorised as <200, 200–349, 350–499 and >500.
Summary of results: 44,322/49,734 participants in the D:A:D Study (89.1%) contributed a TG measurement (median; IQR 1.52; 1.00–2.45), 45,169 (90.8%) a TC measurement (4.80; 4.00–5.70) and 38,604 (77.6%) a HDL-C measurement (1.12; 0.90–1.40). Most participants were male (74%), of white ethnicity (51%), without AIDS (78%), were not receiving lipid-lowering drugs (4%) and were ART experienced (61%) with 47% previously exposed to PIs, 61% previously exposed to NRTIs and 29% previously exposed to NNRTIs. The median (IQR) age, current CD4 count and CD4 nadir were 38 (36–45) years, 400 (242–590) cells/μl and 240 (100–410) cells/μl respectively. Compared to those on ART with a suppressed VL, all lipids were lower for those off ART (Table); non-suppressive ART was also associated with lower TC and HDL-C levels (no impact on TG). A low current CD4 count was associated with lower lipid levels, whereas a low nadir CD4 count was associated with higher TC and TG levels. Prior AIDS diagnosis was associated with higher TG and TC, but lower HDL-C levels.
Conclusion: Although specific drug classes were not considered, lipid levels are considerably higher in those on a suppressive ART regimen. The higher TC/TG and lower HDL-C levels seen among those with low nadir CD4 count and with a prior AIDS diagnosis suggests severe immunosuppression may be associated with dyslipidaemia over the long-term.

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P35

Longitudinal comparison of inflammatory, coagulation and metabolic biomarkers in patients who start ART versus patients who remain ART-na ve

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There are very limited data on the impact of ART initiation on inflammatory and coagulation biomarkers compared to patients who remain ART naïve [1]. We designed a prospective comparative study to evaluate these changes. Prospective observational cohort study of HIV-infected patients who start ART and a group of age-matched controls who remain ART-naïve. Blood levels of insulin, fibrinogen, D-dimer, high-sensitivity PCR, inflammatory (IL-1β, IL-6, MCP-1 and sCD40) and anti-inflammatory cytokines (IL-4), were compared at baseline, 24 weeks and 48 weeks. Summary of results: 94 patients included (57 treated, 37 controls). Baseline characteristics were balanced except for (treated/controls): median [IQR], HIV duration (0.9 [0.4–2.4] / 2.7 [0.6–5.5]) years, CD4 nadir (262 [198–317] / 452 [367–553]) cells/μl, viral load (4.4 [4–5.1] / 3.8 [3.1–4.4]) log cop/ml, current CD4 count (283 [213–323] / 525 [449–669]) cells/μl, HDL cholesterol (38 [29–45] / 41 [36–50]) mg/dl and female gender (8.8%/35%). There were no differences between groups in baseline biomarkers levels except that those starting ART had lower median [IQR] IL-1β (4.1 [3.5–4.7] vs. 4.6 [3.7–6.8] pg/ml; p = 0.019) and lower IL–6 levels (4 [3.4–4.6] vs. 5.2 [4.2–6.6] pg/ml; p < 0.001). No significant correlation was found between biomarkers and baseline viral load. 91% of treated patients achieved viral suppression (<50 c/ml). There were statistically significant differences between groups at week 48 with lower (mean [95% CI]) D-dimer (−138.2 [−268.0, −8.4] mg/L; p = 0.001), IL-1β (−0.6 [−0.9, −0.4] pg/ml; p < 0.001) and higher IL-4 (0.6 [0.2, 0.9] pg/ml; p = 0.004) in those starting ART. In the ART-naïve group there were significant increases

of IL-1β (1.3 [0.9, 1.6] pg/ml; p < 0.001), sCD40 (22.7 [0.8, 44.6] AU; p = 0.043), IL-6 (0.5 [0.0, 0.9] pg/ml; p = 0.049) and a significant decrease of IL-4 (−0.7 [−1.1, −0.3] pg/ml; p = 0.001) levels. After 48 weeks of ART there were statistically significant decreases in pro-inflammatory and coagulation markers (Figure 1) while levels of anti-inflammatory cytokines (e.g. IL-4) were significantly increased. Opposite trends were found in controls.

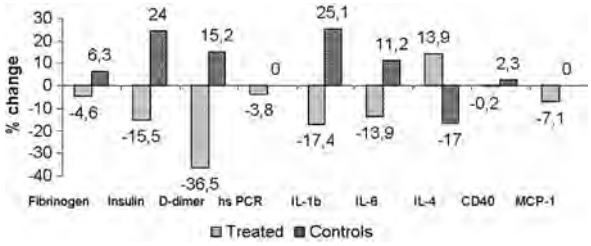

Figure 1. Median percentage changes in bio markers from baseline to week 48.

In conclusion, compared to untreated controls, 48 weeks of effective ART significantly reduces pro-inflammatory (IL-1β, IL-6), coagulation (fibrinogen, D-dimer), and metabolic (insulin) markers and increases levels of an anti-inflammatory cytokines like IL-4.

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P36

Differences in body circumferences, skin-fold thicknesses and lipid profiles among HIV-infected African children on and not on stavudine

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Purpose of the study: To compare body circumferences, skin-fold thickness (SFT) and lipid levels (LL), as measures of lipodystrophy, among antiretroviral therapy (ART)-naïve and experienced children at enrolment into the CHAPAS-3 trial.
Methods: HIV-infected children in Uganda and Zambia, either ART-naïve or on stavudine (d4T) for ≥2 years without clinical lipodystrophy, were randomised to receive d4T, abacavir (ABC) or zidovudine (ZDV) with lamivudine and efavirenz (EFV) or nevirapine. At enrolment, mid-upper arm (MUAC) and calf (CC) circumferences, SFT (biceps, triceps, sub-scapular, supra-iliac) and fasting lipids (total cholesterol (TC), low density lipo-protein (LDL), high density lipoprotein (HDL), triglycerides (TRIG)) were measured. Age/sex adjusted z-scores of MUAC, CC, SFT and the sum of SFT (SSF) used Dutch reference data. ART-naïve and ART-experienced children were compared with t-tests using Stata v11.0.
Summary of results: Among 444 children, 224 (51%) were male and 331 (74.5%) ART-naïve. Mean (sd) CD4% was 19.7% (10.2) versus (vs) 34.2% (7.7) in ART-naïve vs ART-experienced children. The ART-naïve were younger than the ART-experienced children (median [IQR] age 2.5 [1.5, 4.0] vs 6.0 [5.5, 7.0] years, p < 0.0001). Among the ART-experienced, 4/108 (3.7%) were on EFV and median (IQR) d4T use was 3.5 (2.7, 4.2) years. As expected, MUAC, CC, weight-for-age (WAZ) and height-for-age (HAZ) z-scores were lower in the ART-naïve; the ART-experienced had lower SFT z-scores and higher TC and HDL, but lower TRIG (Table 1).
Conclusions: Failure-to-thrive likely contributed to lower circumference values in ART-naïve children. Among the ART-experienced, thinner SFT and higher TC values could be ART (particularly d4T)-related. Normal values, currently unavailable for African children, are being collected. During trial follow-up, we will evaluate the effect of ABC, ZDV and d4T on development of lipodystrophy in naïve children and its reversibility in d4T-treated children randomised to switch to ZDV/ABC.

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	Mean (sd)		Difference	
Z-score/ LL	ART-na ve	ART-experienced	Mean (95% CI)	p-value
MUAC	−1.6 (1.3)	−1.2 (1.0)	0.3 (0.1, 0.6)	0.018
CC	−2.3 (1.5)	−1.8 (1.0)	0.5 (0.2, 0.8)	0.0006
Biceps SFT	−0.2 (0.9)	−0.4 (0.9)	−0.3 (−0.5, −0.1)	0.009
Triceps SFT	−0.4 (1.0)	−1.0 (0.8)	−0.6 (−0.8, −0.4)	<0.0001
Sub-scapular SFT	0.1 (1.2)	0.2 (1.2)	0.1 (0.2, 0.3)	0.751
Supra-iliac SFT	−0.3 (1.1)	−0.9 (0.9)	−0.7 (−0.9, −0.4)	<0.0001
SSF	−3.8 (0.4)	−3.9 (0.4)	−0.1 (−0.2, −0.1)	0.035
WAZ (WHO 2007 reference)	−1.5 (1.3)	−0.9 (0.9)	0.6 (0.3, 0.9)	<0.0001
HAZ (WHO 2007 reference)	−2.5 (1.6)	−1.5 (1.2)	1.0 (0.6, 1.3)	<0.0001
TC (mg/dl)	126.1 (33.8)	154.4 (27.6)	21.7 (12.5, 31.0) (age/sex adjusted)	<0.0001
LDL (mg/dl)	71.3 (29.4)	83.1 (21.2)	7.2 (−1.2, 15.5) (age/sex adjusted)	0.093
HDL (mg/dl)	26.9 (11.6)	54.1 (16.1)	23.2 (19.4, 27.1) (age/sex adjusted)	<0.0001
TRIG (mg/dl)	94.4 (70.3)	45.1 (38.6)	−30.8 (−49.6, −12.0) (age/sex adjusted)	0.001

P37

Combined use of waist and thigh circumference to identify high-risk, abdominally obese HIV+ patients

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Background: We examined whether the combination of waist (WC) and thigh (ThC) circumference improves the prediction of visceral adipose tissue (VAT) over WC and ThC independently in HIV-infected men and women after correction for age. We also examined the independent associations between VAT, and the combination of WC and ThC with metabolic risk factors, metabolic syndrome, type 2 diabetes mellitus (T2DM) and prior cardiovascular events in HIV-infected individuals.
Methods: Consecutive patients attending the metabolic clinic of the University of Modena in Italy between 2005 and 2009 were recruited in this cross-sectional study. Total and regional fat mass and lean mass were quantified using DEXA. A single CT image was taken for quantification of VAT and CAC. Prior cardiovascular events which occurred within a 5-year period of the clinical evaluation were analysed. A cross-fold test was used to explore different models in the ability to predict VAT in order to build an algorithm for VAT estimation (e-VAT). Regression analysis were performed to determine the univariate and multivariate relations between WC, ThC, and age with VAT. A comparison of beta coefficients for VAT and e-VAT to predict cardio-metabolic risk and events were performed using multivariable regression models after correction for BMI and age.
Results: 2322 HIV-infected patients were recruited: median duration of HIV infection was 182 months (IQR 126–236); median nadir and current CD4 were 172 (IQR 68–262) and 515.5 (IQR 369–700) and 75% of them had undetectable HIV1-VL. In this abstract only the results of men will be presented. Men (n = 1481) had a mean age of 45.9 ± 7.3 years, a BMI of 24.1 ± 3.8 kg/m^2, a WC of 88.0 ± 10.1 cm and a ThC of 47.8 ± 4.3 cm. e-VAT algorithm for men was: (5.44*WC) − (1.35*ThC) − (1.70*age) − 348.1 In men, at multivariable regression models after correction for BMI and age, e-VAT was concordant to VAT in predicting HOMA, MetS Risk, prior cardiovascular events (OR = 1.01), was better than VAT in predicting T2DM (OR = 1.00) and CAC > 10 (OR = 1.01) but was worse than VAT in predicting TC/HDL and TG.
Discussion: We confirm that ThC is inversely associated to VAT after correction for WC. e-VAT is a sensitive tool to predict VAT more accurately than WC and ThC independently. e-VAT proved to predict cardio-metabolic risks and events in men and women, qualifying this variable for a potential clinical use.

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P38

Effect of the treatment of hepatitis C with interferon (IFN) and ribavirin (RBV) in body composition measurement by DEXA in HIV-HCV infected patients

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Purpose of the study: HIV infection and antiretroviral therapy (ART) have been associated with lipodystrophy (LD), but we unknown the effect of IFN/RBV on the body composition, mainly body fat, in HIV patients, already with a degree of LD. Our objective: to assess the body composition in HIV-HCV patients that start treatment with IFN/RBV and the changes at its ending.
Material and Methods: Pilot and prospective study of HIV-HCV patients. We performed (baseline and at the end of treatment) clinical and laboratory parameters, HIV and HCV-related. Total and regional body fat contents were measured in the same periods with DEXA (dual-energy X-ray absorptiometry) scanners. For LD diagnostic we used the definition of fat/mass ratio (FMR): absence, < 1, obvious > 1.5, and between 1–1.5 it could have LD but is better to see the evolution. Data are expressed in median.
Results: We included 10 male patients; age 45 yo; time on ART 115 months. HIV VL < 20 in 9; CD4 count 577/mm^3. Genotype 1 in 8, and 3 in 2. Time on IFN/RBV: 10 months. At the end of the treatment we observed a decrease in the level of total, HDL and LDL-cholesterol (expressed in percentage: 4, 16 and 1.5 respectively) and a slightly increase in the level of TGR (9%). The total body mass decreased 7% (from 76.2 kg to 70.6), the total body fat decreased 18.4% (from 21.060 g to 17.172) and the total lean mass decreased only 3%. Results expressed in percentage and by regional parts, we observed also a decrease in all the parameters: 11% in total body fat (from 26.3 to 23.4), 6% in the fat in arms (21.9 to 20.5), 10% in total fat in legs (22.5 to 20.3) and 12.5% in total trunk fat (30.3 to 26.5). The FMR also decreased from 1.5 to 1.4.
Conclusions: Trend to LD at baseline, as the FMR was 1.5. After 10 months on treatment with IFN/RBV there was a decrease in the total body mass (7%), mainly due to the loss of total body fat and less in the lean mass. Regarding the percentage of fat loss, we observed the biggest decrease in the trunk fat and the lesser in the limb fat. So, the FMR also decreased. This effect does not get worse the baseline LD; on the contrary it improves it, although very slightly (decrease of 0.1 in FMR), and could serve to advise the patients and not to be afraid of a possible worsening of LD. The study is ongoing and the next objective will be to perform DXA one year after the end of treatment and to expand the cohort to study clinical or laboratory factors related with these results.

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P39

Iron overload, an immunosuppression marker in HIV-infected patients

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Purpose: Iron overload (IO) has been associated with increased cardiovascular risk (CVR) and metabolic syndrome (MS) in the general population; both elevated CVR and MS are frequent in HIV-patients. Our aim was to analyze the prevalence of IO in a cohort of asymptomatic patients with HIV infection, and related factors.
Methods: Cross-sectional study of a cohort of HIV outpatients in regular follow-up. Demographic, epidemiological, clinical, analytical and therapeutic data were collected. Patients completed a questionnaire about CVR factors and 10-year CV disease risk estimation (Framingham score), underwent a physical exam, and a fasting blood analysis. IO was defined as a plasma ferritin level higher than 200 μ/L in women and 300 μ/L in men.
Results: 571 patients (446 men, 125 women), with a mean age of 43.2 years, sexual transmission of HIV in 68.5%, median CD4 count 474 cell/μL (IQR: 308–666), and 36.3% Aids cases. 86.2% were on antiretroviral therapy (ART), and 74.8% of them had undetectable HIV viral load. 14.6% met MS criteria, and mean CVR at 10 years was 6.67%. IO was detected in 11% of cases. Patients with IO were more immunosuppressed (CD4 count 369 vs 483/μL, p < 0.0001), presented a higher prevalence of detectable HIV viral load (17.6% vs 8.9%; p < 0.005), and of Aids cases (14.9% vs 8.7%; p < 0.023), and lower plasma levels of cholesterol, HDLc and LDLc (154 vs 183, 34 vs

43, 93 *vs* 110 mg/dL, respectively; $p < 0.0001$. In the multivariate analysis, the only related factor was CD4 count < 350 cell/μL (OR 2.86, 95% CI 1.6–4.9; $p < 0.0001$). IO was not associated with CVR nor with MS.
Conclusions: IO is not uncommon in HIV patients, and it is only related with immunosuppression defined as CD4 count < 350 cell/μL, and in contrast to general population, it is not related with increased CVR nor with MS.

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P40

The effect of zinc sulphate supplementation on atazanavir/ritonavir-associated hyperbilirubinemia

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Background: Atazanavir (ATV) causes an exposure dependent elevation of unconjugated hyperbilirubinemia (HBR) as a result of UGT1A1 inhibition. Zinc sulphate reduces unconjugated hyperbilirubinemia in individuals with Gilbert's syndrome. We assessed the changes in total and conjugated bilirubin following single dose and 14 daily doses of zinc sulphate ($ZnSO_4$) and its impact on ATV pharmacokinetics (PK).
Methods: HIV-infected individuals stable on ATV/ritonavir (r) containing regimens with a total bilirubin level > 25 mmol/L were administered 125 mg once daily of as solvazinc effervescent tablets for 14 days. ATV and bilirubin concentrations were measured pre-ATV-dose, 2, 4, 6, 8 and 24 hours post-ATV-dose before $ZnSO_4$ intake initiation (phase 1), after a single dose of $ZnSO_4$ (phase 2), and following 14 days of $ZnSO_4$ intake (phase 3). Changes in bilirubin and ATV concentrations in the absence and presence of $ZnSO_4$ were evaluated by geometric mean ratios (GMR) and 90% confidence intervals (CI, phase 1 as reference).
Results: All 16 male patients completed the study maintaining virologic suppression throughout. $ZnSO_4$ was well tolerated. We observed statistically significant declines in total bilirubin C_{max} and AUC_{0-24} of -12 and -13% after single dose $ZnSO_4$ and -19 and -20% after steady state, compared to reference phase; GM C_{max} decreasing from 57 nmol/L before zinc intake to 50 and 46 nmol/L after $ZnSO_4$ single dose and steady state, respectively. No significant changes in conjugated bilirubin were observed, indicating that the changes were secondary to declines in the unconjugated fraction (data pending). ATV GMR (90% CI) for C_{trough}, C_{max} and AUC were -16% (-33 to $+6$), -8% (-20 to $+8$) and -12% (-23 to $+0.1$) after single dose $ZnSO_4$, but changed by -26% (-38 to -11) -18% (-30 to -3) and -22% (31 to -12) after multiple dose $ZnSO_4$ compared to reference. All individuals with the exception of one (whose levels were low throughout the study) maintained ATV concentration above the suggested MEC of 150 ng/mL.
Conclusions: The intake of $ZnSO_4$ led to a moderate decrease in total bilirubin maximum concentration and overall exposure. However, a decrease in ATV concentrations was also observed. $ZnSO_4$ supplementation may represent a useful tool in the management of ATV-related HBR.

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P41

Maraviroc shows differential effects on glucose uptake and lipolysis in human subcutaneous cultured adipocytes in comparison with omental adipocytes

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Maraviroc (MVC), the first approved CC-chemokine receptor 5 (CCR5) antagonist, is used for treating HIV-1-infected patients with CCR5 tropism. MVC has been proved safe in all respects and showed beneficial effects on lipid profile of HIV patients with dislipidemia. Adipocyte dysfunction seems to be responsible for many metabolic alterations such as insulin resistance and dislipidemia. Subcutaneous and visceral fat depots are not only physiologically but also metabolically different and metabolic disturbances are more closely associated with visceral than subcutaneous fat accumulation. It has been suggested that antiretrovirals affect both fat depots in a different extent. Thus, whether isolated human adipocytes display regio-specific sensitivity to the metabolic effects of MVC have been tested in this study. Human subcutaneous and omental preadipocytes were used as the source of human adipocytes. These cells were treated with therapeutic concentrations of MVC (0.5–25 μM) at day 14 post-differentiation (4 and 24 hours of treatment). Glucose utilization, lactate production and glycerol released into the media were measured using an autoanalyzer. Adiponectin secretion was determined by an ELISA array. A dose-dependent increase in glucose uptake was observed in subcutaneous adipocytes treated with MVC ($+72$% of stimulation for MVC 25 μM, $p < 0.01$). This stimulatory effect was tissue specific, as no effects were observed in omental adipocytes. MVC did not exert any significant effect on adiponectin secretion. No significant effects were observed on lactate production neither in subcutaneous nor omental adipocytes. Interestingly, 4 hours of treatment with MVC induced a significant increase in the amount of glycerol released into the media by subcutaneous adipocytes ($p < 0.001$), but this effect disappeared with longer exposure of adipocytes to MVC (24 h). No effects were observed on lipolysis in omental adipocytes although a slight tendency to decrease lipolysis was observed ($p = 0.08$). These data suggest that MVC exerts direct and differential effects on adipocytes depending on their origin. Thus, a stimulation of glucose uptake has been reported in subcutaneous but not in omental adipocytes and a slight decrease of lipolysis was observed in omental adipocytes whereas no effects were observed in subcutaneous adipocytes. These actions could underline the neutral and even beneficial effects demonstrated for MVC in lipid and glucose metabolism of HIV-infected patients.

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P42

Experience with polymethylmethacrylate 30% (PMMA) facial filling in patients with facial HIV lipoatrophy using of local anesthesia dentistry

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Background: HIV-associated lipoatrophy in a common and stigmatizing side effect of HIV infection, is aggravated by antiretroviral therapy; its presence causes distress and compromises adherence to therapy. PMMA filling is often associated with pain and discomfort.
Objective: To evaluate outpatient intervention using local dentistry anesthesia.
Methods: Patients complaining of facial lipoatrophy, from 10/2007 to 11/2011, were offered the filling with PMMA. Cases with bleeding potential, acute or decompensated chronic diseases or use of immunosuppressors or chemotherapy were excluded. Inclusion

criteria: perception of distressing malar lipoatrophy and both the assisting physician and the applicant agreeing with potential benefit. After informed consent, patients were infused with 30 mg prilocaine/0.03 IU felypressin in 1.8 ml, using a carpule type syringe aiming to block the posterior superior alveolar nerve. This was followed by PMMA infiltration in different points at the malar region. At first return a simple questionnaire evaluating pain, satisfaction, grading 0 to 10 and if would repeat the procedure.
Results: All 64 eligible patients were included. Mean age 46 (13 to 73) years, mostly white (71.87%), males (68.75%), 37.5% of them MSM. Arterial hypertension was the most prevalent comorbidity (17%), 78% with viral load <50 c/mL, with a median 585 CD4 cells/mL (95–2063). On a median of 8 years on treatment, 1/3 had been exposed to three classes (NRTI/ NNRTI/PI), one antiretroviral-naïve. Of the 12 patients who had detectable viral load in the first procedure, seven were suppressed to below 50 copies/mL during follow up. Two of the five patients remaining with detectable viremia died from other causes, 2 transferred and 1 remained naïve. 127 procedures were made in 64 patients, a median of 2 (1–6) per patient. After a mean follow-up of 33 weeks, no infection or late complications were observed. Mean dispensed volume was 9 mL (1.5 to 22). Pain grade was documented in 105 procedures; grade <4 reported by 46%, 4–6 by 34%; 7–8 by 16%, 9 by 2%. All reported that the pain would not hamper future procedures; 94% refer an overall satisfaction from 8 to 10.
Conclusion: The use of local anesthesia in dental facial filling with PMMA in patients with HIV lipoatrophy of the face is safe, decreases pain to tolerable levels and allows high levels of satisfaction with the procedure. The procedure may improve patient adherence to ARV.

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Renal

P43

Tenofovir-induced acute kidney injury in HIV-infected patients in western India: a resource limited setting perspective

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Background and objective: Tenofovir use in HIV positive patients is associated with 0.5–2.5% risk of acute kidney injury (AKI). Data on AKI due to tenofovir use in resource limited settings like India is sparse. Objective of this study is to determine incidence, risk factors and outcome of tenofovir-induced acute kidney injury (serum creatinine >2 mg/dl or creatinine clearance decrease by 50% compared to baseline) in HIV infected patients attending tertiary level HIV clinic in Western India.
Methods: All patients enrolled at the clinic from 2009 to 2012 who were initiated on tenofovir-based ART and had regular follow up creatinine clearance values available were included in this retrospective observational cohort analysis. Patients already on tenofovir-based ART during enrollment were also included.
Summary of results: 512 patients were enrolled in the study with 70% being males. Average age of the cohort was 41 years, average body weight 56 kilograms and median baseline CD4 count 164 cells/mm^3. Mean baseline creatinine clearance was 90 ml/min. Median duration of follow up was 26 months. Tenofovir-induced AKI developed in 25 patients (incidence 4.88 %). Median time to developing AKI was 6 months. On stopping tenofovir, 15 patients had complete recovery of renal function, 5 had partial recovery while 5 patients died. Hemodialysis as a treatment option was used in 3 patients. Age >50 yrs ($p=0.001$), baseline creatinine clearance <50 ml/min ($p=0.0001$), diabetes mellitus ($p=0.0001$), use of tenofovir with protease inhibitors ($p=0.001$), presence of renal calculus disease ($p=0.0001$) and use of concomitant nephrotoxic medications ($p=0.001$) were significantly associated with risk of tenofovir AKI on applying Pearson's Chi square test.
Conclusions: Incidence of tenofovir-induced AKI in our cohort is higher than previously reported and could be attributed to lower body weight, lower baseline creatinine clearance, higher incidence of advanced HIV disease and higher incidence of co-morbidities in our patients.

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P45

Incidence and risk factors of chronic renal disease in a cohort of Greek HIV-1-infected adults

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Background: Chronic kidney disease (CKD) in HIV-infected patients is associated with both HIV and non-HIV-related factors. Initial renal dysfunction is silent and detectable only by laboratory tests such as the glomerular filtration rate (GFR) estimated by the Cockcroft-Gault equation. Our objective was to assess possible risk factors for CKD in a cohort of Greek HIV-1-infected adults.
Methods: Patients in the AMACS (Athens Multicenter AIDS Cohort Study) cohort with at least two available creatinine values were enrolled in the study. Renal dysfunction was defined as eGFR below 90 mL/min/1.73 m^2. The Kaplan-Meier estimator and the Cox proportional hazards model were used to analyze the occurrence and predictors of renal dysfunction.
Results: A total of 1073 patients were enrolled in the study; 255 (23.76%) had baseline eGFR below 90 mL/min/1.73 m^2 and were excluded. Characteristics of the study population: men 88.4%, MSM 62.6%, median baseline age, CD4+count and viral load were 32.6 years, 413 cells/μL and 3.77 $\log_{10}$ copies/mL, respectively. 240 (29.3%) patients experienced an eGFR decrease below 90 mL/min/1.73 m^2 during follow-up period. Older age, female gender,

heterosexual mode of transmission, lower baseline eGFR (all $p < 0.001$), lower baseline CD4+ ($p = 0.001$), stage C ($p = 0.023$), administration of cART ($p < 0.001$) or other nephrotoxic agent ($p = 0.035$) were the major risk factors in univariable analysis. Multivariable analysis identified older age [hazard ratio (HR) 1.289 per 10 years, $p < 0.001$] and female gender (HR vs male: 1.899, $p < 0.001$), as the major factors associated with increased hazard of developing CRD, whereas baseline eGFR <110 (HR vs eGFR <110: 0.245, $p < 0.001$) and current CD4+ count ≥350 cells/μL (HR 0.564, $p = 0.003$) were significant protective factors.
Conclusion: In this large cohort of HIV-infected Greek patients, almost one-third (29.3%) experienced some degree of renal dysfunction during HIV infection. Older age and female gender were major predictors of CKD, whereas high current CD4+ count and baseline eGFR were protective.

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P46

Association of fibroblast growth factor 23 and hypophosphatemia in well-suppressed HIV-infected patients receiving antiretroviral therapy

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Introduction: Prolong hypophosphatemia may result in future bone loss which will have effect on patient's quality of life. Hypophosphatemia is observed in 4–31% of HIV-infected patients receiving highly active antiretroviral therapy (HAART). Fibroblast growth factor 23 (FGF-23), a potent phosphaturic hormone, has not been well studied in HIV-infected Thai patients. We aimed to investigate whether FGF-23 is involved in the etiology of hypophosphatemia in our HIV-positive patients on HAART.
Method: This study was a case-controlled study at HIV-NAT, Thai Red Cross AIDS Research Centre, Bangkok, Thailand during June 2011-May 2012. Serum and urine phosphate was studied in 696 well-suppressed HIV-infected patients. Hypophosphatemia was defined as a serum phosphate level <2.5 mg/dl. All fasting blood and urine samples were taken between 7.00 and 10.00 hr to measure serum phosphate, calcium, 1,25 OHD, parathyroid hormone (PTH), FGF-23 and urinary phosphate excretion. The renal phosphate threshold tubular maximum phosphate reabsorption per glomerular filtration rate (TmP/GFR) was calculated. eGFR was calculated using the MDRD.
Results: Totally 65 (9.3%) subjects were identified for hypophosphatemia. The prevalence of hypophosphatemia was not difference between TDF exposure [(46/544: 8.5%) and TDF unexposure (19/154: 12.5%), $p = 0.13$]. However, only 56 subjects for a case group (hypophosphatemia group) and 65 subjects with normal phosphate (normophosphatemia group were included in this analysis. In the hypophosphatemia group, they were more likely younger, less female, and lower CD4 cell counts than the control group. About 80% and 74% of the case and control group had TDF exposure, respectively. The renal phosphate reabsorption threshold was significantly lower in hypophosphatemia group than in the control [43 (2.19–2.6) vs 3.16 (2.92–3.61) mg/dl, $p < 0.001$]. FGF-23 was significantly higher in hypophosphatemia group [31.9 (24.7–40.0) vs 26.2 (19.3–34.1) pg/dl, $p < 0.017$]. TmP/GFR was strongly related to FGF-23 levels ($p < 0.04$), but not for PTH ($p < 0.06$), and urine calcium ($p < 0.07$).
Conclusion: FGF-23 is involved in pathogenesis of hypophosphatemia in our HIV-positive patients on HAART.

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P47

Impact of emtricitabine/tenofovir (FTC/TDF) on renal function in antiretroviral-na ve patients ≥50 years - TRIP study

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Purpose: In the last decade the prevalence of HIV-infected patients ≥50 years of age has increased. FTC/TDF is nowadays one of the cornerstones of cART in naïve patients, generally considered safe and well tolerated; nevertheless there is a continuous debate about the renal safety of TDF, due to the report of cases linking this treatment with renal failure and tubular dysfunction. In addition, there is a well-recognized age-related decline in renal function. Our aim was to describe the impact of cART regimen (FTC/TDF vs. others) on renal function of subjects who start cART at ≥50 years old.

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	Overall	Among TDF users	
	No TDF vs. TDF/FTC	PI vs. NNRTI	LPV vs. EFV
Glomerular filtration rate by CKD-EPI (mL/min/1.73 m^2)			
Baseline (median)*	91.6 vs. 93.7	90.7 vs. 95.7	93.7 vs. 95.8
Month 12 (median)*	98.0 vs. 95.1	89.2 vs. 96.7	71.2 vs. 97.8 ($p < 0.05$)
Renal deterioration:			
Cases (n, %)	4/38 (10.5%) vs. 9/79 (11.4%)	5/33 (15.1) vs. 4/45 (8.9)	4/21 (19.0) vs. 3/40 (7.5)
Log rank (time to event)	0.883	0.278	0.055
Crude HR (95% CI)	1.09 (0.34, 3.55)	2.06 (0.54, 7.86)	3.96 (0.87, 17.93)
Adjusted HR** (95% CI)	0.60 (0.15, 2.35)	3.37 (0.76, 14.87)	8.20 (1.30, 51.75)

*All comparisons between arms, and between baseline and month 24 were not statistically significant unless otherwise indicated.
**Adjusted by age, sex, transmission category and baseline CD4 count and viral load.

Methods: National, retrospective cohort analysis of HIV-infected patients >50 y at the time they began the first cART (Jan 1, 2006–Dec 31, 2009). Patients were selected in a proportion 2:1 to FTC/TDF versus other NRTI regimens (no TDF). For this analysis we excluded subjects taking potentially nephrotoxic drugs at baseline. We compared the impact of FTC/TDF vs. no-TDF regimens (main groups) on renal function by means of the changes, during the first 12 months of treatment, in glomerular filtration rate estimated by the CKD-EPI formula, and by the analysis of time to renal deterioration during the complete follow up (defined as progression to an EPI-CKD value <60 mL/min/1.73 m^2 in subjects with baseline values >60). We also compared these outcomes among FTC/TDF users, according to the third agent: PI vs. NNRTI, and lopinavir/r vs. efavirenz.
Results: We included 125 patients, median age: 54.8 y, 82% males, median CD4 count 235 cells/μl, median viral load 4.7 log, follow up: median 19 months, max: 66 months. Of them, 82 started with FTC/TDF and 43 with other NRTIs (no TDF). During the follow-up 13/125 patients taking FTC/TDF (11%) presented with renal deterioration. The Cox regression model including age, sex, transmission category, baseline CD4 count and viral load, FTC/TDF use, PI/NNRTI use, and LPVr/EFV use showed a hazard ratio for renal deterioration of 4.13 (95% CI 0.92, 18.5) for LPV/r users. The table shows the evolution of glomerular filtration rate, and proportion and risk of renal deterioration.
Conclusion: In subjects starting cART after 50 years of age, we have not found significant changes in glomerular filtration rate associated with the use of FTC/TDF-based regimens. Overall, the risk of renal deterioration was 4.1 times higher for LPV/r users (almost statistically significant). Among FTC/TDF users, this risk was 8 times higher for LPV/r as compared to EFV.

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P48

Renal dysfunction and factors associated among newly identified HIV-infected patients in Brazzaville, Republic of Congo

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Background: With the introduction of nephrotoxic in recent WHO recommendation, it became necessary to determine prevalence and factors associated with renal dysfunction among patients newly identified HIV-infected in Brazzaville.
Methods: Descriptive and analytical study of patients newly diagnosed HIV-infected at the Ambulatory Treatment Center in Brazzaville, Republic of Congo between January 1st, 2009 and December 31st, 2010. Estimated glomerular filtration rate (eGFR) was assessed using the Cockroft-Gault formula (CGCl) and modification of diet in renal disease (MDRD) equation. Patients had renal dysfunction mild, moderate or severe when eGFR were respectively 60–89 ml/min, 30–59 ml/min and <30 ml/min with the GCCl and MDRD. To determine factors associated with renal failure (defined as GCCl <60 ml/min), univariate analysis followed by multivariate logistic regression analysis was performed.
Results: We evaluated 562 patients newly identified HIV-infected, median age was 38.84 (interquartile range (IQR): 33.18–46.24) years, all patients were of African origin, 61.1% were female, median BMI was 20.30 (IQR: 17.96–22.89) kg/m^2, median CD4 count was 192 (IQR: 81–350) cells/mm^3 and 70.8% were at WHO stage III/IV. GFR was lower using CGCl (median 74.99 ml/min, 26.1% <60 ml/min) versus MDRD (95.59 ml/min/1.73 m^2, 7.9% <60 ml/min/1.73 m^2). Two hundred and fifty-seven patients (47.2%) using CGCl versus 138 (32.6%) with the MDRD had mild, 126 patients (23.1%) versus 33 (5.9%) respectively had moderate, and 16 patients (3%) versus 11 patients (2%) respectively had severe renal dysfunction. Factors associated with renal dysfunction in multivariate analysis included age superior to 40 years (adjusted odds ratio (aOR): 0.37 [95% CI: 0.22-0.61]; p = 0.0001), CD4+ T-cell count below 200 cells/mm^3 (aOR: 1.72 [95% CI: 1.04–2.83]; p = 0.035) and BMI less than 18.5 kg/m^2 (aOR: 4.39 [95% CI: 2.63–7.33]; p <0.0001).
Conclusions: This study shows a high prevalence of renal dysfunction in patients newly diagnosed HIV positive in Brazzaville. Necessity is now beside serum creatinine assay performed in the initial assessment as recommended by WHO, to also perform urine dipstick for better monitoring of these patients before initiating antiretroviral therapy.

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Hepatic

P49

HIV-associated idiopathic non-cirrhotic portal hypertension is an underdiagnosed disorder: results of a large cohort study

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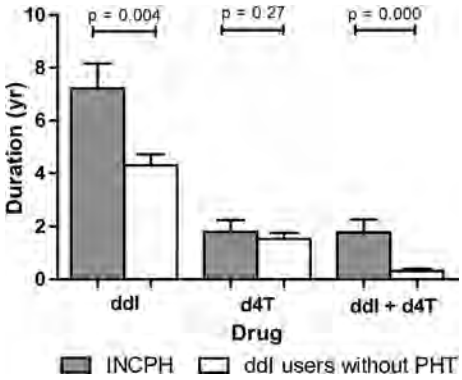
Purpose of the study: Idiopathic non-cirrhotic portal hypertension (INCPH) has been reported increasingly in patients with chronic HIV infection. However, several aspects of this disorder remain to be elucidated. The aim of our study was to evaluate the prevalence and risk factors of HIV associated INCPH.
Methods: All adult HIV patients attending the outpatient clinic between February and September 2011 underwent sonographical spleen size determination and assessment of portosystemic collaterals. Patients with splenomegaly underwent an extensive ultrasound examination. Gastroscopy was performed when additional signs of portal hypertension or collaterals were observed. All children with HIV infection underwent extensive ultrasound examination. INCPH was diagnosed according to the general definition. Differences between INCPH cases (group 1) and HIV patients treated with didanosine (ddI) without portal hypertension (group 2) were assessed at HIV diagnosis, start of ddI and INCPH diagnosis.
Summary of results: Four out of 1010 screened adult HIV patients were diagnosed with INCPH (prevalence of 4‰). Hundred of the 1010 screened patients were treated with ddI. All INCPH patients were treated with ddI, representing an INCPH prevalence of 4% in patients exposed to ddI. In The Netherlands, 7000 patients were treated with ddI and only 17 are diagnosed with INCPH, suggesting underdiagnosis in 260 patients. No differences in clinical characteristics predictive for the development of INCPH could be demonstrated between group 1 and group 2 at HIV infection or start of ddI treatment. INCPH patients were treated longer with ddI [86 vs. 51 months, p <0.01] and concomitant treatment with ddI and stavudine [21 vs. 4 months, p <0.01]. Corrected for age and duration of follow-up of HIV, active protein c [0.64 vs. 1.13, p <0.01] and active protein s [0.67 vs. 1.01, p <0.01] levels were lower in the INCPH group. None of the 38 children with HIV infection were diagnosed with INCPH. None of these children were ever treated with ddI.
Conclusions: In our study HIV-associated INCPH only occurred in patients exposed to ddI. Awareness for this disorder is warranted considering the suggested underdiagnosis based on these study results. Risk factors are long term treatment with ddI and concomitant treatment with stavudine and screening for signs of



portal hypertension in this subgroup may be recommended. A possible pathophysiological role for thrombophilia remains to be elucidated.

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Mitochondrial Toxicity

P50

Incidence of lactic acidosis toxicity among patients on stavudine or zidovudine containing antiretroviral therapy at Lighthouse clinics

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Although stavudine and zidovudine remain frequently used in low-income countries in Africa, they are associated with long-term toxicities. Lactic acidosis is one of the most serious toxicities in antiretroviral treatment (ART) and occurs predominantly in regimens containing stavudine (D4T) or zidovudine (AZT). We conducted this study to determine the incidence and risk factors for lactic acidosis among HIV-positive patients that have been on ART for at least 6 months. This study will bridge the gap that exists due to scarcity of data on the extent of toxicities due to long-term use of D4T and AZT. We conducted a retrospective cohort study using routine clinic data from the Lighthouse and Martin Preuss Centre electronic data systems. We used the clinic data collected between 1st January 2004 and 31st December 2011. We included into the analysis all patients that have been on D4T- or AZT-containing ARV drugs for at least 6 months. We analysed the data using Poisson regression of the number of cases of lactic acidosis (LA) on gender, age at ART initiation, baseline BMI, and lipodystrophy in order to determine the incidence and risk factors for lactic acidosis. All statistical analyses were done at 5% significance level. We identified 14,854 patients that have ever been on D4T- or AZT-containing ARV drugs for longer than 5 months. Of these, 43% were male and median age was 34 years. The total number of cases of confirmed LA was 342 with observed mortality rate 40% more than the patients without confirmed LA. There were 23.02 cases of LA for every 1000 patient-years on D4T- or AZT-containing ART regimens. The strongest risk factor identified for developing LA was having a baseline BMI >25 with incidence rate ratio (IRR) 3.11 (95% CI: 2.49, 3.88). The IRR for patients with a diagnosis of lipodystrophy was 1.77 (95% CI: 1.35, 2.32). Patients aged <30 years at ART initiation had 31% reduced risk of developing LA as compared to patients aged >39 years at ART initiation. We were unable to detect any increased risk associated with gender. Clinicians should always have significantly higher index of suspicion of LA in patients with established lipodystrophy, aged more than 30 years at ART initiation and patients with higher baseline BMIs. The number of cases of fatal lactic acidosis that did not present to the clinic is unknown but is likely to be significant.

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P51

The NRTI BMS-986001 does not degrade mitochondrial DNA in long-term primary cultures of cells isolated from human kidney, muscle and subcutaneous fat

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Background: Nucleoside reverse transcriptase inhibitors (NRTIs) are often used in the treatment of HIV infections, although their use has been in some cases been limited by adverse side effects attributed to inhibition of eukaryotic mitochondrial DNA polymerase gamma (mtDNA polγ). The primary objective of this study was to compare the in vitro toxicity of the novel HIV thymidine-analogue NRTI, BMS-986001 (OBP-601) to that of five other NRTIs: tenofovir (TFV), adefovir (ADV), azidothymidine (AZT), stavudine (D4T), and abacavir (ABC).
Methods: Primary cultures of human renal proximal tubule epithelium, muscle, preadipocytes and differentiated adipocytes (subcutaneous) were exposed to each of the NRTIs at their reported C_{max} concentration and at 200 M for 5, 10, 14 and 19 days. Six in vitro cytotoxicity parameters were measured: percent dead cells, cell protein and ATP content, lactate concentration in the media, and mtDNA (ATP8) content by qPCR. Results were analyzed by analysis of variance followed by Dunnet's post hoc test.
Results: BMS-986001 was not cytotoxic in any of the 4 cell culture systems tested. TFV was cytotoxic in muscle cells and preadipocytes with regard to mtDNA content which decreased in a concentration- and time-dependent manner to approximately 40% control values. In contrast, ADV, AZT and d4T were cytotoxic in all 4 cell culture systems and with regard to all measured parameters. ABC was only significantly cytotoxic at the higher concentration (200 M) tested.
Conclusions: Based on in vitro assessments, when compared to five other NRTIs (TFV, ADV, AZT, d4T and ABC) in primary cultures of human cells, BMS-986001 was the least cytotoxic. The most cytotoxic were ADV, AZT, and d4T. In spite of their very close structural similarity, the relative lack of toxicity of BMS-986001 compared to d4T is consistent with the 100-fold greater potency of d4T for inhibition of mtDNA polγ.

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Bone

P52

Tenofovir accelerates bone mass loss of the lumbar spine in the first years of menopause in HIV-infected women

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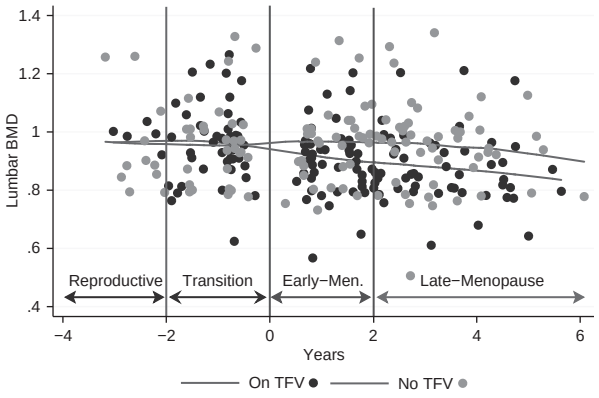
Background: HIV-infected postmenopausal women have higher rates of bone loss than HIV negative women. We aimed to identify

predictors of body mass density (BMD) in HIV infected women entering menopause and to evaluate the pre- and post-menopausal BMD change, with regard to tenofovir (TDF) use.

Methods: Women with at least one DEXA measurement were enrolled. The observation period was divided into: ''Reproductive period'', ''Menopause transition period'', ''Early menopause period'', ''Late menopause period''. BMD of the lumbar spine (L1-4) and femur neck were measured by DEXA. Lowess smoothing curves were drawn to analyze impact of menopause and TDF on BMD. Three different longitudinal linear regression models with random effects were built. Longitudinal regression analysis fits cross sectional time series regression models and allows to analyze repeated measures for each patient.

Results: Fifty-five women were included. Median age at enrollment was 46 years (IQ range 44–49). Median observation period was 16 months (IQ range 8; 23) and 33 months (IQ range 23; 72) for pre- and post-menopausal respectively. At enrollment mean CD4 cell count was 553 cell/mL (±269.62) and HIV-VL was undetectable in 77.5% of patients: 6 women were not undergoing ART. Most common backbone TDF/FTC (46.9%) and ABC/3TC (20.4%). At the time of inclusion in the cohort osteopenia and ostoeporosis were present in 60% and 3.64%, respectively. At the time of last DEXA evaluation osteopenia and osteoporosis were present in 78.18% and 36.36%, respectively. The impact of menopause on lumbar BMD was depicted (fig. 1) using a lowess smoothing analysis according to current TDF exposure (as treated model). Lumbar BMD change predictors were years from menopause and TDF current exposure in the ''Early menopause period'' and years from menopause, Baseline lumbar BMD, BMI and vitD supplementation in the ''Late menopause period''.

Discussion: This is the first study analyzing BMD across menopause. BMD was stable in the pre-menopause period while BMD loss characterized the post-menopause period. Traditional risk factors contributed to BMD change in the post -menopause period. Current TDF exposure was independently associated with BMD change in the ''Early menopause period'' only, but not confirmed in the ''Late menopause period'', suggesting a compensating mechanism occurring after the second year post-menopause.



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P53

Moderate aerobic exercise (brisk walking) increases bone density in cART-treated persons

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Moderate intensity aerobic activity reduces the risk of cardiovascular disease, diabetes and metabolic syndrome in the general population and has a potential in preventing bone loss. We evaluated the effects of brisk walking, with or without strength exercise, on bone mineral density in HIV-infected treated persons. Twenty-eight HIV-infected, cART-treated, sedentary subjects with VL < 50 c/mL were enrolled in a 12-week exercise program, consisting of 3 outdoor sessions/week of 60 min walking at 67–70% of HR (heart rate) max ± 30 min circuit training at 65% of 1-RM (repetition maximum). Subjects were examined at baseline (BL) and 12 weeks (W12) by 6-minute walking test (6MWT) and by counting the number of repetitions for each strength exercise; and by dual energy X-ray absorptiometry (DEXA) to evaluate lumbar spine and femoral bone mineral density with t- and z-scores - in addition to morphometric (BMI, waist, hip and leg circumference) and blood examination (cytometry, fasting total, HDL and LDL cholesterol, triglycerides, glucose, insulin; AST/ALT, ALP, gGT, creatinine, CPK, HbA1c; CD4+ and CD8+, plasma HIV-RNA). Differences over time were tested by Wilcoxon-signed rank test and between groups by Mann-Whitney test. Twenty-seven (96%) participants (19M, 8F; median 48 y-o, IQR 43–54; median CD4+624/μL, IQR 478–708; ART with PI: 13 patients, with NNRTI: 7 patients, and including TDF: 15 patients) completed the 12-week program with a median adherence of 61% (IQR 50–70): 18 in the 'walk only' only group and 9 in the 'walk and strength' group. At W12, participants showed significant improvement of distance by 6MWT (Table), and of performance in all strength exercises (crunch $p = 0.023$, lat machine $p = 0.016$, chest press $p = 0.016$, leg extension $p = 0.016$, sitting calf $p = 0.008$, leg press $p = 0.016$). DEXA spine z-score improved significantly in the whole group, and femoral z-scores in the 'walk only' group. There was no z-score difference at BL between patients with/out PIs, NNRTIs or TDF. However, spine

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	Transitional period			Early menopause			Late menopause		
	β	95% CI	p-value	β	95% CI	p-value	β	95% CI	p-value
Years to (from*) menopause	−0.1	−0.03; 0.01	0.407	−0.01	−0.02; −0.01	<0.001	−0.1	−0.2; −0.003	0.009
Baseline lumbar BMD	0.0002	−0.001; 0.003	0.078	0.0002	−0.0001; 0.0004	0.074	0.9	0.70 −1.09	<0.001
PTH	−0.0005	−0.001; 0.0004	0.280	0.0001	−0.0004; 0.0002	0.535	−0.0001	−0.0002; 0.0002	0.800
BMI	0.003	−0.005; 0.010	0.489	0.004	−0.001; 0.010	0.142	0.008	0.002; 0.014	0.010
VitD supplementation	−0.003	−0.05; 0.04	0.865	0.008	−0.010; 0.026	0.392	0.03	0.001; 0.054	0.038
TDF current exposure	−0.03	−0.07; 0.01	0.125	−0.03	−0.05; −0.01	0.012	−0.04	−0.09; 0.01	0.129

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	BL-median (IQR)	W12-median (IQR)	p
Distance at 6MWT (m)	658 (605–691)	715 (IQR 690–830)	<0.0001
DEXA spine (z-score)	−1.15 (−1.7/ −0.7)	−1.05 (−1.4/ −0.3)	0.002
DEXA spine (z-score)(TDF-treated pts)	−1.4 (−1.7/ −0.7)	−1.3 (−1.55/ −0.5)	0.002
DEXA femoral neck (z-score)(walk only)	−0.8 (−1.4/ −0.2)	−0.5 (−1.2/ −0.2)	0.047
DEXA femoral ward (z-score)(walk only)	−1 (−1.9/ −0.6)	−0.75 (−1.4/ −0.2)	0.004
BMI	25.7 (24.6–26.3)	24.9 (21.4 −26)	0.0016
Waist circumference (cm)	93 (87 −100)	92 (85.5 −98.5)	0.029
LDL cholesterol (mg/dL)	126 (113 −154.5)	116 (96–137.5)	0.0003

z-score improved significantly in patients receiving TDF. At W12 BMI, waist circumference, and LDL also improved significantly in the whole group, whereas no significant changes were observed for the other variables, The above 12-week program improved fitness and bone density in HIV-infected treated subjects, in addition to some morphometric variables and serum LDL. Brisk walking, with or without strength exercise, might help control the long-term consequences of cART.

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P54

Secondary hyperparathyroidism in HIV-infected patients: relationship with bone remodeling and response to vitamin D supplementation

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Purpose of the study: Secondary hyperparathyroidism (SH) is frequent in HIV-infected patients. However, the causes and consequences are not well established. The aim of our study was to determine the relationship between parathyroid hormone (PTH), vitamin D and bone mineral density (BMD) in HIV-infected patients, and the effect of vitamin D replacement on PTH levels.
Methods: Prospective study of 506 patients with at least two sequential serum determinations of PTH and 25-hydroxyvitamin D levels. In all cases, a bone dual X-ray absorptiometry (DEXA) was performed at inclusion. Hyperparathyroidism was defined as a PTH level above 65 pg/ml.
Summary of results: Mean age was 44 yrs (24–78), and 75% were male. Mean BMI was 23.7 (17.97–33.11), and only 3% were of black race. Median nadir CD4+ was 200 cells/μL (9–499), and median time of HIV infection was 15.3 yrs (1.7–25.2). At inclusion, 488 patients (86%) were on HAART (31% TDF + PI, 44% TDF + NNRTI, 25% non-TDF based regimen) for a median of 929.5 days (154–1969), and 40% were HCV-coinfected. Median eGFR was 97.9 ml/min (62.14–134.08). Overall, mean serum PTH was 56.3 pg/mL (27.2–95.07). SH was observed in 27% of cases, with a marked influence of seasonality (from 44% in January to 10% in August). Mean levels of vitamin D were 17.45 ng/mL (7.6–40.78), with 16% below 10 ng/ml, 59% <20 ng/ml (deficiency), 85% <30 ng/ml (insufficiency). SH was related to vitamin D deficiency (relative risk, RR, 2.44), age (RR 1.04 per year), and a higher decrease in eGFR (RR 1.03 per ml/min), after adjustment by season, antiretroviral therapy, GFR at baseline, and HCV coinfection. DEXA scan showed 18% osteoporosis and 54% osteopenia, and there was an inverse correlation between PTH levels and T and Z score in femoral neck ($r = -0.14$, $p < 0.01$), higher in those patients below 40 yrs. Vitamin D supplementation in 181 patients produced a significant decrease in serum PTH (57.2 if not treated vs 50.5 pg/ml, $p = 0.02$, 23% continues with SH) and the only factor associated with lack of response was persistent vitamin D deficiency.
Conclusion: SH is relatively frequent in HIV patients, in close relation with vitamin D deficiency. It is associated with bone resorption, especially in the femoral neck. The use of vitamin D supplementation improves SH when levels above 20 ng/ml are achieved.

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P55

Antiretroviral therapy and pregnancy: effect on cortical bone status of HIV-infected women

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Purpose of the study: Vertical transmission of HIV can be almost eliminated by an appropriate combination of preventative measures, which include the use of combination antiretroviral therapy (ARV) during pregnancy, elective cesarean delivery, and avoidance of breastfeeding. Although current ARV demonstrated to be very effective to control virus infection, it has numerous side effects, including negative repercussions on bone mass. Currently there are no data regarding the bone status of HIV-infected women who received ARV during pregnancy. The aim of this study was to evaluate cortical bone status at delivery in a group of HIV-infected women who received ARV during pregnancy, to monitor the changes occurring during the first year post-partum and to compare the results with those obtained in healthy mothers.
Methods: We studied 17 HIV-infected and 55 HIV-uninfected healthy women within 3 days from delivery, at 4 and 12 months postpartum (median age 36.4 years). The majority (68%) of the HIV-infected mothers was on ARV containing two nucleoside reverse transcriptase inhibitors (NRTI) and a protease inhibitor (PI), and 16% was on a regimen containing two NRTIs and two PIs. Other ARV regimens included the use of two NRTIs and one non-NRTI (10%), one NRTI plus one PI (3%), or two NRTIs and three PIs (3%). The median (range) exposure to ARV during gestation was 14 (5–35) weeks. The great majority (91%) of the women showed an undetectable viral load (<50 cp/mL) at delivery. Median CD4 number at delivery was 610 (128 to 1415). Cortical bone status was evaluated by quantitative ultrasonography at the mid-tibia, and bone measurements were expressed as the speed-of-sound (SOS).
Summary of results: HIV-infected women after delivery had a median SOS of 3985 (3567–4242) m/s, while the median SOS of healthy women was 4025 (3643–4250). The difference was not significant ($t = 0.39$; $P = 0.69$). SOS measurements at baseline, at 4, and at 12 months are shown in Table 1. SOS values did not change significantly in the HIV-infected mothers' group ($F = 0.02$; $P = 0.88$), while they changed over time in the healthy mothers' group ($F = 0.15$; $P = 0.02$). No significant differences were observed between ARV-exposed and control subjects at 4 and 12 months.

Conclusion: Our data suggest that ARV during pregnancy and the first year after delivery does not affect negatively cortical bone status and that QUS results are equivalent to those of HIV-negative healthy women.

Variable	HIV-infected women	Healthy women
Subjects (n)	17	55
Age of delivery (y)	33.8 (23.7–40.9)	35.2 (21.8–42.3)
Height (cm)	163.5 (151–173)	163 (150–178)
Weight baseline (kg)	65 (55–92)	72 (53–94)
Weight 4 months (kg)	58 (47–88)	63 (45–93)
Weight 12 months (kg)	59 (50–84)	61.5 (46.5–90)
SOS baseline (m/s)	4089 (3821–4242)	4013 (3070–4215)
SOS 4 months (m/s)	4043 (3814–4337)	4015 (3672–4191)
SOS 12 months (m/s)	4038 (3814–4337)	3958 (3713–4176)
SOS z-score baseline	1.6 (−1.1–3.0)	0.8 (−2.4–2.7)
SOS z-score 4 months	1.2 (−1.1–3.6)	0.9 (−3.0–2.5)
SOS z-score 12 months	1.2 (−1.3–3.7)	0.5 (−1.8–2.4)

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P56

Bone turnover markers in HIV-infected patients before starting antiretroviral therapy

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Purpose: Bone turnover markers (BTM) - aminoterminal propeptide of type 1 collagen (P1NP) and C-terminal telopeptide of type 1 collagen (β-CTX) - are related to bone density and fracture risk. A high prevalence of osteopenia/osteoporosis and hypovitaminosis D has been reported in HIV patients, however there are few data about BTM in this population. Our aim was to analyse the prevalence of elevated serum levels of BTM in HIV patients before starting antiretroviral therapy (ART), and related factors.
Methods: Cross-sectional study of a series of HIV-patients who started ART during June/11–June/12 in our hospital. Patients with presence of diseases or treatments known to affect bone metabolism were excluded. Epidemiological, clinical, and immunovirological data in addition to serum fasting levels of glucose, lipid profile, calcium, phosphate, alkaline phosphatase, 25-hydroxyvitamin D3 (25OHD), parathyroid hormone (PTH), P1NP, and β-CTX were collected. Definitions: hypovitaminosis D if 25OHD <30 ng/ml, vitamin D deficiency if 25OHD <20 ng/ml; elevated levels of BTM if β-CTX (ng/ml) >0.64 (men <70 years), >0.85 (men >70 years), >0.58 (pre-menopause women), >0.99 (post-menopause women), or P1NP (ng/mL) >69.4 (men <60 years), >71.1 (men >60 years), >55.7 (pre-menopause women), >61.2 (post-menopause women).
Results: 47 patients were included, 91.5% men, median age 37.1 years (30.0–44.3), and 93.6% sexual transmission of HIV (34 HMX, 10 HTX). Median time since the diagnosis of HIV was 3.4 months (1.4–31.7); there were 7 (14.9%) Aids cases, median CD4 count was 277/mm^3 (155–433), and HIV-VL 4.8 $\log_{10}$ (4.1–5.2). Median serum 25OHD was 29 μg/L (21.9–41.1), with a prevalence of hypovitaminosis of 52.2%, and deficiency of 17.4%. PTH was in range in all cases. Median serum P1NP was 33.3 ng/mL (24.5–52.5) and β-CTX 0.25 ng/mL (0.20–0.45); five (11.4%) patients presented high levels of BTM: 4 men, median age 37.1 years, median CD4 count 247/mm^3, median HIV-VL 5.18 $\log_{10}$, and one with hypovitaminosis D. Elevated BTM were related with no clinical, analytical, immunovirological parameters nor with serum levels of 25OHD nor PTH.
Conclusions: The prevalence of elevated BTM was high in this series of HIV-patients, mostly young men, with short time of HIV infection and with no immunovirologic control. BTM were related with no clinical nor analytical data.

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P57

Densitometric disorders in children infected with HIV

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The aim of study was to assess the prevalence of densitometric disorders and deficiencies of vitamin D3 in children vertically HIV-infected, treated with cART. In 34 children vertically HIV-infected aged 10–16 years (mean 13 years), receiving cART ≥ 5, bone densitometry and the titer of 25-OHD3 was done. We analyzed at the time of diagnosis of HIV infection and at the time of the study: age, clinical and immunological classification, the length, effectiveness of cART, the lowest immunological classification. 15/34 (44%) children had abnormal dual-energy X-ray absorptiometry examination (DEXA) of the lumbar aged-matched mean Z-score -2.1 (range -1.2 to -3.5), of which 8 also had abnormal DEXA whole spine aged-matched mean Z-score -1.6 (range -1.1 to -2.2). Level of 25-OHD3 was abnormal (<20 ng/ml) in 29/34 (85%), in 7 of them the level was very low (<4.0 ng /ml). 4/5 children with normal values of 25-OHD3 parallel had correct densitometry; 1/5 with a normal value of 25-OHD3 had significant abnormalities of bone density, visible in radiographs of the hand. Clinical classification at diagnosis was: N/A in 17, B in 12, C in 5 and immunological classification: 1 in 11, 2 in 9, 3 in 13 cases. The lowest classification was AIDS in 9 children, 15 had moderate signs of infection, and 10 mild signs; deep immune deficiency occurred in 17 children, 15 had moderate and 2 have never had immunodeficiency. The regimens based on PI received 9 children, NNTRI -6, all 3 classes received 19. At the time of the study 31 children were successfully treated, 32 had no immunodeficiency, two had moderate deficiency. 32 children were qualified to N/A group, one was in the classification of B and one in C. All children unsuccessfully treated (3) had low levels of 25-OHD3. In a significant percentage of older children receiving antiretroviral treatment ≥ 5 years, had abnormal results of densytometry examination. There was no correlation between age, duration of the cART, the severity of the clinical, immunological classification, viral load and bone density disorders. Level of 25-OHD3 was abnormal in the majority of children. Disorders were also found in children successfully treated.

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P58

Vitamin D status in an urban Spanish HIV-infected patient cohort and its relationship with most frequent antiretroviral therapy regimens

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Purpose: We assessed vitamin D status in HIV-infected patients and its relation to classic, related-HIV risk factors and therapeutic regimens.

	vitDd n = 155 (44%)	vitDi n = 97 (27.6%)	vitDo n = 100 (28.4%)	p
Age	28 (23–34)	28 (25–35)	27 (23–35)	0.77
Gender n (%) Female/male	59 (38.1%) 96 (61.6%)	23 (23.7%) 74 (76.39%)	34 (34%) 66 (66%)	0.06
Ethnic background n (%)	125 (80.6%) 22 (14.2%)	83 (85.6%) 7 (7.2%)	91 (91%) 1 (1%)	0.07 0.001* 0.64
Caucasian/Black/Hispanic	8 (5.2%)	7 (7.2%)	8 (8%)	
Risk factor HTX/MSM/IDU/other	76 (49.1%) 18 (11.6%)	34 (35.1%) 27 (27.8%)	27 (27%) 9 (9%)	0.001* 0.0001*
	59 (38.1%) 2 (1.3%)	33 (34%) 3 (3.1%)	63 (63%) 1 (1%)	0.0001* 0.45
Calcium (mg/dL)	9.3 (9–9.6)	9.2 (8.5–9.5)	9.2 (8.9–9.5)	0.08
Albumin (g/dL)	4.4 (4.2–4.6)	4.4 (4.1–4.6)	4.4 (4.2–4.6)	0.59
iPTH (pg/mL)	48.2 (34.2–67.8)	46 (32.8–59.45)	45.2 (34.57–59.9)	0.51
Phosphorus (mg/dL)	3.29 (3.1–3.6)	3.296 (2.9–3.3)	3.296 (3–3.296)	0.053
Glomerular filtration rate (MDRD)	88.2 (77.3–102)	85.9 (74.7–95.5)	84 (73.9–92.3)	0.03
GFR < 60 n (%)	6 (3.9%)	1 (1%)	9 (9%)	0.02
Blood glucose (mg/dL)	96 (88–104)	96 (89–104)	97 (89–104)	0.99
HCV (%)	92 (59.4%)	58 (59.8%)	33 (33%)	0.0001*
HBV (%)	3 (1.9%)	6 (6.2%)	4 (4%)	0.22
CD4+	519 (334–700)	449 (307–637)	505 (360–660)	0.36
HIV copies/mL (%) > 50 < 50	35 (22.6%) 120 (77.4%)	31 (32.4%) 66 (68%)	9 (9%) 91 (91%)	0.0001*
HAART, n (%)	73 (47.1%)	45 (46.4%)	67 (67%)	0.003*
Season, n (%) spring/summer/	52 (33.5%) 20 (12.9%)	15 (15%) 25 (25.8%)	1 (1%) 37 (37%)	0.0001* 0.0001*
autumn/winter	35 (22.6%) 48 (31%)	38 (39.2%) 19 (19.6%)	58 (58%) 4 (4%)	0.0001* 0.0001*
HAART regimens (patients with < 50 copies)	vitDd n = 118	VitDi n = 64	VitDo n = 91	
Duration (months)	85 (40–143)	64 (28–138)	86 (43–140)	0.344
NNRTI + TDF	36 (30.51%)	23 (35.94%)	21 (23.07%)	0.258
NNRTI + no_TDF	16 (13.56%)	8 (12.5%)	9 (9.89%)	0.745
PI + TDF	28 (23.73%)	15 (23.44%)	25 (27.47%)	0.728
PI + no − TDF	14 (11.28%)	9 (14.06%)	15 (16.48%)	0.602
NNRTI + PI + TDF	1 (0.85%)	0 (0%)	0 (0%)	0.519
NNRTI + PI + no − TDF	3 (3%)	1 (1.56%)	3 (3.29%)	0.781
Other + TDF	2 (2.54%)	1 (1.56%)	0 (0%)	0.475
Other + no TDF	9 (7.63%)	5 (7.81%)	5 (5.49%)	0.821
PI monotherapy	9 (7.63%)	2 (3.12%)	13 (14.28%)	0.039*

Methods: Out of 450 HIV-infected patients followed in the H. Severo Ochoa (Madrid, Spain), we selected 352 patients in which vitamin D levels had been assessed (2009 to 2010). We describe demographics, cART duration, cART, viral load (VL), CD4+ cell count, 25(OH)D levels, iPTH, MDRD, serum albumin and calcium. Vitamin D status cutoff points were: 1. deficiency (vitDd): 25(OH)D levels < 20 ng/mL; 2. insuficiency (vitDi): 20 to 29.99 ng/mL and 3. optimal (vitDo): 25(OH)D ≥ 30 ng/mL.

Results: Median CD4+ cell count was 501 cells/μL; median VL 40 copies/mL. 277 patients (78.7%) had less than 50 copies/mL. 310 patients (88.1%) were on cART. The proportions of patients with vitDd, vitDi and vitDo were 155/352 (44%), 97 (27.6%) and 100 (28.5%). Black patients had 14.2% of vitDd (22 patients out of 155 patients with vitDd), 7.2% (7/97) vitDi and 1% (1/100) vitDo (p = .001) vs. global sample; therefore, 29 out of 30 (96.7%) black patients had vitDd/vitDi, vs. 71.6% in global sample. Former IDUs had more vidDo (p < 0.001 vs. other risk groups). Among patients with less than 50 copies/mL, the proportions of vitDd, vitDi and vitDo were 77.4%, 68% and 91% respectively, (p = .0001). Of the cART, only PI monotherapy was associated with significant differences in vitD (see Table).

On multivariate analysis following variables were related to increased risk of vitD insuficiency/deficiency, black vs. white race (OR 10.6 [95% CI 1.2–94], p = .033); heterosexual/MSM risk vsm IDU risk groups (OR 2.37 [95% CI 1.13–4.93], p = .022) and (OR 3.25 [95% CI 1.25–8.50], p = .016) and VL > 50 copies/mL (OR 2.56 [95% CI 1.10–7.25], p = .040). Less risk of vitamin D insufficiency/deficiency was found in patients on PI monotherapy vs. no treatment (OR 0.08 [95% CI 0.01–0.6], p = .018); Hispanic (South American) patients vs. white (OR 0.18 [95% CI 0.05–0.68], p = .012) and summer/autumn vs. spring samples (OR 0.015 [95% CI 0.002–0.116], p = .0001 summer) and (OR 0.013 [95% CI 0.02–0.099), p = .0001, for autumn).

Conclusions: 1: Vitamin D status was associated with ethnic background, season and non-suppressed VL. 2: Former IDUs had less vitamin D deficiency/insufficiency, perhaps due to more outdoor jobs. 3: As in the MONET study, PI monotherapy had a positive impact on vitD.

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P59

Prevalence of vitamin D deficiency in human immunodeficiency virus-infected patients

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Purpose of the study: Vitamin D deficiency in the adults could produce osteomalacia, secondary hyperparathyroidism with bone loss and increased risk of fractures. An increased prevalence of osteopenia, osteoporosis, decreased bone density, vitamin D deficiency and increased risk of fracture was found in HIV-positive patients. A study performed in Buenos Aires, Argentina that included non-HIV-infected adult patients showed 15% prevalence of vitamin D deficiency in winter and 0% prevalence in summer. There is no local data published of vitamin D deficiency in HIV-positive populations. The aim of the study is to determinate the prevalence of vitamin deficiency in our HIV-positive population receiving HAART.
Methods: An observational, retrospective study was performed. We reviewed the clinical charts of the HIV-positive adult patients attending the infectious disease clinic. We collected data of vitamin D, parathormone and beta cross laps value; we recorded if the test was performed in winter or summer. We considered vitamin D deficiency if <10 ng/ml. We recorded age, sex, comorbidities (diabetes mellitus, renal failure, hepatic failure, HBV and/or HCV coinfection, menopause, malignancy and metabolic syndrome), months since HIV diagnosis, CD4 count, viral load and HAART.
Summary of results: 60 patients were included, 49 (65%) of whom were male. Mean age was 49.15 years. Mean time from diagnosis was 112 months. Mean CD4 count was 548 cells/mm^3 and 6.6% presented CD4 <200; 83.3% had viral load <50 copies/mm^3. All patients were on HAART; 50% received efavirenz, 65% received tenofovir and 11.6% recived atazanavir. Mean vitamin D value was 23.58 ng/ml (5–66.5 ng/ml). In winter, 15.3% of the patients had <10 ng/ml of vitamin D and mean value was 24.16 ng/ml (10–40 ng/ml). Although the mean value in summer was 25.8 ng/ml (11.6–66 ng/ml) 10% of the patients had vitamin D deficiency. PTH value was abnormal in 31.6% of patients and beta cross laps was abnormal in 10% of patients.
Conclusions: Although the small number of patient included, we observed a high prevalence of vitamin D deficiency even in summer. A systematic assessment of vitamin D must be included in HIV positive patient care.

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P60

Avascular necrosis of femoral head in patients with human immunodeficiency virus type 1 (HIV-1) infection: a single-centre experience

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Purpose of the study: Introduction of highly active antiretroviral therapy (HAART) has led to an improvement of life expectancy and quality of life in patients living with HIV. Concomitantly, concerns are arising about long-term side effects of chronic use of antiretroviral therapy. Avascular necrosis of the femoral head (ANFH) and other epiphyses is increasingly reported as one of these debilitating complications. The objective of this study is to analyse clinical characteristics and outcome of patients with avascular necrosis (AN) followed in our centre.
Patients and methods: We analysed retrospectively the charts of 1020 HIV-1 infected patients followed in our centre and focused on symptomatic patients with radiologicaly proven AN. We analysed risk factors, demographic and clinical characteristics, treatment and outcome in these patients.
Summary of results: Ten patients with AN were identified (prevalence of 0.98%). The average interval between HIV diagnosis and diagnosis of AN was 89.1 months (1–254). Four patients had no evidence of risk factors (40%) whereas 6 (60%) had at least one risk factor. One patient had three cumulated risk factors and for him the onset time for AN was shorter (36 months). All patients had been treated by antiretroviral therapy when AN was diagnosed, but one of the patients developed symptoms prior to start of antiretroviral treatment. All classes of antiretroviral drugs have been used: protease inhibitors (mean use duration of 34.7 months before the ONFH onset), non-nucleoside reverse transcriptase inhibitors (12 months), and nucleoside reverse transcriptase inhibitors (40.5 months). ANFH was unilateral in 4 patients and bilateral in 6 patients. In one of these 6 cases, multiple AN locations were present (table). In eight patients, total hip arthroplasty (THA) (88.8%)

Median age	**Years (min–max)**
Age	46.2 (24–84)
Age at AN diagnosis	40.8 (22–69)
Men	6 (60%)
Caucasian	7 (70%)
Median CD4 count (/µl)	CD4/µl (range)
Nadir	65 (4–242)
At diagnosis of AN	405 (13–957)
Viral load at AN diagnosis	N (%)
Undetectable	5 (50%)
Detectable	5 (50%)
Lipid Profile	mg/dl (range)
TC	234 (145–335)
LDL	134 (65–230)
TG	214 (78–512)
Haemoglobin electrophoresis:	N (%)
Normal	8 (80%)
Abnormal (heterozygote)	1 (10%)
Risk factors:	N (%)
Cortisone	1 (10%)
Alcohol	4 (40%)
Chemotherapy	2 (20%)
Smoking	1 (10%)
Radiotherapy	1 (10%)
Average duration of HAART use	Month (range)
PI	34.2
NNRTI	12
NRTI	40.5
Average time between HIV diagnosis and AN (months)	89.1 (1–254)
Average time between onset of symptoms and first arthroplasty (months)	10.5 (2–20)

was the definitive treatment. Diagnosis of ANFH in the two patients who were not operated is very recent (5 and 13 months) but surgery is already indicated. The average interval between ANFH diagnosis and the first THA was 10.5 months.
Conclusion: AN, and particularly ANFH, is a rare but debilitating complication in HIV-1 infected patients. The role of ARV in the pathogenesis of AN remains unclear. However, classical risk factors play an essential role and accumulation of several risk factors could shorten the time before onset of AN. In the presence of advanced disease (stage III–IV) the final treatment remains arthroplasty.

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P61

Efficacy of long-term osteopenia/osteoporosis treatment in the Slovene HIV-infected male population

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Purpose of study: In our study from 2006, high prevalence of reduced bone mineral density (BMD) among Slovene HIV-infected male population was observed. The aim of the present study was to evaluate bone status six years after treatment intervention.
Methods: 69 HIV-infected male patients (out of 96, studied in 2006) were assessed for change in BMD using dual X-ray absorptiometry and markers of bone turnover. The effects of HIV-associated factors (time since infection, ART duration, viral load, CD4+count), changes in life-style risk factors (smoking, physical activity, alcohol consumption, amount of milk in diet) and treatment of osteopenia/osteoporosis were assessed. Therapy for osteopenia/osteoporosis was used in 30 patients; vitamin D and calcium supplementation in 20 patients with osteopenia and additionally bisphophonates in 15 patients with osteoporosis or androgens in case of hypogonadism, respectively. 39 patients were not treated.
Summary of results: Therapy of osteopenia/osteoporosis maintained BMD values in 18 (66.7%) patients, as compared to only 8 (25%) patients without therapy ($p = 0.002$). Lumbar spine BMD increased by 4.1% during the 6-year period for patients with therapy, as compared with an increase of 0.9% for patients without therapy ($p = 0.033$). The difference in total hip values was even more significant, with a 2.6% increase in BMD with therapy, compared to a 1.95% decrease without therapy ($p < 0.0001$). Some increase in the physical activity and milk consumption among HIV-infected population was observed, while the smoking rate and alcohol consumption remained the same. Risk-factors associated with life-style did not have any effect on BMD change. According to the logistic regression model, long-term vitamin D and calcium supplementation was the most significant factor associated with maintaining BMD values ($p = 0.010$; OR = 14.4).
Conclusions: Long-term treatment, especially with vitamin D and calcium, was safe and efficient in the treatment of osteopenia/osteoporosis in HIV infected patients. As BMD values decreased in a majority of individuals without therapy, and given the absence of any association between life-style change and BMD improvement, early vitamin D and calcium supplementation in the HIV-infected population is required.

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Other

P62

Temporal changes of sleep disturbances and their associations with CYP450 2B6 polymorphism and plasma drug level in HIV patients on efavirenz

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Neurological and sleep disturbances were commonly reported among HIV patients on efavirenz (EFV), the pharmacokinetic pattern varies with different CYP450 2B6 G516T genotypes. This prospective study aims to detect temporal changes and differences in the profile of these adverse reactions and their relation to plasma EFV level and host genotypes. HIV patients of Chinese ethnicity on an EFV-containing HAART regimen were recruited from a specialist clinic. Blood for CYP2B6 G516T genotypes was taken. A questionnaire assessing adverse neurological problems and sleep disturbance was administered, alongside testing for plasma EFV levels at baseline, 4 weeks, 8 months and 1 year intervals after treatment. Analysis was performed using χ^2 and t-test. A total of 64 patients (31 GG, 27 GT, 6 TT genotypes, 59 male, and 5 female, mean age of 41 ± 9.9) were recruited. At 4 weeks after EFV, 49 (76%) gave a history of any one of the neurological side effects: dizziness, headache and drunk feeling. Sleep disturbances were common: bizarre dream (45%), nightmares (35%), waking at night (73%), poor sleep quality (31%), nocturia (84%) and difficulty in falling asleep (67%). The mean plasma EFV level of GG genotype was 2.8 μg/ml and 3 μg/ml, GT genotype was 3.8 μg/ml and 3.9 μg/ml, at 4 weeks and 1 year respectively. The mean plasma EFV level of TT genotype was 11.9 μg/ml and 9.7 μg/ml at 4 weeks and 1 year respectively. There was no significant variation of drug level within each genotype over time ($p > 0.08$), while EFV level of TT was significantly higher at all time points ($p < 0.01$). Overall, nightmares and difficulty to fall asleep were significantly related to the plasma EFV level ($p = 0.021$ and 0.017 respectively). However, the sleep quality, nocturnal awakening, nocturia or requirement of sleeping pills was not significantly associated with EFV level ($p = 0.28$, 0.06, 0.1 and 0.5 respectively). When the side effects were separately evaluated according to time points, they all became insignificantly related to plasma EFV level at 12 weeks. In conclusion, very high plasma EFV level was observed in TT genotype (9.4% of patients). There was no relationship between genotype GG/GT and the occurrence of neurological side effects. While selected sleep disturbances like nightmares and difficulty to fall asleep were associated with plasma EFV levels, the general sleep quality was not significantly affected. The influence of plasma EFV levels on side effects diminished over time.

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P64

Viral load rebound in presumed elite controllers: a small case series of the potential use of non-prescribed HAART in African patients

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Introduction: HIV elite controllers are rare with an incidence of <1/300 [1]. We report 4 cases of presumed elite control with subsequent

viral load rebound possibly due to non-prescribed HAART. Case 1: A 37-year-old African woman trafficked to the UK was diagnosed HIV-positive with viral load (VL) <40 copies/mL and CD4 count of 436 cells/cmm. She denied prior diagnosis and was presumed an elite controller until a rise in VL to 26,5205 copies/mL 6 months later (Table 1).

Time from diagnosis	CD4 (cells/cmm)	Viral load (copies/mL)
0	436 (26%)	<40
1 month	424 (18%)	<40
3 months	N/A	<40
6 months	387 (29%)	265,205
6 months	264 (18%)	338,291

A resistance test reported HIV-1 subtype C with a minor protease inhibitor mutation (A71T). It was subsequently disclosed she was given unidentified tablets by traffickers. Case 2: A 31-year-old African woman presented 37 weeks pregnant and was diagnosed HIV-positive with VL 147 copies/mL and CD4 count of 1065 cells/cmm. She denied prior diagnosis, however stated an African doctor visited her ex-partner's home and supplied tablets identified as lopinavir/ritonavir and zidovudine/lamivudine. Clinics in this area were contacted but had no record of this patient. There was a rise in VL with a resistance test reporting HIV-1 subtype C/D with no mutations. Case 3: A 53-year-old African woman presented 6 weeks after a sexual assault in her home country and was diagnosed HIV-positive with VL <40 copies/mL and CD4 count of 609 cells/cmm. She denied prior diagnosis but stated her employers gave her unidentified tablets after the assault. Over 3 months VL increased to 390,751 copies/mL (Table 2).

Time from diagnosis	CD4 (cells/cmm)	Viral load (copies/mL)
0	609 (30%)	<40
1 month	763 (29%)	<40
2 months	N/A	417
4 months	616 (19%)	390,751
6 months	237 (18%)	67,833

A resistance test reported HIV-1 subtype A with no mutations. Case 4: A 42-year-old African man was diagnosed HIV positive with VL 269 copies/mL and CD4 count of 562 cells/cmm. A resistance test reported HIV-1 subtype B with minor PI and NRTI mutations (L10V and V118L respectively). HIV parameters remained stable until 20 months later with an increase in VL to 1,463,132 copies/mL (Table 3).

Time from diagnosis	CD4 (cells/cmm)	Viral load (copies/mL)
0	562 (33%)	269
3 months	454 (37%)	810
6 months	456 (29%)	1110
9 months	492 (31%)	1013
14 months	473 (27%)	199
20 months	279 (13%)	1,463,132
20 months	299 (12%)	1,070,823

A resistance test excluded super-infection reporting a similar sequence and no new mutations. Co-existing pathology was also excluded. He subsequently disclosed taking medication supplied by his family but denied this was HAART.

Conclusion: The viral load rebound seen in these cases may be due to a viral or immune mediated phenomenon; however, the possibility of non-prescribed HAART has to be considered. Home test kits for HIV are widely available and there are reports of counterfeit HAART in the developing world [2]. The HIV community has to be vigilant in reporting cases of this nature which create many anxieties regarding toxicity and resistance.

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CLINICAL PHARMACOLOGY

P65

Therapeutic drug monitoring (TDM) of atazanavir in pregnancy

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Purpose of the study: Pregnant women experience physiological changes during pregnancy resulting in clinically significant alterations in antiretroviral pharmacokinetics (PK). Therefore, achieving and maintaining optimal plasma concentrations of antiretroviral drugs is essential for maternal health and minimising the risk of mother-to-child transmission of HIV. The aim of this study is to describe atazanavir/ritonavir (ATV/r) PK during pregnancy.

Methods: Pregnant HIV-positive women received ATV/r as part of their routine pre-natal care. Demographic and clinical data were collected, and ATV plasma concentrations [ATV] were determined in the first (T1), second (T2) and third (T3) trimester using HPLC-MS/MS (LLQ = 0.05 μg/mL). Postpartum (PP) sampling was performed where applicable. Antepartum (AP) and PP PK parameters were compared using a one-way ANOVA.

Summary of results: From January 2007, 44 women (37 black African) were enrolled in the study. All received ATV/r at a standard dose of 1 tablet once daily (300/100 mg od). 24 women were receiving ART prior to pregnancy, and 20 women initiated ATV/r during pregnancy. Median (range) gestation at treatment initiation in these patients was 23.5 weeks (7–35). At the time nearest to delivery 31 patients had an undetectable plasma viral load (pVL), 6 patients had detectable pVL and 2 were unavailable. [ATV] were determined in 11/44 (T1); 25/44 (T2); 35/44 (T3) and 28/44 (PP) patients. Time of TDM sampling, gestation time and [ATV] (geometric mean; 95% CI) are given in the Table. 6 patients were either below or approaching the ATV MEC (0.15 μg/mL) during pregnancy; of these, 4/6 achieved undetectable pVL at the time of delivery (1 = pVL of 291 copies/mL; 1 unavailable). [ATV] were significantly lower at T2/T3 relative to T1/PP. Equally, in a paired analysis of 28 patients (T2/T3 vs. PP), [ATV] were significantly reduced at T2/T3 (P = 0.003).

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	T1 (n = 11)	T2 (n = 25)	T3 (n = 35)	PP (n = 28)	P value
[ATV], μg/mL	1.07 (0.15–1.99)	0.68 (0.39–0.97)	0.63 (0.47–0.78)	1.22 (0.96–1.49)	0.002
CV, %	102	83	61	49	–
Time of sampling, h	12.0 (8.8–15.3)	18.2 (15.8–20.5)	18.9 (17.2–20.7)	18.9 (16.5–21.3)	0.003
Gestation/PP, weeks	9 (6–12)	20 (14–26)	32 (25–39)	10.5 (5–50)	–

Conclusions: This study represents one of the larger cohorts of women undergoing TDM for ATV in pregnancy. Lower [ATV] were seen in T2 and T3 when compared to T1. However, such findings were not associated with viral breakthrough or HIV transmissions. Nonetheless, careful monitoring of women in pregnancy is required, and if there is concern for inadequate levels, dose adjustment of ATV upward from 300 mg to 400 mg may be an option.

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Simultaneous population pharmacokinetic modelling of darunavir and ritonavir Once daily in HIV-infected patients: evaluation of lower ritonavir dose

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Purpose of study: Once-daily ritonavir-boosted darunavir (DRV/RTV) is a preferred antiretroviral regimen for treatment-naïve patients. Population pharmacokinetic modelling of the interaction between DRV and RTV allows evaluation of alternative dosing strategies, particularly lower RTV doses (e.g. 800/50 mg once daily) and assessment of factors that may influence DRV/RTV PK.
Methods: Data were pooled from 3 DRV/RTV PK studies. Fifty-one HIV-infected patients (7 female) stable on DRV/RTV (800/100 mg or 900/100 mg once daily; n = 32 and 19, respectively) were included. Median age, weight and baseline CD4 cell count were 39 yr (21–63), 74 kg (57–105) and 500 cells/mm^3 (227–1129), respectively; 49 had undetectable viral load. Nonlinear mixed effects modelling (Monolix v.4.1.2) was applied simultaneously to DRV and RTV to determine PK parameters, interindividual variability and residual error. Covariates evaluated included: age, weight, sex and study. The model was validated by simulation and visual predictive check. DRV/RTV 800/50 mg once daily was simulated.
Summary of results: RTV and DRV were described by a 1 and 2-compartment model, respectively with first-order absorption and lag-time. A maximum effect model, in which RTV inhibited DRV clearance (CL/F), best described the relationship between the two drugs. A RTV concentration of 0.33 mg/L was associated with 50% maximum inhibition of DRV CL/F with the maximum inhibitory effect fixed at 1. The population CL/F of DRV in the absence of RTV was 13.7L/h. Inclusion of weight on RTV CL/F and volume and age on DRV CL/F and study on DRV CL/F, volume and absorption improved the fit. Based on visual predictive check 93% and 91% of observed RTV and DRV concentrations were within the 95% prediction interval, indicative of an adequate model. Of 1000 simulated DRV troughs, 10% and 0% were below the MEC for treatment-experienced (<0.55 mg/L) and naïve patients (<0.055 mg/L), respectively. For DRV/RTV 800/50 mg once daily this corresponded to 14% and 0%. Median area under the curve was 17% lower with 50 mg compared to 100 mg RTV (53.5 mg.h/L *vs*. 64.2 mg.h/L), which is consistent with previous data [1].
Conclusions: A population model describing the PK of once-daily DRV/RTV has been developed and validated and included the influence of RTV concentration on DRV CL/F. The model allowed simulation of DRV/RTV 800/50 mg once daily; concentrations were lower but trough concentrations remained within the therapeutic range for treatment-naïve patients.

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P67

Pharmacokinetic profile of maraviroc 150 mg dosed with darunavir/ritonavir once daily, with and without nucleoside analogues, in HIV-infected subjects

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Background: Once-daily nucleoside-sparing combination antiretroviral therapy (cART) regimens, such as maraviroc/darunavir/ritonavir, may be attractive therapeutic options. However, the pharmacokinetic (PK) profiles of such regimens have not been established.
Methods: HIV-1-infected subjects on stable cART comprising of tenofovir/emtricitabine (TDF/FTC) 245/200 mg plus darunavir/ritonavir 800/100 mg once daily with plasma HIV-1 RNA <50 copies/mL were eligible to enter this phase I, open-label, prospective, two-period PK study. On day 1 (period 1) maraviroc 150 mg daily was added to subjects cART regimen and on day 11 (period 2) TDF/FTC discontinued. At steady state (days 10 and 20) intensive PK sampling was undertaken. Geometric mean (GM) ratios for PK parameters between periods 2 versus 1 were calculated. In addition the number of subjects with trough (C_{trough}) and average (C_{ave}) maraviroc concentrations below 25 and 75 ng/mL (values previously associated with optimal virological response) were calculated and factors associated with total maraviroc exposure assessed.
Results: Eleven subjects completed study procedures with a mean age 49 years (range 35–59 years), 82% male and 27% and 73% of black and Caucasian ethnicity, respectively. Maraviroc GM (95% confidence interval [CI]) C_{trough} and C_{ave} concentrations in both study periods (see Table) were >25 and >75 ng/mL (concentrations associated with near maximal efficacy). No individual subjects had a maraviroc C_{ave} below 75 ng/mL in either study period. One subject had a maraviroc C_{trough} concentration below 25 ng/mL in period 1 (14 ng/mL) and one other subject in period 2 (21 ng/mL). Although no statistically significant differences in PK parameters were observed between period 2 and period 1 for any drug (see Table), a trend was observed towards lower maraviroc, darunavir and ritonavir concentrations in period 2 (TDF/FTC discontinued) versus period 1.

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	Period 1	Period 2	
	GM (95% CI)	GM (95% CI)	GMR Period 2/1 (95% CI)
Maraviroc			
C_{trough} ng/mL	47.65 (33.18–68.42)	44.86 (35.75–56.31)	0.92 (0.55–1.54)
C_{ave} ng/mL	149 (126–175)	125 (99–157)	0.84 (0.67–1.05)
AUC_{0-24} ng.h/mL	3567 (3027–4205)	2996 (2374–3781)	0.84 (0.67–1.05)
Darunavir			
C_{trough} ng/mL	1445 (936–2232)	1563 (1166–2094)	1.07 (0.63–1.81)
C_{ave} ng/mL	2891 (2364–3537)	2542 (1997–3234)	0.91 (0.78–1.06)
AUC_{0-24} ng.h/mL	69395 (56726–84893)	61001 (47941–77621)	0.91 (0.78–1.06)
Ritonavir			
C_{trough} ng/mL	46 (33–64)	50 (34–72)	1.04 (0.62–1.75)
C_{ave} ng/mL	175 (137–223)	161 (128–204)	0.91 (0.81–1.03)
$AUC_{0-24\ ng.h/mL}$	4208 (3301–5365)	3873 (3064–4896)	0.91 (0.81–1.03)

AUC, area under the plasma concentration-time curve; CI, confidence interval; GMR, geometic mean ratio. On day 20, in a multivariate model, only total ritonavir exposure (AUC_{0-24}) was statistically significantly associated with total maraviroc exposure (AUC_{0-24}) at day 20 ($p = 0.045$; 95% CI: 0.01–0.89). No clinically relevant safety concerns were observed.

Conclusions: The PK profile of maraviroc/darunavir/ritonavir 150/800/100 mg all once daily appears favourable. Maraviroc exposure is dependent on ritonavir exposure which was slightly reduced in the absence of TDF/FTC.

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Effect of food on the pharmacokinetics of emtricitabine/rilpivirine/tenofovir disoproxil fumarate single-tablet regimen

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Purpose: Emtricitabine/rilpivirine/tenofovir disoproxil fumarate (FTC/RPV/TDF; Complera®/Eviplera®) is a recently approved complete single tablet regimen (STR) for treatment-naïve HIV-1-infected patients. Exposures of rilpivirine single agent Edurant®) are 40% lower when administered under fasted conditions versus standard meal (533 kcal) or high-fat/high caloric meal (928 kcal). The present study evaluated the effect of standard and light meal on FTC/RPV/TDF pharmacokinetics (PK).

Methods: This was a three-period, six-sequence, crossover single-dose study ($N = 24$) in healthy subjects that received FTC/RPV/TDF with a standard meal (540 kcal, 21 g fat), light meal (390 kcal, 12 g fat) or under fasted conditions (each treatment 18 days apart). Blood sampling was done for 192 hrs and PK of RPV, FTC, and tenofovir (TFV) were evaluated. Safety was monitored throughout the study and at 14-day follow-up. Exposures of study drugs from the various treatments were compared to fasted or standard meal as reference using 90% confidence interval (CI) bounds of 80 to 125% about the geometric mean ratio (GMR).

Results: Of the 24 enrolled subjects, 23 completed. There were no Grade 3 or 4 adverse events (AEs), serious AEs, or AEs leading to discontinuation. Compared to fasting conditions, RPV AUC_{inf} was 9% and 16% higher with a light meal or standard meal, respectively. Compared to standard meal, RPV AUC_{inf} was 14% and 6% lower with fasted or light meal administration, respectively. TFV and FTC exposures were consistent with their established PK/food effect (Table 1).

	Exposure versus standard meal	
	GMR (%) 90% CI fasted/standard	GMR (%) 90% CI light meal/standard
Rilpivirine		
AUC_{inf} (ng*h/mL)	85.9 (72.7, 101)	93.8 (79.2, 111)
AUC_{last} (ng*h/mL)	83.7 (70.6, 99.3)	94.9 (79.9, 113)
C_{max} (ng/mL)	79.1 (65.5, 95.5)	106 (87.6, 129)
Emtricitabine		
AUC_{inf} (ng*h/mL)	105 (102, 108)	101 (98.2, 104)
AUC_{last} (ng*h/mL)	105 (102, 108)	101 (98.2, 104)
C_{max} (ng/mL)	107 (101, 114)	103 (96.2, 109)
Tenofovir		
AUC_{inf} (ng*h/mL)	72.5 (68.1, 77.2)	93.0 (87.2, 99.2)
AUC_{last} (ng*h/mL)	70.9 (66.3, 75.8)	92.8 (86.7, 99.4)
C_{max} (ng/mL)	75.8 (67.8, 84.6)	84.8 (75.8, 94.9)

Conclusion: Administration with food has a modest effect on RPV PK as FTC/RPV/TDF STR versus fasted dosing, with no relevant differences between a light meal versus standard meal. FTC/RPV/TDF STR can be administered with a light or standard meal.

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P69

Prevalence and type of drug-drug interactions involving antiretrovirals in patients attending a specialist outpatient clinic in Kampala, Uganda

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Scale-up of HIV services in countries such as Uganda has resulted in a rapid increase in facilities offering antiretrovirals (ARVs) and an increase in healthcare workers trained to deliver care. Consequently, evaluating medication safety is increasingly important in these settings. Data from developed countries suggest that drug-drug interactions (DDIs) involving ARVs are common, occurring at rates of 14–58%. Few data are available from low resource settings, however a study of 996 Kenyan patients found that 33.5% were at risk of

clinically significant DDIs. We evaluated the prevalence and type of ARV DDIs and the patients most at risk in an African outpatient setting. A random sample of patients taking current ARVs and accessing care at the Infectious Diseases Institute, Makerere University, Kampala was selected from the clinic database. The most recent prescription for each patient was screened for DDIs using www.hiv-druginteractions.org. Clinical significance of DDIs was assessed by two of us using a previously developed technique evaluating: likelihood of interaction, therapeutic index of affected drug and severity of potential adverse effect. From 1000 consecutive patients 99.6% were taking ≥ 1 co-medication alongside their ARV regimen (mean 1.89). 24.5% had ≥ 1 potential DDI, with a total of 335 DDIs observed. Of these, 255 DDIs were considered clinically significant, affecting 18.8% of patients. Only 0.3% of DDIs involved a contraindicated combination. There was a higher rate of potential DDIs observed in patients taking TB treatment ($p = 0.0047$), who were WHO stage 3 or 4 ($p = 0.001$), or patients taking ≥ 2 co-medications alongside ARVs ($p < 0.0001$) (Fishers exact test). Patient age, gender, CD4 count and weight did not affect risk for DDIs. Co-medications commonly associated with potential DDIs were antibiotics (6.2% of 1000 patients), anthelminthics (4.6%) and antifungals (3.5%). Potential DDIs involving ARVs occur at similar rates in resource-limited settings and developed countries. Drug combinations which most frequently cause DDIs, however, differ between settings; for example CNS and cardiovascular drugs in the UK and anti-infectives in Kenya and Uganda. Development of tools which are relevant to particular settings are essential for recognition of DDIs. Initiatives such as incorporation of WHO essential medicines into the Liverpool DDI database and the AIDS Treatment Information Centre in Uganda are important in achieving this.

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Development and validation of a LC-MS/MS assay to quantify intracellular tenofovir-diphosphate (TFV-DP) and emtricitabine-triphosphate (FTC-TP)

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Introduction: Combination antiretroviral therapy has been associated with dramatic reductions in morbidity and mortality in HIV-infected patients. The key to successful HIV treatment is strict adherence to the prescribed regimen. The combination of tenofovir, emtricitabine and efavirenz co-formulated in a single tablet (Atripla) provides a 'one tablet once a day' regimen, making adherence easier for patients. Tenofovir and emtricitabine are converted intracellularly to active phosphate anabolites. Therefore, knowledge of intracellular pharmacokinetics should aid understanding of the virological response and toxicity of these agents. This intracellular methodology has been developed and applied to clinical trial samples.
Method: Peripheral blood mononuclear cells (PBMC) were isolated from whole blood by gradient centrifugation using ficoll. PBMC were counted and lysed (70% MeOH) giving a final cell density of 2×10^6 cells/ml. Lysate was centrifuged, supernatant (intracellular matrix), was spiked with drug anabolites at various concentrations to produce standard curves and quality controls (QC). Samples were extracted by protein precipitation (acetonitrile), evaporated to dryness, internal standard (IS) added, and reconstituted in 5 mM ammonuim formate. Weak anion exchange chromatography with an optimised step-wise gradient, interfaced with a triple quadrupole mass spectrometer operated in SRM with positive ionisation mode was used for quantification.
Results: Analytes eluted within 12 minutes run-time with adequate separation. Calibration curves were validated over the following range TFV-DP $= 0.35–10.91$ ng/mL, FTC-TP $= 0.38–103.17$ ng/mL (r^2 values > 0.99; linear 1/x). The lower limit of quantification was $< 20\%$, 20%, signal to noise was $> 5\%$ and carryover $< 0.1\%$. The precision (relative standard deviation,% RSD) of the assays as determined from analysis of quality control samples was; TFV-DP $= 6.3–11\%$ and FTC-TP $= 6–18.6\%$, and accuracy was TFV-DP $= 97.5–100.8\%$, FTC-TP $= 98–100.3\%$.
Conclusions: A direct, highly sensitive intracellular anabolite assay has been developed and validated which elutes analytes and IS rapidly and has been applied to patient samples from a pivotal trial the results of which are crucial in our understanding of antiretroviral drug 'forgiveness'.

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Absence of a pharmacokinetic interaction of rilpivirine with the P-glycoprotein substrate digoxin in healthy volunteers

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Rilpivirine (RPV, TMC278, Edurant®) is a next-generation non-nucleoside reverse transcriptase inhibitor (NNRTI), which demonstrated high virologic response rates and non-inferiority versus efavirenz in two Phase III trials in HIV-infected patients through 96 weeks [1,2]. RPV has been shown to inhibit P-glycoprotein (P-gp) in vitro with an apparent IC_{50} of 9.2 μM (3.4 μg/mL). This study evaluated the in-vivo effect of steady-state RPV 25 mg once daily (qd) on the single-dose pharmacokinetics of the probe P-gp substrate digoxin. This was a Phase I, open-label, randomised, crossover trial in 22 HIV-negative volunteers. Participants received in one session a single 0.5 mg dose of digoxin, and in another session RPV 25 mg qd for 16 days with a single 0.5 mg dose of digoxin in the morning of Day 11. All study drugs were taken with a breakfast. Pharmacokinetic profiles of digoxin in plasma and urine were determined over 144 hours after dosing in each session. Steady-state RPV 24-hour pharmacokinetic profiles in plasma were determined on Day 11.

Table 1. Single dose pharmacokinetic parameters of digoxin in the absense and presence of steady-state RPV

Parameter	digoxin 0.5 mg alone (reference)	digoxin 0.5 mg + RPV 25 mg qd (test)
N	21	22
AUC_{4h} ng.h/mL	4.44 ± 1.21	4.46 ± 1.31
AUC_{last} ng.h/mL	26.6 ± 7.38	26.0 ± 7.86
C_{max}, ng/mL	1.93 ± 0.637	2.05 ± 0.678
t_{max}, h	1.50 (0.68–3.00)	1.74 (0.65–3.02)
t , h	38.8 ± 6.30	38.3 ± 8.17
D_{urine} total, %	47.7 ± 9.51	55.7 ± 12.2
CL_R, L/h	9.46 ± 2.54	11.2 ± 2.66
LS means (90% CI) of digoxin pharmacokinetic parameter ratios*		
AUC_{last}	0.98 (0.93–1.04)[a]	
C_{max}	1.06 (0.97–1.17)[a]	
CL_R	1.16 (1.07–1.25)[b]	

*Ratios presented as test/reference, calculated based on log-transformed pharmacokinetic parameters.
[a]N = 21 for test and N = 22 for reference.
[b]N = 18 for test and N = 22 for reference.

Plasma and urine samples were analysed using validated LC-MS/MS methods. Pharmacokinetic parameters were calculated with non-compartmental methods. The least square (LS) means and associated 90% confidence intervals (CI) of treatment ratios were calculated based on log-transformed pharmacokinetic parameters. Safety and tolerability were assessed throughout the trial. Digoxin pharmacokinetic parameters and statistical results are summarised in Table 1. The plasma and urine digoxin pharmacokinetics were unaffected by co-administration of steady-state RPV. The 90% CIs of the LS means ratios of the main pharmacokinetic parameters were contained within the 0.80–1.25 boundaries of no effect. The terminal elimination half-life of digoxin was similar in the absence or the presence of steady-state RPV. RPV pharmacokinetic parameters were comparable to those in previous clinical trials in healthy volunteers. Administration of digoxin and RPV was generally safe and well tolerated. There were no discontinuations due to adverse events. In conclusion, RPV does not affect the pharmacokinetics of the probe P-gp substrate digoxin. In vivo, at the recommended RPV dose of 25mg qd, the observed in-vitro inhibition of P-gp by RPV is not clinically relevant.

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P72

GAM analysis of the relationship between DRV PK and pharmacodynamics following DRV/r 800/100 mg qd in the phase III trials ARTEMIS and ODIN

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Background: Once-daily (qd) darunavir/ritonavir (DRV/r) 800/100mg was evaluated in two randomised and controlled Phase III trials, showing high response rates in treatment-naïve (ARTEMIS; TMC114-C211) and treatment-experienced patients with no DRV resistance-associated mutations (ODIN; TMC114-C229). Treatment interruptions, medical co-morbidities, drug-drug interactions, and challenges to adherence can decrease exposures and result in suboptimal DRV coverage. Consequences of suboptimal dosing could be detrimental to patients, namely the selection of drug-resistant HIV strains. No relevant relationship between DRV area under the plasma concentration-time curve over 24 hours (AUC_{24h}) or plasma trough concentrations (C_{0h}) and efficacy or safety were observed in ARTEMIS or ODIN [1,2]. The PK/PD analysis for efficacy has been extended using a generalized additive model (GAM).
Methods: A univariate GAM analysis was undertaken for each trial, exploring the relationship between DRV C_{0h} and virological response at Week 48. A quadratic spline (2 degrees of freedom) was selected, based on the Akaike information criterion value. Additionally, a linear logistic regression model was applied to model virologic response as a function of DRV C_{0h}.
Results: In ARTEMIS, there was no relationship between DRV C_{0h} and the observed virological response or virological response predicated in the GAM analysis, with no indication that lower values within the observed DRV C_{0h} range are associated with lower predicted virological response (Figure A). The mean predicted virological response was 92.8% in the total population (N = 304). A 50% reduction in DRV C_{0h} would result in a similar predicted mean virological response (93.9%). In ODIN, for values of DRV C_{0h} up to 3000ng/mL, there was no clear relationship between DRV C_{0h} and observed virological response. The GAM analysis showed a counter-intuitive inverse relationship between DRV C_{0h} and predicted virological response (Figure B). The mean predicted virological response was 80.6% in the total population (N = 252). For each trial, similar results to GAM were obtained when a linear logistic regression model was applied.
Conclusion: In patients who received 800/100mg qd DRV/r in the ARTEMIS and ODIN trials, a reduction in DRV C_{0h} of up to 50% is not associated with a reduced virologic response at Week 48, as predicted by both the GAM and logistic regression model. DRV/r doses below 800/100mg qd should not be administered.

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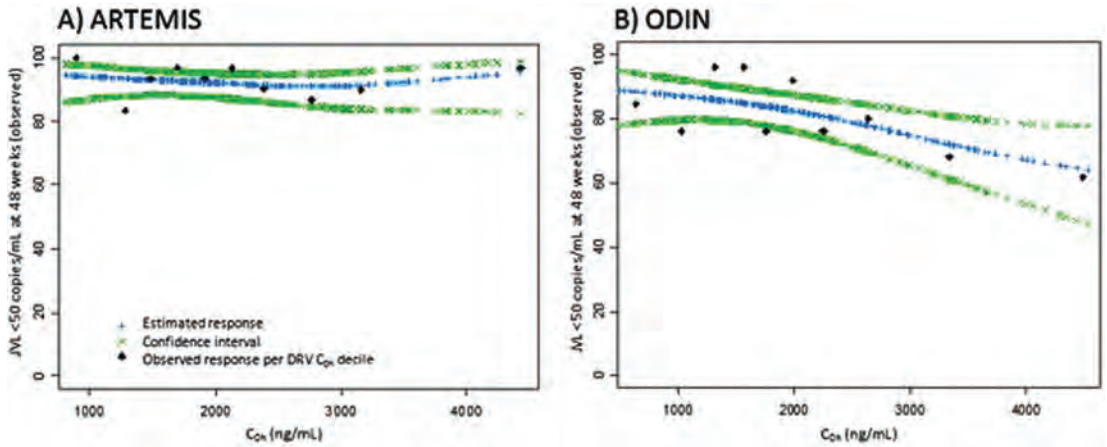

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P73

Prediction of drug-drug interactions between various antidepressants and ritonavir using a physiologically based pharmacokinetic model

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Depression can impact on the treatment of HIV infection, and effective treatment of depressive conditions can have a beneficial effect improving adherence. However antidepressant treatment requires long-term maintenance, and is prone to pharmacokinetic drug-drug interactions (DDI) with antiretrovirals. The aim of this study was to predict the magnitude of DDI between ritonavir (RTV) and the most commonly prescribed antidepressants using a physiologically based pharmacokinetic (PBPK) model simulating virtual clinical trials. In vitro data describing the physiochemical properties, absorption, metabolism, induction and inhibitory potential of RTV and five antidepressants were obtained from published literature. Interactions between RTV and antidepressants were evaluated using the full PBPK model implemented in the Simcyp Population-based Simulator (Version 11.1, Simcyp Limited, UK) and virtual clinical studies were simulated on 50 Caucasian subjects receiving 100mg bid of RTV for 21 days plus sertraline (100mg qd), citalopram (40mg qd), fluoxetine (20mg qd), venlafaxine (25mg qd) and then from day 14–21. Simulated pharmacokinetic parameters were compared with observed values available in the literature. The simulated PK parameters of RTV, sertraline, citalopram, fluoxetine, mirtazepine and venlafaxine given alone at standard dosage were similar to reference values obtain from published clinical studies. The effect of simulated RTV co-administration on sertaline, fluoxetine and venlaflaxine was an AUC decrease of 40%, 26% and 6%, respectively and on mirtazepine and citalopram, an AUC increase of 60% and 20% respectively. The magnitude of the simulated DDI between RTV and the antidepressants was overall weak to moderate according to the classification of the FDA. The modest magnitude of these drug-drug interactions could be explained by the fact that antidepressants are substrates of multiple isoforms thus metabolism can still occur through CYPs that are not or weakly impacted by RTV. Although from a pharmacokinetic point of view, venlafaxine or citalopram represent better candidates for patients on RTV, there are many considerations in seeking to optimize antidepressant therapy. The next stage in this work is to simulate DDI between boosted protease inhibitors and antidepressants. IVIVE is a useful tool for both prediction of drug-drug interactions and design of prospective clinical trials, simulating optimal sample size, and selection of doses.

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P74

Total and unbound darunavir (DRV) pharmacokinetics (PK) in HIV-1-infected pregnant women

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Antiretroviral (ARV) therapy during pregnancy is recommended to reduce the risk of mother-to-child transmission (MTCT). Physiologic changes during pregnancy can affect PK. We present the PK of total and unbound (pharmacologically active) DRV in HIV-1-infected pregnant women receiving twice-daily (bid) DRV/ritonavir (rtv). This Phase IIIb study enrolled HIV-1-infected pregnant women ≥18 years old in the 2nd trimester of pregnancy receiving DRV/rtv 600/100 mg bid and other ARVs. DRV (total and unbound) and rtv (total) plasma concentrations were obtained predose and 1, 2, 3, 4, 6, 9 and

Pharmacokinetic parameters[a] LS mean ratio, (90% CI)	**2nd trimester vs postpartum**	**3rd trimester vs postpartum**
Darunavir (total)		
N	11[b] vs 11	11 vs 11
C_{min}	1.43 (0.39, 5.22)	1.86 (0.49, 7.04)
C_{max}	0.72 (0.61, 0.86)	0.81 (0.69, 0.96)
AUC_{12h}	0.76 (0.63, 0.90)	0.83 (0.72, 0.97)
Darunavir (unbound)		
N	6[d] vs 11	7[e] vs 11
C^{c}_{min}	1.10 (0.59, 2.06)	1.14 (0.59, 2.20)
C_{max}	0.78 (0.52, 1.18)	0.82 (0.57, 1.16)
AUC_{12h}	0.92 (0.66, 1.30)	0.93 (0.69, 1.24)
Ritonavir (total)		
N	11[f] vs 11	11[g] vs 11
C_{min}	1.08 (0.31, 3.81)	1.22 (0.41, 3.59)
C_{max}	0.66 (0.41, 1.08)	0.63 (0.40, 0.98)
AUC_{12h}	0.72 (0.44, 1.17)	0.67 (0.43, 1.04)

Efficacy parameters

Parameter	**Baseline, n = 15[h]**	**2nd trimester, n = 14**	**3rd trimester, n = 11**
Log_{10} viral load, mean (SD)	2.17 (0.770)	1.99 (0.514)	1.88 (0.598)
CD4+ cell count, cells/mm^3, median (range)	419 (104, 793)	429 (81, 933)	470 (103, 960)
Virologic response (HIV RNA < 50 copies/mL), n (%)	5 (33.3)	9 (64.3)	9[i] (81.8)

[a]One patient was excluded from the PK analysis due to low adherence;
[b]n = 10 for AUC_{12h};
[c]n = 10 for postpartum;
[d]n = 9 for C_{min} and n = 7 for C_{max};
[e]n = 8 for C_{min} and C_{max};
[f]n = 12 for C_{max};
[g]n = 10 for C_{min};
[h]n = 14 for CD4+ cell count;
[i]1 patient had VL 50– < 400 copies/mL and 1 patient had VL ≥ 1000 copies/mL; LS, least squares;
CI, confidence interval; C_{min}, minimum plasma concentration;
C_{max}, maximum plasma concentration; AUC_{12h}, area under the plasma concentration-time curve over 12 hours;
SD, standard deviation; PK, pharmacokinetic.

12 hours postdose during the 2nd and 3rd trimesters and postpartum. Total DRV and rtv plasma concentrations were determined using a previously validated HPLC-MS/MS assay (lower limit of quantification 5.00 ng/mL). Unbound DRV was determined by fortifying plasma samples with 14-C DRV and separating total and unbound DRV using ultrafiltration. Total and unbound 14-C DRV were measured using liquid scintillation counting. Total and unbound PK parameters were derived using a noncompartmental analysis. Safety and efficacy were investigated at each visit and summarized using descriptive statistics. Sixteen women (10 black, 4 Hispanic, 2 white) were enrolled; 11 had evaluable PK data. Total DRV AUC_{12h} was 24% and 17% lower during 2nd and 3rd trimesters, respectively, vs postpartum (Table). Unbound DRV AUC_{12h} was unchanged during 2nd and 3rd trimesters vs postpartum. Total and unbound DRV C_{min} increased by 43% and 10%, respectively, during 2nd trimester and by 86% and 14%, respectively, during 3rd trimester vs postpartum. Unbound DRV was above the EC_{50} (27.5 ng/mL) for PI-resistant HIV in all patients. Albumin and α_1-acid glycoprotein (AAG) concentrations were 22%–29% lower during pregnancy vs postpartum. Viral load decreased and CD4+ count increased over time. One serious adverse event was reported (increased transaminase). Three of 12 infants were born prior to 37 weeks (30, 36 and 36 weeks), and all 12 infants were HIV-1-negative by standard PCR testing. Total DRV and rtv PK decreased during pregnancy likely due to pregnancy-related dilution of albumin and/or AAG. No clinically relevant change in unbound DRV AUC_{12h} and C_{min} occurred during pregnancy, and there was no MTCT; therefore no dose adjustment is required for DRV/rtv 600/100mg bid in pregnant women. This ongoing trial will further evaluate the effects of pregnancy on DRV/rtv once daily, etravirine and rilpivirine PK.

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P75

Etravirine concentrations in seminal plasma in HIV-infected patients

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Purpose of the study: Good penetration of antiretroviral drugs to the seminal plasma may be associated with a decrease in viral replication and play an important role in the prevention of sexual transmission of HIV. We present data from a series of HIV-infected ARV-experienced patients receiving etravirine-containing regimens, in whom etravirine concentrations and viral loads were determined in blood plasma and seminal plasma. The objective was to determine etravirine concentrations and HIV-1 viral load (VL) in blood plasma (BP) and seminal plasma (SP) of HIV-infected patients.
Methods: Ten HIV-1 adult antiretroviral-experienced patients receiving an etravirine-containing regimen for at least 1 month were enrolled. Semen and blood samples were both collected around 12–24 h after the last etravirine dose, depending on once-daily or twice-daily dosing, respectively. HPLC/MS/MS was used to determine etravirine concentrations, and HIV-1 VL was determined by real-time PCR (limit of detection, VL 40 copies/mL).
Results: Ten blood and twenty semen samples were collected. Median (range) CD4 count was 502 cells/mm^3 (252–817) and median (range) BP VL was <40 copies/mL (40–362). Median (range) time on etravirine was 52 weeks (12–124). Median (range) BP etravirine concentration was 452.5 ng/mL (258–751). Median (range) SP etravirine concentration was 62.9 ng/mL (31.2–166), and values were above the protein-free IC_{50} range (0.39–2.4 ng/mL) in all cases. Median (range) etravirine SP:BP ratio was 0.16 (0.07–0.26). SP VL was <40 copies/mL in all patients, whereas BP VL was detectable in one patient with poor adherence to treatment.

Patient	SP (ng/ml)	BP (ng/ml)	SP VL (copies/ml)	BP VL (copies/ml)	SP:BP	Concomitant ARV
1	31.2	375	<40	<40	0.08	DRVr/TDF
2*	57.1	307	<40	<40	0.18	3TC/ABC
3*	36.9	506	<40	<40	0.07	TDF/FTC
4*	60.6	399	<40	<40	0.15	3TC/ABC
5	68.1	258	<40	<40	0.26	LPVr/TDF
6*	104	414	<40	<40	0.25	3TC/ABC
7	107	491	<40	362	0.21	DRVr/TDF/FTC
8*	65.3	592	<40	<40	0.11	TDF/FTC
9	52.2	518	<40	<40	0.1	DRVr
10	166	751	<40	<40	0.22	TDF/FTC
Median	62.9	452.5	<40	<40	0.16	

*Patients taking ETR once a day.

Conclusions: Total etravirine concentrations in male genital secretion are modest, reaching only 16% of the BP concentration, but nevertheless, more than 10 times above the wild type IC_{50} range.

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P76

Lack of correlation between UGT1A1*6, *28 genotypes, and plasma raltegravir concentrations in Japanese HIV-1-infected patients

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Background: Raltegravir is metabolized by glucuronidation via UGT1A1. Among the genetic polymorphisms of UGT1A1, the *6, *27 and *28 alleles are associated with reduced levels of UGT1A1. In particular, the *28 allele accounts for most of the UGT1A1 polymorphisms, and the level of UGT1A1 activity has been the focus of most studies. On the other hand, among Asians, the *6 and *27 alleles are more commonly found in comparison with white populations. In this study, we aimed to clarify the contribution of UGT1A1 polymorphisms (*6, *27) to plasma raltegravir concentrations in Japanese HIV-1-infected patients.
Materials & Methods: We analyzed the presence of genotypic variants (*6, *27 and *28) among the 74 patients recruited at the National Hospital Organization Nagoya Medical Center. Genotyping of *6 and *27 in UGT1A1 was performed using the TaqMan drug metabolism genotyping assay. Genotyping of *28 in UGT1A1 was performed using the primers described by Ehmer et al. Plasma raltegravir concentrations were determined by a LC-MS method.
Results: Among the 74 patients, the UGT1A1 genotype in 3 patients (two male, one female) was *6 homozygote. Heterozygous variants were found in 20 patients for *6, and in 14 patients for *28, while all of the patients were found to carry wild-type sequences at the

position corresponding to the *27 allele. The male *6 homozygote patient had modestly higher plasma raltegravir concentration (0.53 μg/ml) than other patients who were wild type (0.12 μg/ml) or heterozygous (0.16 μg/ml) for the *6 polymorphism. The other two UGT1A1*6 homozygote patients had a lower plasma raltegravir concentration (0.03 and 0.05 μg/ml). On the other hand, plasma raltegravir concentrations were 0.12 μg/ml (*6 −/− *28 −/−; n = 37), 0.11 μg/ml (*6 −/− *28 −/+; n = 14), 0.16 μg/ml (*6 −/+ *28 −/−; n = 20). There were no statistically significant differences in the plasma raltegravir concentrations between patients carrying wild-type alleles and those heterozygous for *6 or *28.

Conclusions: Patients heterozygous for the *6 or *28 allele did not display significantly different plasma raltegravir concentrations compared to patients homozygous for the respective wild-type allele. In this study, we showed that heterozygosity for the reduced-function *6 and *28 alleles had no significant effect on plasma raltegravir concentrations in Japanese HIV-1-infected patients.

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P77

Use of antacid preparations with HAART

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Background: Concurrent prescription and consumption of antacid and ulcer healing preparations can affect the absorption of some antiretrovirals (ARV) due to increases in intra-gastric pH and should therefore be avoided in drugs dependent on gastric pH for absorption.

Methods: Questionnaires were given to consecutive consenting patients presenting to outpatient pharmacy who were receiving antiretroviral therapy (ART) which consisted of either atazanavir (TAZ), darunavir (DRV) or efavirenz (EFV) for greater than 1 year. All patients receiving TAZ are routinely advised on the need for caution with co-administration of antacid preparations when they commence the drug. Information was gathered on the awareness of potential interactions between ARVs and antacid/ulcer healing medication and the use of such preparations over the past year. Viral load (VL) data was observed for each patient and any VL blips in the preceding year recorded.

Results: A total of 215 patients were questioned, of whom 30% were aware of interactions between ART and antacids/ulcer healing medication; 38% of patients receiving TAZ, 30% on DRV and 25% and on EFV were aware of the drug interaction. 62% of individuals receiving TAZ were therefore unaware of the need not to receive antacid preparations with this drug. 30% (n = 66) of patients had either been prescribed or bought antacid/ulcer healing medication in the previous year. 16 out of the 215 patients were recorded as having at least one VL blip in the last year; 9 on TAZ, 6 on DRV and 1 on EFV. 7 of these patients had either bought or been prescribed antacids in the previous year. Four of the patients with viral blips on TAZ had taken antacid preparations.

	TAZ	DRV	EFV
n	63	53	99
Aware of interactions with ART	24	16	25
Prescribed PPI/antacid	5	13	9
Bought PPI/antacid	15	15	19

Conclusion: The majority of patients are unaware of potential interactions between ARVs and antacids. However, few patients developed a positive viral load during the period studied. Patients receiving TAZ were not more aware of the potential drug interaction than those receiving other agents. It is essential that information is given to patients at each clinic visit to reinforce interactions between antacids and HAART.

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P78

Darunavir plasma level in HIV overweight patients

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Purpose of the study: Darunavir (DRV) boosted with ritonavir is now regularly used in HIV infection. With an increasing population of HIV-infected patients receiving antiretroviral therapy and having over-weight problems we decided to conduct a transversal study on DRV plasma concentration in overweight patients.

Methods: Measures of drug plasma level were proposed to all patients having their routine blood test between 2010 and 2011 in our outpatient HIV clinic. With their consent they were included in our transversal study. DRV plasma concentrations (C12 h = 12 ± 3 hours) were determined using HPLC coupled with photodiode array detection (limit of quantification 0.05 mg/L), with DRV C12 h = 1.3 mg/L and 0.55 (IC_{50}) as target levels. Weight and height were also measured to calculate body mass index (BMI).

Results: We included 52 patients; 35 women and 17 men, mean age was 40 (±8.8). Majority of them (62%) were African patients. The median CD4 cell count was: 387 [297–551]. The viral load was < 35 copies for 77% of the patients. We had 28 overweight patients: 12 patients had BMI ≥ 30 and 16 patients had BMI between 25 and 29; 87% of the patients had DRV/RTV 800/100 OAD regimen associated with tenofovir/emtricitabine (72%) or abacavir/lamivudine (17%). The mean DRV plasma trough concentrations (C12 h) according BMI are shown in Table 1. Six patients with BMI ≥ 25 had a low plasma concentration of DRV with OAD regimen of DRV/RTV 800/100: 2 in BMI 25–29 group and 4 in BMI ≥ 30 group. Among the six patients no adherence issues was recorded and every patient had undetectable viral load. Only one patient has a C12 h lower than the IC_{50} from the DRV (0.55 mg/L) and 3 others have very probably C_{min} close to the ECC_{50}.

Body Mass Index	< 25	25–29	≥ 30
Number of patients (n)	24	16	12
DRV plasma concentration (mg/L), Means ± SD	3.54 ± 1.60	3.07 ± 1.57	2.58 ± 1.62
Patients with [DRV] C12 h < 1.3 mg/L (n)	0	2	4
Patients with [DRV] C12 h < 0.55 mg/L (n)	0	0	1

Conclusion: Our results show a possible lower plasma concentration of DRV in overweight/obese patients in a small cohort. In our data, this reduced plasma concentration is not related to detectable viral load, possibly due to IC_{min} of DRV. More studies are needed to manage carefully antiretroviral therapy in overweight patients.

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P79

No change of plasma darunavir concentrations by switching from ritonavir soft capsule to tablet

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Background: Darunavir, a second-generation protease inihibitor, is used with a low boosting dose of ritonavir to improve its clinical efficacy. The boosting dose of ritonavir acts as an inhibitor of CYP3A4, thereby increasing darunavir bioavailability. Recently, ritonavir tablet has been on sale in place of soft capsule. However, pharmacokinetic study of darunavir by changing ritonavir form is still not clear. In this study, we aimed to compare with plasma darunavir concentrations by switching ritinavir soft capsule to tablet in Japanese HIV-1 infected patients.
Methods: We analyzed 34 Japanese HIV-1 infected patients (32 males: 2 females) recruited at the National Hospital Organization Nagoya Medical Center. All patients had been administered with 800/100 mg darunavir/ritonavir once daily in combination with other antiretrovirals. Plasma darunavir concentrations were determined by an HPLC method. A pared t-test was used to compare with their concentrations by switching from ritonavir soft capsule to tablet.
Results: The mean of age, body weight, and duration of antiretroviral therapy for 34 patients were 41.9 (range: 24–62) years, 66.3 (range: 51.4–90.0) kg, and 436 (range: 182–739) days, respectively. The mean ± SD darunavir concentration was 3.44 ± 1.78 μg/ml when ritonavir soft capsule was co-administered. After switching to ritonavir tablet, the mean ± SD darunavir concentration was 3.30 ± 2.02 μg/ml. Statistical difference was not found in plasma trough darunavir concentration between ritonavir soft capsule and tablet ($P = 0.826$). On the other hand, the mean of viral load was 78 copies/ml when ritonavir soft capsule was administered. After switching to ritonavir tablet, the mean viral load was 33 copies/ml.
Conclusion: Recruited all patients have been sustained an ndetectable viral load (less than 40 copies/ml) after switching to ritonavir tablet. In this study, switching to ritonavir tablet had no significant difference on plasma darunavir concentrations in Japanese HIV-1 infected patients.

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P80

Determination of rilpivirine (TMC-278) plasma concentrations by the conventional LC-MS method

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Background: Rilpivirine (TMC-278) is a second-generation NNRTI that is highly potent against both wild-type and drug-resistant HIV-1 strains. The quantification of rilpivirine in human plasma is important to support clinical studies and determine pharmacokinetic parameters of rilpivirine. Until now there has been a methodological report for the determination of rilpivirine using LC-MS/MS. However, the MS-MS detector needs to be delicately set and it is expensive. To bypass these difficulties, we aimed to develop more conventional procedures for determining rilpivirine plasma concentration by LC-MS method.
Methods: A Waters Alliance 2695 HPLC and a Micromass ZQ-2000 MS, controlled with MassLynx version 4.0 software, were used for detection. Our method involves rapid liquid-liquid drug extraction from plasma and use of gradient elution on a reversed-phase C18 column. The mobile phase comprised 0.1 mM EDTA in 0.1% acetic acid (65%), acetonitrile (15%), and methanol (20%). Quantitative analysis detected rilpivirine at m/z 367, and the internal standard, at m/z 313, all in the form of ions.
Results: The established LC-MS method was validated by estimating the precision and accuracy for inter- and intraday analysis in the concentration range of 18–715 ng/ml. The calibration curve was linear in this range. Average accuracy ranged from 100.0 to 100.6%. Relative standard deviations of both inter- and intraday assays were less than 3.3%. Recovery of rilpivirine was more than 82.0%.
Conclusions: Our newly developed LC-MS method achieves the same level of reproducibility and accuracy as the LC-MS/MS method. Our method provides a conventional, accurate and precise way to determine rilpivirine in human plasma. This method can be used in routine clinical application for HIV-1 infected patients, and permits management of drug interactions and toxicity for rilpivirine.

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P81

Interaction of antiretroviral medications with finasteride

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Antiretroviral medications are known inhibitors and inducers of cytochrome p450 enzymes and can affect levels of non-HIV medications. Finasteride 1 mg (Propecia), which prevents the conversion of testosterone (T) to dihydrotestosterone (DHT) is commonly prescribed for prevention of hair loss. This medication is a substrate of p450 3A4. Its efficacy may therefore be affected by HIV medications which induce or inhibit this enzyme. Levels of DHT to prevent hair loss are not well established, but likely need to be <15–20 ng/dl, or a DHT/T ratio of <0.02. Observational analysis in a private practice, measuring DHT and T levels in patients on finasteride and various antiretrovirals 21 patients were identified. 7 patients were taking protease inhibitors and had DHT levels <12 ng/dL; DHT/T <0.20. Three of these patients decreased their finasteride dose to 1 mg every-other-day and still have DHT <10. 8 patients were taking potent p450 inducers (efavirenz or etravirine) and had DHT levels between >20; DHT/T >0.025. Two of these patients increased the dose of finasteride to 2 mg/day and subsequently decreased DHT to 14 and 17. Two additional patients on efavirenz, however, had DHT levels of <15 without dose adjustment. Four patients taking nevirapine, a less potent inducer of p450 had DHT levels of <15, as did one patient on raltegravir, which does not affect CYP450. Antiretrovirals that affect CYP 3A4 may interact with finasteride. While it is unlikely that this interaction is dangerous, it may affect its efficacy of the finasteride. Evaluation of DHT/T levels, and/or dose adjustment of finasteride may be appropriate in men being treated for HIV.

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P82

Potential drug-drug interactions in HIV-infected children on highly active antiretroviral therapy in Lagos, Nigeria

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Objective: Multiple therapies are common in HIV-infected children on highly active antiretroviral therapy (HAART). These children are at

risk for clinically significant drug interactions (CSDIs). While CSDIs are under-recognized in developed countries, data are lacking for developing African countries. We aimed to investigate the prevalence of CSDIs between antiretrovirals (ARVs) and co-prescribed drugs for children attending a large HIV clinic in Lagos, Nigeria.
Methods: We retrospectively assessed the risk for clinically significant drug interactions in children on HAART. Of the 417 patients enrolled for treatment, 80 were eligible for inclusion. We defined CSDIs as 'major' (capable of causing severe or permanent damage, contraindicated, avoid or not recommended by the manufacturer, or requiring dose modification) or 'moderate' (manufacturers advise caution, or close monitoring, or capable of causing clinical deterioration).
Results: A total of 60 (75%) patients were at risk for a CSDI resulting in major interactions in 13 (16.3%) patients and could potentially lower the plasma concentration of antiretroviral drugs in 9 (15%) patients. Major interactions most frequently involved rifampicin in 9 (11.3%) patients and artemisinin combination therapies (ACTs) in 8 (10%) patients whereas moderate interactions frequently involved ACTs (48.8%), fluconazole (36.3%), and rifampicin (11.3%). Age ($p = 0.392$), gender ($p = 0.813$), and moderate ($p = 0.692$) or severe ($p = 0.788$) malnourished state of the children were not associated with risk for CSDIs.
Conclusions: Three-quarters of children receiving ARV drugs are at risk for CSDIs. Strategies are needed to be put in place to prevent important drug interactions and to manage unavoidable interactions.

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P83

Moderator effect of CYP2B6 genotype in HIV-1 patients with tuberculosis treated with rifampicin and efavirenz

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Efavirenz (EFV) is the preferred non-nucleoside reverse transcriptase inhibitor component of the ARV regimen in HIV-TB patients. Concomitant use of EFV with rifampicin (RIF), an important component of first-line tuberculosis treatment, induces various hepatic cytochrome P450 enzymes and is known to decrease EFV plasma concentrations in healthy volunteers and HIV-1 patients and EFV plasma concentrations below 1,000 μg/mL have been associated with an increased risk of virological failure [1]. Moreover, previous studies have shown that inter-individual variability in EFV plasma concentrations are associated with the presence of allelic variants in CYP2B6 gene. Carriers of the T allele of polymorphism 516 G > T are reported to be associated with slower EFV oral clearance. The aim of our study was to determine the influence of CYP2B6 genotype in EFV levels in HIV patients with TB treated with RIF. Four HIV patients who started ARV treatment concomitantly with TB treatment were analyzed. These patients started a regimen based on EFV at doses higher than standard due to RIF interaction. Viral load, CD4+ cell count and plasma levels of EFV in plasma were measured at each visit, and genotyping for CYP2B6 (516G > T) polymorphism were performed. The self-reported rates of adherence to HAART were very high. One patient, who had TT genotype, required progressive dose reduction by toxic levels (C_{min}: 20 μg/mL) and effects on the central nervous system. Dose was adjusted to 600 mg qd despite treatment with RIF, and he required even lower doses after completion of TB treatment, 400 mg qd. Two other patients with non-mutated genotype (GG) required dose escalation up to 1000 mg qd to achieve minimum recommended EFV concentrations between 1 and 4 μg/mL. All of them achieved virological suppression at six months. The fourth patient, who had non-mutated genotype, required dose increases for several months until dose adjustment. He needed 1600 mg qd during treatment with RIF. He presented virological failure, likely to maintain infratherapeutic levels of EFV for several months. Our study shows that the variability in EFV pharmacokinetic behaviour justifies the use of therapeutic drug monitoring (TDM) in situations in which there are potential interactions with other drug. Also, it is recommended to know CYP2B6 genotype in patients receiving HIV-TB to predict their metabolizing behaviour. TDM in clinical practise continues to be the best tool for optimizing the dosing of EFV.

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COMMUNITY INITIATIVES

P84

A randomized controlled trial of a web-based psychological intervention for patients under treatment for chronic HIV infection

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Purpose of the study: One of the most prevalent mental conditions in people with HIV is depression as uniquely characterized by low positive affect. This study examined the effect of a web-based intervention (Avanti) on overall mood and depressive symptoms among patients with HIV infection.
Methods: Patients treated with effective antiretroviral treatment were included in a two-armed trial with substance abuse as an exclusion criterion and randomized to Avanti ($n = 36$) or control ($n = 31$). Patients were surveyed at baseline, as well as 1 and 3 months after the initiation of a 5-week intervention period. Outcomes were Center for Epidemiological Studies-Depression scale and the Positive and Negative Affect Schedule which was combined into an overall mood index. Changes within groups were tested by Wilcoxon matched pairs test and baseline differences between groups by chi-square and Mann-Whitney independent samples test.
Summary of results: Baseline scores for both groups were similar. However, patients in the intervention group had an improvement in median (M) overall mood from baseline ($M = 67.6$) to 1 month ($M = 71$, $p = 0.02$) which was also maintained from 1 to 3 months ($M = 71.9$). Moreover, these patients had a favorable reduction in negative affect from 1 ($M = 24$) to 3 months ($M = 22$, $p = 0.01$) and a transient improvement in positive affect from baseline ($M = 31.7$) to 1 month after intervention onset ($M = 35$, $p < 0.01$) which almost returned to baseline levels at month 3 ($M = 32$, $p = 0.01$). In contrast, no significant changes were observed within the control group, except for a reduction in negative affect from 1 ($M = 23$) to 3 months ($M = 21.6$, $p = 0.05$). Notably, symptoms of depression at baseline were low in both the Avanti ($M = 13$) and control ($M = 12$) groups, possibly explaining why no further reduction in depression was observed from baseline to 3 months in either of the two groups.
Conclusions: The results of this study lend support to the promise of a web-based psychological intervention among patients with HIV and

its ability to improve overall mood with favorable intervention-related changes in negative and positive affect. Avanti had no effect on depression but this was probably due to low initial symptoms of depression. The findings suggest that a prolonged web-based intervention with regular contact could maintain the positive effects on mood seen in this study. If so, Avanti could potentially provide an easily accessible and cost-effective adjunct to traditional psychotherapy.

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P86

When doctors come to prison – a pilot project for better HIV care in correctional facilities

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Recent rearrangements in national policies regarding follow-up of HIV-infected inmates have determined that hospitals closest to the prison facility be responsible for their care. Our HIV Unit and the two prison facilities in the area have established a clinical protocol whereby a clinical team goes to the prisons for blood collecting and visits instead of having the inmates transported to the hospital. The purpose of the protocol, from a clinical point of view, was to: (i) promote adherence to blood tests and clinical visits; (ii) promote adherence to antiretroviral (ARV) therapy; (iii) facilitate ARV administration by promoting once-daily-dosing. This retrospective review looks back at the first year of protocol implementation between the HIV Unit of HPP Cascais Hospital and the prisons of Tires and Linhó. The purpose of this study is to characterize the demographics of our inmate population; assess the number of inmates on ARV and describe the regimens as PI- or NNRTI-based and as once- or twice-daily dosed; evaluate ARV efficacy by HIV viral load undetectability; and assess opportunity for ARV switch from twice- to once-daily dosing. From April 2011 until June 2012 a total of 53 inmates were included in this protocol. The majority of patients were female (55%) as one of the prisons is mainly for female inmates. The median age is 36 years (from 23–59). The average time of follow-up was 11 months (15 months maximum). From the total of 53 patients under study, 40 are currently under care, the other 13 having been released or transferred to other prison facilities. The majority of these patients are on ARV therapy (83%). By the end of follow-up time 88% of patients were on a once-daily dosed regimen; these are PI-based in 69% and NNRTI-based in 31%. At their last evaluation, 32/33 patients on therapy had undetectable HIV viremia (97%). As a conclusion, we assess that this protocol implementation has benefitted all parts: patients assure regular laboratory and clinical follow-up, and avoid constraintful displacements to the hospital; prisons guarantee regular specialized medical assistance to inmates and save on multiple trips to the hospital; finally, the clinical team is rewarded with 100% adherence to visits and therapy, which is evident by 97% viral load undetectability. The major constraint found in this protocol was the difficulty in providing adequate discharge planning and linkage to care in the community due to frequent unannounced release of inmates.

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P87

Late presentation for HIV diagnosis: a single-centre experience

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Purpose of the study: Antiretroviral therapy reduces mortality and morbidity in HIV-infected individuals, most markedly when initiated early, before advanced immunodeficiency has developed. All international guidelines (IAS 2010, EACS 2011, DHHS 2012) tend to recommend starting ART in patients with high CD4 cell count. Some challenges need to be met before reaching this goal, particularly HIV-infected patients with late presentation-diagnosis. The objective of this study was to determine the frequency of and demographic features associated with delayed presentation to care in our centre.

Methods: All patients, newly diagnosed with HIV between January 2007 and December 2011 and on follow-up in our AIDS Reference Centre, were included. 'Late presenter patient' was defined as patient with CD4 count $<350/mm^3$ at the time of diagnosis. Demographic (age, sex, ethnicity, migration) and clinical characteristics (transmission, CD4 cell count, viral load, CDC stage) were collected. We then compared these features with those identified in our centre between 1997–2006.

Summary of results: Of the 601 patients diagnosed between 1997–2006, 57.1% were late presenters for HIV diagnosis. Among the 359 patients included between 2007–2011, 42.9% patients were late

Abstract P87–Table 1. Characteristics of patients with late presentation (CD4 $<350/mm^3$) for HIV diagnosis between 2007–2011

	n total	n (%)			
Total	**359**	**154 (42.9)**	**p value**	**OR (95% CI)**	**Adjusted OR (95% CI)**
Age, years					
< 30	64	21 (32.8)		1.00	1.00
30–39	135	52 (38.5)		1.28 (0.68–2.40)	1.27 (0.66–2.44)
40–49	95	41 (43.1)		1.55 (0.80–3.01)	1.66 (0.83–3.32)
> 50	65	40 (61.5)	<0,001	3.27 (1.59–6.74)	2.84 (1.25–6.41)
Sex					
Female	103	54 (52.4)		1.00	1.00
Male**Origine**	256	100 (39)	0,021	0.58 (0.36–0.92)	0.92 (0.48–1.75)
non-migrant	141	45 (31.9)		1.00	1.00
Migrant	218	109 (50)	<0,001	2.13 (1.37–3.32)	1.70 (1.02–2.83)
HIV transmission					
MSM	164	49 (29.8)		1.00	1.00
Heterosexual	191	102 (53.4)	<0,001	2.68 (1.73–4.17)	1.84 (0.99–3.41)

presenters. Demographic characteristic are summarized in Table 1. In the univariate analysis, patient age >50 years, female sex, immigrant status and heterosexual contact were associated with late presentation for HIV diagnosis. In the multivariate analysis, patients aged >50 and migrant women were the only independent risk factors for late presentation. Except gender, other risk factors remain identical to those that were identified in our centre between 1997–2006 [1].

Conclusion: A considerable proportion of patients continue to be diagnosed with advanced HIV disease, despite the fact that risk factors for late presentation have been identified clearly. In order to be able to treat all patient at high CD4 cell counts as recommended in all guidelines, we need to develop policies focused directly to categories of people at high risk of late presentation.

Conflict of interest: None. All co-authors have participated in, and agree with the content and conclusions. This work is original and does not infringe any copyright.

Acknowledgement: A. Sasse, Institut de Santé Publique, Belgium

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P88

The SHE programme: a European initiative to improve the care of women living with HIV

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Purpose of the study: In Europe, the number of women living with HIV is increasing, but data are limited and guidelines scarce. HIV care poses unique challenges for women living with HIV and their healthcare providers. The SHE programme is a response to these unmet needs. SHE supports women living with HIV to feel empowered to get the most from their healthcare services and provides education to healthcare providers. The objective of SHE is to improve the quality of life of women living with HIV.

Methods: SHE is run by a community faculty and a scientific faculty. Both faculties include women living with HIV and healthcare professionals. SHE scientific faculty reviewed available data pertaining to HIV in women. Data gaps were validated and prioritised at a scientific meeting held in June 2011, attended by 80 invited delegates from 13 European countries. SHE community faculty held advisory workshops to examine the challenges faced by women living with HIV. Following these activities, medical and community toolkits have been developed. To integrate scientific and community activities, 'SHE units' are being launched at specific sites. Each SHE unit will be a multidisciplinary team working to improve and promote best clinical practice.

Summary of results: The scientific faculty identified five key topics: 1. situation of women with HIV in Europe; 2. challenges of testing; 3. antiretroviral treatment (ART); 4. women with HIV of childbearing age; and 5. long-term treatment. The highest priority gaps were guidance on the management of women living with HIV, coordination of registries of ART in pregnant women, and more gender-specific data. An educational 'medical toolkit' has been developed including an overview of current data on these topics and a summary of continuing data gaps. A peer support toolkit has been developed for women living with HIV who wish to facilitate peer support sessions. The toolkit includes topics such as diagnosis, accessing healthcare, relationships, and HIV treatment, and was launched at the 2011 IAS Conference. The toolkit is online at http://www.shetoshe.org and being translated into seven European languages. SHE units have been established in France, Germany and Portugal. Additional units are planned across Europe.

Conclusions: SHE is a successful ongoing programme providing education and support in clinical and community settings to improve the care of women living with HIV. SHE is integrated to reflect both patient and physician perspectives.

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P89

What's the buzz about BUZZ? A workshop to enhance communication between patients and their health care teams

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Objective: BUZZ is a workshop designed to enhance communication between patients and health care providers (HCPs) and results to date will be described.

Background: A study of HIV patients interviewed about their treatment, identified several barriers to communication with their health care teams. Another study called BEAHIV, demonstrated low levels of agreement between patients and HCPs surrounding bothersome symptoms of ARV treatment. With a grant from Janssen, a workshop was designed by a faculty of HIV clinicians from across Canada, in conjunction with a behavioural specialist. The workshop covered several topics: identifying barriers to communication for HIV patients, learning about one's own preferred communication style, how to determine a patient's communication style, and ways to uncover issues associated with the patient's treatment, such as ARV-associated side effects. To date, 15 workshops have been conducted across the country.

Results: At the end of the workshop, 85% of participants said they would start or continue to identify barriers to communication. At the start of each workshop, several before/after questions were asked. Only 45% of HCPs felt comfortable in adapting their communication towards patients with different behavioural styles prior to participating in the workshop. This increased to 84% after the workshop. Prior to the workshop, 68% of HCPs said they currently engage patients in proactive discussions surrounding ARV-associated side effects, increasing to 82% post-workshop. Prior to the workshop, 60% proactively engaged patients on the impact of ARV side effects on quality of life, which increased to 80% post-workshop. Several weeks after each workshop, a follow up with participants was conducted and it was found that many implemented changes in their practices as a result of what they learned.

Conclusion: A workshop designed to enhance communication may have a beneficial effect on reducing communication barriers and enhancing HIV patient care.

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P90

Prevalence of HIV 2: A retrospective study from a HIV/AIDS consult

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The western Africa is the origin of the HIV2 infection where Guinea Bissau has been the country where the rate of infection is higher. This infection have extended to Europe through the relationship established between European countries and there African colonies in the past. At 2010, 1.295 cases of HIV 2 infection were notified in Portugal, which represents nearly 3.3% of all HIV infections. Almost 510 of these cases are classified as AIDS. Although the majority of notified cases is from African patients there is still a significant contribution of the Portuguese people in these numbers. Retrospective analysis of HIV2 infected women and men followed at Faro's Hospital HIV/AIDS consult between January 1992 and June 2012. In this sample were included every patient older than 15 years and were excluded every patient than haven't been at the consult for a period superior to 18–24 months. Deceased patients and address change were also exclusion factors. Of all 1500 patients followed in consult, 35 of them were infected with HIV2 (2.3%); 18 women and 17 men. There were 3 patients that were co-infected with HIV1 and HIV2. Mean age were 52.9 years. 19 of the infected patients were leucodermic and 16 were melanodermic. The majority of patients (19 cases) were Portuguese. The rest of them were from Africa where Guinea Bissau were the only country represented. In opposition to the HIV1 infection, the sexual transmission is by far the more common way of being infected. There's no case of vertical transmission known in our population. At the first contact, the majority of patients appear asymptomatic (16 cases) while a minority (4 cases) manifest themselves by AIDS. There is an AIDS case that result from HIV1 and HIV2 co-infection (only one intravenous drug user in the group). The more common treatment is the association of NRTI and PI. The HIV2 infection is characterized by a longer clinical evolution when compared to the HIV1 infection. That fact explains why the mean age of patients is higher in the first case. This study shows that there isn't a gender incidence difference between men and women. Despite what happens at a national level, at local level the HIV2 infection is more prevalent among patients born in Portugal. It's important to notice that the HIV1 and HIV2 co-infection is rising and that leads to some questions like viral synergism with consequent rapid disease progression.

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COST-EFFECTIVENESS

P91

Cost of switching darunavir + ritonavir (DRV + RTV) to lopinavir/ritonavir (LPV/r) in HIV-1-infected treatment-na ve women of child-bearing age (WOCBA)

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Guidelines consider LPV/r a preferred protease inhibitor for use during pregnancy. When an HIV-infected woman receiving DRV + RTV becomes pregnant, a switch to LPV/r may be warranted. The budget implications of proactively initiating LPV/r versus initiating DRV + RTV and then switching has not been examined. A cost-minimization analysis was performed from the US healthcare perspective for HIV-1-infected, treatment-naïve WOCBA comparing: initiating LPV/r in all patients versus initiating DRV + RTV and switching to LPV/r when pregnant. A discrete event simulation was employed to represent antiretroviral (ARV) therapy management. Healthcare utilization and clinical trial data [1] were used to model pregnancy rates [2], ARV regimen switch rates, and impact of treatment as a function of CD4-cell count and viral load, adherence, treatment response, acquired resistance mutations, and ensuing treatment changes. Five- and 10-year costs incurred due to ARV therapy, clinician visits and management of AIDS-related, non-AIDS related, and cardiovascular events were estimated. Base-case analysis assumptions: switching to LPV/r can occur only once at first pregnancy, 30% of WOBCA switch to LPV/r circa time of pregnancy, and women's adherence to medication improves by 15% when becoming pregnant. Sensitivity analyses varied the rate of switching to LPV/r at time of pregnancy, pregnancy rates, adherence improvement, and healthcare costs. Daily drug cost of LPV/r + TDF/FTC was $56.59 while DRV + RTV + TDF/FTC was $73.89. Costs were discounted at 3% per annum. Survival was similar in both groups. Five- and 10-year total healthcare costs of ARV-naïve HIV-positive WOCBA who initiate LPV/r were $108,200 and $192,600 per patient, respectively, compared to $132,200 and $234,400 when women initiated DRV + RTV and then 30% switched to LPV/r. Initiating with LPV/r resulted in 5- and 10-year savings of $24,000 and $41,800 per patient, respectively. If 100% of patients who initiated with DRV + RTV switched to LPV/r upon pregnancy, the savings per patient were $21,300 at 5 years or $33,140 at 10 years, since a greater number of patients switch to the less expensive LPV/r. Sensitivity analyses showed that initiating with LPV/r was always cost-saving relative to DRV + RTV. Initiating HIV-infected, treatment-naïve WOCBA on LPV/r was cost-saving compared to initiating DRV + RTV. Limitations of the analysis include the uncertainty of long-term outcomes projections driven by short-term clinical trial endpoints.

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P92

Cost-efficacy analysis of darunavir/r monotherapy in clinical practice

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Purpose of the study: To evaluate the economic impact of a swiching strategy to DRV/r mx in clinical practice using Spanish prices.
Methods: Multicenter retrospective study of four tertiary hospitals in Spain. The analysis includes 147 patients switching to DRV/r mx mainly due to toxicity or simplification from March 2009 to June 2011. The Spanish costs (ex-factory price + VAT) per patient with HIV RNA < 50 copies/ml were calculated, accounting for additional/switch antiretroviral taken after initial treatment failure and management of adverse events. Cost of adverse events were based on

a Spanish publication [1] (updated by the inflation rate until april 2012) The horizon of the analysis was of 48 weeks.
Summary of results: Baseline characteristics were: women (30.6%), median age (49 yr), IDU (45%), AIDS stage (32%), HCV coinfected (48%, 40% with advanced fibrosis), length of HIV-RNA <1.7 before DRV/rtv mtx 67.6. Most frequent reasons for switching to DRVr mx were toxicity (62.6%) and simplification (23.8%). If a hospital with 600 patients in ART treatment, switched from 10% to 20% of its patients to DRV/r mx, there is a potential to save up to 448,000€/year.
Conclusions: Switching to DRV/r mx is a cost-effective strategy that allows more patients to be treated for a fixed budget. Higher cost saving is expected when toxicity is the reason for switching.

Abstract P92–48 Weeks Cost-Efficacy analysis: Simplification strategy to DRV/r monotherapy

	Baseline HAART	DRV/r Monotherapy	Difference
Mean cost per patient (ARV)	8.471€	5.773€ -	2.698€
Mean cost per patient (AEs)	70€	5€ -	65€
Total Mean cost per patient*	8.541€	5.778€ -	2.762€
Number treated for 1,000,000	117	173	56
% HIV RNA <50 copies/ml (OTT)	93,10%	93,10%	0,00%
Cost per success	9.174€	6.207€ -	2.967€
Number of success	109	161	52
ICER (Incremental Cost Efficacy Ratio)			Dominated

*Includes ARV and AEs treatment costs.

Hospital Budget Impact Analysis: assuming that 10%–20% of 600 patients in ARV treatment simplifies to DRV/r monotherapy

	% of patients that Switches to DRV/r monotherapy		
	10%	**15%**	**20%**
Number of patients in ARV treatment	600	600	600
Number of patients in DRV/r Monotherapy	60	90	120
Before Switch: 1 year cost	512.441€	768.662€	1.024.883€
After Switch: 1 year cost	346.698€	520.048€	693.397€
Total Cost Saving	165.743€	248.614€	331.486€

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P93

Cost-efficacy of European AIDS Clinical Society-recommended initial antiretroviral regimens for treatment of HIV infection in Portugal

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Purpose of the study: Guidelines are based on clinical trial data as well as expert opinion and do not reflect economic considerations. Cost-efficacy analysis of recommended regimens allows for a ranking which takes into account both clinical and economic considerations. The aim of the present analysis was thus complement the information provided by the EACS (v6) guidelines regarding recommended initial treatment for HIV-1 infection.
Methods: The methodology used was that described in Blasco et al. 2011 [1], but applied to Portugal in terms of (i) resource prices, (ii) resource utilization upon ART initiation, regimen switch and treatment of adverse events, and (iii) subsequent regimen selection according to the initial regimen and the reason for switch. Regarding costs, the payer (National Healthcare Service) perspective was considered taking into account only differential direct costs. The time horizon was 48 weeks.
Summary of results: In this analysis, efficacy ranged from 66% with ABC/3TC+LPV/r to 86% for TDF/FTC+RAL. TDF/FTC+NVP was the least expensive regimen both in terms of the 48 weeks' cost of the initial regimen and in terms of the total 48 weeks' costs (i.e., including sequential therapy and other direct medical costs) (7,592€). Nonetheless, once cost and efficacy are considered simultaneously,

TDF/FTC + NVP ranks third (11,419€), ABC/3TC + EFV ranks second (11,073€) and TDF/FTC + EFV (also available, in a single tablet regimen) ranks first (10,888€) indicating that this is the regimen yielding the lowest cost per suppressed patient. Among regimens containing boosted protease inhibitors, TDF/FTC + DRV/r was the regimen with the lowest cost/efficacy ratio (13,020€) and TDF/FTC + ATV/r had the highest ratio (15,102€).
Conclusions: Viral suppression is a relevant efficacy outcome not only due to individual benefits but also from a public health perspective. In this analysis, TDF/FTC + EFV was the initial ART regimen with the lowest cost per suppressed patient at 48 weeks.

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P94

Budget impact analysis of introducing the new single-tablet regimen rilpivirine/emtricitabine/tenofovir for the treatment of HIV in Portugal

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Purpose of the study: Rilpivirine/emtricitabine/tenofovir (RPV/FTC/TDF) is a new single-tablet regimen (STR) approved for the initial treatment of HIV-1 infection. The aim of this study was to estimate the impact on the State Budget of this new STR introduction in the Portuguese Health System (PHS) using secondary data from official statistics and observational studies.
Methods: The analysis considers a time frame of three years, does not include mortality, assumes a constant flow of new patients, and deals only with antiretroviral therapy (ART) costs. Values are not discounted. The stock and flow data of total HIV-1 patients comes from official statistics from the National Committee for HIV/AIDS. The model starts with recent historical data on the percentage of different ART drugs used for the treatment of naïve patients. Estimates from an observational study also provide 1) the probability that a patient in a given regimen switches to another therapy and 2) the probability distribution for the new therapy choices given that the patient has switched. The penetration of the new STR is also linked with the prevalence of adverse effects of other ART, in particular teratogenic effects, central nervous systems effects and possible interactions with methadone. The distribution of patients according to ART drug, together with price information, allow us to estimate average costs of treatment per year and per patient for each class of ART. Estimates of patients' numbers for the second and third years assume the same inflow as in the first year, a given annual percentage of non-switchers from RPV/FTC/TDF and additional flows from patients switching to non-nucleoside reverse transcriptase inhibitors from other third-agent classes.
Summary of results: The model predicts a flow of 245 new naïve patients on RPV/FTC/TDF per year, with 209 and 194 of these patients staying with RPV/FTC/TDF in the second and third years, respectively. Given that the average cost of treatment is lower in the scenarios with RPV/FTC/TDF (because the percentage of patients on the more expensive PI class are lower), the overall budget impact consists in savings of about €2.3 million.
Conclusions: The introduction of the new STR RPV/FTC/TDF in the PHS will lead to cost savings in the resources spent on the anti-retroviral therapy of HIV-1.

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P95

Budget impact analysis of switch to darunavir/ritonavir monotherapy in Greece

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Background: In virologically suppressed patients, simplifying to darunavir/ ritonavir (DRV/r) monotherapy maintains HIV RNA suppression and could lower treatment costs. Monotherapy is mentioned as an alternative treatment option in the Greek therapeutic guidelines (posted in the Greek Health Authority website), even though it is not included in the label of darunavir or any other PI.
Methods: In the MONET trial 256 patients with HIV RNA < 50 copies/mL and no history of virological failure on HAART were switched to DRV/r 800/100 mg once daily, either as monotherapy (n = 127) or with 2NRTI (n = 129). The three-year analysis of the MONET trial was used to calculate the overall nationwide cost of switching to DRV/r monotherapy in Greek patients. We used a 'switch included' analysis at Week 144 to account for additional antiretrovirals taken after initial treatment failure. Published Greek hospital prices of antiretrovirals were used in this analysis. Data from a local expert panel were used to estimate the number of patients currently receiving NNRTI versus PI-based treatment in Greece, and the number of patients eligible for DRV/r monotherapy.
Results: In the ITT switch included analysis, HIV RNA < 50 copies/mL by Week 144 was 86.1% versus 84.3% in the DRV/r monotherapy and control arms. No patients developed resistance to DRV as measured by virtual phenotype. Before the trial, the mean annual cost of antiretrovirals was €5,625 for patients on NNRTI-based HAART, and €6,935 for patients on PI-based HAART. The mean per-patient cost in the monotherapy arm was €4,514 in the MONET trial (including the cost of intensification with NRTIs where needed): this annual cost of antiretrovirals was €1,111 lower (20%) than NNRTI-based treatment, and €2,421 (35%) lower than PI-based treatment taken before the trial, respectively. According to the local expert panel feedback 5,230 people are treated with antiretrovirals in Greece (40% NNRTI-based, 60% PI-based) and 20% of patients (n = 1,046) are eligible for PI monotherapy. Based on the MONET results, a switch to DRV/r monotherapy in 20% of patients could reduce the three-year cost of antiretroviral treatment for these patients, from €20.11 million to €14.26 million.
Conclusions: Based on the MONET trial results, if the 1,046 eligible patients were to switch to PI monotherapy the lower cost of DRV/r monotherapy versus triple therapy in Greece would allow a potential saving of up to €5.85 million over three years.

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P96

Cost-effectiveness analysis of first-line HAART

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Combining various antiretroviral agents into one single pill (STR, single-tablet regimen) is a strategy to reduce pill burden, enhance adherence and improve efficacy of HAART. We evaluated STR from a cost-effectiveness point of view in a large, unselected cohort of patients starting their first HAART. The incremental cost-effectiveness analysis was carried out by means of a Markov model simulating QoL and costs for a patient, according to the given regimen, through 1-year cycles. The considered outcome measure was quality-adjusted life years (QALYs) and all direct health costs were computed. From January 2006 to January 2012, 793 naïve patients started their first regimen at our center and were included in the analysis. They were mostly males (74.5%) with a mean age of 39 years, a baseline mean HIV-RNA of 200K copies/ml and a mean baseline CD4 count of 292 cells/μL. We adopted several definitions to describe STR use trying to reflect the clinical indications of single-tablet regimens: a) any EFV-based regimen followed by STR treatment; b) TDF + FTC + EFV followed by STR; c) any HAART regimen followed by STR; d) use since the beginning of STR. We run the analysis for each of these different STR treatment definitions and compared the results with those of two different control groups: patients receiving a PI-based OD treatment or patients receiving a PI-based BID treatment. For the considered definitions of STR, the mean year-cost per patient ranged from 6,766 to 7,083€ with a mean per patient QALYs ranging from 0.955 to 0.973. In the case of OD PI-based regimens the cost range was from 8,484 to 8,532€ and the QALYs mean varied from 0.923 to 0.925. The same values for BID PI-based regimens were from 8,040 to 8,303€ and from 0.930 to 0.931. In all cases STR dominated (i.e. was more effective and less costly) any comparator HAART regimen. The incremental cost-effectiveness ratio (ICER) values comparing the different STR definitions are reported in the table. STR compared to boosted PI-based regimens either OD or BID resulted highly cost-effective showing in any case the lowest cost and the best efficacy as measured by QALYs. The comparison of different strategies including STR use revealed that starting with an STR regimen is cost-effective compared to simplification strategies, assuming a commonly internationally accepted threshold of 50.000€ to define cost-effectiveness.

Abstract P96

Treatment	C Mean cost per patient	E Mean QALYs per patient	Delta C Delta Cost	Delta E Delta QALYs	DC/DE ICER QALYs
OD EFV - based HAART? switch STR	€6.766	0,960			
Start with STR	€7.083	0.973	317	0,013	€23.770
TDF + FTC + EFV? switch STR	€6.867	0,961			
Start with STR	€7.083	0,973	216	0.012	€17.783
Any HAART? switch STR	€6.947	0,955			
Start with STR	€7.083	0,973	136	0,018	€7.555

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P97

Cost-effectiveness of atazanavir + ritonavir (ATV + RTV) vs. lopinavir/ritonavir (LPV/r) in women of childbearing age in the United Kingdom

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Purpose of the study: In the UK, an increasing proportion of individuals with HIV are women of childbearing age (WOCBA). Literature on the potential effects of antiretroviral therapy (ART) on certain risk factors for coronary heart disease (CHD), such as total cholesterol (TC), has not differentiated the reported ART-associated risk by other risk factors for CHD (e.g. age and gender). Given the different age-specific CHD risk estimates for men and women, particularly the low risk of CHD in WOCBA, the cost-effectiveness of LPV/r vs ATV + RTV specifically among WOCBA warrants examination. Therefore, the objective of this study was to perform a cost-effectiveness and budget impact analysis of two first-line protease inhibitor-based regimens, LPV/r versus ATV + RTV, among HIV-infected, ARV-naïve WOCBA in the UK.

Methods: A modified version of a previously published Markov model was utilized [1]. CHD risk estimates were based on the Framingham risk score. Baseline assumptions were that 33% of women were smokers with a mean age of 25 years. Guidelines regarding therapeutic drug monitoring among pregnant women in the 3rd trimester who receive ATV + RTV were incorporated [2]. Age-specific pregnancy rates were estimated in order to determine ARV utilization during gestation. The model employed a lifetime horizon under a NHS perspective and a discount rate of 3.5%. Costs were presented in 2011 GBP.

Summary of results: The model predicted no appreciable difference in quality-adjusted survival (in terms of QALYs) between the two regimens over a lifetime (0.2 days in favor of ATV + RTV) and an increased cost of £3,003 per patient on the ATV + RTV regimen. Cost savings of £1,977 over 5 years and £2,916 over 10 years were predicted for patients who initiated LPV/r. Furthermore, for every 100 patients started on LPV/r, the savings accrued after one year allow for the treatment of 6 additional patients. After 10 years, the number of additional patients that can be treated accumulated to 42. The model predicted a mean of 1.4 pregnancies per woman, and an overall difference between the regimens of 0.3% in CHD events after 10 years.

Conclusions: Initiating HIV infected, ARV-naïve WOCBA on a LPV/r-based regimen compared to an ATV + RTV-based regimen produces substantial short- and long-term cost savings with similar life expectancy. These results warrant consideration, as selecting LPV/r over ATV + RTV may provide an opportunity for improving access to ART for WOCBA living with HIV in the UK.

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P98

Cost-effectiveness evaluation of initial HAART regimens for managing HIV-infected patients according to real clinical practice

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We evaluated the single-tablet regimen (STR) versus multiple-tablet regimen (MTR) strategies through an incremental cost-effectiveness analysis in a large cohort of patients starting their first HAART. Adult HIV-1-naïve patients, followed at the San Raffaele Hospital, starting their first-line regimen from June 2008 to April 2012, were included in the analysis. First-line HAART regimens more frequently used ($>10\%$) were grouped into two classes as follows: a) single-tablet regimen (STR) of TDF + FTC + EFV; b) multiple-tablet regimen (MTR) including TDF + FTC + EFV, TDF + FTC + ATV/r, TDF + FTC + DRV/r TDF + FTC + LPV/r. The incremental cost-effectiveness analysis was carried out by means of a Markov model calculating quality of life and costs for each patient, according to the given regimen (including any subsequent switch if occurred), through 1-year cycles. The outcome measure was quality-adjusted life-years (QALYs). Data were analysed from the point of view of the Lombardy Regional Health Service (RHS): HAART, hospitalisations, visits, examinations and other concomitant non-HAART drugs costs were evaluated, price variations included. 474 naïve patients: 90% males, mean age 42.2 years, mean baseline HIV-RNA 4.50 $\log_{10}$copies/ml and CD4+ count of 310 cells/μL with a mean follow-up of 28 months. Patients starting with an STR treatment were less frequently HCVAb positive (4% vs 11%, $P=0.040$), had higher mean CD4+ values [351 vs 297, $P=0.004$] as compared to MTR patients. The mean year cost/patient was €9,213 (range: €6,574.71–€33,570.00) with a mean per patient QALYs of 0.986 (range: 0.878–0.999) among STR patients; the mean year cost/patient was €14,277 (range: €5,908.89–€82,310.30) with a mean QALY of 0.933 (0.830–0.976) among MTR patients. STR dominates (i.e. is more effective and less costly) compared to MTR. (Fig. 1) At multivariable analysis, after adjustment for age, gender, HCVAb status, HIV risk factor, baseline CD4+ and HIV-RNA, the cost-effectiveness ratio was significantly lower among patients starting an STR treatment as compared to a MTR regimen (adjusted mean: €12,096 vs. €16,106; $P=0.0001$). The incremental cost-effectiveness ratio (ICER) values comparing the two treatment strategies reported in the table. Starting with a first-line STR regimen compared to multiple-tablet regimens resulted cost-effective showing lower costs and better efficacy as measured by QALYs.

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P99

A MultiFactorial Risk Score to weigh toxicities and co-morbidities relative to costs of antiretrovirals in a cohort of HIV-infected patients

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Purpose of the study: Considering costs of antiretrovirals (ARVs) for HIV patients is increasingly needed. A simple and comprehensive tool weighing comorbidities and ARV-related toxicities could be useful to judge the appropriateness of use of more expensive drugs. We conceived a MultiFactorial Risk Score (MFRS) to evaluate the appropriateness of ARVs prescription relative to their costs.
Methods: HIV patients were consecutively enrolled in 2010-2011. We considered socio-demographic characteristics, HIV history, cardiovascular risk factors, low energy fractures, bone density. Psychological factors were assessed by BDI, DS14 and TAS-20. The MFRS was calculated as the sum of the following: age (<30y 1 point; 1 point increase every 5y, 10 for ≥ 70); AIDS diagnosis (5); CD4 nadir (5 if <100; 1 point less every 100 CD4 increase); ART line (0 first, up to 5 for ≥ 6 lines); lipodistrophy (5); HCV coinfection (7); education (1 degree, 2 secondary, 3 primary); alcohol (3) and drug abuse (5); working activity (3 if unemployed); hypertension (3); cholesterol ≥ 200 mg/dl (3); diabetes (3); Framingham score (7 if $>7\%$); creatinine (0 if <1 mg/dl, 1 if <1.2; 2 if $<1.5>1.2$, 5 if $<2>1.5$, 7 if ≥ 2); bone fractures (7); bone status at DEXA (0 normal, 3 osteopenic, 5 osteoporotic); cancer (5); depression (3 if BDI >17); other psychiatric illness (5). Annual costs of individual ART regimens were calculated. MFRS was correlated in univariate and multivariate models with all variables. All statistical analyses were carried out using Stata 10.1.
Summary of results: We enrolled 241 HIV patients, 74.3% males, aged 44.5 ± 9.9y; 19 patients (7.8%) were untreated, 74.8% of treated had undetectable HIV RNA. Mean Nadir CD4 counts were 218 ± 168, 38.5% of patients had an AIDS diagnosis. Mean individual ARV annual cost was $10{,}976\pm5{,}360$. Mean MFRS was 28.5 ± 13.9 (4–64). MFRS was significantly higher ($p<0.001$) in patients with older age, longer duration of HIV infection, lower CD4 nadirs, AIDS diagnosis, lipodistrophy, HCV, smoking, lower education, alcohol/drug abuse, hypertension, carotid plaques, higher Framingham score, diabetes, bone fractures or disorders, depression, alexithymia, and higher ARV costs. In multivariate models, ARV costs were significantly higher in patients with older age, previous AIDS diagnosis, lower CD4 nadir and higher MFRS.
Conclusions: MFRS may be a simple and reliable tool to match patients' complexity and ARV costs, deserving further validation on larger samples.

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Abstract P98

Treatment	C Mean cost per patient	E Mean QALYs per patient	ΔC Delta cost	ΔE Delta QALYs	ΔC ΔE ICER QALYs
STR (Single Tablet Regimen):	€9,213	0.986			
MTR (Multiple Tablet Regimen):	€14,277	0.933	€5,064	–0.053	Dominated

Figure 1. Incremental Cost Effectiveness Ratio of HAART Regimens.

P100

A survey of patients' willingness to switch from a single-tablet regimen to 2 pills once a day as a cost-saving strategy

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With the patent on efavirenz due to expire a potential cost-saving strategy is to switch HIV-infected patients who are stable on Atripla® (tenofovir, emtricitabine & efavirenz) to a regimen of 2 pills once a day of generic efavirenz and co-formulated tenofovir & emtricitabine. We assessed patients' willingness to switch and whether it would be perceived to affect their adherence to their antiretroviral (ARV) regimen and quality of life (QOL). Consecutive patients who had been prescribed Atripla® for at least 3 months were asked to anonymously complete a questionnaire detailing the number of pills they took and how many times a day they took them. They were asked about their willingness to switch for cost-saving reasons and whether they perceived their adherence and QOL would change if they were to switch to 2 pills once a day. The questions were assessed using visual analogue scales with values from 0 to 10. Univariate and multivariable logistic regression models were employed to determine statistical difference. 143 patients completed questionnaires, mean age was 42.3 years and 121 (85%) were male. 57 (40%) were taking other regular medicines and 125 (88%) took their pills once a day. Patients' willingness to switch scored a median of 2 (0 = not willing at all, 5 = neutral, 10 = very willing). Perceived change in adherence and QOL both scored a median of 5 (0 = considerably worse, 5 = stay the same, 10 = better). No significant associations were found between patients' willingness to switch and age, gender, in those taking other regular medicines and in those taking their pills twice or more times a day. In those taking other regular medicines an increased willingness to switch was associated with increasing number of pills taken daily ($p = 0.037$). Willingness to switch was significantly less likely in those who perceived poorer adherence (RR 0.20, $p < 0.001$) and reduced QOL (RR 0.16, $p < 0.001$). Adherence is key to viral load suppression and hence treatment success and what is essentially a lifelong treatment should maintain or even improve quality of life. These are critical factors to consider if switching strategies are to be implemented to reduce drug expenditure as strategies which could potentially lead to poorer adherence could result in treatment failure and counteractively increase drug costs by necessitating the use of more expensive 2nd- or 3rd-line ARVs. It is therefore important to ensure patient involvement and address patient concerns in such strategies.

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P101

Loss to follow up within an HIV cohort

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BHIVA guidelines recommend that all ARV-naïve and stable on-treatment patients are monitored at least 6 monthly [1]. Studies have shown that loss to follow up (LFU) not only worsens outcomes [2] but has increased potential for onward transmission. Case notes of 1275 HIV patients registered under our care up to January 2011 were examined for attendance within the previous 6 months. 788 (61%) patients had not been seen within the previous 6 months. Reasons for non attendance were identified. These are outlined below:

Patient group	Number
Deceased	61
Transferred care to another HIV clinic	455
Moved out of the UK	54
Lost to follow up - no means to contact	130
Lost to follow up - eligible for recall	88

76% of the 130 LFU whose demographics were further examined were of Black African ethnicity, 54% female, 51% of single marital status and 48% of patients had been taking ARVs at the time of LFU. Interestingly, 53% of patients were lost to follow up within 1 year of diagnosis. The LFU patients (88) that had a local GP and a registered current address were sent recall letters. A small number of patients reengaged with care as a result of this action, some having not attended for over 5 years. Partner notification led to a number of new diagnoses in these cases. Failure to respond led to subsequent letters inviting them to clinic and finally a letter to their GP informing them of non attendance. In September 2011, a new recall system using Lillie Electronic Patient Records (EPR) was introduced to promptly recognise if a patient had not attended for care as planned. Prior to this, recall was a manual process carried out by the Health Advising Team. We conclude that within our cohort we had a particularly mobile group of patients; 455 (36%) transferring care to another clinic within the UK, 54 (4%) moving out of UK. 76% of the LFU group being of Black African ethnicity highlights the ongoing problem of retention of care in this group. Further exploration is needed to identify additional issues besides housing and immigration that lead to LFU. Furthermore, the disportionate number of patients (53%) disengaging with services within 1 year of diagnosis should encourage HIV services to provide additional support within this time period to reduce LFU. This study highlights the need for robust recall systems within clinics to identify those individuals not engaging with services or not attending for routine monitoring. These may be easier to implement with the increasing use of EPR. An audit of the recall system is planned in September 2012 to re-examine loss to follow up rates after its implementation.

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EVALUATION OF ARV DELIVERY AND COVERAGE

P102

Analysis of the evolution of direct costs of antiretroviral delivery in Argentina

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Background: In Argentina, antiretroviral treatment (ART) is covered by the State for all the persons who do not have health insurances, who represent 70% of all HIV infected patients in the country. Since

1992, the Direction of Aids (Ministry of Health) buys and delivers ART, treatments for opportunistic infections and reagents to diagnose and follow-up HIV infection. Nevertheless, until now, an analysis of the evolution of the costs of the drugs acquired by the Direction of Aids has not been performed. The aim of this study was to analyze the direct costs of ART for the Direction of Aids in Argentina since 2006, and evaluate progression over time.
Methods: The expenditure on ART and drugs for opportunistic infections was obtained. All values (in pesos) were converted to dollars. The cost of ART per patient per year was calculated. Changes in cost were determined for the total and per patient expenditures, and the reasons for the changes analyzed.
Results: Total expenditure for ART (in uS dollars) went from 33.7 million in 2006 to 75 million in 2011 (123% increase). The number of patients on ART covered by the Aids Direction increased from 23228 in 2006 to 33279 (43%) by the end of 2011. The cost (u$s) of ART per person per year was: *06*: 1449; *07*: 1645; *08*: 1516; *09*: 1543; *10*: 1968; *11*: 2255. This represents a 56% increase from 2006 to 2011, though this change was uneven through the years. This was driven mainly by a decrease from 07 to 08, due to lack of acquisition of ART for political reasons; and a very steep increase in 09-10 due to incorporation of more expensive drugs such as tenofovir/emtricitabine, raltegravir and maraviroc.
Conclusions: Annual cost of ART per person in Argentina has been increasing considerably in the last years. Even though this cost is much lower than those informed by some European countries (Italy: u$ 7500[1]; UK: u$ 9000[2], Germany: u$ 18000); it is one of the highest in Latin-America, where median cost is u$1200 (range: 200–3300). According to PAHO, the delivered ART in Argentina should cost u$ 1200 per person per year, or less. In view of the policy for treatment expansion (new Ministry of Health guidelines recommend ART with CD4 $\leq 500/mm^3$), it is important to seek ways of lowering the cost of ART. Some of the strategies might be the incorporation of generics (Argentina has a young patents law, barriers to generic use seem not to be very strong but this might change in the future) and buying via strategic funds.

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P104

Prescription patterns and costs of antiretroviral therapy in HIV-infected na ve patients: theoretical impact of a regional therapeutic protocol

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In the Lazio region, about 10.000 HIV+subjects receive combination antiretroviral therapy (cART) with a medication expense of 78.177.632,28. In 2011, in order to standardize prescriptions, to monitor appropriateness, and to decrease drug costs, the Protocol for Regional Therapeutics (PTR) for cART was developed. Aim was to describe prescription patterns and costs of first-line cART in 2010 and to estimate the theoretical impact of PTR application on medication costs. A cross-sectional evaluation of first-line cART prescribed during 2010 at the National Institute for Infectious Diseases was carried out. Data collected: age, date of HIV diagnosis, CD4, HIV-RNA, antiretroviral drugs. cART were classified based on the PTR ranks as follows: a) recommended regimen (rank A1/A1); b) alternative regimens (ranks A1/B1; B1/A1; B1/B1); c) not recommended regimens. A descriptive analysis of prescription patterns together with their economic impact was carried out. A multivariate analysis was performed to identify predictive factors of higher regimen costs. The hypothetical transition of not recommended regimens to recommended or alternative regimens was assessed. 370 naïve patients were evaluated: mean age 42 y (range, 1–84), mean duration of HIV 41 months (range, 1–84); median CD4 269/mmc (135–349), log_{10}HIV RNA 4.91 (4.4–5.4). A1/A1 regimens were prescribed in 62.2% (€163.789,28); A1/B1-B1/A1-B1/B1 in 22.8% (€73.831,75); not recommended cART in 15% (€54.929,95). Among A1/A1 regimes the most frequent were: TDF/FTC+EFV/(TDF+ FTC+EFV) in 39.4% and TDF+FTC+atazanavir/ritonavir in 22.7%. Up to 30 different cART (79% of all prescribed regimens) were used, each with a prescription prevalence lower than 1%. Mean patient-month cART expense was €790,68. At multivariate analysis, higher plasma HIV RNA was associated with significantly higher first-line regimen costs (coeff. B 48.64; 95% CI 22.78–74.50; $P < 0.0001$). When applying the simulation model with the transition of all patients treated with not recommended regimens to recommended or alternative regimens, a total of €18.036,41 and €10.078,35 may have been achieved, respectively. A high prescription variability of cART has emerged. This finding is unlikely to be determined by clinical needs, especially because of the high frequency of not recommended regimens. Our findings highlight the need of standardized prescription strategies and that the introduction of PTR may allow a saving of up 10.4% of total cART expenses.

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P105

Engagement and retention in care of patients diagnosed with HIV infection and enrolled in the Modena HIV Surveillance Cohort

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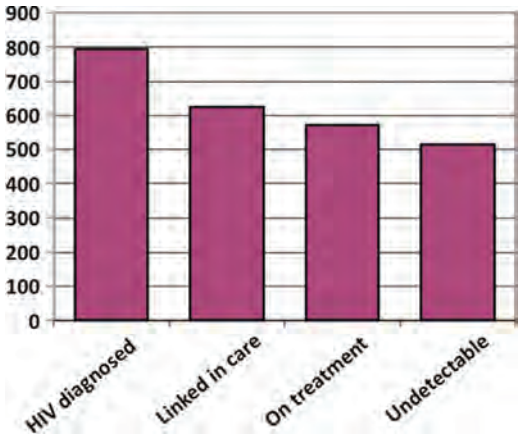
Engagment and retention in care is one of the main aspects not only for the prognosis of the single patient, but also for the treatment as prevention strategy. American data showed a percentage of engagement in care ranging between 50 and 59%. Aim of our study was to evaluate the engagement in care after diagnosis and the percentage of viral load suppression in an Italian Public Health System. A retrospective study was conducted in the Modena HIV Surveillance Cohort, which includes all HIV test performed at the Laboratory of Virology of Modena. All new HIV infections diagnosed in subjects older than 17 years and resident in the province of Modena between January 1996 and December 2011 were included. Subjects were classified as currently in care (IC) if followed until June 2011, and lost to follow-up (LF) if their last visit was recorded more than one year before June 2011. 962 subjects, 638 males (66.3%), had an HIV diagnosis during the study period. 71 (7.4%) were not linked to care, 891 were linked to care (92.6%) and 96 (10.8) of them died during the study period. In the 15 years, 625 out of 795 prevalent patients (excluding dead) (78.6%) were IC and 170 (21.4%) were LF. As June 2011, 570 patients were on antiretroviral treatment and 516 (90.5%) of them had an undetectable HIV RNA. At univariate analysis LF were younger than IC (median 32 vs 36 years; $p < 0.001$); more frequently had a foreign origin (49.4% vs 30.6%; $p < 0.001$) and were drug users (17.1% vs 7.0%; $P < 0.001$). Determinants to be a LF, by using a multivariate model, were: age (OR 0.97; 95% CI 0.94-0.99;

p ≤0.001), foreign origin (OR 3.45; 95% CI 2.24–5.33; p <0.001); while, being MSM vs drug user (p =0.001), heterosexual vs drug users (p <0.001) and having received an HIV diagnosis in more recent years, i.e. 2006–2011 vs 1996–2000 (p <0.001) were good predictors to be a IC. Considering the all prevalence, 962 subjects, the percentage of subject receiving antiretroviral treatment was 71.7% and that of those with an undetectable HIV RNA was 64.9%.



In conclusion, in a public health system setting, the percentage of patients not engaged in care or lost to follow-up could be lower than in other situations as the American one. Nevertheless, if we consider the strategy of treatment as prevention, there is still a lot to do, especially following the patients for a long period.

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P106

Comprehensive care with antiretroviral therapy for injecting-drug users associates to low community viral load and restriction of HIV outbreak

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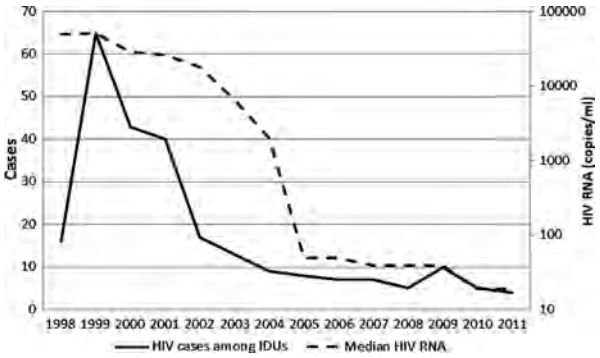
An outbreak of HIV was detected amongst Finnish injecting-drug users (IDUs) in 1998. The outbreak was caused by CRF01-AE virus [1]. A comprehensive care programme including infectious diseases, addiction medicine, low threshold methadone program, needle exchange, accommodation and other social services started in December 2000. Funding was provided by municipalities. We have described earlier how the outbreak became geographically and socially restricted [2]. The data of newly diagnosed HIV infections in the hospital district of Helsinki and Uusimaa (Helsinki region) amongst IDUs and HIV-1 subtypes were obtained from the Finnish national HIV registry. The Helsinki University Central Hospital (HUCH) registry was used to obtain the number of IDUs in HIV care, on antiretroviral therapy (ART), and plasma HIV-1 RNA (VL) amongst IDUs. The HUCH registry also includes IDUs diagnosed with HIV infection in other Finnish regions, but currently living in Helsinki region. The highest number (n =65) of newly diagnosed HIV infections among IDUs in Helsinki region was observed in 1999 (Figure 1). Between 1998 and 2011, 249 IDUs were diagnosed with HIV infection. From 1998 to 2004 the subtype was CRF01-AE in 187 (92%) cases, other subtypes in 5 (2%) cases and not subtyped in 11 (5%) cases. From 2005 to 2011 the subtype was CRF01-AE in 25 (54%) cases, other subtypes in 15 (33%) cases and not subtyped in 6 (13%) cases. In 2011 there were 4 IDUs diagnosed with HIV, one of them with CRF01-AE. In the Helsinki region out of 183 HIV-infected IDUs in 2005, 100 (55%) had VL <50 copies/ml and out of 167 HIV-infected IDUs in 2011, 133 (80%) had VL <50 copies/ml in 2011. We propose that from 2005 the low HIV-1 RNA in plasma of IDUs has contributed to the low incidence of HIV among IDUs in Helsinki region. However, the incidence of HIV started to decline before the decline of VL in the cohort (Figure 1). This suggests that other factors besides ART may have decreased the risk of HIV infection among IDUs before ART coverage of the cohort became considerable. Other subtypes of HIV circulated among IDUs in the Helsinki region during the observation period, which emphasises the necessity of health promoting services (e.g. needle exchange) to be available to all IDUs.



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P107

Patterns of retention in clinical care among HIV-positive men in the UK CHIC Study

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We examined disparities in engagement and retention-in-care among men in the UK Collaborative HIV Cohort (CHIC) Study according to ethnic group and mode of HIV infection. All male subjects in UK CHIC from 1996–2011 were included. We considered factors associated with both *initial engagement* (follow-up >1 day) and *consistent retention in care* (no interval between consecutive CD4/viral load (VL) measures >6 months). Logistic regression was used to identify associations with ethnic group and mode of HIV infection after adjusting for covariates at study entry (age, year, use of antiretrovirals (ART), AIDS). Analyses of retention also adjusted for VL/CD4 at entry and clinic. The 33210 men had a median (interquartile range) age of 36 (30,42) years at study entry, ethnic group was white (21851, 65.8%), black African (4374, 13.2%), black other (1539,

4.6%), Asian (967, 2.9%), other (2337, 7.0%) and unknown (2142, 6.5%). Mode of infection was sex between men (MSM) (22260, 67.0%), heterosexual sex (HET) (6286, 18.9%), other (1556, 4.7%) and unknown (3108, 9.4%). 32045 (96.5%) men were initially engaged in care, with no major differences by ethnic group after adjustment. Compared to MSM, initial engagement was less likely in those with heterosexual (adjusted odds ratio 0.77 [95% confidence interval 0.63–0.95]) or other (0.43 [0.33–0.56]) modes of infection. Other factors associated with initial engagement were older age, receipt of ART and having AIDS at entry; those entering UK CHIC in 2008–2011 were less likely to engage due to the shorter follow-up time. Of the men initially engaged in care, 12644 (44.0%) were consistently retained with no interval between consecutive CD4/VL >6 months. Consistent retention was more likely in MSM than in those with other modes of infection (HET: 0.76 [0.68–0.84]; other 0.54 [0.46–0.62]). Ethnic group again did not impact greatly on subsequent retention. Other independent predictors of retention were older age, receipt of ART and AIDS at entry. Those entering UK CHIC in later years were more likely to exhibit consistent retention as were those with higher VL and lower CD4 at entry. Our study demonstrates high rates of initial engagement in care. Those infected with HIV through heterosexual sex and younger men are less likely to engage in care and, once engaged, are less likely to attend consistently. The reasons behind these differences need to be explored further to ensure equitable health care delivery.

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P108

The effect on survival of a multidimensional intervention project (SEAD) in HIV/AIDS patients with follow-up and adherence (FUP/ADH) barriers

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Purpose of the study: Irregular FUP/ADH were associated with higher mortality and resource use [1]. SEAD was a multidimensional intervention project, designed from the patient's perspective, to specifically attend patients with poor FUP/ADH in an HIV/AIDS outpatient clinic.
Methods: From Jan 2006 to May 2010, patients with poor FUP/ADH were offered SEAD inclusion, all were evaluated by a nurse or a psychologist (adherence collaborators) who assessed all the reasons and barriers precluding a correct FUP/ADH. For each identified problem, different interventions were planned, using our own resources or coordinating others. Follow-up was censored in Nov 2011. Time to death after being admitted to SEAD and the effect of SEAD program intervention were assessed with Kaplan-Meier curves, log-Rank test and a Cox regression model.
Summary of results: Overall, 215 patients were assessed: mean age 45 years, 24% women, IDU 75%, with baseline ADH >90% in only 23%; median HIV-RNA and CD4 cell count were 377 copies/ml and 326 cell/mcL. Patients entered in SEAD due to poor ADH in 17%, FUP problems in 23%, and both 60%. Main reasons driving poor FUP/ADH were severe bio-psycho-social problems 28%, severe drug and/or alcohol abuse 26%, logistic problems 18%, other psychiatric disorders 13%, oversights 9%, unknown 4% and antiretroviral intolerance 2%. Only 54% of patients received; >50% of planned interventions, due to population complexity. Cocaine/heroin and alcohol abuse were reported by 34% and 17% respectively. Afer a median follow-up of 3.7 [3.31–4.4] years 193 patients received a mean of 8 (2.5–12) interventions/year, achieving virological control in 64%. Probability of survival was 92%, 89% and 86% after 1, 2 and 3 years respectively. In Cox regression model an intervention of SEAD project higher than 50% of planned was an independent predictor of survival HR 0.336 (95% CI 0.156–0.725); p = 0.005, after adjusting for age, alcohol or cocaine abuse, psychological attention, degree of adherence and follow-up, intravenous acquisition of HIV, and family support. Alcohol and cocaine abuse were associated with higher mortality HR 2.964 (95% CI 1.378–6.374); p = 0.005 and HR 2.444 (95% CI 1.161–5.145); p = 0.019.
Conclusions: Being admitted to SEAD intervention project and receiving more than 50% of planned interventions increased survival expectancy.

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P109

cART prescription trends in a prospective HIV cohort in rural Tanzania from 2007 to 2011

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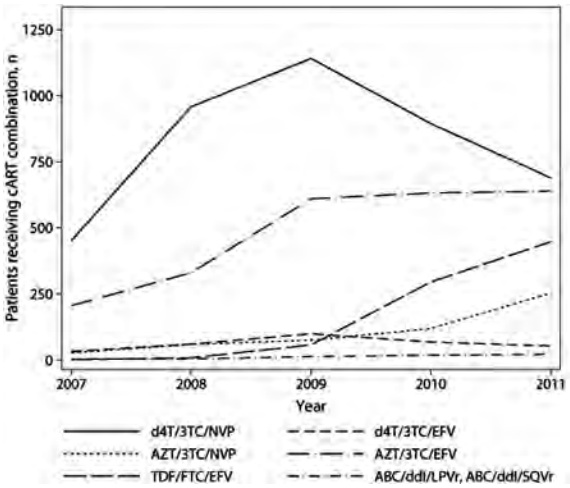
Comprehensive information on combined antiretroviral therapy (cART) regimens in rural Sub-Saharan Africa over time is scarce, particularly on the use of stavudine (d4T) and second-line regimens. Since 2010, World Health Organization (WHO) guidelines discourage using stavudine in first-line regimens due to frequent and severe side-effects. This study examined the practical adaption of this phasing-out and described trends in use of various cART combinations in a rural Tanzanian setting. We analyzed longitudinal, prospectively collected data of HIV-1-infected adults initiating cART within the Kilombero Ulanga Antiretroviral Cohort (KIULARCO) in Ifakara, Tanzania from 2007–2011. This analysis included data of 3068 patients over a 5-year period. Of these subjects, 1997 (66.9%) were female, median age was 37 (interquartile range [IQR] 31–44) years and median CD4 cell count at enrollment was 178 cells/μl (IQR 88-291). The percentage of prescriptions containing stavudine in initial regimens (Table 1) fell from a peak of 75% in 2008 to 12.2% in 2011 (p for trend <0.001). TDF/FTC/EFV became available in 2009 and was used in 117 (41.6%) patients initiating cART in 2011. An overall on-treatment analysis (Figure 1) revealed that d4T/3TC/NVP and AZT/3TC/EFV were the most prescribed combinations in each year, including 2011 (684 [32.5%] and 642 [30.5%] patients respectively). Of those on d4T/3TC/NVP in 2011, 632 (92.4%) were initiated in earlier years. The ratio of second-line to total regimens remained stable over time (p for trend = 0.19) with a maximum of 34 (1.2%) patients in 2011, whereof 32 (94.1%) received a combination of ABC/ddI/LPVr.

Initial cART with stavudine declined to low levels according to recommendations but the overall use of stavudine remains substantial. The usage of second-line treatment is unusually low in view of expected therapeutic failure rates, indicating potential difficulties in management of suspected treatment failure cases. Monitoring of prescription trends is a simple and feasible approach to identify

Abstract P109–Table 1. Initial cART combinations prescribed by year

	2007	2008	2009	2010	2011
d4T/3TC/NVP	426 (66.6%) 536	536 (71.2%)	362 (46.8%)	93 (19.4%)	52 (12.2%)
d4T/3TC/EFV	25 (3.9%)	29 (3.8%)	25 (3.2%)	6 (1.2%)	0 (0%)
AZT/3TC/EFV	177 (27.7%)	174 (23.1%)	324 (41.9%)	160 (33.4%)	138 (32.4%)
AZT/3TC/NVP	7 (1.1%)	10 (1.3%)	5 (0.6%)	21 (4.4%)	54 (12.7%)
TDF/FTC/EFV	2 (0.3%)	2 (0.2%)	57 (7.3%)	199 (41.5%)	177 (41.6%)
Total	639	752	773	479	425



Abstract P109–Figure 1. Overall on-treatment count of patients on cART combinations by year.

deficits in the implementation of treatment guidelines for optimal outcomes.

Abbreviations: 3TC, lamivudine; ABC, abacavir; AZT, zidovudine; d4T, stavudine; ddI, didanosine; EFV, efavirenz; LPVr, lopinavir/ritonavir; NVP, nevirapine; SQVr, saquinavir/ritonavir; TDF, tenofovir.

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P110

Observational study on HIV-1-infected patients treated with an ARV combination therapy including raltegravir: the RACING cohort results at month 12

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The French RACING cohort study is a 24-month, observational, longitudinal, prospective, multicenter study on HIV-1 infected patients being treated with an antiretroviral combination therapy containing raltegravir. The objectives of this study are to describe the viro-immunological course, characterize and document adverse events (AEs), describe patient adherence at M6 (month 6) and examine clinical-biological data for patients undergoing ARV therapy including raltegravir at M12 (month 12). Demographic, viro-immunological, safety and clinical-biological data were collected at M6 and M12 and self-reported patient adherence to treatment regimen at M6. Data from 478 of 482 patients were available at M12. The median age was 45.9 years (IQR: 40.0–52.2), 64.1% were male and the median duration of infection was 13.2 years (IQR: 5.5–21). At the baseline, 64.1% of patients had a cardiovascular risk factor or a history of cardiovascular events and 65.2% had received concomitant treatment (psychotropic drugs: 33.5%, lipid-lowering drugs: 30% and antihypertensive agents: 24.8%). The virological response, viral load and CD4 cell count are shown in Table 1 (based on data available at M6 and M12). Of the 134 reported and treatment-related AEs, the symptoms most frequently described (>5%) were myalgia (6.7%) and nausea (5.2%). A total of 34 serious adverse events were reported, of which 5 were possibly or probably related to raltegravir. Self-reported patient adherence at M6 is described as follows: 'high' for 56% of patients, 'average' for 36% of patients and 'low' for 8% of patients (205 questionnaires). To conclude, in a real-life setting concerning patients with a strong proportion of co-morbidity and variation in adherence, the efficacy and safety data observed after 12 months are comparable to the data observed (not shown) in clinical studies.

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Table 1. Viro-immunological data

	Na ve No previous treatment n=65		**Switch** Previous treatment with a viral load <50 copies/mL n=258		**Failure** Previous treatment with a viral load >50 copies/Ml n=151	
Median Viral Load (copies/mL) at baseline	64,513		–		1,891	
Median CD4 (cells/mm^3) at baseline	308		556		365	
	M6	**M12**	**M6**	**M12**	**M6**	**M12**
Virological Response% (HIV-RNA <50 copies/mL)	77% n=56	87% n=62	92% n=191	94% n=211	70% n=112	73% n=125
Immunological Response Median CD4 count (cells/mm^3)	461 n=58	514 n=63	592 n=205	591 n=209	451 n=124	490 n=126

P111

The Australian experiment: general practitioner care of HIV

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Over 20,000 people are living with HIV infection in Australia. From the early days of the epidemic general practitioners (GPs) have been closely involved in providing HIV care including antiretroviral therapy (ART). Training programs began in 1990 with about 200 GPs currently trained to provide ART. However there are limited data available on uptake and outcomes of GP HIV care. This review will present data on current GP involvement in providing HIV care as well as treatment outcomes. A Medline search was conducted using the terms general practice, HIV and Australia. Abstracts from local conferences were also reviewed. The major identified study of treatment uptake is HIV Futures [1], a national survey of approximately 1000 HIV+ve people performed every 2 years. Over the last 10 years this study consistently reports that about 50% of all HIV specific care is provided by GPs. One study describes an audit of 500 HIV+ve patients starting treatment in primary and hospital sites [2]. This found that there were comparable and high levels of adherence to guidelines on ART initiation in both general and specialist practice. A cohort of 168 patients followed for over 10 years in an Australian GP reported that 24% had been lost to follow-up, 7% died and 68% continued in care with 98% receiving ART with 96% having an undetectable viral load (<400) [3]. These outcomes were similar to those reported in the long-running national Australian HIV Observational Database (AHOD). Robust data show that about half of all HIV care in Australia is provided by GPs. Limited published data on adherence to guideline and treatment outcomes suggest comparable result in general practice versus specialist settings. GP care appears to be an acceptable and effective approach to HIV management although more research on treatment outcomes is needed.

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P112

The impact of introducing a satellite dispensary service at an outpatient HIV clinic

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Background: Studies have demonstrated the potential impact of pharmaceutical services in HIV care [1]. We sought to extend HIV pharmacy services at the Dean Street outpatient HIV/GUM clinic to improve efficiency and enhance client satisfaction. The pharmacy team was expanded and a satellite dispensary was opened in the clinic. This project compares the new dispensary service with the previous one offered.
Method: Comparisons were made between the pre- and post-change period across a range of pharmaceutical services provided and patient satisfaction feedback. Medicine-related interventions, repeat prescription requests, waiting and dispensing times were recorded. Service satisfaction questionnaires were designed for patients to quantify aspects of service provision.
Results: Types of interventions remain broadly similar ($p=0.353$), with an increase in the daily number of interventions ($p=0.0038$) and a decrease in time spent per intervention ($p=0.006$) in the new service delivery model. A greater dispensing time ($p=0.035$, $p=0.001$) and time per item ($p=0.043$, $p=0.002$) for prescriptions with related queries was seen across both periods. However, the time taken to dispense prescriptions remained similar pre- and post change ($p=0.8$). The patient satisfaction survey had a series of statements relating to pharmacy services; there was a stronger association with patient satisfaction seen for the provided services during the post-change period. The number and types of repeat prescription requests remain unchanged ($p=0.342$); however, patient prescription requests were completed more efficiently post-change (mean time 5.4 minutes) as compared to pre-change (mean 12.6 minutes; $p=0.001$). There was also a significantly lower rate of FP10 prescriptions issued in the post-change period due to a greater choice of available medications.
Conclusion: The care contributions of HIV pharmacists to a multidisciplinary HIV clinic providing patient-centred care were measured before and after the introduction of a satellite dispensary service. The expanded pharmacy service has increased efficiency by completing more tasks in less time and increased access to medications for patients. Its focus is dealing with patient-related queries and providing support for the patients seen at the clinic.

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HIV-RELATED INFECTIONS, CO-INFECTIONS AND CANCERS

Opportunistic Infections

P113

High seroprevalence of human herpes virus 8 (HHV-8) antibodies among vertically HIV-infected pediatric patients living in Germany

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Background: Human herpes virus 8 (HHV-8), a gamma herpes virus, is the etiological agent for Kaposi sarcoma (KS). HIV-infected adults

with advanced immunodeficiency are at risk. Prevalence data of HHV-8 infection in HIV-infected children living in non-endemic areas are limited. Serologic studies indicate low seroprevalence rates of 3–4% for healthy children living in United States and Germany [1].

Purpose of the study: The aim of the study was to determine the seroprevalence of HHV-8 antibodies among vertically HIV-infected pediatric patients in Germany and to evaluate their association with age, gender, ethnicity, and other demographic factors.

Methods: In 2012, a multi-center cross-sectional study was conducted in four University Hospitals in Germany. Stored frozen serum specimens obtained from vertically HIV-infected children and adolescents were tested for antibodies against lytic and latent HHV-8 antigens. Data on patients' demographic characteristics and medical history were recorded.

Results: A total of 214 HIV-infected children and adolescents (105 males, 109 females) were included. The median age was 10.2 years (range 1 months–22.6 years). A high proportion of these children (62%) was born in Western Europe, whereas 65% (139/214) of their mothers were born in countries outside Western Europe. The majoritiy (91%) of the children had been treated with highly active antiretroviral therapy and 55.2% (116/210) had a HIV-viral load <50 copies/mL. The median CD4 cell count was 1000/L (range 3–4400). The overall seroprevalence of HHV-8 antibodies was 23.8% (51/214). Seroprevalence rates did not show significant differences between age or gender. In the group of young children aged 1 month to 35 months, 19.4% (46/31) had HHV-8 antibodies, compared to 25% (25/100) in children aged 36 months to 11 years, and 24.1% (20/83) children 12 years and older. In the study group, seroprevalence rates were significantly lower in children who were born in Western Europe ($p < 0.01$) compared to those born in Africa, Asia, or Eastern Europe. Clinical symptoms of HHV-8 infection were reported to be uncommon; only one child had a history of KS at 2 years of age.

Conclusions: Vertically HIV-infected pediatric patients living in Germany showed a high HHV-8 seroprevalence of 23.8%. These rates were higher as expected in the normal pediatric population. The findings suggest that HHV-8 infection occurred already in the first years of life.

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P115

Hospital admissions of HIV-infected patients at a Lisbon reference centre: comparison among previously known and in-ward HIV-diagnosed patients

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Comparison of hospital admission causes for previously known (group A) and HIV-infected patients diagnosed during in-ward stay (group B), from 2009 to 2011. Retrospective evaluation of demographic, epidemiologic, clinical, immunologic, virologic and treatment parameters at time of admission. 1167 patients were admitted; of those 617 (52,9%) were HIV-infected: 92% HIV-1 and 8% HIV-2. 83% had previously known HIV infection and 15% were diagnosed during hospital stay (missing data in 2%). 66% were male, mean age was 46 years and 52% were Portuguese. The most frequent transmission routes were heterosexual exposure (36%) and iv drug use (29%). Mean length of hospital stay was 17 days (group A) and 28 days (group B) ($p = 0{,}004$). At admission, the mean TCD4+ count was 280 cells/mm^3 in group A, and 132 cells/mm^3 in group B ($p < 0{,}001$). The majority of group B patients had clinical or immunological AIDS criteria at admission (84%) while group A presented a 71% rate for the same parameter ($p = 0{,}011$). In group A, 52% of patients were on antiretroviral therapy but of those only 33% presented undetectable HIV plasma RNA, non-adherence being an important cause of therapeutic failure identified in 40% of cases. Respiratory infection was the principal cause of hospital admission in both groups (33% in group A vs. 35% in group B). The most prevalent nosological entities were community acquired pneumonia in group A (18,1% vs. 11,5%-$p = 0{,}118$) and *Pneumocystis jirovecii* pneumonia in group B (4% vs. 18%-$p < 0{,}001$). *Mycobacterium tuberculosis* was frequently identified as an agent of opportunistic infection (10% in group A vs. 24% in group B-$p = < 0{,}001$). HCV coinfection was a comorbidity found in 37% in group A vs. 11% in group B ($p < 0{,}001$). Other relevant comorbidities were psychiatric disturbances (16% vs. 3%-$p = 0{,}001$) and neoplastic conditions (11% vs. 0%-$p = 0{,}001$), mostly present in group A. Mortality rate was not significantly different between groups (10% group A vs. 11% group B) ($p = 0{,}773$). This analysis evidenced that, a significant percentage of HIV patients diagnosed at admission were late presenters. Slightly a half of patients with previous known HIV infection were prescribed cARV and only a third presented undetectable HIV viral load. Non-adherence was a major concern in this population. Respiratory infections had a significant clinical impact in both groups, justifying the importance of vaccination prevention strategies in immunocompromised individuals.

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P116

Clinical manifestations and survival of HIV/AIDS-infected patients, southern region of Thailand

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Objective: The purpose of this study was to determine magnitude of clinical manifestations on survival of HIV/AIDS patients.

Methods: The HIV/AIDS information system, a database containing demographic factors and clinical manifestations was used. A prospective, hospital-based cohort study was conducted in HIV/AIDS patients registered in both provincial and community hospitals from 14 provinces in southern region of Thailand, between January 1993 and April 2010. Totally, 52,459 of HIV/AIDS patients were routinely observed and followed up. One-fifth of the HIV/AIDS patients died ($n = 11{,}767$, 22.43%) during the follow-up period. The outcome was timed from diagnosis of HIV/AIDS infection to death. Cox's proportional hazard model was used to analyze the magnitude of clinical manifestations on survival of HIV/AIDS patients.

Results: A statistically significant corresponding risk of clinical manifestation on death was found. HIV/AIDS patients who had clinical manifestations including: invasive cervical cancer (HR = 0.14, 95% CI: 0.44 to 0.43), herpes simplex (0.81, 0.66 to 0.98), histoplasmosis (0.67, 0.46 to 0.97), *Mycobacterium* other species (0.78, 0.64 to 0.97) were more likely to have a longer life. However, patients expressed clinical manifestations including; candidiasis (1.45, 1.34 to 1.56), cryptococcosis (1.77, 1.64 to 1.91), cytomegalovirus retinitis (1.58, 1.26 to 1.98), HIV encephalopathy (2.17, 1.92 to 2.47), *Mycobacterium avium* complex (1.76, 1.32 to 2.33) *Mycobacterium tuberculosis* (1.25, 1.21 to 1.30), pneumonia recurrent (1.78, 1.61 to 1.96), *Pneumocystis carinii* (1.71, 1.63 to 1.78), salmonella septicemia (1.85, 1.43 to 2.39) toxoplasmosis (1.47, 1.30 to 1.66) and wasting syndrome (2.13, 2.04 to 2.21) were more likely to die faster.
Conclusion: In conclusion, HIV/AIDS patients expressed clinical manifestations which were a risk of death must be monitored closely and intensively care to extend their life and increase their quality of life.

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P117

Reasons of hospitalization for HIV-positive patients in the Infectology Center of Latvia in the period from 2009 to 2011

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Introduction: In Latvia, HIV-positive patient count increases every year. 5189 HIV patients were registered in Latvia until January 2012. 1047 of them were in the AIDS stage. For the moment, healthcare of HIV patients is realized in two inpatient departments and one outpatient department; only patients with dual infection - HIV and TB - are observed in the TB center.
Aim of study: To identify problems, which are related to hospitalization of HIV-positive patients, by improving patient care standards and if necessary change it.
Materials: 1205 patient cards of hospitalization were analyzed in the period from January 2009 till December 2011 (year 2009 - 351 patients, 2010 - 391 patients, 2011 - 463 patients). Statistical data analysis made by software - SPSS and Microsoft Excel and described methods.
Results: Within three years 1205 patients were hospitalized. In late AIDS stage, 714 patients were hospitalized. For the treatment of these patients ART, OI prophylactic treatment and OI therapy had to be included. Most common cause of hospitalization was opportunistic infection: 2009 - 168 patients (47.8%); 2010 - 201 patients (51.4%); 2011 - 193 patients (41.9%). Second most common cause of hospitalization was liver disease: 2009 - 37 patients (10.5%); 2010 - 55 patients (14%); 2011 - 47 patients (10.1%). Other reasons of hospitalization were lower respiratory tract infections-pneumonia, bronchitis. Only in 5.9% cause of hospitalization was acute retroviral syndrome. In 4.4% hospitalizations outcome was death, only in 0.2% cases cause of death was associated with non-AIDS disease. Average time of hospitalization was 12.8 days.
Conclusions: 1. HIV-positive patient hospitalization count increases every year. 2. More often hospitalized patients are in late stage of HIV infection and reason of hospitalization is opportunistic infection, which extends time of hospitalization and costs. 3. Recommended immunization against VHB and *S. pneumoniae*, which would protect against non-AIDS diseases. 4. Medical staff education needs to be updated, which would help to diagnose HIV infection in early stage of disease.

Table 1. Patients' distribution by HIV/AIDS stage

Clinical categories/CD4	A	B	C
>500 c/mm^3	79	22	41
499–200 c/mm^3	141	55	115
<200 c/mm^3	75	119	558

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P118

Dynamics of Epstein-Barr Virus DNA concentrations in whole blood of HIV-1-infected patients during primary HIV-1 infection

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Introduction: Epstein-Barr virus (EBV) viraemia is associated with nasopharyngeal carcinoma and lymphoproliferative diseases. In HIV-1 infection, persistent EBV viraemia is a common phenomenon. The underlying mechanism of these high EBV DNA loads has not been clarified. We studied EBV viraemia during primary HIV-1 infection (PHI) to explore the mechanism of EBV viraemia in HIV-1 infection.
Methods: Patients with PHI, participating in Primo-SHM study, a clinical trial with three study arms: no treatment, 24 weeks of combination antiretroviral therapy (cART) and 60 weeks of cART, were sampled longitudinally during PHI and 24 and 48 weeks thereafter. EBV DNA was assayed by PCR on stored samples of lysed whole blood.
Results: 39 patients were tested, in 22 of whom EBV DNA was detected at one or more time points. All patients tested positive for anti-VCA and anti-EBNA antibodies, most patients that had EBV viraemia did not receive cART or interrupted cART. The prevalence of EBV viraemia at baseline was 29%, 18% and 33% for the untreated, 24 weeks cART and continuous cART groups. At week 48, these percentages were 38, 64 and 17 respectively ($p < 0.05$). Individual concentrations of EBV DNA for the three groups are shown in Figure 1.
Conclusion: Intermittent EBV viraemia is highly prevalent in patients with PHI. Assuming that patients with very early HIV-1 infection are still immunocompetent, this indicates that EBV viraemia is not caused by immunodeficiency. Antiretroviral therapy started during PHI but not later during chronic HIV infection might reduce the prevalence of EBV viraemia in HIV-1 infection.

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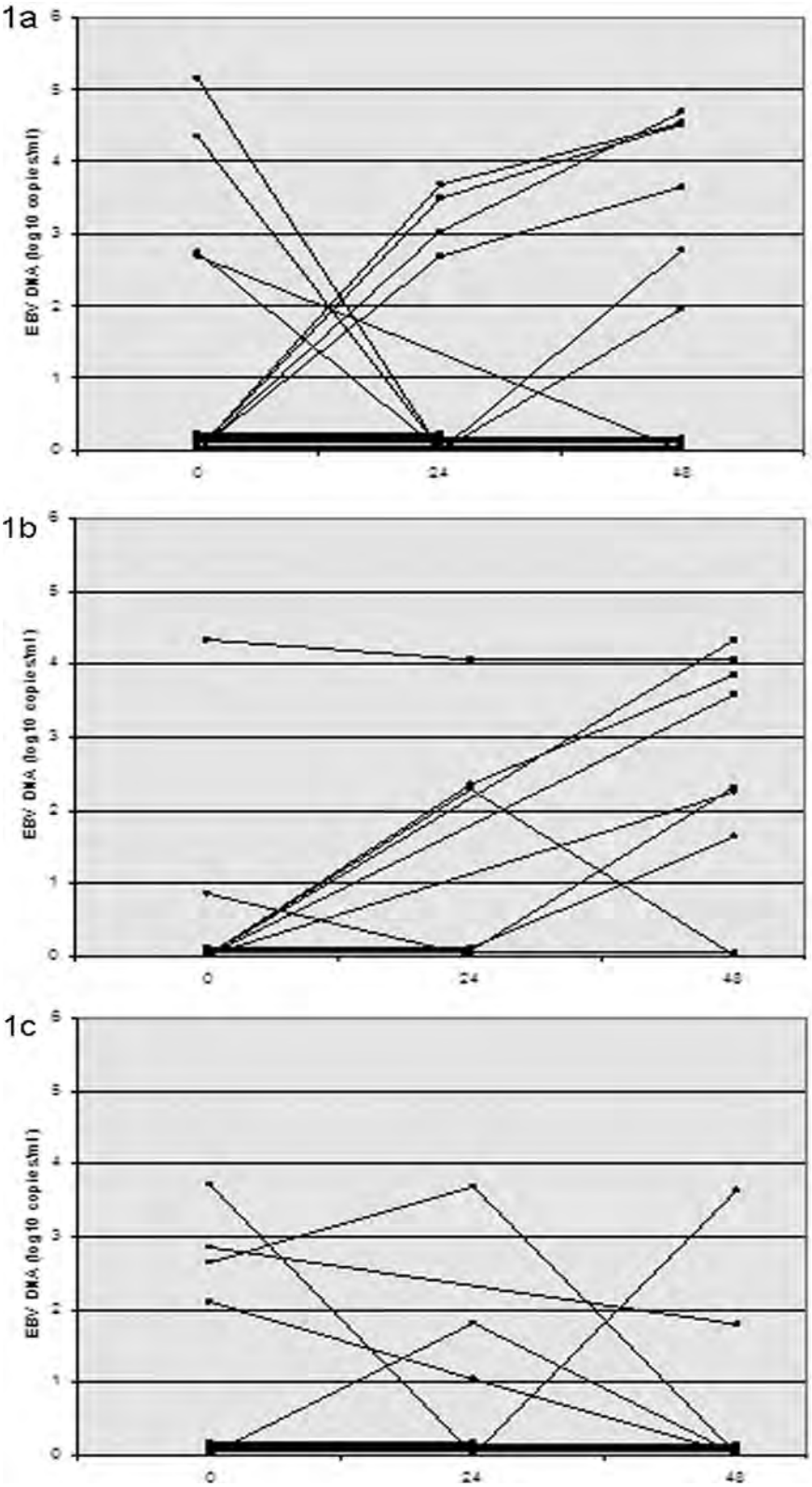

Figure 1. The black lines show the individual log10 transformed EBV DNA concentrations in whole blood in patients that remained untreated (panel a), patients that were treated for 24 weeks with cART (panel b) and patients that were treated continuously with cART (Panel c).

P119

Changing spectrum of clinical presentation in visceral leishmania in HIV+patients: preliminary results from a clinical registry in Northern Italy

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Purpose: Visceral leishmania (VL) and HIV were related since the beginning of AIDS era but the impact of HAART has completely changed the pattern. Aim of the study is to describe the current presentation of this opportunistic infection.
Methods: Demographics, clinical, laboratory and therapeutic findings were recorded in patients (pts) enrolled in the Ligurian registry for VL from January 1st 2007 to December 31st 2010. From these data we obtained the HIV+features. Statistical analysis was performed using: STATA 11.0 and SPSS software 13. Statistical significance was defined as a P value <0.05.
Summary of results: A total of 65 episodes in 55 pts (36 adult) were accumulated: median age 48.7 years (yrs) in adults (37.5 months in pediatric pts). All children were immunocompetent (ICC), adults included both ICC (17) and immunosuppressed (19) (ISS) pts. HIV was the leading cause of immunosuppression (10–59%) all pts. belonged to CDC stage C and they sustained 15 cases of infection; 4 were not on HAART and 4 on a failing regimen. Mean age in HIV +pts was 38 yrs, average CD4+count and HIV RNA at first diagnosis were respectively 135/l$\pm$101 and 6,974 $\times 10^4$ cp/ml (0–2.8 $\times 10^5$). No significant CD4 r differences at first diagnosis were present among who would not recur compared to those for whom a VL recurrence was observed. Main clinical presentations were: Fever (F)+hepatosplenomegaly 8, F+lymphoadenoathy 2, F+pancytopenia 2, thrombocytopenia 2, other 1. Detection of urinary antigen and serology (IFAT) were the most frequently used diagnostic tools (respectively in 14/15 and 11/15 pts). Bone marrow detection of intracellular parasites (Giemsa) was performed only in 4/15 cases. Liposomal amphotericin B was the most frequently (98.2% of cases) prescribed drug with 100% clinical cure. VL relapses (n°5) represented a crucial finding: they occurred in 3 pts and time to relapse presented a significant difference among ICC and ISS; CD4+cell numbers at VL recurrence were not different compared to those for the pts at baseline. Three deaths were reported, accounting for significant (15.8%) mortality.
Conclusions: The main findings can be summarized as follows: clinical presentation among HIV pts is heterogeneous with frequent recurrence and remarkable mortality. Moreover, the use of both serology and urinary antigens detection for diagnostic purposes allows a reliable performance and could be very useful in pts not eligible for bone marrow aspiration.

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Tuberculosis

P120

Particularities of tuberculosis in HIV-infected patients: 10-year experience of a Portuguese hospital

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The incidence of tuberculosis (TB) has dramatically increased since the advent of the human immunodeficiency virus (HIV) pandemic. In Portugal, tuberculosis is still common in HIV-negative patients, despite earlier diagnosis and countrywide directly observed therapy strategies. With the purpose of comparing some demographic and clinical aspects of TB in HIV-infected and uninfected patients, the authors reviewed the files of patients admitted with a diagnosis of tuberculosis between January 2002 and December 2011. During this time period, there were 234 cases of tuberculosis, 43 (18%) of which occurred in HIV-infected patients. In this group, 74% of patients were male, with a mean age of 38$\pm$11 years and the majority (51%) acquired HIV from heterosexual risk behavior. The most common site of infection was the lung, in both groups, but cases of extra-pulmonary TB were significantly higher in the HIV-infected group (67% versus 39%, $p<0.01$). Disseminated TB was the most common extrapulmonary diagnosis in the former group (28%) and lymph node TB (8%) in the latter. The duration of hospitalization was not statistically different between the two groups (mean of 26$\pm$16 days in HIV-infected patients and 21$\pm$15 days in the HIV-negative group, $p=0.21$). The mean CD4 count at TB diagnosis was 180$\pm$177/mm^3. In 11 (26%) of the patients, HIV was diagnosed during the TB episode and in 5 cases, the diagnosis of tuberculosis occurred with immune reconstitution syndrome. In the majority of patients (60%), TB was the first AIDS-defining condition. In 26 (60%) of patients there was microbiologic confirmation of TB, mainly by direct observation (69%), positive culture (46%) and molecular diagnostic technics (27%). While most patients were treated with the 4-drug standard regimen, 16 (37%) of cases received alternative treatment. The mean duration of treatment was 8.5$\pm$4.8 months and the majority of patients (58%) were considered cured. About one-third of patients were lost to follow-up (32%). Tuberculosis is a heterogeneous disease, varying accordingly with the immunologic status of the host. The risk of extrapulmonary and disseminated TB increases with immunosuppression but, in this cohort, it did not seem to influence the length of hospitalization. The authors alert to the need of HIV screening whenever TB occurs, allowing for earlier diagnosis and prompt start of antiretroviral therapy.

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P121

CYP2B6 G516T and *ABCB-1* C3435T polymorphisms: implications for efavirenz-associated liver toxicity in HIV/tuberculosis co-infected Thai adults

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Cytochrome P450 2B6 (*CYP2B6*) and ATP-binding cassette, sub-family B (*ABCB-1*) play an important role in metabolism and transport of anti-retroviral therapy (ART) agents. *CYP2B6* 516TT and *ABCB-1* 3435CT polymorphisms affected plasma efavirenz levels. Efavirenz-based ART was proofed to be beneficial in HIV/tuberculosis co-infection management; however, the drug-drug interactions and toxicity are major concerns. Factors affecting adverse drug events and liver toxicity were investigated in this study. Seventy-one HIV patients with tuberculosis receiving efavirenz (600 mg/day)-based ART were enrolled in the randomized trial: the N2R study in Bamrasnaradura Infectious Diseases Institute, Thailand. After 12 weeks of ART, 65 rifampicin recipients continued in the analysis of the factors influenced drug toxicity. Plasma efavirenz, serum levels of

aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), total and direct bilirubins were determined. *CYP2B6* and *ABCB-1* polymorphisms were genotyped. Mann-Whitney U test was used to compare genotypes and laboratory parameters. *CYP2B6* 516TT and *ABCB-1* 3435CT genotypes were found in 9 (13.85%) and 33 (50.77%) patients, respectively, while six (9.23%) carry both -516TT and -3435CT genotypes. Patients with 516TT genotype had significantly higher mean rank plasma efavirenz than GT and GG genotypes (54.78 vs. 29.50, $p = 1.97x10^{-4}$) while those carrying 3435CT had slightly higher than CC and TT genotypes. Patients carrying both -516TT and -3435CT had higher mean rank efavirenz levels than those without these two genotypes (60.17 vs. 30.24, $p = 2.21x10^{-4}$), and had significantly different ALT, total and direct bilirubin levels ($p = 0.044$, 0.009, 0.021, respectively). *CYP2B6* 516TT and *ABCB-1* 3435CT influenced plasma efavirenz levels and related to higher levels of ALT, total and direct bilirubin in patients implication for drug toxicity. The results might be useful for personalized therapy due to their impact on ART adherence related to drug resistance and treatment failure.

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P122

Impact of pharmacogenetic markers of CYP2B6 and clinical factors on plasma efavirenz level in HIV/tuberculosis co-infected Thai patients

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Purpose of study: Polymorphisms of CYP2B6 are associated with altered activity of cytochrome P450 2B6 which has an effect on plasma efavirenz level. The data of these polymorphisms and their effect, particularly in HIV/TB co-infected patients, is still limited.
Methods: A total of 150 HIV-infected Thai adults with active tuberculosis (TB) and receiving rifampicin-containing anti-TB regimen were prospectively enrolled to receive a once-daily regimen of efavirenz 600 mg/tenofovir/lamivudine. Nine single nucleotide polymorphisms (SNPs) within CYP2B6 were genotyped using real-time PCR-based allelic discrimination. At 12 weeks after ART, plasma efavirenz levels at 12 hours after dosing were measured by HPLC assay.
Summary of results: Of all, the median (IQR) CD4 count was 44 (17–113) cells/mm^3 and median (IQR) plasma HIV-1 RNA was 5.8 (5.4–6.3) log copies/mL. Eight (5.3%) patients discontinued efavirenz due to adverse events prior to measuring efavirenz level. Of 142 patients, the frequencies of wild type, heterozygous mutant, and homozygous mutant of each SNP were 64C > T (89%, 10%, 1%), 499C > G (99%, 1%, 0%), 516G > T (45%, 47%, 8%), 785A > G (36%, 54%, 10%), 1375A > G (100%, 0%, 0%), 1459C > T (97%, 3%, 0%), 3003C > T (29%, 44%, 27%), 18492T > C (55, 39%, 6%), and 21563C > T (38%, 57%, 5%). Median (IQR) plasma efavirenz level of 102 patients who were concurrently receiving efavirenz and rifampicin was 2.08 (1.33–3.51) mg/dL and those of 40 patients who did not received rifampicin was 2.72 (1.80–5.21) mg/dL. Of 102 patients, heterozygous/homozygous mutant vs. wild type of 5 SNPs associated with high mean efavirenz level were 516G > T (3.6 vs. 1.9 mg/dL, $P < 0.001$), 785A > G (3.2 vs. 2.0 mg/dL, $P = 0.001$), 3003C > T (4.0 vs. 2.4 mg/dL, $P = 0.012$), 18492T > C (3.5 vs. 2.0, $P < 0.001$), 21563C; > T (3.4 vs. 1.9 mg/dL, $P < 0.001$). Three of 9 haplotypes identified, including *6/*6, *1/*6, and *4/*6, were associated with high efavirenz level. By multivariate analysis, factors associated with high efavirenz level included specific haplotype ($P < 0.001$), low body weight ($P = 0.003$), and receiving rifampicin ($P = 0.058$).
Conclusions: Particular SNPs and haplotype of CYP2B6, especially *6/*6, has the greatest impact on efavirenz level in HIV/TB co-infected Thai patients whereas low body weight and concurrent receiving rifampicin have lesser effects.

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P123

Integrating TB screening tool in medical clinical records improves TB screening and detection among HIV and AIDS patients; a case TASO Uganda

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Background: Tuberculosis remains a major public health problem in Uganda with an annual incidence of 330 cases of all forms and 136 new smear-positive cases per 100,000 people per year. The expected case load per year is 102,000 as per WHO 2010 Global Report. The 2010 Global WHO Report ranked Uganda 16th among the 22 TB high-burden countries. Uganda, like most of Sub-Saharan Africa, is battling with the dual tuberculosis and HIV/AIDS epidemic. TB stands as the number one killer of HIV/AIDS patients, and the clinical presentation of TB among the dually infected persons changed and this has a bearing on the clinical management and design of public health interventions to respond to the dual epidemic. TASO integrated TB screening tool clinical records to remind clinicians to screen for active TB among under TASO care.
Methodology: Clinicians complete a section of the clinical record form entitled TB screening by assessing if the patient enrolled for TASO care is symptomatic for TB using a screening tool. Patients who screened positive for one or more signs/symptoms of TB were further investigated to confirm active TB by sputum analysis, chest X-ray, lymph node aspirates and pleural tap for analysis. Cases with confirmed TB received respective treatment as they continue to attend the usual medical review on appointment.
Results: Overall percentage of patients screened for TB improved from 78% to 96% between fourth quarter, 2011 and first quarter, 2012. Of those screened the percentage of patients with at least one or more positive signs/symptoms of TB increased from 23.3% to 42.5% within the same period TASO Tororo MIS, out of those with a positive screen who took a test, the percentage of patients diagnosed with TB increased from (26/126) 15.9% to (68/192) 35% within the same period.
Conclusion/recommendation: Integrating screening tool in clinical record will prompt clinicians to screen for active TB at each clinic visit, allow continuity and quality of TB care, prevent unmasking of TB through immune reconstitution syndrome in patients with lower CD4 cell count initiating ART, and monitors TB investigation results, treatment, progress and outcomes.

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P124

Mortality among HIV/AIDS patients with/without *Mycobacterium tuberculosis* infection in southern region of Thailand

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Object: The purpose of this study was to gain knowledge of tuberculosis infection in HIV/AIDS-infected patients, the purpose of this study was to investigate an association between tuberculosis infection and mortality in HIV/AIDS-infected patients.
Methods: A prospective, hospital-based cohort study was conducted in HIV/AIDS patients registered in hospitals between January 1993 and April 2010. In total, 52,459 patients with HIV/AIDS infection were routinely observed and followed up, covering 14 provinces in southern region of Thailand.
Results: The main results found that one-third of the HIV/AIDS patients were infected with *Mycobacterium tuberculosis* (27.94%) during the follow-up period. However, the risk of *Mycobacterium tuberculosis* infection was not statistically significant in terms of association with mortality among HIV/AIDS patients (HR: 1.01; 95% CI: 0.96 to 1.05). In contrary, HIV/AIDS patients with pulmonary tuberculosis were more likely to have a longer life by about 19% (HR: 0.81, 95% CI: 0.73 to 0.91). As well, HIV/AIDS patients with extrapulmonary tuberculosis were more likely to have a longer life by about 31% (HR: 0.69; 95% CI: 0.57 to 0.83).
Conclusion: In conclusion, tuberculosis infection was associated with mortality among HIV/AIDS patients. Early treatment of tuberculosis is needed for HIV/AIDS patients, in order to decrease morbidity and mortality among HIV/AIDS patients with tuberculosis.

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P125

Characteristics of tuberculous meningitis in HIV-infected patients

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Background: Tuberculous meningitis (TBM) has a substantial mortality even with anti-tuberculous treatment, in HIV-non-infected patients. Purpose of the study. The objectives were to describe clinical and laboratory differences of TBM in HIV-infected versus HIV non-infected patients and to assess risk factors of death in HIV-infected patients.
Methods: We retrospectively analyzed patients admitted to four infectious diseases hospitals in Romania, between 2001 and 2011, with TBM. Patients were defined as having TBM according to a consensus definition published by Marais et al. [1] and further divided into three categories of TBM (definite, probable and possible).
Results: We identified 162 patients with TBM of which 47 (29%) tested positive for HIV infection. Sixty-six patients had definite, 53 probable and 43 possible TBM. Out of the 47 HIV-infected patients 25 had definite, 17 probable and 5 possible TBM. TBM in HIV-infected patients vs. HIV non-infected patients was significantly associated in multivariable analysis with younger age ($p = 0.01$), in-hospital mortality ($p < 0.001$), absence of meningean syndrome ($p = 0.021$), and absence of cranial nerve palsy ($p = 0.036$). HIV-infected patients who died had a median CD4 count of 61 cells/mm^3 (IQR 21-132) vs. 135 cells/mm^3 (IQR 61–255) in patients who survived ($p = 0.014$). HIV infection was diagnosed before TBM episode in 35 (75%) patients. Twenty-four (51%) HIV-infected patients had concomitant extra-central nervous system tuberculosis.
Conclusions: HIV infection is associated with increased mortality in patients with TBM. Most of our patients with TBM were late presenters. Death in HIV infected patients was associated with a lower median CD4 count.

	HIV-infected	HIV-non-infected	p-value
Male N (%)	32 (68)	68 (59)	0.287
Age (years) (median, IQR)	22 (18–34)	34 (20–51)	0.005
Duration of symptoms before admission (days) (median, IQR)	10 (7–14)	10 (7–14)	0.878
Cranial nerve palsy N (%)	6 (13)	31 (27)	0.051
Meningean syndrome N (%)	34 (72)	102 (89)	0.010
Glasgow Coma Scale <7 N (%)	11 (23)	18 (16)	0.243
Cell number in CSF (cells/mm^3) (median, IQR)	180 (91–457)	200 (86–400)	0.799
Protein CSF level (mg/dl) (median, IQR)	175 (120–542)	198 (129–279)	0.701
CSF/serum glucose <0.5 N (%)	32 (71)	96 (84)	0.079
In-hospital mortality N (%)	18 (38)	13 (11)	<0.001

Reference

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P126

Status of HIV serology among pulmonary tuberculosis patients: the pattern of pulmonary tuberculosis and the characteristics of patients

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Tuberculosis (TB) is a leading cause of death among people with HIV. In 2009, there was an estimate of 380,000 deaths due to TB among HIV patients. 78% of TB/HIV co-infection cases reside in sub-Saharan Africa; HIV prevalence is as high as 80% in some countries. Therefore, the prevalence of HIV infection in the study population of TB was determined. Clinical, laboratory and radiological presentation of TB were analyzed and compared between HIV sero-ve and HIV sero +ve patients. Observational case-finding hospital-based study was done on 60 TB patients, performed in 3 hospitals in Sudan. Interview-based questionnaires and medical records were used for data collection. Prevalence of HIV-infected TB patients among the study population was 16.7%. The study revealed that 50% of the HIV+ve TB patients were younger than 30 years. There was no major sex difference between HIV+ve and −ve TB patients ($P = 0.905$). However, males were predominant among the whole study population of TB patients. 60% of HIV+ve patients originated from the north, whereas the origins of the HIV-ve patients were more or less equally distributed ($P = 0.012$). Clinical presentations of HIV+ve and −ve TB patients were similar and the differences were not statistically significant. When comparing the lab findings; +ve sputum smear was found more common among HIV+ve patients (70% vs. 54%) and a +ve PPD test was also more common among HIV+ve patients (75% vs. 50%). A clear CXR was the only statistically significant difference between the two groups, being more common in HIV+ve (40% vs. 6%) ($P = 0.002$). The study concluded that the prevalence found was low in comparison to most of the countries in the region but high in

comparison to developed countries. The main differences between HIV+ve and −ve was a+ve sputum smear, +ve PPD test, and a clear CXR, all of which were more common in HIV+ve TB patients. Therefore, the TB/HIV programme should be strengthened; starting by knowing the exact incidence of TB/HIV among the population, implementing better diagnostic tools and more researches to be conducted on a larger scale.

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Hepatitis Co-infection (HCV and HBV)

P127

Safety and efficacy of raltegravir in patients co-infected with HIV and hepatitis B and/or C virus: complete data from Phase III double-blind studies

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Purpose of study: Safety and efficacy of raltegravir (RAL) in patients (pts) with HIV and hepatitis B and/or C (HBV/HCV) co-infection were evaluated in a double-blind fashion for 5 years in STARTMRK and 3 years in BENCHMRK-1&2.
Methods: In STARTMRK, treatment-naïve pts received RAL 400 mg bid or efavirenz (EFV) 600 mg qhs, both with tenofovir+emtricitabine (TDF/FTC), for up to 240 weeks. In BENCHMRK-1&2, highly treatment-experienced pts with multidrug-resistant virus and failing other therapies received double-blind RAL 400 mg bid or placebo, both with optimized background therapy (OBT), for up to 156 weeks. Pts with stable chronic HBV/HCV could enroll if baseline AST and ALT were = 5 × upper limit of normal.
Summary of results: 743 pts received RAL and 519 received comparator. Hepatitis co-infection was present in 6% (34/563) of treatment-naïve pts (HBV = 4%, HCV = 2%, HBV+HCV = 0.2%) and 16% (114/699) of treatment-experienced pts (HBV = 6%, HCV = 9%, HBV+HCV = 1%). Safety and efficacy results at the end of double-blind treatment are shown by study, treatment group and co-infection status. Liver enzyme elevations were more common in pts with HIV+HBV/HCV co-infection than in pts with HIV infection alone, in the RAL and control groups. Most liver enzyme changes occurred in the first 48 weeks of treatment, with minimal further increases (data not shown).
Conclusion: RAL was efficacious and generally well tolerated for up to 5 years in pts with HIV+HBV/HCV co-infection. The majority of grade 3 and grade 4 liver enzyme elevations occurred during the first year of treatment and were more common among co-infected pts than among HIV mono-infected pts, irrespective of treatment group.

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P128

Long-term safety and tolerability of nevirapine and efavirenz-containing regimens in HIV/HCV-coinfected patients

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Abstract P127

	STARTMRK (treatment-naive), 240 weeks				BENCHMRK (treatment-experienced), 156 weeks			
	RAL+TDF/FTC		EFV+TDF/FTC		RAL+OBT		Placebo+OBT	
	HBV or HCV positive N = 18 %	HBV & HCV negative N = 263 %	HBV or HCV positive N = 16 %	HBV & HCV negative N = 266 %	HBV or HCV positive N = 77 (PYR = 182) % (rate/100 PYR)†	HBV & HCV negative N = 385 (PYR = 869) % (rate/100 PYR)†	HBV or HCV positive N = 37 (PYR = 43) % (rate/100 PYR)†	HBV & HCV negative N = 200 (PYR = 280) % (rate/100 PYR)†
Aspartate aminotransferase (AST) increased								
Grade 3‡	5.6	4.6	0	3.0	9.1 (3.8)	3.4 (1.5)	2.7 (2.3)	3.0 (2.1)
Grade 4‡	5.6	0.8	6.3	0	2.6 (1.1)	0.3 (0.1)	0	1.5 (1.1)
Alanine aminotransferase (ALT) increased								
Grade 3‡	0	1.9	6.3	1.9	10.4 (4.4)	3.6 (1.6)	8.1 (7.0)	1.5 (1.1)
Grade 4‡	5.6	1.5	6.3	0.4	3.9 (1.6)	0.8 (0.3)	0	2.0 (1.4)
Bilirubin increased								
Grade 3‡	0	0.8	0	0	3.9 (1.6)	2.9 (1.3)	5.4 (4.7)	2.0 (1.4)
Grade 4‡	0	0.4	0	0	1.3 (0.5)	0.8 (0.3)	0	0
Clinical adverse events, %								
Any clinical AE	94.4	96.6	93.8	98.1	93.6	94.0	86.5	90.5
Discontinued	5.6	4.9	6.3	8.3	3.8	4.7	2.7	6.0
Hepatobiliary AE	5.6	5.7	0	3.4	7.8	4.2	5.4	5.5
Discontinued	5.6	0.4	0	0.4	0	0.5	0	0.4
Efficacy: % with HIV RNA < 50 copies/mL (Observed Failure approach)								
	90.9	89.1	91.7	80.0	62.3	57.9	14.7	26.3

†Exposure-adjusted rates per 100 patient-years at risk (PYR); shown for BENCHMRK studies only, due to longer exposure in RAL group.
‡Division of AIDS toxicity criteria.

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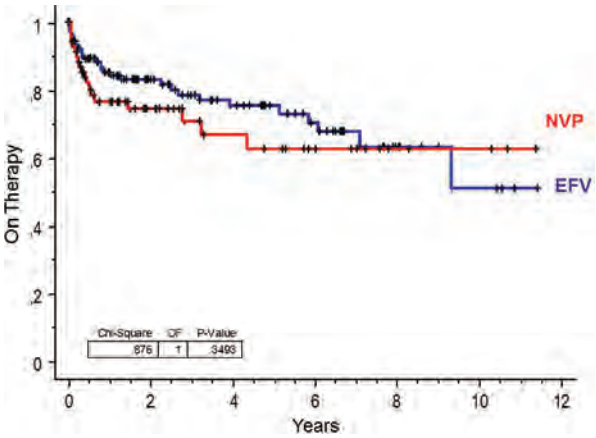
Purpose: There is some controversy about the hepatic safety of nevirapine (NVP) and current US guidelines discourage NVP use in HCV-coinfected patients. We evaluated the long-term safety and tolerability of antiretroviral therapies containing NVP or efavirenz (EFV) in this difficult-to-treat population.
Methods: This retrospective observational cohort study included all HIV/HCV-coinfected patients who initiated a regimen including NVP or EFV between January 2000 and July 2011 in two HIV centers. A detailed analysis of the HIV/HCV status at the time of NNRTI start was performed as well as of the reason for NNRTI discontinuation.
Results: In total, 195 cases were identified (121 on EFV, 74 on NVP). Mean age was 38 years, 77% were men and intravenous drug use (59%) was the most frequent mode of transmission. In 66%, HCV infection was viremic while 34% had an aviremic infection. The estimated median time on NNRTI was 5.2 years. During a total of 566 patient-years, no NNRTI-associated fatal event was observed. Treatment was discontinued due to adverse events (AEs) in 23.1% patients on EFV and 23.0% in patients on NVP. The main AE leading to discontinuation were CNS side effects in patients on EFV (20.7%) and hepatic events in patients on NVP (21.6%, grade 3 or 4 events: 9.5%). The majority of AEs in patients on NVP occurred during the first 12 months while AEs in patients on EFV were observed continuously during the observation period (Figure).



Discontinuations due to hepatotoxicity were not more frequent in patients viremic for HCV compared to aviremic patients. Pre-treatment levels of ALT, GGT or CD4 cells were also not predictive for discontinuation of ART due to an hepatic event.
Conclusions: Antiretroviral regimens, including NVP or EFV, were generally safe in HIV/HCV-coinfected patients. Severe AEs were rare. However, 23% of the patients discontinued their NNRTI regimen due to AEs. Discontinuations of NVP due to hepatotoxicity were not more frequent in patients viremic for HCV compared to aviremic patients.

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P129

Menage a trois: increased prevalence of syphilis infection in HIV-positive MSM with acute hepatitis C

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In recent years, an increase in acute hepatitis C (HCV) infection has been observed in human immuno-deficiency virus (HIV)-positive men who have sex with men (MSM). Since sexual transmission of hepatitis C does not play as significant a role in other populations, there is much speculation surrounding its transmission in HIV-infected MSM. While injection-drug use appears to play only a minor role, other drug use and specific sexual practices are frequently reported. The purpose of this observational study was to investigate for a correlation with other sexually transmitted diseases (STDs). Data on 133 HIV-positive MSM with documented acute HCV infection were included in the analysis. We investigated for new or recurrent infections with *Chlamydia trachomatis*, *Neisseria gonorrhea* (direct detection of the pathogen) and *Treponema pallidum* (serological examination) within a time frame of 24 weeks prior to or after the acute HCV infection. The control group consisted of 1034 HIV-positive MSM without HCV infection with a follow-up of one year. HIV-infected MSM with acute HCV had a higher rate of syphilis infection when compared to HIV-positive HCV-negative controls (73% vs. 43%). 31% of patients in the HCV group acquired a new (seroconversion) or recurrent syphilis infection (significant titre increase using the *Treponema pallidum* particle agglutination test = TPPA) compared to 12% of controls ($p < 0.05$). Further, 12 cases of *Neisseria gonorrhea* and 6 cases of *Chlamydia trachomatis* infection were observed in the HCV group. Due to the lack of routine screening for these infections in the control group, a comparison could not be made. Conclusions: We report a higher prevalence of other sexually transmitted diseases in HIV-infected MSM within 24 weeks before or after acute HCV infection. This observation however does not prove a pathophysiological connection between acute hepatitis C and other STDs. The high frequency of syphilis infections primarily affecting the ano-genital region suggests a possible correlation.

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P130

Boceprevir in combination with HIV protease inhibitors in patients with advanced fibrosis-altered drug-drug interactions?

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In HIV/HCV co-infected patients improved treatment outcomes have been reported for the HCV protease inhibitors (PIs) boceprevir (BOC) and telaprevir (TVR), reaching SVR rates of up to 70% in pilot trials. Due to complex drug-drug-interactions triple therapy is substantially limited in HIV/HCV-coinfected individuals. Co-administration of BOC with the commonly available HIV PIs has been reported not only to decrease the level of BOC but also to lead to relevant decreases in the respective HIV PI. Here, we report on two patients who received BOC-containing HCV triple therapy in combination with a HIV PI. Patient 1 was on darunavir 800 mg/ritonavir 100 mg once-daily mono-therapy. Using FibroScan a liver stiffness of 34 kPa suggested liver cirrhosis prior to start of HCV triple therapy. At week 5 of HCV triple therapy darunavir trough concentration was measured in the reference range with 3777 ng/ml (reference trough concentration 2400–4600 ng/ml). HCV-RNA became negative at week 10 and HIV-RNA was below detection limit (< 40 copies/ml) at all times. Patient 2 was on a simplified FTC qd and fos-amprenavir 700 mg/ritonavir 100 mg bid regimen. Liver disease had also progressed to liver cirrhosis, confirmed in FibroScan, with a liver stiffness of 32 kPa. At week 8 of HCV triple therapy fos-amprenavir trough level was measured in the normal reference range with 1699 ng/ml (reference trough concentration 750–2500 ng/ml). At week 11 HCV-RNA was < 12 IU/ml and HIV viral load was below detection limit of

<40 copies/ml at all times. Our clinical data suggest that in patients with advanced liver disease possibly drug levels of HIV PIs which are coadministered with BOC may be within the normal range. In order to better understand the true amount of drug interactions between BOC and commonly used HIV PIs in HIV/HCV-coinfected patients with more advanced liver fibrosis, urgently more PK studies are required to make HCV triple therapy accessible for a wider number of HIV/HCV-coinfected patients in desperate need of these drugs.

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P131

Raltegravir switch improves hepatitis C transaminitis in HIV-1 and hepatitis C (HCV) co-infected individuals

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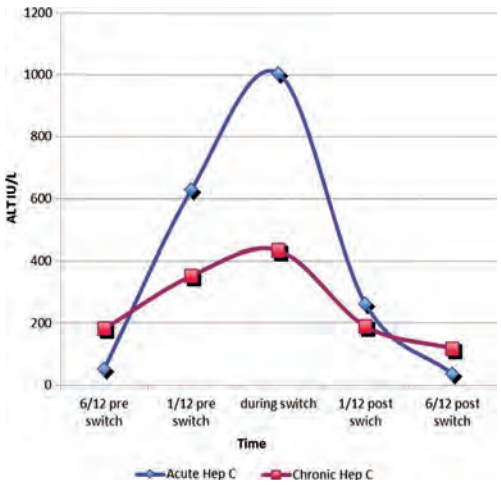
Purpose of the study: HCV is one of the most relevant co-morbidities seen in HIV-infected individuals as evidenced by the negative impact that HIV exerts on the course of HCV infection. Despite remarkable results on HIV infection alone, the impact of highly active antiretroviral therapy (HAART) on liver disease in co-infection remains unknown. We sought to explore the impact of raltegravir (RAL) on amino transferase (ALT) in HIV/HCV co-infected individuals.
Methods: HIV-infected individuals co-infected with HCV within the last 5 years receiving non-integrase inhibitor containing HAART with a subsequent switch to RAL-containing HAART were identified from a retrospectively maintained outpatient database. Patient demographics were extracted. Biochemical, virological and immunological parameters were collated and individuals received pegylated interferon with ribavirin were excluded. ALT levels at switch and post switch were compared using Kruskal-Wallis test. Spearman's Rank correlation was used to assess the relationship between ALT and HCV-RNA.
Summary of results: Twenty-seven HIV-HCV co-infected individuals were identified between January 2007 and January 2012 and seven individuals were excluded. Median age was 44 years (range: 31–68). Five had acute and fifteen had chronic HCV infection during the switch. Twenty (100%) had HIV-RNA-1 <40 copies/mL at time of RAL switch. In chronic HCV infected individuals, median ALT levels at the time of switch were 465 IU/L, decreased significantly to 179 IU/L 1 month following switch ($p = 0.0261$) and to 140 IU/L 6 months later ($p = 0.0225$). On the other hand, in acute HCV infected individuals median ALT levels were 1005 IU/L at time of switch but decreased significantly to 220 IU/L 1 month later ($p = 0.0034$) and to 35 IU/L 6 month later ($p = 0.0026$). Sustained improvement in ALT levels from baseline to 1 month and up to 24 weeks after switch to RAL was observed in both groups but the reduction in ALT levels was statistically more significant in acutely infected individuals. ALT and HCV-RNA levels showed a positive correlation at 6 months pre, post and at time of switch both in acute and chronic HCV-infected individuals (Spearman's Rank correlation).
Conclusion: In our study, RAL had a favourable effect on the liver up to 24 weeks after switch in HIV/HCV infected individuals.



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P132

Distribution of HCV genotype and single nucleotide polymorphisms (SNPs) of IL-28B gene in HIV/HCV-coinfected Thai populations

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Introduction: Hepatitis C virus (HCV) infection remains a major silent killer, worldwide, particularly in resource poor settings where treatment of hepatitis C is mainly impossible. Pegylated interferon-α (PEG-IFN) plus ribavirin (RBV) are the recommended treatment for patients with chronic hepatitis C genotype 2/3. Recent study revealed that treatment responses against HCV infection by PEG-IFN and RBV are significantly associated with the single nucleotide polymorphisms (SNPs) of interleukin-28B (IL-28B) gene. There is limited data about the HCV genotype and SNPs of IL-28B in HIV-infected Thai population. Therefore, we aimed to investigate HCV genotype and the SNP patterns of the IL-28B gene in our HIV/HCV coinfection.
Methods: Quantification of HCV RNA was done by a real-time polymerase chain reaction assay (Abbott with lower limit of detection of <12 copies/ml). HCV RNA-positive samples based on reverse transcriptase-polymerase chain reaction (RT-PCR) of the 5'UTR were amplified with primer specific for the core and NS5B regions. Nucleotide sequences of both regions were analyzed for the genotype by phylogenetic analysis. DNA sample was extracted from PBMCs or sera. Then SNPs within IL-28B gene were detected by TaqMan real-time PCR (rs8099917 and rs12979860). The data were analyzed by allelic discrimination (AD) software on the ABI-7900HT.
Results: Totally 60 HIV/HCV-coinfected patients were studied. Median HCV RNA were 5.8 $\log_{10}$ copies/mL, 70% of them had HCV RNA >100,000 copies/mL. After sequencing, the phylogenetic analyses in this study showed that genotype 3 was the most prevalent in this population (56%); following by genotype 1 (30%) and 6 (13%). Approximately 4% of them had infected for both genotypes 1 and 3. For IL-28B at rs8099917 and rs12979860 position, 95% of them were major allele (T/T or C/C) and 5% were heterozygous (T/G or C/T).
Conclusions: HCV genotype 3 is the most prevalent in our HIV/HCV coinfection. 95% of our patients have favorable IL-28B gene. This data is useful for further chronic hepatitis C treatment in Thailand.

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P133

Optimizing ribavirin dose in HIV/hepatitis C (HCV) co-infected individuals treated for HCV

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Hepatitis C (HCV) and HIV share common transmission pathways and the acquisition of both viruses are relatively common. Concurrent treatment for HCV with highly active anti-retroviral therapy (HAART) should be considered in HIV co-infected individuals to decrease the progression of liver damage. Adverse effects and less satisfactory treatment outcomes are often concerns when treating co-infected individuals. Although, direct acting antivirals (DAAs) may increase SVR, they may not be possible because of drug-drug interactions. he objective of this study is to investigate the difference in response rates of HCV treatment in HIV co-infected inmates with varying doses of ribavirin. Retrospective medical chart reviews of 52 HCV/HIV co-infected inmates who underwent HCV therapy between 2003 and 2010. All received standard doses of pegylated interferon alpha 2a or 2b and 800–1600 mg of ribavirin depending on weight. The recommended dosage for genotypes 2 and 3 is 800 mg/day. For other genotypes, if weight is <75 kg, the recommended ribavirin dose is 1000 mg/day or 1200 mg/day if >75 kg. Efficacy was defined as attaining sustained virological response (SVR) six months post treatment. Univariate analyses was performed using SPSS-18; Chi-square test with p-value <0.05 was defined significant. 52 co-infected (3 females & 49 males) were identified. Mean age was 40 ± 7 years. Caucasians accounted for 84.6%; First Nations for 13.5% and Asians 1.9%. 36 were concurrently on HAART. The genotype distribution was: geno 1, 66.0%; geno 2, 7.5%; geno 3, 26.4%. SVR by ribavirin dosage ratio (actual dosage/recommended dosage): $=1.0$; 41.2% (14/34), >1.0; 58.8% (20/34). Doses greater than 1.5 times were associated with higher adverse events and lower SVR. Suboptimal doses of weight-based ribavirin may be contributing to a lower treatment response in HCV/HIV co-infectants. In our experience, the optimal dose of ribavirin is between 1 and 1.2 times the current recommended dose. We recommend that ribavirin dose be individualized in co-infected in order to enhance the likelihood of achieving SVR. Dual therapy is more practical in many of our population because of chaotic lifestyle. Therefore optimizing the ribavirin dose should be initially undertaken.

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P134

Re-infection of hepatitis C virus infection in HIV/HCV co-infected inmates of correctional institutions, Canada

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Hepatitis C (HCV) and HIV are commonly acquired through intravenous drug use (IDU). Treatment of HCV is beneficial in reducing hepatic complications and likely decelerating the rate of progression of HIV. HCV therapy in HCV/HIV co-infected individuals is increasingly being reported to be feasible. However, re-infection is emerging as an important concern, especially in the prison population where likely related to surreptitious IDU. In this study, we report the re-infection rate of inmates in the Pacific region of Canada who have HCV/HIV and were successfully treated for HCV. Retrospective medical chart reviews of 57 co-infected inmates with a history of IDU who received HCV therapy between April 2003 and June 2012. All received standard doses of pegylated interferon alpha 2a or 2b and weight-base ribavirin for durations of 24–48 weeks depending on genotypes. After successfully attaining SVR, inmates are routinely monitored for re-infection every 6–12 months with HCV RNA qualitative analysis. Of the 57 inmates with HCV/HIV, 48 (82.8%) were Caucasians and 10 (17.2%) were First Nations. 94.7% (54) of the study population were males. The mean age at the start of treatment was 39.6 ± 7.5 years. 100% (inclusion criteria) admitted to IDU before treatment and 7 (12.1%) admitted IDU after treatment. Genotype 1 made up 56.1% (32), followed by genotype 3 at 35.1% (20) and genotype 2 at 8.8% (5). Treatment was discontinued due to adverse side effects in 4 (6.9%) and discontinued due to no response in 9 (15.5%) inmates. 2 (3.7%) were lost to follow up due to discharge to community. SVR was attained in 33 (56.9%) inmates and of those 30.3% (10) were re-infected. These re-infected cases were noted mainly in genotype 3 (60%) and genotype 1 (40%). Six had viral relapsed. SVR results are pending for three. Achieving a SVR is encouraging in HCV/HIV co-infected. Our study revealed that 30.3 % of the inmate population became re-infected after treatment. Of note, these numbers are relatively small. However, it is important that counseling regarding harm reduction and strategies should be provided before, during and after treatment to help reduce the rate of re-infection.

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P135

Adherence with screening guidelines for hepatitis C testing among HIV-infected patients

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Purpose of the study: Co-infection with HIV / hepatitis C virus (HCV) occurs commonly due to similar routes of transmission, mainly in MSM and IVDU patients. In 2009, EACS guidelines introduced the notion of systematic annual HCV screening among HIV-infected patients. This study evaluated staff knowledge, adherence to HCV screening recommendations and seroconversion rates for HCV in our HIV Reference Centre.
Methods: Eight physicians (HIV specialists) were interviewed on recommendations and perceived adherence to EACS clinical guidelines on HCV screening [1]. We then reviewed medical records of our cohort of HIV-infected patients on regular follow-up in our centre each year, from 2008 to 2011. We considered a patient to be on regular follow-up when records showed at least two clinical reviews and one HIV viral load testing during the year. Demographic features and HCV serology tests were collected from the operating software of our institution (Medical Explorer v3r9, 2008). Diagnosis of HCV was retained when serology became positive and HCV RNA was detected.
Summary of results: Though knowledge of current guidelines was excellent (100%), staff claimed a 87.5% adherence rate to these recommendations. Rate of screening rose gradually between 2008 and 2011, especially after introduction of EACS guidelines in 2009 (Table 1 and Fig 1). The maximal screening rate was in 2011, with 44% of patients tested among the general HIV population and 57% among MSM bisexual patients. This trend was statistically significant in both populations ($p<0.01$). The year 2011 displayed a marked increase in diagnosis of HCV infection, with 8 new patients diagnosed in a 963-patient-large cohort (all were MSM).

Year	Patients on regular f/un	MSM-Bisexual patients on regular f/un (%)	HCV serology tests n (%)	HCV tests among MSM-Bisexual patients n (%)
2008	818	258 (31)	292 (35)	118 (45)
2009	869	290 (33)	314 (28)	132 (45)
2010	938	308 (33)	389 (41)	198 (56)
2011	963	335 (35)	425 (44)	193 (57)

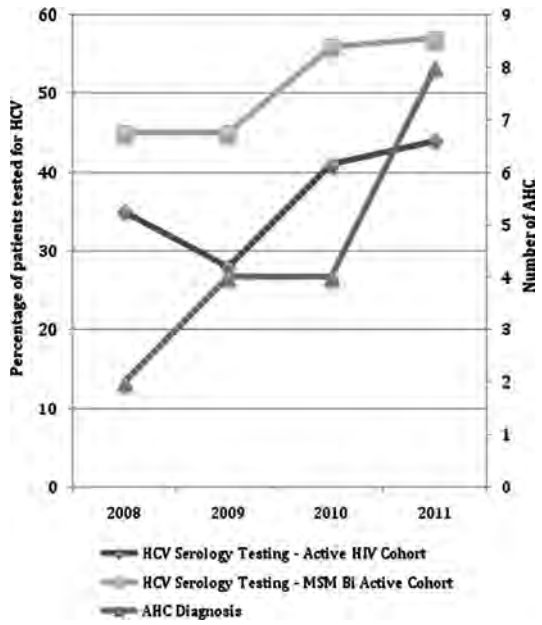

Figure 1. Evolution of HCV Screening & Acute HCV Hepatitis Diagnosis (2008–2011).

Conclusion: In our centre, knowledge of EACS guidelines on screening for HCV was good but adherence to these recommendations is poor, though it improves over time. It is consistent with published rates of compliance to clinical guidelines on screening policies for HCV among STD/HIV specialists (47–54%) [2]. However, it remains low compared to expected rates of 70–100%. Education of clinicians is warranted to increase awareness and further improve adherence to guidelines. Peer review and computer-based algorithms/reminders could be used in order to increase systematic screening.

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P136

Telaprevir-based triple-therapy in patients with chronic hepatitis C in Germany: a 12-week interim analysis of real-life data

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Telaprevir (TVR)-based triple therapy in patients (pts) with chronic hepatitis C (HCV) in daily practice in Germany is investigated in this non-interventional study. Aims are the evaluation of the implementation of futility rules, as well as safety and efficacy of TVR-based therapy. This prospective, multi-center study investigates TVR-based therapy in therapy-naïve and pretreated pts with genotype 1 chronic HCV in Germany, including pts with HIV co-infection. Patients are treated with a combination of TVR, ribavirin and peg-interferon. This interim analysis includes data from the first 100 pts (12.5% of the planned total) at 32 sites completing 12 weeks (W) of treatment. 66% of pts were pretreated for HCV. 36.4% of pts with pre-treatment were prior relapsers and 30.3% null or partial responders. Cirrhosis was present in 11% of all pts at baseline. HCV RNA levels below 800.000 IU/ml at baseline were present in 50% of pts. 67% of pts showed rapid virological response (RVR, undetectable HCV RNA at W4). Adherence to the futility rule (treatment stop if HCV-RNA $>$1000 IU/ml at W4) was 100% (N = 9). At W12, 91.4% of pts had undetectable HCV RNA. 57.7% of therapy-naïve pts and 86.4% of previous relapsers were HCV-RNA negative at both W4 and 12 (70.8% in total). Only one patient achieving RVR at W4 suffered a virologic breakthrough. Nearly all pts (99%) had adverse events (AE) during the first 12W, 6% reported serious adverse events (SAE). AEs were mostly mild (63.9%) or moderate (34.6%) and frequently mentioned dry skin/pruritus (54%), gastrointestinal disorders (48%), anorectal discomfort (30%), rash (29%) and anemia (23%). Rash was mostly rated as mild or moderate (97.1%). An Hb decrease $<$12 g/dl (female) or $<$13 g/dl (male) was reported in 87% of pts. Mean Hb levels decreased from 14.8 g/dl at baseline to 10.6 g/dl at W12; Hb levels $<$8.5 g/dl at any time within the first 12W of treatment were present in 11% of anemia cases and 6.6% required transfusion. Only one patient received erythropoietin treatment. 2 cases each of anemia and rash were considered as SAE. These interim results suggest that TVR-based triple-therapy is efficient against GT1 chronic hepatitis C in a real life setting. Adherence to futility rules was confirmed in all patients. As observed in clinical trials, adverse events were reported frequently, including anemia and rash. As more data become available, results will be updated.

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P137

Depressive disorders in HIV-HCV patients undergoing interferon-α treatment for hepatitis C

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Effective clearance rates of HCV with interferon alpha plus ribavirin treatment are reported to be reduced in the co-infected HIV/HCV population when compared to the HCV monoinfected population [1]. Neuropsychiatric adverse events are associated with hepatitis C treatment and interferon alpha-induced major depressive disorder is commonly reported [2]. This study examined the rate and predictors of depression during interferon alpha plus ribavirin treatment in a Brighton, UK cohort of HCV-infected patients including a subsample with HIV coinfection. Depressive disorder was explored at baseline and monthly up to 6 months using the Structured Clinical Interview for DSMIV and the Hamilton Rating Scale for depression. Six month treatment response was determined using viral load assay (clearance achieved if HCV RNA $<$400 IU/mL). A cohort of 237 HCV patients consented to participate in the study, including 38 coinfected with HIV. The HCV monoinfected group had a mean age of 45.60 years (SD = 8.93) and 64.3% were male. The HIV/HCV coinfected group had a mean age of 41.34 (SD = 9.8) and 94.7% were male. The most common mode of HCV transmission was intravenous drug use in both groups. Notably, clearance rates at 6 months were equivalent in both groups: 88.3% in the HCV group vs 86.5% in the coinfected group. Baseline DSMIV depressive disorder rates and mean HAMD scores were not significantly

different between groups. For Hamilton depression scores over time, a significant multivariate effect was found [Wilks' Lambda = .33, F (6, 203) = 67.73, $p < .001$, $\eta_p^2 = .67$] with the co-infected group having lower scores. For the whole sample, post-hoc comparisons revealed that all depression scores after week 8 were significantly different from baseline scores and scores at week 4. Multiple regression analysis revealed DSMIV depressive disorder at week 4 was significantly predicted by baseline DSMIV depression ($\beta = .30$), past psychiatric history ($\beta = .25$), and not being coinfected ($\beta = -.16$). Age and gender had no significant effect. Only baseline depression predicted depression at later time points. Lower rates of depression in this coinfected group may relate to antiretroviral treatment effects. Limitations of our study include a small coinfected sample size and the absence of immunological data over the time course.

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P138

Why don't we treat chronic hepatitis C in HIV patients? Results from a cohort of HIV-HCV coinfected patients from the southeast of Spain

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Purpose of the study: To know the different reasons why we decide not to treat or to delay the antiviral treatment against HCV in HIV coinfected patients.
Methods: Prospective cohort of HIV and HCV coinfected patients, followed in the Infectious Diseases Department of the Santa Lucia Universitary Hospital (Cartagena, Spain) between 1/12/2011 and 28/02/2012 in which we made transitory elastography. We evaluated the main reasons that moved us to decide not to treat or to delay the antiviral treatment against HCV: social-familiar-laboral reasons; neuro-psychiatric severe diseases; patient decision; low grade hepatic fibrosis; previous failure to pegylated interferon (IFN) and ribavirin (RBV) in no-1 genotype patients; delay in the approval of the triple therapy with INF-RBV and a protease inhibitor (boceprevir or telaprevir) by the Regional Sanitary Authority; active alcohol abuse; active diseases that contraindicate the antiviral treatment, incomplete study of HCV (VL of HCV, genotype, ILB28, abdominal ecography); previous intolerance against IFN-RBV and severe thrombocytopenia ($< 50 \times 10^9$/L).
Summary of results: The cohort included 109 patients, being 27 of them females (25%) and 82 males (75%), with a median of age of 45.8 years (SD: 6.2). In 98 patients (90%) we decided not to treat or to delay the antiviral treatment against HCV for one or more of the following reasons: 37 (34%) presented low grade hepatic fibrosis ($<$9.5 kpascal or F0-F2); 19 (17%) had neuro-psychiatric diseases; 18 (16.5%) were waiting for the approval of triple therapy by the Regional Sanitary Authority; 10 (9.2%) did not want to be treated; 10 (9.2%) had failure to IFN-RBV in no-1 genotype; 6 (5.5%) had social-familiar-laboral reasons; 6 (5.5%) presented active severe diseases; 4 (3.7%) were waiting to complete HCV study; 3 (2.8%) presented active alcohol abuse; 3 (2.8%) had previous intolerance against IFN-RBV treatment and 2 (2%) had severe thrombocytopenia.
Conclusions: In our cohort of HIV-HCV coinfected patients it was decided to delay or not to treat chronic hepatitis C in a significant proportion of subjects. The low grade of hepatic fibrosis measured with transitory elastography was the main reason for delaying the HCV antiviral treatment. The neuro-psychiatric disease was the main clinical reason to not treat HCV. The delay of the approval of triple therapy treatment by the Regional Sanitary Authority was the most relevant non- clinical reason in our prospective study.

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P139

Evaluation of the HIV-HCV co-infection status in a cohort of southeastern of Spain

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Purpose of the study: To know the main epidemiological, virological and therapeutic characteristics of HCV infection and the degree of hepatic fibrosis in a cohort of HIV-HCV co-infected patients in a health area of southeastern of Spain.
Methods: Prospective cohort of co-infected HIV-HCV patients followed in the University Hospital of Saint Lucia (Spain), which describes the main epidemiological characteristics, degree of liver fibrosis assessed by transient elastography and the level of response to treatment for HCV during the period November 30, 2011–February 28, 2012.
Summary of results: The cohort included 109 patients, of whom 27 were females (25%) and 82 males (75%), with a mean age of 45.8 (SD: 6.2) years and a mean time of infection of 18.8 (SD: 5.7) years. The main route of transmission was in this order: IDUs in 90 patients (83%), 13 (12%) by heterosexual intercourse and 3 (2.8%) in MSM. There were no statistically significant differences between the years of evolution of HCV based on the route of transmission ($p = 0.36$). In the genotypic analysis, 55 patients were genotype 1a (51%), 13 genotype 1b (13%), 19 genotype 3 (17%) and 9 genotype 4 (8.3%). The median HCV viral load was 868,000 IU/ml (6.15 $\log_{10}$). In this cohort 31 patients (28%) received antiviral therapy for HCV: 2 (1.8%) Interferon (INF) non-pegylated, 3 (2.8%) INF non-pegylated with Ribavirin (RBV) and 25 (23%) INF pegylated with RBV. In 6 cases (19%) were achieved sustained viral response (SVR). In the 25 cases without SVR (81%), 9 (36%) were partial responders, 7 (28%) null responders, 6 (24%) relapsers and 3 (12%) discontinued treatment due to problems of tolerability. In 108 patients were determined the degree of liver fibrosis by transient elastography: 48 patients (44%) had significant fibrosis (F3–F4; $>$9.5 kpascal) and 30 (28%) liver cirrhosis (F4; $>$14.5 kpascal). In patients with F4, 5 (17%) had values between 14.5–20 kpascal, 14 (47%) values between 21–40 kpascal and 11 (37%) values over 40 kpascal.
Conclusions: In our cohort, the gender predominant was male and the abuse of intravenous drugs was the main cause of HCV transmission. Most patients had genotype 1a, high viral load ($>$800,000 UI/mL) and a poor rate of SVR (19.3%), predominating the partial response rate among non-responders. A high proportion of patients (28%) had liver cirrhosis (F4), of which, a significant

proportion of subjects (37%) were at high risk of hepatic decompensation (>40 kpascal).

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P140

Insights on treatment of a Portuguese cohort of HCV/HIV coinfected patients

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Purpose of the study: This study intends to characterize a Portuguese patient population with chronic HCV and HIV coinfection, followed at our Research Unit, underline the importance of early treatment and incorporate the importance of DDA for retreatment of HCV infection.
Methods: Retrospective, observational analysis of medical records of 348 HCV/HIV coinfected patients from 2001 to 2011. Demographic, epidemiological, clinical and laboratory data and virologic response were collected.
Summary of results: Review of 348 HCV/HIV coinfected patients, 121 of those (34.7%) under treatment, predominantly male (77.0%) and Caucasians (94.8%) with a median age of 44 yrs old (min 25; max 77 yrs). Intravenous drug use was the main route of HCV infection, in 71.3% of patients, and 8.3% were related with MSM. Frequent morbidities were alcohol abuse (46.8%), illicit drug use (70.1%), methadone (25.6%) and mental disturbances (12.3%) of patients. Regarding HIV infection, six were HIV-2 and 342 HIV-1; 36.1% were stage A and 29.6% were stage C (CDC Atlanta), 94.8% on antiretroviral treatment and only 21.9% of them with more than 350 TCD4 cell count. Genotype 1 was the most prevalent (58.1%–117 genotype 1a, 26 genotype 1b); 1.6% were genotype 2, 22.8% genotype 3 and 17.5% genotype 4. Previous to treatment initiation, HCV ARN was above 600.000 IU/mL in 56.9% patients. Fibrosis was evaluated by fibroelastography in 41.1% and hepatic biopsy in 26.3% of patients; in those, 44.0% had a score above F2 (METAVIR) and ALT was elevated 2 times the limit in 38.0%, with an average value of 94 UI/L. IL 28B testing was performed in only 35 patients at the time, with 45.7% CC and 17.1% CT genotype. Treatment was started in 34.8% of patients, with 1.7 treatments per individual, and regimen was based on peguilated interferon with ribavirin in 93.6% of cases (72.1% with peginterferon alfa 2a). The SVR rate was 51.2%, with 28.9% non responders, 3 relapsers and 9 treatment interruptions due to major toxicities.
Conclusions: Our data presents a low HCV treatment initiation, illustrated by 65.2% patients who did not begin any treatment. The majority completed treatment and the SVR rate was similar to literature. Individualized approach is essential to determine the optimal time to initiate HCV treatment, to assess patient adherence and adverse events management, in order to optimize treatment and reserve DDA drugs to experienced patients with worse predictive factors.

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P142

Using phosphazide in regimes of ART in patients co-infected with HIV and HCV receiving treatment of hepatitis

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Purpose: Comparing of the efficacy and safety of treatment of chronic hepatitis C PegIFN and RBV in HIV-infected patients receiving HAART with phosphazide (PhAZT) or abacavir (ABC).
Methods: 81 co-infected with HIV/HCV patients with ART >3 months, treated by PegIFN and RBV (1000–1200 mg/day by weight) during 24–48 weeks. 50 patients (group 1) received PhAZT + 3TC + EFV or PIs, and 31 patients (group 2) -ABC + 3TC + EFV or PIs. Patients in both groups did not differ by sex, age, stage of HIV infection, body mass index, HCV genotype, HCV RNA levels, the degree of hepatic fibrosis.
Results: Virologic response EOT in 1st group was 74% (genotype 1–56%, genotype 3–92%), in 2nd group-75.9% (genotype 1–61.5%; genotype 3–87.5%). Sustained virological response (SVR) in 1st group was 62% (genotype 1–44%, genotype 3–80%), and in 2nd group –53.3% (genotype 1–46.7%, genotype 3–60%). Relapse of HCV replication within 24 wks after therapy was observed in 12% of pts with 1st group and 22.6%-2nd group ($p < 0.05$). The frequency of relapse in pts with G1 was 12% and 14.8%, with G3-12% and 27.5% (in 1st and 2nd groups, $p < 0.05$). If the duration of HCV therapy was <48 wks, SVR rates in pts of both groups was 50% and 41.1%, and if 48 wks and more –73.1% and 71.4%, respectively ($p < 0.05$). When using PIs-SVR was 52% and 57% in 1st and 2nd groups. In appointing EFV SVR in 1st group –76.2% (genotype 1–70%, genotype 3–81.8%), in 2nd group –50% (genotype 1–44.4%, genotype 3–57.1%), $p < 0.05$. Inclusion in the regime of HAART PhAZT had no significant effect on the performance of peripheral blood. Decreased hemoglobin, neutrophil and platelet counts were similar in both groups and no more than 1–2 degrees of toxicity. Reducing the CD4 + count during HCV treatment has been less pronounced when using PhAZT (compared with ABC) in combination with EFV, and with PI.
Conclusions: PegIFN and RBV therapy in pts with HIV/HCV co-infection receiving HAART, is effective in 44–47% (genotype 1) and 60–80% (genotype 3). Application of the regime PhAZT + 3TC + EFV was safe and allowed to reach the maximum frequency of SVR –76.2%.

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P143

Hepatotoxicity of antiretrovirals in patients with human immunodeficiency virus and viral hepatitis coinfections

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Background: Antiretroviral drugs used to treat HIV may cause hepatotoxicity. The high prevalence of persons with chronic hepatitis B or C coinfected, raised aminotransferases have many causes and neither specific markers is a indicator of liver injury, difficulties in interpreting the hepatotoxicity.
Objective: We evaluated hepatotoxicity in HIV/HCV- and/or HBV-coinfected patients, risk factors and severity.
Methods: Prospective study of HIV-1 patients with start HAART in Hospital Provincial del Centenario from Rosario, Argentina. Patients were classified into two groups, HCV and/or HBV coinfected vs. no coinfected. The major endpoint was hepatotoxicity defined as Benichou's Score within the first 6 months. This score is among the few validated, but little used in clinical practice. Secondary endpoints were risk factors and severity of hepatotoxicity.
Results: 140 patients were included, 39% coinfected and 61% no coinfected. Females were similar in both groups; 21% and 27% respectively. The hepatotoxicity within the first 6 month was 44.3%,

75% in coinfected patients and 25% in no-coinfected. RR 3.97 (95% confidence interval 2.34–6.75, $p < 0.0001$). The hepatotoxicity was associated with the use of illicit drugs and alcohol, symptoms, high level aminotransferases previous to HAART and NNRTI + PI. 3% of hepatotoxicity was severe.
Conclusions: 44% of HIV patients experienced hepatotoxicity, 75% in coinfected vs 25% in no coinfected. The relative risk of hepatoxocity was almost 4 times higher among in chronic hepatitis-coinfected patients, compared with those with HIV non-coinfected. In multivariate analysis, the risk factors were illicit drugs, alcohol, symptoms, high level aminotransferases and NRTI + PI. Only 3% of hepatotoxicity was severe. The Benichou's Score is better than level of aminotransferase for evaluated hepatotoxicity, so it would be recommended for use in clinical practice.

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P144

Sexually transmitted infection with an immune-escape mutant hepatitis B virus (HBV) in an HBV-vaccinated individual with acute HIV-HCV infection

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Immune pressure exerted on HBV by anti-HBV antibodies and long-term therapy with drugs that mutagenize the viral polymerase gene can select for mutations in its surface gene, leading to vaccine escape and evasion from serological detection. In general, these mutations are considered to be poorly transmissible. However, cases of HBV infection with vaccine-escape mutant viruses have been reported in vaccinated individuals, mainly from high-prevalence regions of the world. The possibility of an infection with HBV despite an effective vaccination may pose a major health issue, requiring a change in routine diagnostic and screening programmes. Here, we report a case of a HBV vaccine escape mutant infection in an effectively vaccinated individual. The patient was a 27-year old man who has sex with men (MSM) who presented in September 2011 for the first time in a Berlin outpatient HIV clinic due to a newly diagnosed HIV infection. He was aware of several sexual high-risk contacts within the past, but had a negative HIV and HCV antibody test (ELISA) in April 2011. He complained about slight fever, swollen cervical and axillary lymph nodes and general muscle pain. The Western blot confirmed an HIV infection. The HIV viral load was 24,000 copies/mL, the CD4 count was 550/mm^3. His ALT levels were elevated to 10 × the upper limit of normal (ULN) and he was additionally found to have acute HCV infection: The HCV viral load was 2 million IU/mL, the HCV genotype was 2c. Furthermore, he was anti-HBc negative, HBsAG negative, and his anti-HBs level was 121 IU/L. He reported to have been vaccinated for HBV in the past. Three months later, the patient was routinely retested. At this time point, his HBsAg turned out to be positive and anti-HBs antibodies had vanished. His HBV viral load was 600 million IU/mL, and ALT had decreased to 2 × ULN. Population sequencing revealed a genotype F and a S143L mutation in the surface gene consistent with a vaccine escape mutant HBV. A retrospective analysis of the initial blood sample showed a HBV DNA of 90 IU/mL.
Conclusion: To our knowledge, this is the first report of a sexually transmitted HBV virus with vaccine-escape mutation in a vaccinated individual. Despite a fairly high CD4 count, the transmission may have been promoted by a loss of immunity through an acute HIV infection. Clinicians need to be aware of the possibility of HBV infections with mutant viruses.

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P145

Hepatitis B virus infection in adolescents and young adults with human immunodeficiency virus infection in an urban clinic in a resource-limited setting

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Purpose of the study: Patients with HBV/HIV co-infection are at an increased risk of progression to hepatic cirrhosis and eventual liver-related death. There is limited data on HBV/HIV co-infection prevalence in adolescents and young adults in developing countries. The objective of the study was to estimate the prevalence of hepatitis B virus co-infection among HIV-positive adolescents and young adults attending an urban clinic in Kampala, Uganda.
Methods: Prospective study in HIV-infected adolescents and young adults aged from 15–24 years.
Summary of results: From the adolescent/young adult HIV clinic, we purposively selected a sample of 148 adolescents and young adults who had been diagnosed with sexually transmitted infections between April 2011 and March 2012. A total of 148 HIV-positive adolescents and young adults, 10 males and 138 females, aged between 15 and 24 years, were examined. Nine participants (6.1%) were HBsAg-positive and were diagnosed with hepatitis B. Hepatitis B was predominant amongst the female participants compared to the male participants: 6.1% vs 0%. The median age of the participants diagnosed with hepatitis B was 22 years (IQR: 18.5–24.0). Of the 9 HBV/HIV co-infected participants, 7 (77.8%) had CD4 + counts of > 250 cells/μl while 2 (22.2%) had CD4 + counts < 250 cells/μl ($p < 0.001$). The median CD4 + counts for the HBV/HIV co-infected participants whose CD4 + counts > 250 cells/μl was 434 cells/μl (IQR: 289–577). On the other hand, the participants whose CD4 + counts < 250 cells/μl had a median CD4 + count of 120 cells/μl. There was very strong evidence to show that the 8 (88.9%) HBV/HIV co-infected participants who were in WHO stage I and II were more as compared to 1 (11.1%) HBV/HIV co-infected patients who was in WHO stage III and IV ($p < 0.001$).
Conclusion: Only 6.1% of the HIV-positive adolescents/young adults had hepatitis B co-infection. HIV/HBV co-infection was predominant among female adolescents/young adults and there was very strong evidence to show that HIV/HBV co-infection was largely associated with WHO stage I and II disease.

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P146

HBV and neurological impairment in HIV-infected patients

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Objective: HIV can affect CNS in early stages of disease and determine neurological impairment. HBV DNA was found in CSF of HIV co-infected patients, but little is known about the neurotropic character of this virus. Here we assessed the degree of association between HBV infection and neurological impairment in a large cohort of long-term survivors, HIV-infected patients that experienced multiple therapeutic schemes over time.
Methods: A total of 462 HIV-1-infected patients were retrospectively followed up for 10 years for HBV infection and neurological impairment. The patients were tested for immune (flow cytometry) and virological parameters of HIV infection (Roche Amplicor, version 1.5/ COBAS AmpliPrep/COBAS TaqMan HIV-1 test) and for HBV

infection markers (HBsAg, anti HBc: Murex Biotech ELISA tests). Many of these patients have experienced between one and six regimens such as: 2 NRTIs, 3 NRTIs, 2 NRTIs + 1 NNRTI, 1 NRTI + 1 NNRTI + 1 PI, 2 NRTIs + 2 PIs.

Results: After 10 years 29.87% of the patients presented neurological impairment. Out of them 56.52% were HBV-infected. The prevalence of HIV encephalopathy (HE) in our studied cohort was 22.7% and 50.4% of these patients were HBV-infected. The median HIV diagnosis age was 7 and the median age of HE diagnosis was 10. In order to establish a possible correlation between HBV infection and HE we first reviewed and excluded the main risk factors associated with HE at the moment of diagnosis: low weight, anemia, constitutional symptoms, low CD4 + count, high plasma HIV-RNA load. No patient was infected with HCV. The groups of patients that presented HE and HBsAg and HE without HBsAg were balanced regarding sex, number of deceased patients, number of class C3 patients, but the patients in first group presented lower CD4 values at HE diagnosis vs patients from second group 2: 44.5 vs 95 cells/μL, $p = 0.3$; lower nadir CD4 count: 38 vs 51 cell/μL, $p = 0.1$; and slightly higher HIV viral load: 5.2 vs 5 $\log_{10}$ copies/mL, $p = 0.2$. There were only 53 patients that presented at the same time HE and HBV infection and the majority, 78.69%, were first infected with HBV.

Conclusions: In our studied cohort HBV infection was associated with HE but further studies are needed to prove HBV neurotropic potential. Absolute CD4 nadir count and class C3 are proved to be strong predictors of HE in HIV-infected patients even after several changes in antiretroviral therapy schemes.

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Cancers

P147

Persistence and clearance of HPV infection at anal site in a cohort of HIV-positive males

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We aimed to assess the persistence and clearance of HPV-DNA at anal site in a cohort of HIV-positive patients (pts) asymptomatic for sexually transmitted diseases (STD). Consecutive HIV-pos males underwent anoscopy, and each anal sample was analyzed for HPV-PCR detection/genotyping (high-risk genotypes: HR-HPV) and for cytologic abnormalities (Bethesda System 2001: low and high grade SIL, LSIL-HSIL). Immune activation in peripheral blood (CD8/CD38 +) was assessed by flow cytometry. Pts were re-examined at a 12–18 months follow-up visit. Comparisons were assessed by Mann-Whitney and chi-square test. Factors related to HPV persistence were identified by logistic regression. 105 HIV-pos males were studied: 89 (84%) were MSM, 76 (72%) were on HAART, median age was 42 (IQR:34–47), median CD4 count of 500 cell/mmc (IQR:366–680). HPV-DNA was detected in anal swabs from 96 (91.4%) pts, 77 of them (80%) harbored HR-HPV; 46 were coinfected with > 1 HR-HPV. Most frequent genotypes were HPV-16 (30%), HPV-58 (25%). In a median follow up of 18 months (IQR 12–24), 83/96 (86.4%) pts showed persistent HPV infection, while 13 (13.5%) became negative; conversely, 6 (5%) pts, HPV-negative at baseline, acquired HPV infection. Younger pts and those with a shorter duration of HIV infection showed a higher prevalence of HPV persistence (Table).

Conversely being on HAART and a longer duration of therapy were associated to viral clearance. Interestingly, pts with persistent HPV infection showed an activated immune profile at baseline, with significantly higher CD8 + CD38 + %. In the multivariate analysis only SIL at baseline (AOR 4.11, 95% CI 0.89–18.9, $p = .06$), being MSM (AOR 5.11, 95% CI 0.87–29.8, $p = .06$) and higher CD8 + CD38 + % (AOR 1.93, 95% CI 0.88–4.24, $p = .09$) were borderline associated with persistent anal HPV infection. Our results confirm a higher prevalence and persistence of anal HPV infection in HIV-positive males; HIV-pos pts with anal HPV infection should be thus strictly followed-up for the early detection of pre-cancerous lesions.

Table. Demographic characteristics of study population at baseline according to persistence of HPV infection

Characteristics at baseline	HPV + pts that become negative at follow-up (n = 13)	HPV + pts that remain positive at follow-up (n = 83)	p
Age*	48 (42–60)	41 (33–46)	**0.008**
MSM°	9 (69%)	74 (89%)	0.071
HAART°	13 (100%)	57 (68%)	**0.017**
HAART duration (mths)*	121 (41.5–180)	46 (21.25–119.3)	**0.030**
HIV duration (mths)*	125 (56–202)	43 (22–130)	**0.007**
CD4 + T cells/mmc*	525 (407–656)	500 (362–680)	0.59
Nadir CD4 + T cells/mmc*	285 (173–403.5)	300 (163–396)	0.99
CD8 + T cells/mmc*	846 (638–1008)	884 (748–1060)	0.26
HIV-RNA cp/mL*	59 (39–59)	59 (39–16967)	0.15
CD8 + CD37 + %	1 (1–1)	2 (1–4)	**0.003**
Dysplasia	3 (23%)	52 (62.6%)	**0.011**
HR-HPV°	8 (61.5%)	69 (83%)	0.12
Follow-up duration (mths)*	18 (12.5–30)	18 (12–24)	0.58

*Data are presented as the median (IQ R); °Data are presented as the number (percentage).

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P148

Initiation of an anal cancer screening in HIV + MSM: results of cytology, biopsy and determination of risk factors

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Incidence of anal cancer is increasing and risk of anal cancer is higher in MSM, especially if they are HIV +. European guidelines for treatment of HIV-infected adults recommend anal cancer screening

by digital rectal exam ± Pap test with anuscopy if Pap test is abnormal. A systematic anal cancer screening in HIV + MSM with anal cytology (Pap smears) was established in June 2011 in our reference centre in Brussels. If anal cytology was abnormal, high-resolution anuscopy (HRA) with biopsy was performed. 353 MSM HIV + were screened by anal smears between June 2011 and May 2012. 90% were Caucasians, median age was 44.5 years, 83% were on HAART and 74% had an undetectable viral load, median CD4 was 632/μl and 33% had a nadir CD4 < 200. Thirty-three (9.3%) were excluded because of poor quality. Cytology was abnormal in 46% of the 320 remaining patients: high-grade squamous intraepithelial lesion (HSIL) 3%, low-grade squamous intraepithelial lesion (LSIL) 24%, atypical squamous cells of undetermined significance (ASC-US) 16%, and atypical squamous cells / cannot rule out a high-grade lesion (ASC-H) 3%. Viral load (VL) was more frequently undetectable (82% vs 64%, p = 0.0003) and median duration of HAART was longer (111 vs 61 months, p = 0.0145) in patients with normal cytology. 80 HRA with biopsies have been performed. 12.5% were normal, 44% showed anal intraepithelial neoplasia (AIN) 1, 24% AIN 2 and 19% AIN 3. For this analysis, high-grade AIN (2 and 3) were put together (AIN 2+). Among patients with AIN 2+ (n = 33), cytology had showed 8 (24%) ASC-US, 3 (9%) ASC-H, 19 (57%) LSIL, 3 (9%) HSIL. When patients with normal cytology or normal biopsy and patients with AIN 2+ were compared, the only significant risk factor found for AIN 2+ was a nadir CD4 < 100/μl (32% of the patients with AIN 2+ vs 14% in patients with normal smear, p = 0.0073). Anal precancerous lesions are frequent and at different stages. Among 46% abnormal cytology, 87% had abnormal biopsy including half AIN 2+. Cytology ± biopsy is the only way to detect those lesions and should be performed systematically in HIV + MSM. Risk factor for AIN2+ was a nadir CD4 < 100/μl. A normal cytology was associated with an undetectable VL and a longer duration of HAART. Those results provide further argument for early initiation of HAART.

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P149

Disseminated bone lesions in AIDS-associated Kaposi sarcoma, a bad prognosis? About four cases

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Kaposi sarcoma (KS) can present with a wide range of clinical features ranging from minimal cutaneous disease to a rapidly progressing neoplasm. Bone lesions are most often discovered accidently in the context of radiological investigations done for the screening of KS-visceral involvement [1]. Little is known on clinical outcome and response to antiretroviral therapy (ART) and/or chemotherapy of these lytic osseous lesions. We report four cases with bone involvement in the context of systemic KS and aim at describing the long-term clinical outcome in two of these patients. Cases of AIDS-associated KS with disseminated bone lesions were collected in the HIV Unit, University Hospital Geneva, Switzerland. Patients were compared on clinical, biological and radiological features and therapeutic responses. Between 2002 and 2012, four HIV1-infected patients with T1 stage of KS presented disseminated osseous lesions (Table 1). Mean age was 43 years (range 39–47 years), mean time of follow up until our analysis was 48.5 months (SD 53.8), and mean CD4 count at KS diagnosis was 190.5 c/mL (SD 202.8). All patients showed hypodense bone lesions predominating the axial skeleton (figure 1), but no radiological imaging was performed to search for peripheral bone lesions.
No patient reported pain or experienced pathological fractures. In one patient a dual-energy X-ray absorptiometry (DXA) showed a bone mineral density within normal range after 10 years of KS diagnosis with disseminated bone lesions. No radiological change was observed in that patient despite stable KS disease after 13 cycles of liposomal doxorubicin and ART (figure 1). We describe a well-documented long-term follow up of disseminated osseous AIDS-associated KS disease. In our four cases, lytic bone lesions were asymptomatic and were not associated with bone fragility. We even could confirm the KS nature of the lesions by bone biopsy in patient B (3 months after KS diagnosis), as the differential diagnosis is wide, and include bacillary angiomatosis, cancers or metastasis. Chemotherapy and antiretroviral treatment did not affect bone lesions using CT scan despite a good response on other KS-affected sites. Prognostic factors are well established in AIDS-associated KS [2]; however disseminated bone disease does not seem to have an impact on disease evolution. A larger sample size is needed to confirm this hypothesis.

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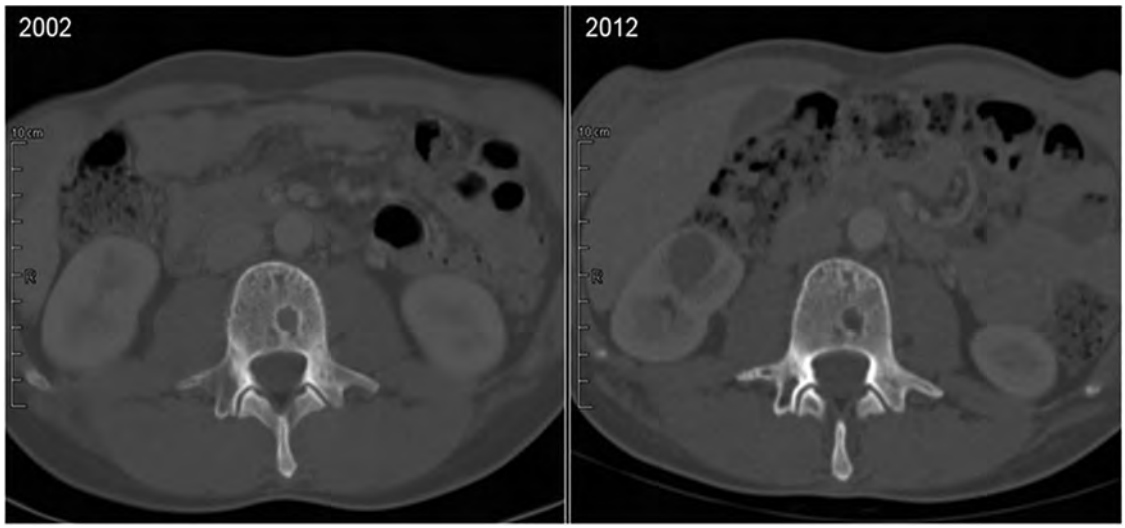

Abstract P149–Figure 1. Patient with 10yr follow up, lumbar vertebre after 6 (2002)and 13 (2012) sycles of chemotherapy with Liposomal Doxorubicin.

Table 1. Baseline characteristics for all four patients with AIDS-related KS and osseous lesions. Staging classification is based on Known SE et al. J Clin Oncol 1989; 7: 1201–7 and includes the following parameters: T for Tumor (T0 = KS confined to skin and minimal oral disease, T1 = all other manifestations), I for Immune system (I0 = CD4 cells >200/ μL and I1 = CD4 cells <200 μL) and S for systemic illness (S0 = no history of opportunistic infections, S1 = history of opportunistic infections and thrush)

Patient	Sex	Age	Ethnicity	Kaposi stage (TIS)	Follow-up time since KS diagnosis	Visceral involvement	Bone lesion (imaging)	HHV8 viremia at KS diagnosis (full blood c/mL)	Chemotherapy (first line, number of cycles, time period)	Last HIV-RNA (c/μL)	ART including PI (y/n)	Special comment
A	M	47 (1965)	CAU	1/1/1	10 years	yes	Axial skeleton, disseminated, hypodense (CT scan)	n.a.	Liposomal Doxorubicin (13, 1999–2004)	<20	yes	DXA-scan BMD within normal range
B	M	45 (1969)	SSA	1/1/1	8 months	Yes	Axial skeleton, disseminated, hypodense (CT scan)	2200	Paclitaxel (4, 2012–ongoing)	45	yes	KS confirmation by bone biopsy
C	M	41 (1971)	SSA	1/0/1	5 years	Yes	Axial skeleton, disseminated, hypodense (CT scan)	Not done	none	94	no	
D	M	39 (1973)	SSA	1/1/1	6 months	Yes	Axial skeleton, single lesions, hypodense (CT scan)	62200	Paclitaxel (3, 2012–ongoing)	<20	yes (but stop May 2012)	

(Abbreviations: SSA = Sub Saharan Africa; CAU = Caucasian; n.a. = not available DXA = Dual-energy X-ray absorptiometry; BMD = bone mineral density)

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P150

Prevalence and predictors of solid or hematological malignancies in a monocentric cohort of HIV patients from central Italy

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Introduction: HIV-infected patients have a higher risk of developing cancer than the general population. Kaposi's sarcoma (KS), non-Hodgkin's lymphoma (NHL), primary CNS lymphoma (PCL) and invasive cervical cancers are considered AIDS-defining. An increased incidence in recent years, however, has been reported also for other malignancies after the introduction of HAART.
Methods: We performed a case-control study to characterize all HIV-infected patients with both AIDS and non-AIDS-defining neoplasms observed among all consecutive patients followed at the Infectious Diseases Unit of Pescara General Hospital, since 1991 through 2012. All cases were matched with equinumerous controls without neoplasia homogeneous for age, sex and AIDS diagnosis.
Results: Out of 626 patients consecutively assisted since 1991, 57 cases of malignancy (9.1%) were observed. Of these, 45 (79.0%) occurred in males; mean age was 43.6 ± 9.3 years; 49 (86.0%) patients were diagnosed with AIDS. Tumors observed were: NHL, 17 (29.8%); SK, 13 (22.8%); HCC, 5 (8.8%); CPL, 6 (10.5%); Hodgkin's lymphoma, 4 (7.0%); solid tumors, 12 (21.1%), including 1 AIDS-defining tumor (anal cancer). Among these, 37 (66.1%) patients died; of them 14 (37.8%) had non-AIDS cancers. Cases were well matched with the 55 controls for sex ($p = 0.9$), age ($p = 0.6$) and AIDS diagnosis ($p = 0.6$). In comparison with controls, CD4 nadirs were not different (153 ± 151 in controls vs 136 ± 154 cells/mmc), while CD4 at tumor diagnosis were very different between controls (463 ± 283 cells/mmc) and cases (226 ± 209 cells/mmc, $p < 0.0001$). Among patients with malignancies, those who died had a non-significant reduction in CD4 counts ($p = 0.14$); seemingly irrelevant were smoking status ($p = 0.9$), working ability ($p = 0.4$), HCV coinfection ($p = 0.4$). Surprisingly, in patients co-infected with HBV, including HBsAg negative, antibody-positive subjects, tumors were significantly more frequent (60.7% vs. 38.8%, $p = 0.009$).
Conclusion: Factors potentially relevant for carcinogenesis in the prolonged survival patients of the HAART era may include HBV coinfection in spite of the lack of active biochemical activity (HbsAg negative) in the majority of coinfected patients. The potential relevance of this finding deserves prompt assessment in a larger multicentric cohort.

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P151

Lung cancer in HIV-infected patients

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Purpose: Several studies have shown that HIV patients are at higher risk of lung cancer. Our aim is to analyse the prevalence and features of lung cancer in HIV-infected patients.
Methods: The clinical charts of 4,721 HIV-infected patients seen in three hospitals of southeast Spain (study period 1992–2012) were reviewed, and all patients with a lung cancer were analysed.
Results: There were 61 lung cancers, giving a prevalence of 1.2%. There was a predominance of men (82.0%), and smokers (96.6%; mean pack-years 35.2), with a median age of 48.0 (41.7–52.9) years, and their distribution according to risk group for HIV was: intravenous drug use 58.3%, homosexual 20.0%, and heterosexual 16.7%. Thirty-four (56.7%) patients were Aids cases, and 29 (47.5%) had prior pulmonar events: tuberculosis 16, bacterial pneumonia 9, and *P. jiroveci* pneumonia 4. The median nadir CD4 count was 149/mm^3 (42–232), the median CD4 count at the time of diagnosis of the lung cancer was 237/mm^3 (85–397), and 66.1% < 350/mm^3. 66.7% were on ART, and 70% of them had undetectable HIV viral load. The most common histological types of lung cancer were adenocarcinoma and epidermoid, with 24 (40.0%) and 23 (38.3%) cases, respectively. There were 49 (80.3%) cases with advanced stages (III and IV) at diagnosis. The distribution of treatments was: only palliative 23 (39.7%), chemotherapy 14 (24.1%), surgery and chemotherapy 8 (13.8%), radiotherapy 7 (12.1%), surgery 4 (6.9%), and other combined treatments 2 (3.4%). Forty-six (76.7%) patients died, with a median survival time of 3 months. The Kaplan-Meier survival rate at 6 months was 42.7% (at 12 months 28.5%).
Conclusions: The prevalence of lung cancer in this cohort of HIV-patients is high. People affected are mainly men, smokers, with transmission of HIV by intravenous drug use, and around half of them with prior opportunistic pulmonary events. Most patients had low nadir CD4 count, and were immunosuppressed at the time of diagnosis. Adenocarcinoma is the most frequent histological type. The diagnosis is usually made at advanced stages of the neoplasm, and mortality is high.

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P152

Improving care for women living with HIV: initial outcomes of an integration experience

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Background: Women living with HIV are at higher risk of developing HPV-related diseases. Albeit they are systematically referred for cervical cancer screening, difficulties in obtaining timely appointments are the main barrier for an adequate gynecological care. In our unit, according to a previous survey, 67% of women reported this problem. Therefore, in January 2011 the integration of HIV and gynecological care was sought through the provision of gynecological care within the Infectious Diseases Unit in our hospital.
Methods: A weekly specific clinic for women living with HIV cared by HIV and gynecological specialists was implemented. Appointments are given at the HIV clinic, with no need of referral. Pap smear and colposcopy are offered in the same place. Data are collected through standardized forms. Baseline data from the first hundred patients referred are presented.
Results: Ninety-six women were assisted. Median age was 40 years (IQR 36–46.5). Median time from HIV diagnosis was 10.6 years (IQR 4.9–16.4). 82% patients were on HAART. Median CD4 cell count was 473 cells/cc (IQR: 287–614) and 49% had viral load <50. 48% lacked a gynecological control for the last 2 years. 24% had been previously diagnosed and/or treated for HPV-related pathology. Cervical Pap smear results ($n=94$): 59% were negative; 20% had LGSIL and 2% had HGSIL. Of those diagnosed with SIL, 29% had history of HPV-related lesions. Of note, 23% had infections or inflammatory results. Clinically significant abnormal colposcopies were seen in 21/93 (23%) patients. Of those, 30% were diagnosed SIL in the Pap smear.
Conclusions: Integrating the gynecologist with the ID Unit allowed women living with HIV easier access to gynecological control. The high number of abnormalities in the Pap smears detected in this pilot study reinforces the need of improving cervical cancer screening for prevention and early treatment through integrated approaches.

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Other

P153

Changes in hospitalizations due to opportunistic infections, chronic conditions and other causes among HIV patients (1989–2011). A study in a HIV unit

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Background: Reduction in mortality and morbidity in HIV patients due to the introduction of HAART have resulted in changes in patterns of hospital admissions.
Objective: To examine trends of HIV patients hospital admissions.
Design and method: Serial cross-sectional analysis of HIV-hospitalized patients from 1989 to 2011 in an HIV Care Unit. Each hospitalization was classified as major categories: opportunistic infections, other infections, drug-related admissions, chronic hepatopathy, AIDS and non-AIDS-related tumours and chronic medical conditions (COPD, diabetes) and as specific diagnosis: tuberculosis, PCP, CMV, bacterial pneumonia and others. We considered 4 periods of time: pre-HAART, 1989–1996; early HAART, 1997–2001; intermediate HAART, 2002–2006; and present HAART, 2007–2011.
Results: We evaluated 2588 admissions. 20.7% of patients were unaware of HIV infection before first admission; this proportion did not change along the time ($p=0.27$). No previous outpatient follow-up was seen in 34.9% of patients. There were differences in diagnosis, mortality, age and mean inpatient stay time (Table 1) between the analyzed periods of time.
Conclusions: (i) HAART and older age have changed the pattern of hospital admissions with a decrease of OI-related admissions and an increase of chronic diseases and non-AIDS-related tumours and with a decrease in mortality and length of inpatient stay. (ii) Proportion of patients with unknown HIV serostatus before admission has not changed along the time. (iii) Pneumonia, respiratory tract infection and tuberculosis were the more common causes of admission.

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P154

High acceptability of cognitive screening in HIV-infected patients: a pilot study

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With combined antiretroviral therapy (cART) life expectancy of HIV-infected persons is close to the one of non-infected persons. Identifying neurocognitive deficits in ageing HIV-infected individuals is important. This study aimed to evaluate the acceptability of screening neurocognitive deficits in HIV-infected patients. Thirty patients (26 men, 4 women) from the HIV clinic were examined with a new screening test and an in-depth neuropsychological examination. The screening tests consisted of questions and

Abstract P153

	OI	HIV tumours	Non-HIV tumours	Chronic diseases	Mortality	Mean age	Mean hospital stay	Pneumonia	Resp infect	TBC	CMV	PCP	PML
Pre-HAART 682 adm.	51.7%*	5.1%*	0.8%*	3.2%*	10.1%*	36.1*	23.9*	12.1%*	14.1%*	14.1%	15%*	9.5%*	5.1%
Early HAART 632 adm.	34.5%	4%	2.2%	9%	4.6%	38.4	17.2*	21.1%	19.9%	11.7%	5%	8.2%	4.1%
Intermediate HAART 613 adm.	31.4%*	2.4%	2.8%	7.7%	4.4%	39.6	15.7	25.6%*	23.2%	11.4%	1.7%*	3.4%*	3%
Present HAART 661 adm.	21.8%*	0.8%*	4.1%*	15.9%*	3.8%*	42.9*	14.2	29.8%*	29.2%*	10.9%	1.9%*	4.2%*	2.2%

*$p<0.05$

examinations on cognition in everyday situations, mood and selected cognitive functions (word list memory, grooved pegboard, psychomotor speed, trail-making test, psychomotor speed and executive functions, digit symbol test). Also, patients received a questionnaire to evaluate test acceptance. The mean age of the patients was 52.5 (30–74) years, mean education 12.5 (8–18) years. Seven patients had HIV-stage CDC A, 12 B and 11 CDC stage C. The mean CD4 count was 657 cells/μl, the mean HIV viral load <20 cop./μl. All patients were treated with cART (7 with efavirenz). The screening test was done assisted by a nurse and lasted 26 minutes (mean). The screening indicated pathological signs of neurocognitive function in 11 (42%) patients. The in-depth neuropsychological assessment revealed pathological conditions in 25 (83%) of patients; i.e. 16 (53%) patients had ANI (asymptomatic neurocognitive impairment), 8 (27%) had MND (mild neurocognitive disorder) and 1 (3%) had HAD (HIV-associated dementia). Most patients (43.3%) judged the test as not too difficult and 56.6% as partly difficult. 96.6% of patients viewed the instructions of nurses as clear, 3.3% as unclear. 93.3% felt the test has not affected privacy and 83.3% estimated the screening as valuable and not worriesome. 83.4% of all patients were interested in their results and for none of the patients the test was too long. The test acceptability by the study nurses was also good. Only in 3.4% of tested persons they judged the test as too difficult for the patient. In 86.7% of tests they estimated the screening as valuable and in again 86.7% as not worrisome. For none of the nurses the test duration was too long. Only 16.6% of the patients had a completely normal neurocognitive testing. A short screening test lasting less than half an hour to search neurocognitive disorders assisted by a nurse is widely accepted by patients and nurses.

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P155

Prevalence of persistent parasitic infections in foreign-born, HIV-infected persons in the north of Spain

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Background: Foreign-born, HIV-infected persons are at risk for subclinical parasitic infections acquired in their countries of origin. This study presents the results of this screening program.
Methods: A prospective, descriptive study was designed to include all the immigrant patients diagnosed of HIV infection attending in Hospital Central de Asturias, Spain, 2006–2011. We included demographic variables, CD4+cells count and viral load at time of diagnosis. Screening comprised blood count, biochemistry, basic urinalysis, hepatitis B virus (HBV), HCV, strongyloidiasis and schistosomiasis serologic analysis, stool parasites, blood test for filarias, PCR for malaria and Chagas disease serologic analysis and PCR in persons from Latin America. Qualitative variables were compared using the χ^2 test, the Fisher exact test, when necessary. For quantitative variables, the Student t test for nonpaired variables or the Mann-Whitney U test were used. Significance was designated at $p<0.05$.
Results: 57 patients were analyzed. 70% are sub-Saharan immigrant and the rest Latin American. The most frequent countries of origin were Equatorial Guinea (43%), Nigeria (10%), Senegal (9%), Colombia (9%). Average time in Spain: 1,061 days (3–9,876). Average Cd4+ cells were 209 cells/mm^3. The average viral load were 47,000 RNA viral copies. Intestinal parasites were diagnosed in 27 patients: *T. trichuria* (22%), strongyloidiasis (11%), amebiasis (7%), and schistosomiasis (5%), *G. intestinalis* (4%). All infections by *T. trichuria* were diagnosed in Equatorial Guinea patients. Other parasites diseases were: filariasis by *M. perstans* (9%); malaria (9%, all from Equatorial Guinea), Chagas disease (4%). Eight patients had chronic hepatitis B virus and 2 patients had HCV hepatitis. 19% of patients had latent syphilis, significantly more frequent in sub-Saharan patients (9 vs 2; $p=0.04$). In 12 patients the screening did not show any disease.
Conclusions: Given the high prevalence of certain parasite infections and the potential lack of suggestive symptoms and signs, selected screening for strongyloidiasis and schistosomiasis or use of empiric antiparasitic therapy may be appropriate among foreign-born, HIV-infected patients. Identifying and treating helminth infections could prevent long-term complications.

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P156

Syphilis in HIV-infected patients: predictors for serological failure and serofast state

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Purpose: HIV-infected patients treated for syphilis may be at increased risk for serological failure and serofast state. Our aim was to analyse serological response to treatment in HIV-infected patients diagnosed with syphilis, and factors associated with serological cure and serofast state.
Methods: Open-label, no controlled study of a series of HIV-patients diagnosed with syphilis during 2004–2011. Patients were categorized by rapid plasma reagin titer (RPR) into success (4-fold decrease in RPR by 12 or 24 months after treatment of early or late syphilis), serofast (success with persistently stable reactive RPR), and failure/re-infection (failure to decrease 4-fold in RPR by 12 or 24 months after treatment or sustained 4-fold increase in RPR after treatment response).
Results: 141 HIV-patients were diagnosed with syphilis during the study period (104 early syphilis, 36 late or indeterminate latent syphilis). The mean age was 36.3 years, 98.5% were male, and 87.2% homosexual men. In 46 (32.6%) cases, HIV and syphilis infection diagnosis were coincident (mean CD4 457/mm^3 and HIV-VL 4.72 $\log_{10}$). Among patients with prior known HIV infection, 65 were on antiretroviral therapy (ART) at syphilis diagnosis (mean CD4 469/mm^3, 76.9% undetectable HIV-VL). 116 patients satisfied criteria for serological response analysis (89 early, 24 late/indeterminate). At 12 months of early syphilis treatment (89.2% penicillin) there were 16 (18%) failures, and at 24 months of late/indeterminate syphilis (91.7% penicillin) there were 5 (18.5%) failures. Overall, 36 (31.0%) patients presented serofast state. Treatment failure was related with lower CD4 count (295 *vs* 510/mL; $p=0.045$) only in patients with coincident diagnosis. Serofast state was related with older age (41 *vs* 36 years; $p=0.024$), and lower CD4 count (391 *vs* 513/mm^3; $p=0.026$).
Conclusions: In this series of HIV-infected patients, with many patients on ART and with good immunological and virological parameters, serological failure and serofast state were frequent. Immunological status, and age could influence on serological response to syphilis treatment in HIV-infected patients.

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P157

Role and interpretation of FDG-PET/CT in HIV patients with fever of unknown origin: a prospective study

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Purpose of the study: Fever of unknown origin (FUO) is a challenging clinical entity in HIV patients. FDG-PET/CT is well validated in the work-up of FUO in HIV-negative patients but in HIV viremic patients, metabolism of HIV reactive lymph nodes could decrease its specificity. We prospectively evaluated the usefulness of FDG-PET/CT in FUO in HIV-positive patients and in particular whether HIV viremia impacts on FDG-PET/CT performance.
Methods: FDG-PET/CT was performed in 20 HIV patients with FUO and compared with FDG-PET/CT in 10 HIV viremic patients without FUO. Final diagnosis for FUO was based on histopathology, microbiology, or clinical and imaging follow-up. Mode of diagnosis, accordance of FDG-PET/CT with final diagnosis, localization of invasive diagnosis procedures was recorded in order to assess usefulness of FDG-PET/CT.
Results: FDG-PET/CT showed a different pattern in FUO and asymptomatic viremic patients. Reactive HIV lymph nodes in asymptomatic viremic patients were mostly peripheral with mean SUVmax of 6.5. In patients with FUO and underlying focal pathologies, hypermetabolic lymph nodes were central with mean SUVmax of 11.6. Presence of central lymph nodes with high FDG uptake in had a 100% specificity for focal pathology, even in viremic patients and absence of these had 100% negative predictive value. Lymph node biopsy in central hypermetabolic areas allowed identifying underlying disease in all FUO patients. For peripheral lymph nodes, a ROC curve was built in order to define the best cut-off of SUVmax for biopsy: SUVmax of 6–8 showed a sensitivity of 62.5% and specificity of 75%. Lymph nodes with SUVmax <4 had sensitivity of 0%.
Conclusions: FDG-PET/CT contributed to the diagnosis or exclusion of a focal etiology of the febrile state in 80% of HIV patients with FUO. Although number of patients was small, we could highlight several clear-cut features to help interpreting FDG-PET/CT in HIV patients with FUO. As in HIV-negative patients, we showed the usefulness of FDG-PET/CT in FUO in HIV patients even if they are viremic.

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P158

Kidney transplantation in HIV-positive patients: a report of 14 cases

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The HAART reduces the risk of HIV-related renal disease but the incidence of end-stage renal disease (ESRD) is increasing. Therefore, efficacy and safety of renal transplantation (Tx) is an important resource in the HIV-infected population. We reported the results of kidney Tx in HIV+patients from deceased donors from June 2007 to March 2012 at our institution. The patients had to have CD4+ T-cell counts $\geq 200/mm^3$ and undetectable plasma HIV-RNA if on HAART. The induction immunosuppressive therapy consisted of metilprednisolone and basilixmab; tacrolimus and/or mycofenolic acid were used for maintenance therapy. The therapeutic drug monitoring (TDM) has been performed for the adjusting of both their doses [1]. A total of 14 patients underwent kidney Tx. They were on dialysis (haemodialysis = 13, 92.9%; peritoneal = 1, 7.1%) for 5 ± 3.1 years and they were included on the Tx waiting list for 10 ± 8 months. The baseline characteristics are showed in Table 1.

Donor at baseline	
Mean age	38 ± 12.5 years
Deceased	14/14 (100%)
High/unclassified infectious risk	9 (64.29%)
Recipients	
Mean age	44 years
Patients with previous AIDS-defining events	3 (21.4%)
Median follow-up months (IQR range)	42.75 (8.5–55.2)
Patient survival at last follow-up	14/14 (100%)
Graft survival at last follow-up	13/14 (92.9%)
Mean time of acute rejection since Tx	28 ± 20 days
Patients not treated with steroid at last follow-up	6 (43%)
Plasma creatinine at last follow-up	1.87 ± 1.93 mg/dl
Severe infectious complications (CMV pneumonia, malaria, Kaposi sarcoma)	3 (21.4%)
Diabetes	3 (21.4%)
CMV infection without localization	3 (21.4%)
Bacterial pneumonia	4 (28.6%)
Reactivation of HIV RNA	3 (21.4%)

At the last available point of follow-up (median = 42.8 months, IQR = 8.5–55.2), 8 out of the 13 patients (61.6%) without steroid had at least one acute rejection episode, but only 1 patient lost the graft, after 43 months (7.1%) due to chronic rejection associated with infectious and vascular complications. After Tx the median CD4+T-cell count increased from 382.5 (IQR range = 233–415) to 434 (IQR range = 282–605) cells/mm^3 ($p = 0.055$). In Figure 1 are reported the CD4+trends of 9 patients with a follow-up of at least 6 months.

HIV infection was well controlled, with only 2 (14.3%) cases of virological failure which were promptly resolved after HAART regimen modification. Table 1 shows the observed infectious complications. The skin Kaposi sarcoma has been resolved by switching to immunosuppressive therapy with sirolimus [2]. Kidney Tx appears to be safe in HIV-positive patients undergoing HAART. The viro-immunological parameters remained well controlled with no increases in infectious complications or neoplasm and a satisfactory control of HIV infection. However, the high rejection rate is a serious concern and suggests to consider a steroid-containing immunosuppressive regimen also in these patients.

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P159

STI screening in people living with HIV: are we getting the whole story?

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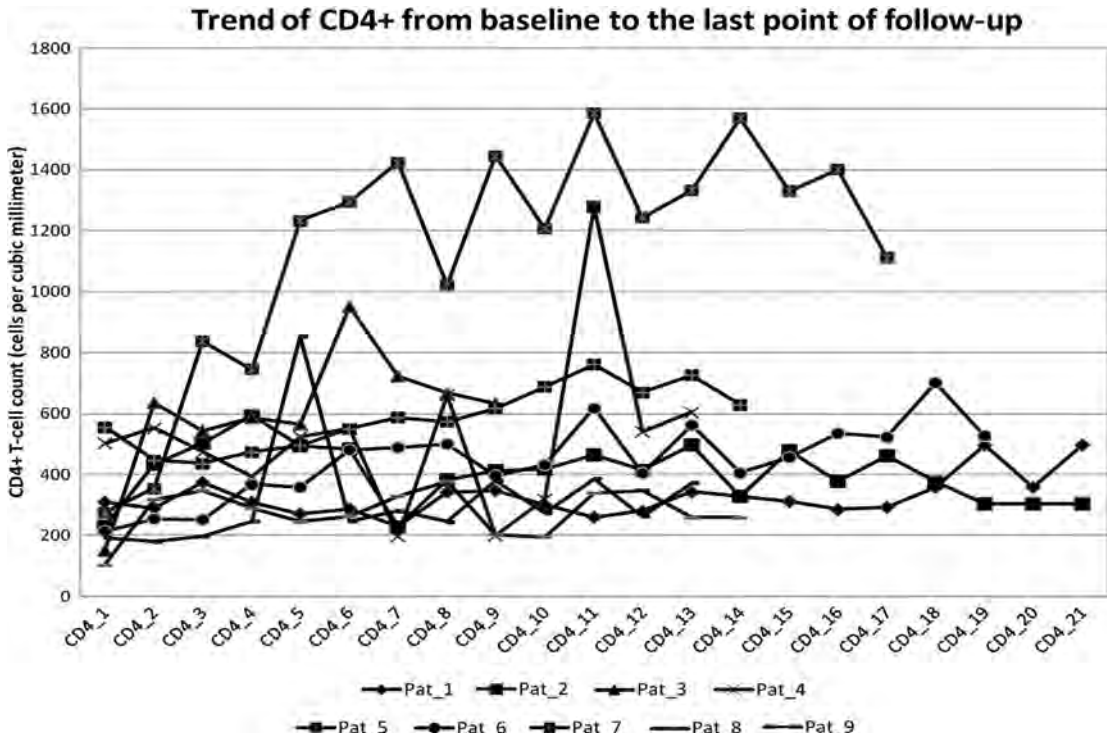
People living with HIV are able to enjoy meaningful sexual relationships; there remains however the key responsibility of reducing transmission to others and within this the prevention and

Abstract P158



management of sexually transmitted infections (STIs). In 2008 and 2011 BHIVA published guidance on STI testing recommending annual STI screening in asymptomatic patients with consideration of more frequent screening dependent on risk. We conducted a retrospective case note review of 385 HIV-positive patients presenting for routine HIV care in a large city teaching hospital HIV clinic during 2010. Data included demographics, HIV parameters, sexual history and STI screening were collected. 297 (77%) were male, 215 (56%) white British, 105 (27%) black African. 229 (56%) were MSM. Median age was 37 years (range 17–75) and the median year of diagnosis was 2005 (range 1998–2010). Median CD4 count was 467 cells/mm^3 (range 1–1849) and undetectable viral load in 248 (64%). 296 (77%) were on HAART. 18 were co-infected with HBV and 17 with HCV. 249 (65%) patients had at least one STI screen. 56 (15%) declined testing and 77 (20%) were not offered. 238 (62%) had regular partner(s) and of these 109 (46%) were known HIV-positive and 128 (32%) reported casual partners. 11 (3%) had sex exclusively with HIV-positive partners. 91 (69%) always used condoms for vaginal sex. With regards to anal sex, 16 (68%) always used condoms. 11% used condoms for oral sex. 25 patients (6.5%) had rectal chlamydia, 27 (7.0%) had rectal gonorrhoea, 8 had dual infection and 3 had LGV. 10 HSV, 12 syphilis and 6 acute HCV infections were diagnosed during this period. 172 patients reported monogamous relationship over 12 months 11 (6.4%) of these had STIs. 160 reported consistent condom use for anal sex; of these 24 (15%) had rectal STIs diagnosed. Routine STI screening is offered annually in our cohort with reasonable uptake rates. STIs are still being diagnosed in people living with HIV despite our repeated safe sex messages and self-reported condom use. In our cohort this was almost exclusively in MSM. Sexual history and safe sex education should be included at each visit. STI screening should be offered annually even in those reporting monogamous relationships and more frequently dependent on sexual history.

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P160

High KSHV prevalence among HIV-infected males in North India

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Background: Kaposi sarcoma is the most common cancer associated with AIDS worldwide. HIV is endemic in India but there are no studies on this co-infection from India. Our present study examined the seroprevalence of HHV8 infections in adult Indian males infected with HIV.
Methods: The study was carried out at AIIMS, a tertiary care hospital in Delhi, India. We enrolled 93 HIV-positive males naïve of ART. We employed whole virus enzyme-linked immunosorbent assay [ELISA; Advanced Biotechnologies Inc, Columbia, MD, USA]. A univariate analysis including age, marital status, mode of HIV transmission and CD4 count were used to determine variables associated with HHV8 seropositivity. Significant variables were adjusted in a logistic regression model expressed in odds ratio (OR) with 95% confidence interval (CI). $P < 0.05$ was considered significant.
Results: The seroprevalence of KSHV infection was 33.3% in HIV-1 infected males. HHV8 seropositivity in HIV-infected males. Age was independently associated with the age group > 25 years [OR $= 9.5$; 95% CI $= 1.98–45.75$.
Conclusion: Taken together, our findings showed high rates of KSHV antibody prevalence in the male cohort of suggesting that KSHV infection may be markedly associated with HIV-1 infection in India especially in the heterosexual group. However, a further KSHV seroepidemiological survey; including a representative number of Indian cohorts of HIV-1-infected outpatients, is needed to further confirm our present findings.

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P161

Infections and cancer after ARV: a Portuguese cohort

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Background and purpose of the study: The advent of antiretroviral therapy (ARV) resulted in a significant decrease in opportunistic infections; however these diseases still represent an important cause of morbidity and mortality. ARV also changed the spectrum of cancers presented by HIV patients as a result of immune recovery and increased life expectancy. We intend to describe the variety of infections and cancers, AIDS or non-AIDS related, identified in our patients in the new era of ARV and also identify possible risk factors related to this conditions.
Methods: Assessment and registry of infectious and neoplastic conditions occurring after initiation of ARV in a cohort of HIV-infected patients who started ARV between January 2007 and December 2011. We included records of these conditions until March 2012. Epidemiological, clinical and laboratory data were analyzed and compared with a control group of HIV-infected patients that started ARV in the same period but did not experience those comorbidities. Patients lost to follow-up were excluded. Statistical significance of the differences encountered was evaluated with T-student test and chi-square; differences were considered statistically significant when $p < 0.05$.
Results: 497 patients were included (71.0% were men) with a mean age of 43.4 ± 12.5 years and average follow-up of 30.9 ± 16.8 months. In the analyzed period there were 112 events in 91 patients: 85 infections and 27 cancers. The most common infectious condition was tuberculosis ($n = 13$) and the most common cancer was non-Hodgkin's lymphoma ($n = 8$). The interval between the introduction of ARV and the onset of these conditions was 15.1 months (min: 0.03, max: 57.40). We identified 22 deaths: 11 were result of infection and 11 from cancer. Statistically significant differences between the groups compared were identified in the following variables: risk factor for HIV infection, co-infection with hepatitis B, clinical stage, viral load and CD4 T lymphocyte count before the beginning of ARV.
Conclusions: We identified a substantial number of infections and cancers in our cohort, with tuberculosis and lymphomas continuing to be particularly noteworthy. Patients who had these conditions initiated ART with more severe immunosuppression and higher viral load which reinforces the importance to establish a prompt diagnosis which enables an efficient treatment and low morbidity associated with infections and cancers, particularly those related to AIDS.

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P162

Hospitalisation causes of HIV-infected patients in 2011 in an HIV reference center in the Paris region, France

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Background: In France, approximately 100,000 HIV-infected patients are regularly followed up in hospitals. Due to the availability and efficacy of antiretrovirals, the number of hospitalised patients is decreasing in favour of outpatient management. In order to optimise the balance between patients' hospitalisation and hospital structures, collection of recent data on the profile of hospitalised patients is essential.
Objectives: Describe the frequency, causes of hospitalisation and characteristics of hospitalised HIV-infected patients.
Methods: Retrospective study of a cohort of HIV-infected patients hospitalised more than a day at the Bégin hospital (Saint-Mandé) between January 1st and December 31, 2011.
Results: During this period, 170 hospitalisations were recorded, corresponding to 78 patients (61 M /17 F). Main causes of hospitalisation were: infections (52%), surgical treatments (10%), haemopathies/cancers (8%), cardiovascular diseases (8%), neurological illnesses (7%), hepatic and digestive tract pathologies (6%). Principal admission wards were: an HIV reference unit (67%), the emergency department (7%), cardiology (7%), surgery ward (7%), internal medicine (6%) and intensive care unit (3%). One out of five patients was admitted for an acquired immune deficiency syndrome-related event (opportunistic infection or cancer). Two-thirds of patients had one or several co-morbidities. Only 61% (48/78) of patients had more than 200 CD4+ lymphocytes/mm^3 and 69% (54/78) an undetectable HIV viral load. The average length of stay was 6.5 days (range: 2–38). Four (5%) fatalities were reported and 85% of patients returned home.
Discussion: Hospitalisation of HIV-infected patients remains significant and the causes are diversifying. Infections, in particular in patients screened at a late stage, cancers and management of comorbidities justify a coordinated referral to the different specialists.

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P163

Aspergillosis in HIV patients: a case series

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Purpose: Aspergillosis is uncommon in HIV patients and has been mostly reported in patients with CD4 $< 50/\mu L$. Data on risk factors and prognosis are scarce. We reviewed 19 cases of aspergillosis diagnosed in our HIV cohort.
Methods: In the Brussels Saint-Pierre HIV cohort, 19 patients were diagnosed with aspergillosis between 1998 and 2012 (0.87/1000 patient/year of follow-up). We analyzed retrospectively and described localization and invasiveness of aspergillosis, risk factors, treatment and outcome of these patients.
Results: Patients were mostly African (74%) and mean age was 40 years (22–60). Clinical presentation were 10 invasive aspergillosis (IA) (53%), 6 pulmonary aspergilloma (31%) and 3 sinus fungal ball (16%). The global mortality was 42%. IA was proven for 3 patients, probable for 4 patients and possible for 3 patients according to IDSA definitions. Risk factors for IA included CD4 $< 200/\mu L$ (70%; 40% < 50 CD4/μL), corticotherapy (50%), neutropenia (20%), intravenous drug use (20%), cirrhosis (20%). IA arose in the time course of septic shock in 30% and opportunistic infections occurred concomitantly in 40%. Seven patients out of 10 with IA died including 3 patients before antifungal therapy. The 3 survivors recovered without relapse. Four patients were treated with voriconazole, 2 with itraconazole, 2 with liposomal amphotericine, 1 with caspofungine, and 2 with bitherapy. Among patients with aspergilloma ($n = 6$), the major associated risk factor was tuberculosis sequelae (80%). Two patients were successfully treated with surgery and voriconazole, 1 died from massive hemoptysis, 2 were lost to follow-up, 1 is currently asymptomatic

without treatment. Among patients with sinus fungal ball (n = 3), all recovered without relapse with surgical treatment associated with voriconazole for one.

Conclusion: Incidence of aspergillosis in HIV patients remains low but in accordance to previous reports, mortality of IA is high (70%). CD4 < 200 is the most common risk factor (70%) but 80% of patients who died had other risk factors, mostly corticotherapy. IA is often concomitant with other infectious diseases (40% with other opportunistic infections and 30% in the time course of septic shock), which can potentially delay diagnosis. Prognosis of pulmonary aspergilloma and sinus fungal ball is better.

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LABORATORY MONITORING OF DISEASE AND THERAPY

P164

Assessment of patient complexity using routinely collected data: The UK CHIC study

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We identified predictors of clinical complexity based on data collected in the UK CHIC Study. All subjects under established care (>1 year) from 2000–2010 were included. Each subject's follow-up (1 year after study entry to last clinic visit, death or 31/12/2010) was stratified into a series of 6–monthly periods and his/her status was assessed at the start of each. Using Poisson regression (with generalised estimating equations to allow for multiple entries per subject), we studied associations between demographic/clinical factors, CD4 count/percent, viral load (VL), calendar year and measures of prior/current antiretroviral (ART) use, and the development of a new AIDS event or death during each period. A complexity score was derived from the coefficients of the final model; subjects were categorised into ten equally sized groups based on the score, and event rates were calculated for each group. The 31,338 eligible subjects had a median (interquartile range) age of 36 (10, 42) years at baseline. Ethnicity was white (55%), black African (27%), black other (5%), other (9%) and unknown (4%). Mode of acquisition was sex between men (52%), heterosexual sex (37%), other (5%) and unknown (5%). Subjects contributed a total of 377,284 periods of follow-up (181,170 person-years [PY]) of which 5796 included a clinical event (rate/1000 PY: 3.20 [95% confidence interval 3.12, 3.28], 4322 AIDS events, 1534 deaths). As an active AIDS-defining event in the past 6 months was the dominant predictor of a new clinical event (relative rate 41.55), subjects with an active event were excluded from further analysis. Risk factors for a clinical event in patients without an active AIDS event (Table 1) were earlier calendar year, non-white ethnicity, older age, lower CD4 count, >80 CD4 cell drop from previous visit, being off ART or on ART with a VL >10,000 copies/ml.

Hepatitis co-infection and previous experience of immune suppression were associated with lower clinical risk. A score based on this model discriminated reasonably well between subjects who did/did not develop an endpoint over the next 6 months (approximate C-statistic: 0.72), with event rates increasing from 0.49/100 PY in the lowest score group to 7.16/100 PY in the highest. A score based on clinical markers may provide a means to identify those who will experience clinical progression over the next 6 months, allowing this group to be targeted for closer monitoring and funds for HIV care to be distributed appropriately.

Table 1. Estimates from multivariable Poisson regression model of factors associated with a new clinical event over subsequent 6-month period (excluding patients with an active AIDS event)

	RR*	(95% CI)	P-value
Calendar year / later year	0.97	(0.96, 0.98)	0.0001
Ethnicity			–
White	1	–	–
Black African	1.23	(1.13, 1.34)	0.0001
Black other	2.34	(2.06, 2.65)	0.0001
Other	1.64	(1.24, 2.17)	0.0001
Unknown	1.64	(1.38, 1.94)	0.0006
Age (years)			
<30	0.59	(0.51, 0.69)	0.0001
≥30, <35	0.72	(0.64, 0.80)	0.0001
≥35, <40	0.75	(0.69, 0.83)	0.0001
≥40, <45	0.84	(0.76, 0.92)	0.0001
≥45	1	–	–
CD4 count (cells/mm^3)			
<200	2.49	(2.25, 2.75)	0.0001
200–349	1	–	–
350–499	0.72	(0.65, 0.80)	0.0001
≥500	0.51	(0.46, 0.57)	0.0001
Unknown	0.71	(0.54, 0.93)	0.01
>6 Months of immune suppression	0.84	(0.76, 0.93)	0.001
>80 Cell drop in CD4 count from previous visit	1.15	(1.05, 1.27)	0.004
Previous (non-active) AIDS event	2.51	(2.31, 2.74)	0.0001
Viral load/HAART status			
On HAART VL <1000 c/ml	1	–	–
On HAART VL ≥1000 c/ml	1.81	(1.62, 2.02)	0.0001
On HAART VL ≤10000 c/ml	1.23	(1.10, 1.38)	0.0002
On HAART VL >10000 c/ml	2.61	(2.38, 2.86)	0.0001
Missing viral load	2.00	(1.55, 2.56)	0.0001
Hepatitis B/C co-infection	0.81	(0.73, 0.89)	0.0001

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P165

Optimisation of baseline genotypic testing for safe and efficient maraviroc administration

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Different diagnostic parameters may affect the tropism prediction reliability. The impact of usage of FPR cut-offs < 20%, use of viral RNA versus proviral DNA samples, single versus triple amplification, and presence of MVC resistance mutations on tropism prediction at baseline were analysed on 101 patients receiving maraviroc (MVC) and correlated with their clinical outcome. This was a non-interventional, retrospective study. 82 RNA and 54 DNA samples from the 101 patients receiving MVC were obtained. The V3 region was sequenced and the tropism predicted using the geno2pheno[coreceptor] and T-CUP tools with FPR cut-offs of 5%, 7.5%, 10%, 15% and 20%. Additionally, 27/82 RNA and 28/54 DNA samples were analysed in triplicate and 34/82 samples with the ESTA assay. The influence of 16 MVC resistance mutations on clinical outcome was studied. The genotypic susceptibility score (GSS) of the concomitant drugs was mapped to numerical values: susceptible to 1 (or 0.5 for NRTIs), intermediate to 0.5 (0.25 for NRTIs) and resistant to 0. Detection of baseline R5 viruses in RNA (by geno2pheno[coreceptor] and T-CUP) or DNA (by T-CUP) samples correlated with MVC-treatment success. Both tools performed very similarly, with PPVs close to 90%, even with FPR cut-offs as low as 5%. The use of triple amplification did not improve the prediction value but reduced the number of patients elegible for MVC treatment. No influence of the GSS or MVC resistance mutations on the clinical outcome was detected. Genotypic tropism testing from viral RNA and proviral DNA using the geno2-pheno[coreceptor] and T-CUP systems is valid to select candidates for MVC treatment. Our data suggest that the use of FPR cut-offs of 5–7.5% and single amplification from RNA or DNA would assure a safe administration of MVC without excluding many patients who could benefit from this potent antiretroviral drug.

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P166

HIV-infected viremic long-term non-progressors and controllers display different immunological mechanisms for preserved CD4 + cell counts

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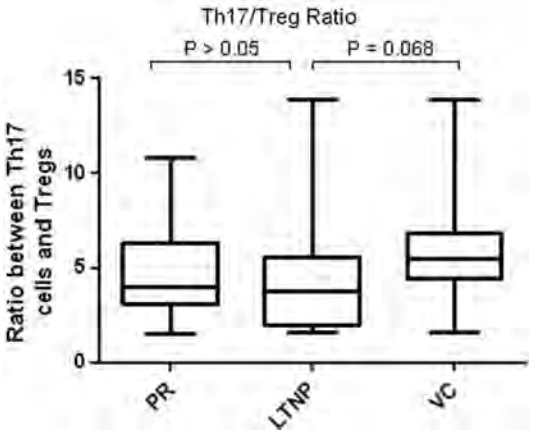
Purpose: Most HIV-infected patients develop immunodeficiency without treatment. However, Long-Term Non Progressors (LTNP) and Viremic Controllers (VC) maintain normal CD4 counts and do not progress in the absence of treatment. While VC are able to control viral replication LTNP are not. Thus, lack of viral replication cannot explain non-progression in LTNP. Therefore we hypothesized that the immunological mechanism responsible for preserved CD4 counts in LTNP is different from that in VC.

Methods: 69 treatment naïve HIV-infected patients were included in a cross-sectional study. A total of 14 LTNP (viral load, VL > 5000 copies/ml, CD4+ cell count > 350 cells/ul, infected > 10 years), 30 VC (VL < 5000 copies/ml, CD4 count > 350 cells/ul), and 25 progressors (PR) (VL > 5.000 copies/ml, CD4 count > 350 cells/ul) were included. Immune activation (CD4+ and CD8+cells co-expressing CD38+HLA-DR+), apoptosis (CD8+CD28-CD95+), Th17 cells (CD4+CD161+), and regulatory T cells (Tregs, CD4+CD25+CD127lowFoxP3+) were evaluated using flow cytometry. For



statistics Kruskal-Wallis test followed by Mann-Whitney U test were used. Data are given as medians.

Summary of results: LTNP had higher frequency of activated CD4+ and CD8+cells compared to VC (3.4% vs. 1.6%, P = 0.007, 21.7% vs. 12.0%, P = 0.051) and similar levels to PR (4.2%, 22.4%, P > 0.05). Likewise, LTNP had higher frequency of apoptotic cells compared to VC (63.7% vs. 48.6%, P = 0.0408) and similar levels to PR (63.8%, P > 0.05). Interestingly, borderline significant trends towards lower Th17/Treg ratio in LTNP compared to VC were found (3.8 vs. 5.5, P = 0.068) while ratios in LTNP and PR were similar (4.0, P > 0.05).

Conclusion: LTNP displayed high levels of immune activation, apoptotic cells and reduced Th17/Treg ratio compared to VC, while LTNP were similar to PR. Thus, the immunological mechanism responsible for preserved CD4 counts in LTNP is still unclear but seems to be different from that in VC.

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P167

CD3+CD8+CD161high Tc17 cells are depleted in HIV-Infection and related to the level of immune reconstitution

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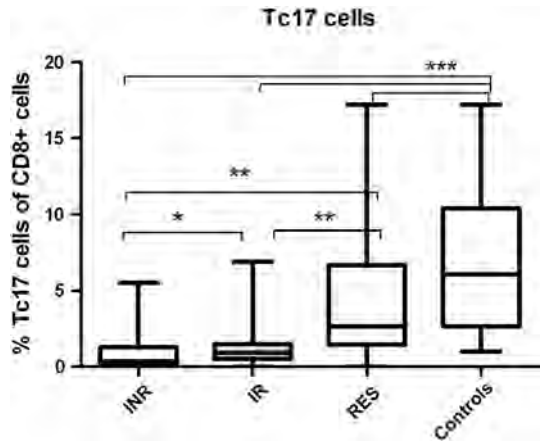
Purpose: The existence of CD8+cells with pro-inflammatory properties referred to as Tc17 cells has recently been acknowledged. While it is evident that CD4+pro-inflammatory IL-17-producing Th17 cells are important in the regulation of chronic viral infections, the role of Tc17 cells is largely unknown. Tc17 cells are characterized by expression of high levels of CD161 (CD161high). We hypothesized that Tc17 cells are involved in immune regulation in HIV- infection.

Methods: 67 HIV-infected patients were included in a cross-sectional study. All patients had nadir CD4 counts < 200 cells/μL, fully suppressed viral loads, and had been on cART for at least 2 years. Three groups were defined: Immunological Non Responders (INR, CD4 counts < 200 cells/μL), Intermediate Responders (IR, CD4 counts 200–500 cells/μL), and Responders (RES, CD4 counts > 500 cells/μL). Percentages of CD8+cells expressing CD3+CD8+CD161high were evaluated using flow cytometry. Additionally, Production of IL-17 in phytohaemagglutinin(PHA)-stimulated peripheral blood was determined by Luminex. For statistics Kruskall Wallis test followed by Mann-Whitney U test was used. Data are given as medians.

Summary of results: INR had lower levels of Tc17 cells compared to IR, RES and controls (0.4%, 1.0%, 2.1%, 6.1%, p values < 0.05).



All HIV-infected patients had lower levels than controls (p values <0.0001). Furthermore, all HIV-infected patients displayed lower production of IL-17 in peripheral blood compared to controls (p values <0.001).

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P168

Persistent enterocyte damage despite decreased microbial translocation in patients on effective antiretroviral therapy

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Intestinal fatty acid binding protein (I-FABP) was proposed as a plasma marker of enterocyte turnover that could be applied to estimate the level of gut damage in HIV-1 infected patients. We investigated the kinetics of I-FABP in patients starting antiretroviral therapy (ART) in a clinical cohort (CC) ($n=32$), and in a clinical trial (RCT), where patients were randomized to lopinavir/r (LPV/r) or efavirenz (EFV)-based therapy ($n=71$). I-FABP was analyzed at baseline (BL) and after 48 and 72 weeks of ART, respectively. Additionally we estimated levels of LPS and sCD14 in both cohorts. At baseline, we found elevated plasma levels of I-FABP, LPS, and sCD14 in patients with HIV-1 infection as compared to controls. During ART I-FABP levels increased from BL to week 48 (1.66 ng/ml [IQR 1.29–2.88] vs. 2.56 ng/ml [IQR 1.29–5.26]; $p=0.02$) in CC group. Similar pattern was seen in the RCT group at week 72 as compared to BL (2.26 ng/ml [IQR 1.4–3.6] vs 3.13 ng/ml [IQR 1.8–4.9]; $p<0.0001$). Levels of sCD14 decreased at the end of study period in both groups. The levels of LPS decreased in RCT cohort but not in CC cohort. Interestingly, we found that the I-FABP levels increased in both cohorts despite 48–72 weeks of efficient ART. A subgroup analysis of the RCT cohort revealed that the I-FABP increase occurred in the patients treated with EFV (2.32 ng/ml [IQR 1.5–3.8] vs. 4.29 ng/ml [IQR 2.4–5.9]; $p<0.0001$), but not in those with LPV/r. This finding was not confirmed in the CC group. The possibility of immune reconstitution in the gut as a cause of the increasing I-FABP levels seems to be less likely, as CD4 T-cell recovery tended to be lower in efavirenz-treated patients. In RCT cohort, the established MT markers lipopolysaccharide (LPS) and sCD14 were both reduced after 72 weeks (data not shown), supporting a reduced MT. Most likely the systemic I-FABP levels in patients on ART do not reflect only MT itself. Further studies should address this issue.

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Progression to AIDS or death in HIV-infected patients initiating cART with CD4 <200 cells/μL: the role of CD4 and viral load changes during follow-up

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Purpose of the study: Our aim was to evaluate factors associated with progression to AIDS/death in HIV-infected naïve pts initiating cART with low CD4 counts.
Methods: Adult HIV-infected ARV-naïve pts with CD4 <200 who initiated NNRTI or PI-containing regimens between 1998 and 2009, were included. Primary end point was progression to AIDS (a first episode or a new AIDS-defining condition in pts with prior AIDS) or death. Kaplan-Meier curves were used to determine progression-free survival and multivariate Cox regression models were used to identify independent predictive factors of progression to AIDS/death.
Summary of results: We included 1427 patients (80% men, median age 38 years, 25% IDU, 37% AIDS, 20% HCV) between 1998 and 2009. At baseline (BL), median (range) CD4 and viral load (VL) was 77 (1–199) cells/μL and 170,000 (19–8,750,000) copies/mL, respectively. After a median follow-up 4.6 years, 70% of pts reached CD4 >200/μL, 65.2% reached undetectable VL and 268 (19%) pts progressed to AIDS/death during follow-up. The probability of AIDS/death at 5 years was 76%, 34%, 3% and 3%, in pts with BL CD4 <100/VL >5 log and CD4 <200/VL detectable during FU, BL CD4 <100/ VL >5 log and CD4 <200/VL undetectable during FU, BL CD4 <100 and/or VL >5 log and CD4 >200/VL undetectable during FU and BL CD4 >100/ VL <5 log and CD4 >200/VL undetectable during FU, respectively. In the multivariate analysis, several variables were associated with AIDS/death: CD4 < 200 during FU (HR 10.89, $p<0.001$), detectable VL during FU (HR 3.49, $p<0.001$), age >50 years (HR 1.75, $p=0.001$), prior AIDS (HR 1.71, $p<0.001$) and BL VL >5 log (HR 1.45, $p=0.011$). If only pts without prior AIDS ($n=895$) were analyzed, the variables independently associated with AIDS/death were: CD4 <200 during FU (HR 9.90, $p<0.001$), detectable VL during FU (HR 2.78, $p<0.001$) and BL VL >5 log (HR 1.62, $p=0.016$).
Conclusions: In immunosuppressed patients initiating cARV therapy, not reaching CD4 >200/μL during FU was the strongest variable associated with progression to AIDS/death. VL at BL and mainly at follow up also played a role in patient outcome.

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P170

Multicenter epidemiological study to describe prevalence of advanced stage disease among newly diagnosed HIV-infected patients in the Russian Federation

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Purpose of the study: The proportion of HIV-infected persons diagnosed in an advanced stage of HIV disease (ASH) varies by country from 15 to 30%. Data are lacking on the proportion of new cases diagnosed in this late stage in Russia. The aim of this study was to estimate the proportion of and further characterize patients with ASH among newly diagnosed HIV-1 infected persons in the Russian Federation.
Methods: This was a cross-sectional, multicenter, epidemiologic study. Adult HIV-1 patients that were newly diagnosed within 90 days and naïve to highly active antiretroviral therapy were included at twelve centers/regions (Moscow Region, St Petersburg, Leningrad Region, Ufa, Kazan, Ulyanovsk, Volgograd, Yekaterinburg, Kemerovo, Krasnoyarsk, Irkutsk and Vladivostok) of the Russian Federation. ASH was defined as a CD4+ cell count $\leq$200 cells/mm^3. Pairwise, two-tailed comparisons were conducted with an unadjusted 5% significance level. For comparison variables between patients with ASH and all other patients, Pearson's chi-square test was used.
Summary of results: 4540 patients were included. The overall proportion of ASH was 16.3% (95% CI; 15.3%, 17.4%). The median plasma HIV-1 RNA was 4.48 (Q1, Q3; 3.81, 5.07) $\log_{10}$ copies/mL. The proportion of patients with CD4+ cell count by categories is presented in Figure 1.

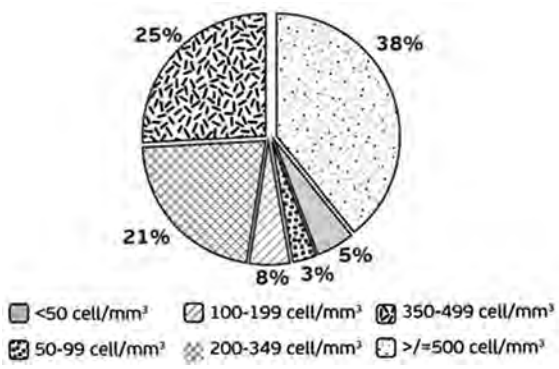

Figure 1. Proportion of newly HIV infected patients by CD4+ count categories, % (n = 4540).

Table 1. Descriptive statistics of newly HIV-infected patients

	Total	CD4+ cell count $\leq$200 cells/mm^3	CD4+ cell count $\geq$200 cells/mm^3	p-value*
	4540	741	3799	
Age				
Mean (SD)	32.6 (8.7)	35.5 (8.9)	32.1 (8.6)	<0.0001
Median	31.0	33.0	30.0	
Age group				
18-25 yr	901 (19.8%)	52 (7.0%)	849 (22.3%)	<0.0001
26-40 yr	2921 (64.3%)	512 (69.1%)	2409 (63.4%)	
>40 yr	718 (15.8%)	177 (23.9%)	541 (14.2%)	
Gender				
Male	2289 (50.4%)	462 (62.3%)	1827 (48.1%)	<0.0001
Female	2251 (49.6%)	279 (37.7%)	1972 (51.9%)	
HIV mode of transmission				
Heterosexual contact	2801 (61.7%)	390 (52.6%)	2411 (63.5%)	<0.0001
Homosexual contact	99 (2.2%)	21 (2.8%)	78 (2.1%)	
Intravenous drug user (IVDU)	1388 (30.6%)	293 (39.5%)	1095 (28.8%)	
Blood transfusion, organ transplant or healthcare contact	3 (0.1%)	1 (0.1%)	2 (0.1%)	
Unknown	249 (5.5%)	36 (4.9%)	213 (5.6%)	
Chronic hepatitis B				
No	4362 (96.1%)	701 (94.6%)	3661 (96.4%)	0.0235
Yes	178 (3.9%)	40 (5.4%)	138 (3.6%)	
Chronic hepatitis C				
No	3001 (66.1%)	415 (56.0%)	2586 (68.1%)	<0.0001
Yes	1539 (33.9%)	326 (44.0%)	1213 (31.9%)	

*Analysis result of comparison of HIV-1-infected patients with advanced stage disease vs. all other patients. Tests resulting in p-values less than or equal to 0.05 are reported as 'statistically significant'.

ASH was associated with male sex (62.3%), 26-40 and >40 years age groups, rural place of residence (18.9%), only primary and/or basic school education (complete or not complete) (39.4%), unemployment (40.5%), intravenous drug user as mode of HIV-1 transmission (39.5%), patient with clinical signs of immunodeficiency or condition related to HIV/AIDS as reason for primary HIV-1 testing (35.2%), HBV (5.4%), HCV (44.0%) as partly shown in Table 1.
Conclusions: The overall prevalence of ASH was 16.3%. At least 9 factors associated with ASH were revealed. Knowledge of these factors is valuable for planning, prevention and post-diagnosis services for HIV-infected patients presenting with advance stage disease.

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Genotypic prediction of HIV-1 subtype CRF01-AE tropism

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Purpose of the study: Determination of HIV-1 coreceptor usage is crucial for the clinical management of HIV-infected patients and for optimizing patient selection prior to coreceptor antagonist use. HIV-1 subtype CRF01-AE predominates in south and south-east Asia and has spread all around the world. As for other subtypes, the HIV-1 subtype CRF01-AE tropism must be assessed before CCR5 antagonists' usage. Genotypic methods would be useful for tropism determination but their correlation with the phenotypic approach has not been assessed.
Methods: We determined the HIV-1 coreceptor usage in 44 subjects infected with subtype CRF01-AE by both a recombinant phenotypic entry assay and sequencing of the V3 region to determine the correlation between them.
Summary of results: We first used genotypic algorithms currently used for subtype B HIV-1. The sensitivity of the Geno2pheno10 genotypic algorithm was 75% but the specificity was poor (46%). In contrast, the sensitivity of the combined 11/25 and net charge rule was poor (50%) but the specificity was 96%. We used a GenBank clonal data set of 69 CRF01-AE V3 sequences of viruses with known phenotype to identify subtype CRF01-AE determinants in the V3 region associated with CXCR4 use and built a new simple genotypic rule for optimizing the genotypic prediction of CRF01-AE tropism. The data showed that loss of the N-linked glycosylation site at the beginning of V3 was an independent determinant of CXCR4 use by the CRF01-AE virus clones. The new genotypic tool based on the 11/25, net charge and glycosylation site mutation criteria was 96% concordant with the phenotype on the GenBank clonal data set. Lastly, this algorithm has been validated using our patients' data set in which the sensitivity was 70% and the specificity was 96% for predicting CXCR4 use.
Conclusions: The concordance between genotype and phenotype was 84% when using the CRF01-AE genotypic tool, approaching the concordance obtained for the tropism prediction of HIV-1 subtype B. The genotypic prediction of HIV-1 subtype CRF01-AE coreceptor usage requires an optimized genotypic tool for a safely use of CCR5 antagonists.

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P172

Long-term therapy with nevirapine and tropism

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Objective: A more potent effect on the residual viraemia was ascribed to nevirapine (NVP) with respect to other antiretroviral drugs; moreover a selection of X4 strains was described in patients (pts) with undetectable viraemia; our aim was to study viro-immunological parameters and tropism for co-receptor in pts on a long term successful therapy with NVP.
Methods: 14 pts on HAART from 130 months (GL, median value, range 118–156 months) without occurrence of blips, as assessable with the available methods at that time, were retrospectively selected from a single center cohort (Bolzano). Tropism for V3 was determined by population sequencing on blood, and using geno2-pheno algorithm; cellular HIV DNA load was analysed by in-house Real-Time. A further eighteen months (mo) follow up was then observed. Data were compared with those obtained from a control group of 50 naïve pts (GS), evaluated after a 36-mo successful therapy (median, range 12–84) with various drug combinations, with median baseline (BL) CD4 of 50/μl, comparable value with the GL cohort.
Results: In 7 pts a R5-tropic (GLR5, FPR median 84.8%) and in 7 an X4-tropic strain (GLX4, FPR median 1.1%) was demonstrated. BL data of GLR5 were 46 y old, CD4 54/l, HIV-RNA 104,000 cps/ml; HAART from 142 mo, with NVP from 125 (one after 70 mo on NVP switched to protease from 57); at follow up CD4 were 679/l, HIV-DNA 60 cps/106 PBMCs (range <5–252). GLX4 were 46 y, at BL 38 CD4/l, HIV-RNA 250,000 cps/ml; in HAART from 121 mo, with NVP from 97; at follow up CD4 902/l, HIV-DNA 60 cps/106 PBMCs (range <5–225). Six out of seven pts of the two groups were on treatment with abacavir+lamivudine (ABC+3TC) and one with tenofo-vir+emtricitabine. In the subsequent 18 mo four blips were observed (21–71 cps/ml); the backbone was changed to raltegravir in two GLR5 and one GLX4 for convenience. In the 50 GS pts at follow up an X4 strain was found in 50% of 14 efavirenz-treated, in 16% of 6 NVP, and 63% of 30 protease.
Discussion: In a group of very long-term treated pts with NVP plus two NRTI (ABC+3TC in 12 out of 14), a tropism for CXCR4 was demonstrated in 50%, without significant differences in the CD4 gain and in the HIV-DNA load archived in the peripheral blood. With respect to pts on various therapies from a median of 36 mo, the type of archived virus does not seem to have a role on the outcome of a very long therapy, 130 mo, with NVP+ABC+3TC; this therapy does not seem able to select a special tropism in pts.

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P173

A systematic literature review examining soluble and cellular biomarkers in HIV patients receiving antiretroviral therapy

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The use of antiretroviral therapies (ART) for treatment of human immunodeficiency virus type 1 (HIV-1) has led to more favorable prognoses for infected individuals, including reduced HIV viral load, improved CD4 +T-cell recovery, and slower disease progression. However, ART-treated HIV+patients may have increased risk of adverse outcomes associated with chronic inflammation and immune activation. Molecules associated with chronic immune system activation and inflammatory cytokine production may be useful biomarkers of HIV pathogenesis and/or ART outcomes. We systematically identified MEDLINE-indexed articles published in the past decade investigating the association of several soluble (IL-6, CRP,

MCP-1, IP-10, D-dimer, soluble CD14, and LPS) and cellular (CD28, CD38, HLA-DR, PD-1, caspase-3, IFNγ and IL-2 ELISpots) biomarkers with clinical outcomes in ART-treated HIV positive (HIV+) patients. Seventy publications were included, consisting mainly of observational studies of soluble biomarkers. One quartile elevations in baseline IL-6, CRP, and D-dimer were associated with increased risk of disease progression or death (ORs 1.8–2.4; $p \leq 0.01$) and all-cause mortality (ORs 4.1–5.3; $p \leq 0.0001$); these elevations were also associated with increased rates of IRIS (ORs 1.59–2.07; $p \leq 0.001$). Additionally, IL-6, CRP, and D-dimer levels were higher in patients who experienced a cardiovascular event than in controls ($p \leq 0.001$). The association between soluble biomarkers and quantitative assessments of HIV viral load has not been studied as thoroughly. However, several studies found an association between D-dimer and viral load. Research is lacking regarding the relationship between CD4 count and soluble biomarkers. Most studies evaluating cellular biomarkers examined their association with HIV viral load and CD4 count, but did not examine clinical outcomes. The most commonly studied cellular biomarkers were the T cell activation markers CD38 and HLA-DR. Studies suggest that CD4 and CD8 activation were increased in patients with higher HIV viral load, and that CD8 activation was higher in patients with low CD4 counts. In our review, we found that several soluble biomarkers were related to the risk of adverse clinical outcomes in ART-treated HIV+patients. More data, particularly regarding cell-associated biomarkers, is required to characterize their association with outcomes of interest, to describe causality, and to document their prognostic importance.

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P174

Use of age and CD4 cell count as criteria for identification of recent HIV infection in resource-limited countries

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Background: Identification of recent HIV infection is crucial for estimating HIV incidence and transmitted drug resistance (TDR) prevalence. Due to limited availability of diagnostic assays, WHO TDR surveys use age <25 yrs and/or CD4 >500 cells/mm^3 at HIV diagnosis as epidemiological criteria to maximize inclusion of recently infected (within 3 yrs) and ARV-naïve individuals. Accuracy of these criteria and variation by geographical region is unknown.
Methods: A literature review of studies on HIV seroconverters (SC) published through March 2012 was performed. Age at SC and CD4 decline in absence of treatment were abstracted. Accuracy of alternative TDR survey criteria was explored.
Results: 11 studies provided age at SC: 7 in Africa, 2 in Latin America, 2 in Asia. Median age at SC ranged between 24 and 33 years in studies in Kenya and Zambia, respectively and was 29 [interquantile range (IQR) 24, 34] in a large cohort study from Africa. Median age at SC was 29 years in studies on MSM in Brazil and China. 7 studies reported CD4 count decline: 5 in Africa, 1 in Latin America and 1 in Asia. Studies used ordinary least square regression or mixed models. None described median CD4 count 3 yrs after SC. The estimated mean CD4 count 3 yrs after SC ranged from 350–420 cells/mm^3 in Africa and was 237 and 282 cells/mm^3 in Asia and Latin America, respectively.
Conclusion: HIV SC occurs at all ages (median 29 yrs) in the assessed geographical regions. Enhancing feasibility of TDR survey implementation by including individuals >25 yrs decreases specificity, particularly in low HIV prevalence settings (Table).
Use of age <25 yrs can maximized specificity to detect recent infection, but misses almost 75% of recent infections thus limiting feasibility of TDR survey implementation, particularly in low HIV prevalence settings. Lower mean CD4 count 3 yrs after SC was observed in Asia and Latin America compared to Africa. Regional differences may be explained by heterogeneity in eligibility criteria and statistical methods as well as contextual factors such as HIV subtypes or co-morbidities. Confirmed CD4 >500 cells/mm^3 would maximize specificity but greatly reduce the number of individuals included in TDR surveys. This review highlights the limitations of using age and CD4 count at HIV diagnosis as criteria to identify recent infections. These criteria should be revised when results of well-designed studies to calibrate misclassification errors become available.

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P175

Fifteen years of HAART: comparison of time to failure and percentage of undetectable in two successive cohorts

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Early and current HAART drug combinations' efficacy is comparable but pill burden and tolerability are strikingly different. Demographic, biological and virological aspects of an early and late cohort from the HAART era were evaluated, focusing on time to failure and percentage of undetectable at first year of treatment. Retrospective observational study of two HIV reactive patients cohorts clustered by the year starting their first HAART; cohort 1 from January 1996 to June 2003; cohort 2 from July 2003 to January 2011. Standarized collected data from clinical records were median age of diagnosis, sex, CDC stage category, median CD4+ count at the time of starting

Abstract P174

Transmitted Drug Resistance Survery Criteria	Evidence of Recent Infection	Feasibility in Low-Prevalence Settings	Feasibility in High-Prevalence Settings
Age <22 years	STRONG	POOR	FAIR
Age <25 years	INTERMEDIATE	FAIR	FAIR
Age <30 years	WEAK	GOOD	GOOD
Confirmed* CD4 >500 cells/mm^3	STRONG	VERY POOR	VERY POOR
Confirmed* CD4 >350 cells/mm^3	INTERMEDIATE	POOR	POOR
CD4 >500 cells/mm^3	INTERMEDIATE	FAIR	FAIR
CD4 >350 cells/mm^3	WEAK	GOOD	GOOD

*Confirmed = At least two consecutive CD4 counts.

treatment, percentage of patients failing their first HAART, time to failure and percentage of undetectable at the first year of treatment. Exclusion criteria: lack of viral load at the first year of initial HAART and loss of patient following. Evaluation of adherence: number of absences to scheduled appointments, number of pills dispensed per patient and accomplishment self-reporting. Taking less than 90% pills in a month was considered as low adherence. Virological rebound was defined as two successive viral loads >50 copies of HIV-1 RNA/ml after one detection of a viral load <50 copies/ml. A percentage analysis was applied to biological and demographic variables, x^2 test was implemented when comparing cohorts. From 958 clinical records, 215 were eligible for the study. Cohort 1 enrolled 84 patients; cohort 2, 131. Table 1 compares demographic, biologic and virological variables. Median CD4+ count when starting first HAART showed no significant difference between groups: 254 and 235 cells/ml; group 2, 235 cells/ml. Failure to first treatment: cohort 1, 38 (45%); cohort 2, 17 (13%). Mean time to failure: 118 and 94 weeks in cohort 1 and 2 respectively (p 0.13). Percentage of undetectable at the first year of treatment: cohort 1, 84%; cohort 2, 82% (p 0.34). This comparison shows that drugs prescribed in early HAART era were equipotent with current ones, since neither the percentage of undetectable at the first year of treatment nor the time to failure showed significant differences. On the contrary, the percentage of failures at any time was significantly higher in cohort 1, mainly because of adverse effects and intolerance. Low CD4 count in both groups indicates a delayed diagnosis. Offering the HIV screening test to the whole community is the remaining challenge.

Characteristics	Cohort 1 (1996–2003) No. (%)	Cohort 2 (2003–2011) No. (%)	p
N	84	131	
Mean age at diagnosis	33	36	
Sex: Men/Women	53 (63)/31 (37)	78 (59)/53 (41)	
CDC stage C3	22 (26) 21 (16)	21 (16)	
Median CD4+ count at treatment start	254	235	
Mean time to failure	118	94	0.13
Percentage of undetectable at first year of treatment (%)	84	82	0.34

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P176

Validation of Cobas AmpliPrep/Cobas TaqMan HIV-1 Test on dried blood spots

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The plasma specimen is the gold standard for viral load monitoring, the key method to assess the effect of antiviral chemotherapy and to monitor progression of the disease toward AIDS. Nevertheless, several works endorse the use of dried blood spots (DBS) on filter paper for the reliable quantification of the levels needed to take therapeutic decisions, detect of treatment failure and monitor the occurrence of drug resistance. The purpose of this study was to validate the use of Cobas AmpliPrep/Cobas TaqMan HIV-1 test version 2.0, with DBS. To evaluate the performance of the above mentioned kit, three stages were involved: 1- Standardization of DBS working conditions, 2- Stability studies at three temperature conditions and 3- Performance evaluation of the kit using this alternative specimen. Additionally, the viral load was quantified in parallel (plasma and DBS) to 43 genetically characterized samples, with different levels of viral load. The Pearson correlation coefficient was calculated and the prediction of the value of RNA in plasma starting from the obtained value in DBS was made. Linear regression analysis was performed and coefficients of variation in precision assays were calculated. The best conditions pickups to the work with DBS were: 100 μL of blood (2 spots/50 μl), dried time between 16 and 18 hours at room temperature and, elution of the blood, 2 hours, between 2 and 8°C; in TRIS-EDTA buffer. The samples on DBS proved to be stable during the study periods. A strong correlation was attained between the measurements of viral load in plasma and DBS samples (r = 0.96). The detection rate was 90.7 and the coefficient of variation between the values obtained in plasma-DBS sample pairs averaged 3.42%. The CAP/CTM HIV-1 test provided a linear response in DBS, from 330 copies/mL to 420 000 copies/mL. Overall, coefficients of variation in precision tests were below 10%. Cobas AmpliPrep/Cobas TaqMan HIV-1 test version 2.0 had a good performance using DBS. High detection rate was obtained with DBS specimen. Our results clearly support the use of CAP/CTM HIV-1 test with DBS, as it reliably quantifies the levels needed for therapeutic decision-making and detection of treatment failure.

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P177

Differential patterns of CD4 recovery following effective treatment with HAART

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CD4 counts rise following treatment with HAART, the pattern of which however varies between individuals and populations. Host, virus and treatment factors may play a part in shaping the trajectory. Through an HIV clinical cohort study, we aim to describe the natural course of CD4 trajectories and evaluate possible factors associated with different patterns. Between 1997 and 2008, HIV-1-infected patients receiving HAART at one major HIV specialist clinic in Hong Kong were included in a study for assessing CD4 changes. The entry criteria were: (a) patients who have been put on HAART according to standard criteria; (b) sustained viral suppression after treatment; (c) having been on HAART for at least 48 months. A total of 141 patients with 3,087 measurements were analysed, covering a total of 11,282 person-months. The median age at initiation of HAART was 37 (IQR 32–44). A majority were male (74%), Chinese (87%) and who have contracted HIV through heterosexual contacts (84%). At baseline, the median CD4 was 39 cells/μL (IQR 13–127 cells/μL) and viral load was 74,100 copies/mL (IQR 26,800–280,000 copies/mL). Over time, 80 (57%) gave a CD4 count of >500/μL during antiretroviral treatment. Clinically, almost all (96%) had presented with an AIDS-defining illness before HAART was started. Around half of the patients were on 2NRTI+1 NNRTI and half on 2NRTI+1 PI. Overall, 3 groups of patients can be differentiated by their temporal pattern of CD4 recovery. Group One (n = 38; 34%) gave a median peak value of 576/μL within 4 years (median interval 40 months). Group Two comprised 96 (68%) patients whose mean CD4 count continued to rise beyond 48 months. Group Three (n = 7) gave little or no response to

treatment, as defined by a change of <100 cells/μL in the mean count by year. Group Three patients were relatively older (median age $=46$ years). Comparing between Group One and Two, there was a higher proportion of men having sex with men whose CD4 had plateaued within 4 years (21% vs 6%, $p=0.017$). Lower baseline CD4 and higher baseline viral load were associated with continued rise of CD4 beyond 4 years. There was no association of CD4 recovery pattern with the HAART regimen. In conclusion, CD4 rise tends to be prolonged following effective virus suppression in a predominantly Chinese HIV population. The differential patterns were largely associated with host factors with little impacts from HAART regimens.

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P178

Analysis of regulatory T-cells and of their na ve and memory-like subsets in long-term treated aviremic HIV+ patients and untreated viremic patients

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Purpose of the study: Although HIV infection impacts the proportion and phenotype of regulatory T-cells (Tregs), discrepant results have been reported depending on the surface markers employed to characterize them and on the patient populations. In addition, the effects of a long-term combined antiretroviral therapy (cART) on Treg cells have not been thoroughly documented. Our study investigated the frequency and number of Tregs and their phenotype in two different groups of HIV-infected patients: one aviremic undergoing long-term cART and one viremic naïve to cART showing a similar CD4+ cell count.
Methods: Thirty-six HIV+ patients with sustained suppression of plasma viremia (<37 copies/mL) on effective cART for more than 6 years and 22 HIV+patients naïve to cART and without clinical signs of opportunistic infections or tumors at the time of study (untreated group) were included in the study. Healthy donors (HD) were used as control. Flow cytometry on fresh whole blood was used to quantify total Tregs (defined as CD25+CD127low/-CD4+ cells) and the following Treg subsets: naïve (CD45RA+CCR7+) Tregs, central-memory like Tregs (CD45RA-CCR7+, TregCM), effector-memory like Tregs (CD45RA-CCR7−, TregEM) Statistical comparisons of the percentages and number of Tregs and Treg subpopulations were performed by ANOVA or Kruskal-Wallis test. Analysis of covariance was employed in order to adjust for the effect of the age. The Spearman's test was used to assess correlations.
Summary of results: In viremic untreated and aviremic long-term cART-treated patients the percentage and number of the total Treg cells were not different from those of HD. However, the analysis of Treg phenotype showed a marked redistribution of the Treg subpopulations: in the untreated viremic patients, both the percentage and number of the TregCM subset decreased compared to HD and cART-treated patients, whereas only the percentage of naïve Tregs increased. In particular, the percentage of TregCM was inversely correlated with the viral load ($r=-0.51$; $p=0.016$).
Conclusions: In our aviremic long-term cART-treated and viremic untreated patients, the total Treg cell population seems to be unaffected by HIV infection. However, our results showed that the analysis of the naïve and memory-like Treg subsets may provide a better understanding of the real contribution of Tregs in HIV disease and therapy.

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P179

Vitamin D deficiency in a cohort of HIV-infected patients: clinical analysis

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Purpose of the study: Observational studies have noted very high rates of low serum 25-hydroxyvitamin D [25(OH)D3] levels in both general and HIV-infected populations. In HIV-infected patients, low 25(OH)D3 levels are secondary to a combination of usual risk factors and HIV-specific risk factors, like antiretroviral therapy [1]. The objective of our study is to analyse the magnitude of vitamin D deficiency or insufficiency and the role of various factors such as age,

Abstract P179

	VitD <20 ng/mL N $=590$	VitD 20–29 ng/mL N $=168$	VitD d30 ng/mL N $=90\geq$
Sex (male/female)	340/250 (58/42)*†	109/59 (65/35)*	73/17 (81/19)
BMI (kg/m^2)	25.7 ± 5.1*†	24.7 ± 4.1	23.8 ± 3.7
Homo- (and bi-) sexuality vs heterosexuality	169/421 (29/71)*†	68/100 (40/60)*	48/42 (53/47)
Ethnicity (Black/Others)	289/301 (49/51)*†	58/110 (35/65)	21/69 (23/77)
Month of dosage			
Dec, Jan, Feb	197 (33)*†	25 (15)	18 (20)
Mar, Apr, May	223 (38)	67 (40)	33 (37)
Jun, Jul, Aug	102 (17)*	60 (36)	29 (32)
Sep, Oct, Nov	68 (10)	16 (10)	10 (11)
HIV viral load			
Undetectable	162/428 (27/73)*	56/112 (33/67)*	45/45 (50/50)
Detectable	52 112 ± 160 671	337 871 ± 2 294 712	94 547 ± 234 335
Treatment			
EFV	85 (14)*	23 (14)	5 (6)
TDF (alone or in combination)	300/290 (51/49)*	80/88 (48/52)	35/55 (39/61)
HAART (naïve/treated)	116/469 (20/80)*	41/124 (24/74)*	38/52 (42/58)

sex, ethnicity, season, and antiretroviral medications in our cohort of HIV-infected patients.

Methods: We prospectively collected data on 25-hydroxyvitamin D levels sampled between January 2009 and June 2011 from our cohort of 930 HIV-infected patients. Vitamin D dosage was performed using immunoassay ('Diasorin' - Saluggia, Italy). We divided vitamin D levels into 3 categories: 25-hydroxyvitamin D levels <20 mg/nl were considered deficient, insufficient between 20 and 29 ng/ml. Levels ≥ 30 ng/ml were defined as normal [2]. Data on demographic features (age, ethnicity, season, heterosexuality vs homosexuality), clinical features and laboratory findings (CD4 cell count, viral load, HAART, BMI) were collected from patients' medical records using our institutional database 'Medical explorer v3r9, 2009'.

Summary of results: Overall, 848 patients were included in our study (Table 1).

Low levels of serum 25(OH)D3 were seen in 89.3% of the study population, from which 69.5% were deficient and 19.8% were insufficient. On univariate analysis, female sex, high BMI, black African, heterosexuality, undetectable viral load and antiretroviral treatment were all predictors of vitamin D deficiency and insufficiency. Treatment with efavirenz and tenofovir were the most associated with low vitamin D levels. On multivariate analysis (multiple linear regression model) only female sex (OR $=1.14$; 95% CI 0.84–0.96; $p<0.001$), dosage during winter months (OR $=1.14$; 95% CI 1–1.15; $p<0.05$) and HAART (OR $=1.12$; 95% CI 1.04–1.19; $p=0.002$) were identified as independent risk factors of low 25(OH)D3 levels.

Conclusion: Vitamin D deficiency is frequent in HIV-infected populations (69.5%). Patients on antiretroviral therapy are at higher risk of vitamin D deficiency. In our cohort, black women and dosage during winter were also independent risk factors for low vitamin D levels.

Conflict of interest: None. All co-authors have participated in, and agree with the content and conclusions.

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P180

Upgraded Cobas TaqMan version 2: hidden consequences at cohort level

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The viral load quantification constitutes a cornerstone of antiretroviral therapy management. After the switch from the Cobas Ampliprep Amplicor HIV-1 Monitor Test, v. 1,5 (CAP/CA) (Roche Diagnostics, Mannheim, Germany) to CTM2 in August 2009 at the HIV department of the General Hospital in Vienna, multiple internal reports accumulated concerning an increase of detectable HIV-1 viral loads in patients with previous long-term virological suppression. In order to evaluate these observations and their clinical consequences, a retrospective analysis of the number of elevated VL measurements in formerly virological suppressed patients during the first year of CTM2 use was performed. Furthermore, we monitored for consecutive numbers of repeated VL measurements, genotypic testing and for changes of antiretroviral therapy (ART). We recruited 373 of 2078 patients meeting the chosen inclusion criteria (Initiation of ART prior to August 6, 2008; ≥ 1 VL measurement in the pre-CTM2 period from August 6, 2008 to August 5, 2009, all VL measurements below the limit of quantification as defined by applied nucleic acid quantification assay (CAP/CA with <50 copies/mL); ≥ 1 VL measurement during the CTM2 period from August 6, 2009 to August 5, 2010). 221 (59.2%) remained with an undetectable HIV-1 viral load after implementation of CTM2, whereas 152 (40.8%) became detectable. The newly detected viremia showed a clear increase at the lower end of the dynamic range of quantification by CTM2. Among our 152 patients, 111 (73.0%) had viral loads ranging from 20–200 copies/mL, 6 (4.0%) between 201–400 copies/mL, while 35 (23.0%) patients showed viral loads measurements above >400 copies/mL. Of these newly detectable patients, 132 had a VL repeat and 72 became undetectable, the remaining 60 patients remained detectable. Remarkably, it was striking to find that in the group of patients who when switching to CTM2 reached at once viral loads exceeding 400 copies/mL, 48.3% became undetectable after viral load repeat using again CTM2, suggesting a high test variability at low detection limit but also beyond. Three genotypic resistance testings were performed and 16 patients underwent subsequent ART changes. In summary, the transition to CTM2 was followed by a dramatic increase of detectable viral loads in patients with stable ART and prior virological suppression, which at least in part could not be reproduced in repeat measurements.

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P181

Factors associated with immune status in the diagnosis of HIV infection

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Introduction: Current guidelines recommend the start of antiretroviral therapy before advanced immunosuppression, which is not always possible. The purpose of this study is to evaluate factors associated with the degree of immunosuppression at the diagnosis of HIV infection.

Methods: We evaluated demographic and epidemiological data of HIV-infected patients observed at the Department of Infectious Diseases diagnosed between 2006–2011, and analyzed the relationship between these data and the immune status at diagnosis. Statistical analysis was performed using SPSS version 20.0 for Windows.

Results: Data from 600 new patients were analyzed. 584 (97.3%) infected by HIV-1. 426 (71%) male. Mean age $=42$ years (SD $=14$). Risk factor for HIV infection: sexual in 548 patients (91.3%) (22.8% homo/bisexual). 153 (25.5%) patients had AIDS -defining illness. Origin of patients: general practitioner - 153 (25.5%), hospitalization in the Department of Infectious Diseases - 110 (18.3%), diagnostic screening after partner's diagnosis - 69 (11.5%), hospital consultation - 68 (11 3%), emergency room - 61 (10.2%), anonymous diagnostic testing center - 46 (7.7%), other hospital inpatient services - 31 (5.2%), hospitalization in another hospital - 30 (5%), attempted blood donation - 15 (2.5%), drug addiction treatment center - 8 (1.3%), pregnancy screening - 3 (0.5%) and patient's own initiative - 6 (1%). The mean CD4+ cell count was 319 cells/cmm (SD $=274$; range: 2–1416). Women were diagnosed at significantly higher CD4+ cell count levels ($p=0.005$), as well as younger patients ($p<0.001$). Homo/bisexual patients had CD4+ cell counts significantly higher

than the other groups ($p < 0.001$). There were differences in CD4+ cell count depending on the origin of the patients ($p < 0.001$): patients diagnosed at anonymous diagnostic center, drug addiction treatment center, blood donors, pregnant women and coming on their own initiative, had higher CD4+ cell count levels ($p < 0.001$). Patients admitted in the Department of Infectious Diseases were those with the lower CD4+ cell counts. No relationship was found between CD4+ cell count level and year of diagnosis.

Conclusion: These results indicate the importance of early HIV screening even in individuals without a perceived risk of acquisition of this infection, so they can benefit from antiretroviral treatment before having advanced immunosuppression.

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P182

HIV elite controllers as a key to novel strategies in treatment of HIV infection

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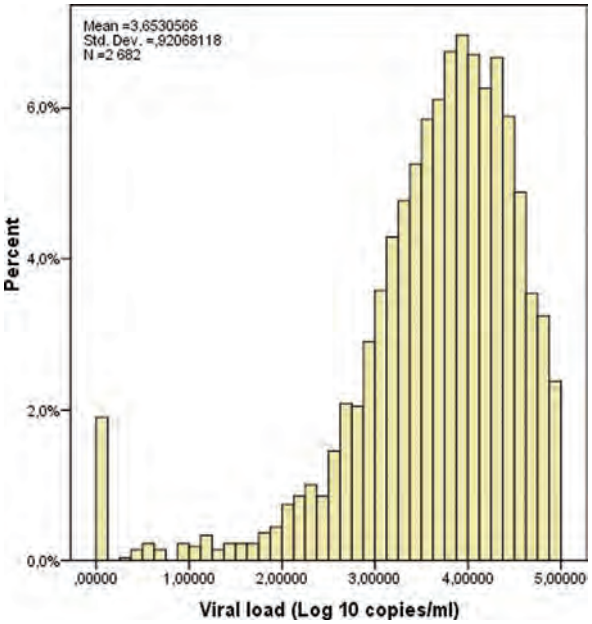
Purpose of the study: To identify and primarily characterize the elite controllers (EC) in Moscow Regional HIV Living People Cohort (Russia).

Methods: 2682 HIV-1-positive individuals with A1 (asymptomatic) stage of HIV infection were under regular physician observation continuously for at least 5 years. Verification antibody testing was performed with ''New Love Blot'' and ''Autoblot 2000'' (Biorad). Patients underwent scheduled HIV viral load and T-lymphocyte subpopulation measurement (twice a year) and did not have indications to HAART (viral load less then 5 $\log_{10}$/ml, $CD4^+$ counts more then 500 cells/mm^3). HIV viral load was detected by PCR m2000rt Abbott Biosystems analyzer, ''RealTime HIV-1'' sets with 20 copies per ml sensitivity) and major subpopulation of T-lymphocytes were analyzed by flow cytometer BD FACSCount, sets of antibodies ÑD3/CD4/CD8/CD45) [1].

Summary of results: Average $\log_{10}$ viral load was defined in each patient for 5-year period, and the distribution appeared to have a bimodal character (Figure 1). 106 EC were primarily identified as having average viral load less then 1.7 $\log_{10}$ (50) HIV copies/ml.



The incidence of EC appeared to be 3.95% (95% CI: 3.2%; 4.7%) of population with A1 (asymptomatic) disease with no indications to HAART, that corresponds to literary data [2]. Belonging to EC was then proved by laboratory dynamics. In EC 3 types of *viral load dynamics* were identified: 1) absence of detectable viremia, 2) single spikes, 3) episodic temporary elevation(s) (at mean 500–900 copies) lasting half a year. All these emphasize the control of virus. In EC 3 types of *$ND4^+$ T-lymphocyte dynamics* were defined: 1) $CD4^+$ elevation (in case beginning from the acute stage of the disease), 2) stable Ñ$D4^+$ cells, 3) $CD4^+$ cell depletion with very small velocity.

12 EC had ''minimal change disease'' defined additionally by the absence or trace appearance of pol 68/66, 52/51, 34/31 antibodies (Table 1) and non-detectable PCR levels in all measurements. These represent 11.32% (95% CI: 5.17%; 17.47%) from EC and 0.45% (95% CI: 0.19%; 0.71%) from population with A1 (asymptomatic) HIV-disease.

	Env	Env	Env	Gag	Gag	Gag	Gag	Pol	Pol	Pol
Patient number	160	120	41	55	40	24/25	18	68/66	52/51	34/31
1	+	*	+	+	+	+	–	–	–	–
2	+	+	+	+	*	+	–	*	*	+
3	+	*	+	*	–	*	–	*	*	*
4	+	+	+	+	+	+	–	+	*	+
5	+	+	+	+	–	+	–	+	+	–
6	+	+	+	+	+	+	*	+	+	*
7	+	+	+	+	+	+	*	*	*	+
8	+	*	+	*	–	*	*	*	–	*
9	+	+	+	+	–	+	*	–	–	–
10	+	–	+	*	–	+	–	–	–	–
11	+	+	+	+	+	+	*	–	–	–
12	+	*	+	+	+	+	–	*	–	–

Signs of antibodies: +, presence; *, traces; –, absence

Conclusions: Among EC patients with ''minimal change disease'' were identified. They may represent: (i) primarily persistent HIV infection (with reduced productive cycle), (ii) low dose (localized) HIV-infection, (iii) rare successful immune-mediated elimination of HIV that could be the model for novel elimination strategies.

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Tropism Assays

P184

Genotypic HIV-coreceptor tropism prediction with geno2pheno [coreceptor]: differences depending on HIV-1-subtype

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Purpose of the study: Determination of HIV-1 coreceptor tropism is a major prerequisite before starting treatment with a CCR5-antagonist. While most of the patients currently under treatment with maraviroc are probably infected with HIV-1 subtype B viruses, recently published data show differences in the distribution of coreceptor tropism in different HIV-1 subtypes.
Methods: In a Germany-wide project within the HIV-GRADE society, V3-loop sequences of 2466 isolates were analysed with geno2pheno for coreceptor tropism using a FPR cut-off of 10%. HIV-1 subtype was determined by using the COMET HIV subtyping tool. Sequences consisted of at least the V3 loop fragment. The ratio of CCR5 vs CXCR4 tropic viruses was calculated for each subtype. A normalized mean for all analyzed subtypes was calculated to extrapolate the overall ratio of coreceptor usage distribution. From this the expected distribution in the particular subtype was calculated and compared to the observed one. Statistical analysis was performed using the chi2 test.
Summary of Results: Most samples were classified as HIV-1 subtype B (79%, n = 1952). Other subtypes present in at least 23 samples were A1 (9.5%, n = 234), C (4.8%, n = 118), CRF01_AE (2.2%, n = 55), G (1.6%, n = 39), D (1.1%, n = 27), F (0.9%, n = 23). The calculated normalized mean distribution over all subtypes was 71% CCR5- vs. 29% CXCR4-tropic viruses. No significant difference compared to the mean distribution could be observed for HIV-1 subtypes B (71/29%), C (76/24%) and F (70/30%). Higher rates of CXCR4 tropic virus were detected in subtypes D (52/48%, p = 0.01) and CRF01_AE (49/51%, p = 0.001), while in HIV-1 subtypes A1 (22/78%, p = 0.02) and G (13/87%, p = 0.02), a higher rate of CCR5-tropic virus was observed.
Conclusions: Our analysis shows a different distribution of CCR5 and CXCR4 tropic virus in some subtypes. In contrast to other publications, we could not observe a statistically significant difference in subtype C compared to the overall mean distribution, while we could confirm a higher rate of CXCR4-tropic virus in subtype D, as previously described. Without further data on treatment success of patients with non-B subtypes under treatment with maraviroc, it remains unclear if subtype-specific differences in the distribution of tropism are biased by differences in clinical variables before test or if there is a bias in the tropism interpretation system. In the latter case, individual interpretation cut-offs for different subtypes may be necessary.

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P185

Improving HIV-1 tropism determination by combining geno2pheno and V3 net charge calculation

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Genotypic tests are the most common methods to identify patients eligible for CCR5 inhibitors administration in Europe. Among the available tools geno2pheno coreceptor (G2P) is the most used online system in routine diagnostics. This study was conceived to assess if the combination of G2P prediction with V3 peptide net charge (NC) value could improve the accuracy of tropism prediction. Sequences (129) were analyzed by G2P according to European Guidelines. NC values were calculated by the online software Peptide Property Calculator. Phenotypic assay was performed cloning the complete env gene into pcDNA 3.1 TOPO vector; infectivity of pseudotyped virions was tested on U87_CD4+CCR5+ and U87_CD4+CXCR4+ cells lines to assess viral tropism. Sequences were stratified into 3 groups according to the agreement between NC values and G2P results. Group 1: sequences assigned to the same group by both tools, group 2: sequences assigned to one group by G2P but

indeterminate by NC and group 3: sequences for which G2P and NC gave discordant results. 61% of sequences predicted as X4 by G2P showed NC values higher than 5; similarly, 76% of sequences predicted as R5 by G2P had NC values below 4 (Group 1). Sequences with NC values between 4 and 5 (Group 2) were associated to different G2P predictions: 59% samples were predicted as R5-tropic and 41% sequences as X4-tropic. These data support the hypothesis that 4 to 5 NC values could be associated to the presence of dual/mixed-tropic variants (DM). Sequences identified as X4 by NC value had at least one positive residue in positions known to be involved in tropism prediction (58%) and positive residues in position 32 (39%). To further verify NC-based prediction, phenotypic assay was performed on a subset of sequences from each group. The assay confirmed the tropism prediction for group 1 sequences and demonstrated that the variants with net charge between 4 and 5 have DM tropism. Moreover, in vitro phenotyping of discordant viruses confirmed NC result, showing that this parameter is strongly associated with phenotypic assay. These results show that the combination of G2P and NC could increase the accuracy of tropism prediction and the ability to discriminate DM viruses. A more reliable identification of X4 variants would be useful for better selecting candidates for maraviroc administration, but also as a predictive marker in coreceptor switching, strongly associated to the phase of infection.

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P186

Test for CCR5 tropism and treatment with maraviroc in Sicily: an observational retrospective multicentre study

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Purpose of the study: Maraviroc (MVC) is the first CCR5 inhibitor licensed for clinical use. A pre-treatment test is mandatory to identify R5 tropic patients. Aim of this study is to detect indications and results of tropism test and to evaluate efficacy and tolerability of MVC-based regimen.
Methods: An observational retrospective multicentre study was performed in Sicily in 15 Infectious Diseases Units. Clinical records of 213 screened for tropism HIV+ subjects were reviewed for age, sex, risk, clinical stage (CDC, CD4 cell count, HIV RNA viral load), therapeutic line, indication and result of test for tropism; within subjects treated with MVC, HIV RNA, CD4 cell count and metabolic parameters trend and adverse events were analysed.
Summary of results: Median age 44 (IQR 30–50) years, 67.1% males; 46.3% heterosexuals, 28.6% MSMs, 21.4% IVDUs; 23.7% CDC A, 32.1% CDC B, 44.2% CDC C; median CD4 was 217 (IQR 121–374) cells/μl and mean of HIV RNA was 4.72 (CI 95% 4.07–4.67) $\log_{10}$ copies/ml; median therapeutic line was 4 (IQR 2–7). 80.8% were submitted to Trofile™ test, 19.2% to genotypic test, 75.5% after a therapeutic failure. 56.8% of subjects screened were R5, 7.5% X4, 21.6% DM, 14% undefined. All X4 patients were tested after a therapeutic failure; patients screened for toxicity were more frequently R5 (75%) ($p < 0.01$). 76 (35.7%) multi-experienced (at baseline 8% HIV RNA < 50 copies/ml, median CD4 cell count 219 (IQR 124–345) cells/μl) subjects were treated with MVC plus an optimized background treatment: MVC was associated in 74% of cases with a protease inhibitors (56% darunavir/ritonavir), in 42% with raltegravir, in 56% with a NUC-sparing regimen. After 12 months of treatment 56.8% (ITT analysis) and 61.7% (AT) of patients had HIV RNA < 50 copies/ml; median CD4 cell count was 387 (IQR 222–455) cells/μl. After 24 months 64.8% (ITT) 80% (AT) had HIV-RNA < 50 copies/ml. Median CD4 cell count was 381 (IQR 218.515) cells/μl with a median increase of 168 (IQR 54–274) cells/μl. At 24 months median value of total and HDL cholesterol and triglycerides were within the normal range. 7 patients stopped the treatment: 2 died, 1 adverse event, 4 virological failure.
Conclusions: Although the test has been proposed to patients with long treatment history and failure, only 3/5 of R5 tropic patients were treated with MVC. An high number of multi-experienced subjects treated with a MVC-based regimen obtained HIV RNA < 50 copies/ml and a satisfactory increase of CD4 cell count.

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MOTHER-TO-CHILD TRANSMISSION

P187

Clinical risk factors on survival among infected children born to HIV-positive mothers

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Objective: The aim of this study was to investigate clinical risk factors on survival among infected children born to HIV-positive mothers in the southern region of Thailand.
Methods: Data from routine prospective cohort studies from 1990–2010 were analyzed. In these studies, totally 1549 infected children born to HIV-positive mothers were enrolled at birth and followed longitudinally. Information on demographic, clinical manifestation, HIV infection status factors was collected. Survival analysis was used to determine risk factors associated with mortality.
Results: The main result found that one-quarter of infected children died (434, 28.02%) during the follow-up period. A total of 135,295 person-months of follow up was available. The incident rate was 1.03 times per 100 person-months (95% CI: 0.97 to 1.08). The median survival time among infected children born to HIV-positive mothers from diagnosis to death was 87.34 months (95% CI: 87.32 to 87.36). Infected children born to HIV-infected mothers were diagnosed to confirm as AIDS (88.44%) and symptomatic HIV positive (11.56%), respectively. Regarding the clinical risk factor on survival among infected children born to HIV-positive mothers were found. Infected children born to HIV-positive mothers were more likely to die, who infected with candidiasis (HR: 1.47, 95% CI: 1.07 to 2.00), *Mycobacterium tuberculosis* (HR: 1.51, 95% CI: 1.26 to 1.81) and *Pneumocystis carinii* (HR: 1.50, 95% CI: 1.27 to 1.76), those compared to infected children without clinical manifestation.

Conclusion: Mortality among infected children born to HIV-positive mothers contributed to high levels in the southern region of Thailand. Consequently, health service system related to prevent mother-to-child HIV transmission is needed to improve child survival by lowering HIV infection and mortality in children born to HIV-positive mothers.

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P188

The incidence of complications after cesarean section in HIV-infected women with advanced WHO stages of HIV disease

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Prevalence of HIV infection in Ukraine is 1.6% overall, with antenatal prevalence of 0.52%, the highest in Europe. According to national protocol, cesarean section has been recommended for women with viral load above 50 copies/mL to further prevent vertical transmission of HIV. The aim of our study was to compare the infectious complication rates after cesarean delivery in HIV-infected women with advanced WHO stages of HIV disease who received HAART, and HIV-infected women with I or II WHO stages.

Materials and methods: A retrospective analysis was performed on data derived from 150 HIV-infected women with advanced WHO stages of HIV disease (group I) and 150 HIV-infected women with I or II WHO stages (group II), who underwent cesarean delivery. Post-operative infectious morbidity in both groups was analyzed according to whether the cesarean section was an elective or emergent delivery. Descriptive, comparison analyses were performed.

Results: There was no significant difference between the both groups in terms of gravidity, parity, number of previous cesarean sections, estimated gestational age at time of delivery. It has been shown that HIV-infected women from the group I have 2 times more factors for the appearance of postpartum infectious complications, such as anemia, the urinary tract infection, sexually transmitted infections. Both groups of women were statistically more likely to experience postpartum endometritis when being delivered by emergent cesarean section than by elective cesarean section (14.6% versus 4.6%, respectively in the group I and 5.3% versus 0.5%, respectively, in the group II), superficial or deep wound breakdown (22.6% versus 4.6%, respectively, in the first group and 5.3% versus 2.6%, respectively, in the second group). Septic pelvic thrombophlebitis was only in 2% of HIV-infected women from the group I. Urinary tract infection had 25% HIV-infected women in the both groups. Overall, the rate of postpartum infectious complications in the first group consist 28%, which was 2 times higher compared the second group.

Conclusion: According to our study, there was no significant difference in infectious postoperative morbidity in HIV-infected women who delivered by elective cesarean section in the both groups. But HIV-infected women with advanced WHO stages of HIV disease undergoing emergency cesarean section are at increased risk for post-operative infectious complications.

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P189

3TC+ PI dual therapy during pregnancy for PMTCT of HIV-1-na ve or pretreated women

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Purpose of the study: Perinatal transmission of HIV has fallen dramatically in countries where access to antiretrovirals is available, placing the focus of research on safety. The aim of this study is to assess whether in naïve or pretreated HIV-1 women, a dual, zidovudine sparing regimen (3TC+ PI) initiated during pregnancy can control maternal viral load while preventing maternal and infant toxicities related to in utero exposure to zidovudine.

Methods: We performed a retrospective, descriptive study between January 2006 and 2012. Seventeen naïve and 28 pretreated women who received dual therapy (3TC +PI) during pregnancy were included in the studied group and compared to 49 women on standard triple therapy (3TC/ ZDV+ PI), who delivered in the same time interval, at the same hospital. The primary endpoint was the % of women with viral loads (VL) $\leq$50 cp/ml at delivery. Secondary endpoints included% of women with VL $\leq$400 cp/ml after one month of dual therapy and of women who remained under dual therapy until delivery and achieved a VL $\leq$50 cp/ml at delivery. We also compared safety outcomes during pregnancy and until 18 months in children.

Summary of results: Groups had indistinguishable median VL at day zero (200 vs. 1680, p = 0.29) and gestational ages at initiation of therapy (19.6 vs 18 weeks, p = 0.18). At initiation of dual therapy (in 80% of cases: 3TC+LPV/r; ATV/r or ATV), the median VL was 21,692 cp/ml (6589 to 31,269) for naïve women and 43 cp/ml (20 to 200) for pretreated women. In intent-to-treat analysis of the dual therapy group, 41/45 women (91.11%, 95% CI 78.7 to 97.5%) achieved their primary endpoint. The table presents proportions of viral success at

ITT	3TC+PI	3TC/ZDV+PI	*p*
VL at delivery			
<50	91.1%	88.5%	0.72
VL at M1			
<400	91.1%	73.4%	0.03
Virological success and maintained therapy			*p*
VL at delivery			
<50	82.2%	85.7%	0.76

primary and secondary endpoints in the dual (N = 45) and control (N = 49) groups. Groups had similar proportions of cesarean section (28.8% vs 34.7%, p = 0.65) and of prematurity and changes in ART due to intolerance. There was one case of MTCT for the controls and none in the dual therapy group. Newborns with prenatal ZDV exposure had higher proportions of clinical syndromes at birth

(50% vs 25%, p = 0.02) and SAE in the first 18 months of life (90.3% vs 68.2%, p = 0.05) and worse haematological values at birth, with lower levels of haemoglobin (15.6 vs 17.5 g/dl, p = 0.05).
Conclusions: The 3TC+ PI dual therapy strategy in naïve or pretreated women achieved a satisfactory virologic effectiveness and resulted in less SAE in the first 18 months of life and better haematological parameters at birth for children.

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P190

Are HIV-related factors associated with pre-term delivery in a UK inner city setting?

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Purpose: In the UK the accepted standards for the management of HIV-positive pregnant women are the British HIV Association Guidelines [1]. The guidelines were updated in 2012 and make reference to conflicting evidence regarding the risk of premature birth; some studies suggest an increased risk of preterm delivery (PTD) in women treated with protease inhibitors (PIs) but others do not. Several of these studies have been conducted in developing countries and not in a setting analogous to UK healthcare. The aim of this study was to examine data from HIV-positive pregnant women attending a large UK teaching hospital, comparing the rates of PTD in women on PI-based regimes to those on non-PI based regimes. In addition, known and possible confounding risk factors for prematurity were considered.
Methods: We analysed retrospective data from the files of HIV-positive women attending a UK maternity center with specialist HIV care between 2003 and 2012. Inclusion criteria were women who delivered live-born infant(s) beyond 24 weeks gestation, and who were taking anti-retroviral treatment at some point during the first 37 weeks of their pregnancy. Preterm delivery was defined as delivery at less than 37 weeks. Multi-variable logistic regression adjusted for repeated measures was used to compare the rates of PTD in women on non-PI-based regimes with those on PI-based regimes; adjusting for possible covariates, including the percentage increase in CD4 count during pregnancy, the timing of HAART initiation, and concurrent genital tract infections.
Results: A total of 208 pregnancies in 157 women were included in the study. The overall prematurity rate was 11.1% (PI = 11.1%, non-PI = 10.8%), of which 5.8% were before 34 weeks. Analysis of the data demonstrated no statistically significant increased risk between PI and non-PI based regimes, which persisted following adjustments for known and possible confounding factors.
Conclusions: In this study 11.1% of HIV-positive women experienced PTD; in the general UK population 7.5% of pregnancies end in PTD [2]. The inclusion of a PI in the mother's HIV drug regime was not associated with an increased risk for PTD. An association between PTD and CD4 count increase in pregnancy of borderline significance was noted; p = 0.053. This is particularly relevant for women commencing HAART during pregnancy in whom, although over 1.5 times as likely to have PTD as those on treatment at conception, this was not statistically significant.

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P191

Treatment interruption after delivery in HIV-infected women without HAART indications is not safe if initial CD4$^+$ count is less than 700 cells/mm^3

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Purpose of the study: To determine safety for the mother of termination after delivery of HAART, initiated with the aim to prevent mother to child transmission.
Methods: 640 HIV-infected women were randomly selected and evaluated at baseline as not having standard HAART indications [1]. 32 of them got pregnant and short termed HAART (with one boosted protease inhibitor and two nucleoside reverse transcriptase inhibitors) was started at 14–26 week of gestation. It was stopped after delivery and women were additionally followed up for 3 years. Women were divided into 2 groups according to initial CD4$^+$ T-lymphocyte count: the *High Count Group* (16 women) 700 to 1200 CD4$^+$cells/mm^3, and the *Low Count Group* (16 women) 500 to 700 CD4$^+$ cells/mm^3. Data was subjected to statistical analisys by least square regression and Kaplan-Meier's method by means of SPSS software [2].
Summary of results: Women in the *High Count Group* had stable disease duration and lost at average only 9 CD4$^+$ cells per year (0,9% of CD4$^+$ cell count per year). The average elevation of viral load was 4306 copies per year. Only 6,3% (1 of 16) of women reinitiated HAART in 3 years. Women in the *Low Count Group* demonstrated immunological disease progression with outstanding loss of 80 CD4$^+$ cells per year (12% of CD4$^+$ cell count per year). Velocity of virological progression was 34940 HIV copies per year. 50% (8 from 16) of women reinitiated HAART in 3 years. 12,5% (2 of 16) of women had symptoms on viral rebound (acute pharyngitis, pneumonia).
Differences in above mentioned indices were statistically significant. Both groups did not differ significantly in age, HIV infection duration, duration of short termed HAART during pregnancy, initial viral load. Even mild immune deficiency 500–700 CD4$^+$ cells/ml results in evidently high velocity of immunological and virological HIV disease progression, leading to soon (within 3 years) HAART reinitiation. Termination of HAART in this case is considered to be not safe.
Conclusions: 1. In case initial CD4$^+$ cell count is less then 700 cells/ml termination of HAART after delivery is not safe and should not be recommended in practice. 2. If initial CD4$^+$ cell count is more then

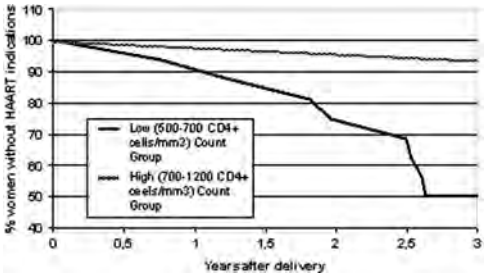

Figure 1. Kaplan-Meier curves, indicating women remaining without HAART indications after delivery.

Abstract P191–Table 1. Comparison of High and Low CD4+ Count Groups

Index	Measure	High (700–1200 cells/mm^3) CD4+ T-lymphocyte Count Group	Low (500–700 cells/mm^3) CD4+ T-lymphocyte Count Group	t	Significance (2-tailed)
Average CD4+ Cell Loss	cells per year	9,30	79,6	2,312	0,028
Average % CD4+ Cell loss	% per year	0,88	12,4	2,727	0,011
Proportion of women, initiated HAART at year 3	%	6,3	50	1,830	0,050
Average Viral Load Year Elevation	copies/ml	4306	34940	1,378	0,178
Age	years	25,84	26,22	0,278	0,783
Disease duration	years	2,43	3,17	0,759	0,454
Short Time HAART Duration	days	83,44	77,75	0,461	0,648
Initial Viral Load	Log_{10} copies/ml	4,09	4,25	0,602	0,551

700 cells/ml HAART may be terminated after delivery but additional studies are needed to evaluate the best appropriate time of termination.

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P192

Breast feeding in HIV: assessing risks in a London clinic

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In the UK, national guidelines recommend that all HIV-positive women should refrain from breastfeeding for prevention of mother to child transmission (PMTCT). However, the World Health Organisation recommends that HIV positive mothers from low income countries should exclusively breastfeed until six months and continue until twelve months with anti-retroviral therapy (ART) for mother and/or child. In our clinic, a high proportion of HIV positive women are from Africa and mixed messages regarding breast feeding may occur. The decision to not breast feed is sensitive and difficult, particularly where bottle feeding may be associated with HIV. A 2010 BHIVA position statement suggests that in exceptional circumstances breastfeeding may be supported with intense monitoring if the mother has an undetectable viral load. However, there is currently not sufficient evidence regarding transmission or ART toxicity. After a clinic disclosure of breastfeeding at four months post-delivery, we examined our current practice to investigate how monitoring may need to change if breastfeeding were supported in certain circumstances. A review of notes was undertaken to consider ART and viral load in the post natal-period to assess potential risks of breastfeeding in our cohort. All HIV-positive pregnant women who delivered during 2009–10 were eligible. 41 women were identified as having a live delivery of which 30 (73.2%) identified as Black African. 18 (44.0%) were new diagnoses in pregnancy. In total, 28 (68.2%) were on ART, or ART was indicated for the mother, and 13 for PMTCT only (Table 1).

	Require or on ART	ART for PMTCT
New HIV diagnosis	7	11
Known HIV positive	21	2

A viral load greater than 100 was found in 4 (9.8%) at delivery. All of the babies delivered were HIV negative. The mean time to post-delivery viral load was 65.4 days (range 24–584). Of those who were meant to be undetectable on ART, 6/28 (21.4%) had a viral load >100 copies/ml. 12(92.3%) of those who took ART for PMTCT were detectable at post-delivery viral load. Our clinic review suggests that if breast feeding is to be supported in certain circumstances: i) increased frequency of monitoring will be necessary for those on ART; ii) those on ART for PMTCT only would need to continue ART in the post natal period with such monitoring.

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P193

HIV-exposed infants on follow up at a PMTCT clinic: risk of HIV transmission and its predictors in north-west Ethiopia

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Background: The HIV pandemic created an enormous challenge to the survival of mankind worldwide. Vertical HIV transmission from mother to child accounts for more than 90% of pediatric AIDS.

Prevention of mother-to-child transmission (PMTCT) programs are provided for dual benefits, i.e. prevention of HIV transmission from mother to child and enrolment of infected pregnant women and their families into antiretroviral treatment. The availability and use of short-course antiretroviral (ARV) prophylaxis, a safe and well-tolerated regimen, can contribute significantly to PMTCT during childbirth. This study assessed risk and predictors of HIV transmission among HIV-exposed infants on follow up at a PMTCT clinic of a referral hospital.

Methods: Institution-based retrospective follow-up study was carried out on all records of HIV-exposed infants enrolled between September 2005 and July 2011 at Gondar University Hospital PMTCT clinic. Secondary data were collected using a structured data extraction format prepared in English by a trained nurse working at the PMTCT clinic. Data were then entered in to EPI INFO Version 3.5.1 statistical software and analyzed by SPSS version 16.0. Both bivariate and multivariate analyses were carried out to identify variables that had association with vertical HIV transmission.

Results: A total of 509 records were included in the analysis. The median age of infants at enrolment to follow up was 6 weeks (IQR = 2 weeks). A total of 51 (10%) infants were infected with HIV. Late enrolment to the exposed infant follow-up clinic (AOR = 2.89, 95% CI: 1.35, 6.21), rural residence (AOR = 5.05, 95% CI: 2.34, 10.9), delivery at home (AOR = 2.82, 95% CI: 1.2, 6.64), absence of maternal PMTCT intervention (AOR = 5.02, 95% CI: 2.43, 10.4) and mixed infant feeding practices (AOR = 4.18, 95% CI: 1.59, 10.99) were significantly and independently associated with maternal-to-child HIV transmission.

Conclusion: There is a high risk of MTCT of HIV among exposed infants on follow up at the PMTCT clinic of the University of Gondar referral hospital. This finding could push decision-makers to enhance commitment and support an adequate and sustainable extension of the use of PMTC services to rural mothers, expand services to rural settings in the PMTCT scaling-up program.

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P194

Efficacy of raltegravir in late-presenting HIV-infected pregnant women: a case series presentation

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The risk of HIV perinatally transmition is highest in the 3rd trimester and is correlated with the imune status and especially with the maternal viral load close to delivery. The speed of the viral load decay is an importante strategy for the prevention of mother-to-child transmition (MTCT) in late-presenting pregnant women. Poor access to prenatal care and HIV late diagnosis during pregnancy remains a major problem in Bahia, Brazil. The integrase inhibitor raltegravir has significantly higher first and second phase viral decay rates, has a high placental transfer with a potential preloading effect for neonate, and demonstrated effective accumulation in cervicovaginal secretions. These characteristics make RGV a potential candidate to treat late-presenting pregant women. We report 13 cases in which raltegravir (400 mg twice daily) was used late in pregnancy, as part of the antirretroviral regimen for MTCT prophylaxis. Table 1 contains the main characteristics of the 13 cases.

Four mothers for whom viral load data were available had undetectable levels (< 50 HIV-RNA cp/ml) at the time of delivery. The remaining 9 women had viral load < 460 cp/ml one week before delivery. All but one infant's HIV-RNA were undetectable at 1 and 3 months. The only positive case was an intrauterine transmission, since the baby viral loads at birth and at 1 month were > 500.000 cp/ml and mother had 64 cp/ml at delivery (elective C-section).

Table 1. Characteristics of the 13 cases. Numbers represent means (range)

Variable	
Maternal age (yr)	28.6 (17–37)
Years since HIV diagnosis	4.6 (< 1–16)
Week of pregnancy at RGV initiation	35.8 (34–38)
Maternal CD4+ T-cell count at RGV initiation (cl/ml)	357 (65–1.203)
Maternal viral load at RGV initiation (cp/ml)	73.765 (636–391.535)
Other ARV in regimen	ZDV + 3TC + LPV/r + RGV (7), ZDV + 3TC + RGV (3), ZDV + 3TC + DRV/r + RGV (2), ZDV + 3TC + ATV + RGV (1)
Exposure to RGV (days)	17.7 (7–35)
Adverse events with RGV	None
Viral load at delivery (cp/ml)	181 (< 50–457)
Gestational age at delivery (wk)	38.3 (37–40)
Mode of delivery	Elective C-section (10), Non-elective C-section (2), Spontaneous vaginal delivery (1)
Infant birth weight (kg)	2.942 (2.215–3.525)
Obstetrical complications	None
Birth defects	None
Intravenus ZDV during labour and delivery	Yes (13)
Oral ZDV post-exposure prophylaxis for infant	Yes (13)

In conclusion, this and other previous reports suggest that RGV is an useful and safe ARV drug to reduce the MTCT in late-presenting HIV-infected pregnant women.

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P195

Adverse outcomes of pregnancy in HIV-positive women in the era of HAART: a perspective from an outer London centre in the UK

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Background: Increasing number of women with HIV are choosing to become pregnant as there is dramatic reduction in the risk of vertical transmission. However, management of HIV in pregnancy still poses a variety of challenges and adverse pregnancy outcomes are still common. We aimed to explore the factors associated with adverse outcomes of pregnancy in our HIV cohort.

Methods: It is a retrospective case note review of all the women attended our unit and had HIV care from 2008–2011. A total of 87 women were followed up. Three women had two pregnancies during the study period. Data collected from Genitourinary Medicine and maternity records were analysed using SPSS program.

Results: Mean age was 34 yrs ranging from 20–43 yrs. Majority (91%) were of African origin; 67% had HIV subtype C; 26% resistant to one or more class of HIV drugs; 55% had a nadir CD4 fewer than 350; 44% diagnosed at an antenatal setting and 62% were planned pregnancies. Prior to the current pregnancy, these women had 121 children: 5% of the children have HIV and 33% not tested for HIV. Of the partners, 38% have HIV and 73% were aware of their partner's HIV status. None of the children born during the study period were infected with HIV; mean birth weight was 2789 g; there were 3 sets of twins; one still birth and one child died soon after birth. Around 46% were on anti-retroviral therapy (ART) during conception, 6% had miscarriages and 16% had emergency caesarean sections. At delivery, viral load was detectable in 23%, mainly due to poor adherence (11%) and late presentation (9%). 38% of the women experienced an obstetric complication, premature labour 9%; premature rupture of membranes and gestational diabetes both accounted to 4% whilst 3% had post-partum haemorrhage. On ART during conception and late HIV diagnosis that is nadir CD4, less than 350 cells were significantly associated ($P < 0.05$) with having a foetal complication such as prematurity 8%, low birth weight 7% or having a foetal abnormality 2.3%. There was no significant association between 1st and 2nd trimester ART exposure and adverse pregnancy outcomes such as prematurity, low birth weight or foetal abnormality.
Conclusion: Late diagnosis of HIV and ART during conception is significantly associated with adverse outcomes of pregnancy. Widespread HIV testing is essential and has to be extended to non-traditional settings. In addition, more studies are needed on ART exposure and adverse pregnancy outcomes.

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P196

An audit of the management of HIV-positive pregnant women and their babies: are we already meeting the 2012 BHIVA guidelines?

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Purpose of the study: In April 2012 the British HIV Association (BHIVA) issued revised guidelines for the management of HIV-positive women in pregnancy and their babies following birth [1]. These reflect the increase in knowledge and developments in HIV care since 2008 when previous guidance was issued [2]. The purpose of this audit was to determine to what extent the management of the patients was consistent with this new guidance, and to identify areas where changes in practice may be required.
Methods: The audit included 100 HIV-positive women and their babies, delivered between 2008 to 2012. The 2008 and 2012 BHIVA perinatal guidelines were reviewed and compared, key changes between the two were identified and auditable outcomes determined from these plus other crucial steps in their care. Data was collected retrospectively from a clinic database and where necessary, case-notes, and compiled on to a spreadsheet, recording compliance with the auditable outcomes.
Summary of results: Compliance with the 2012 guidelines was demonstrated in most aspects of the maternal and neonatal care examined. Areas of less than optimal compliance include testing for hepatitis delta virus (HDV) in hepatitis B co-infected women and performing resistance testing postnatally following antiretroviral therapy which is stopped postnatally. It was also found that in some cases antiretroviral therapy was switched in pregnancy, although this was most often due to reasons unrelated to the pregnancy such as toxicity or resistance, and where women were prescribed drunavir this was the once-daily rather than the twice-daily regime, although in all cases with good effect. Plans for appropriate mode of delivery were made for all women. In terms of neonatal antiretroviral prophylaxis, 99% received zidovudine monotherapy or triple therapy as appropriate depending on maternal viral load, and in 90% of cases this was started within 4 hours of birth in line with the 2012 guidelines.
Conclusions: The care provided to HIV-positive women and their babies managed at our centre between 2008 to 2012 is largely of the standard set in the 2012 BHIVA guidelines. Areas for improvement identified by the audit include continuing HIV therapy without change during pregnancy, considering increasing the dose of darunavir, testing for HDV when appropriate, performing resistance tests when therapy is stopped post-partum and increasing the proportion of neonates receiving prophylaxis within 4 hours of birth.

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P197

Reasons why HIV-positive women do not want to have a child: the questionnaire-based DIDI study

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Given that the majority of HIV-positive women are of reproductive age, it is necessary to understand the interaction between HIV and family planning, especially as antiretroviral medications allow to live longer, healthier lives. Aim of this analysis form the DIDI study was to assess prevalence of motherhood desire in current years and to identify variables associated pregnancy decision-making in HIV-infected women. DIDI is an Italian, 16-center, questionnaire-based survey performed in 585 HIV-positive women between Nov. 2010 and Feb. 2011. The items covered in the self-administered questionnaire included: socio-demographic characteristics, sexual and gynecological health, motherhood desire, strategies adopted to become pregnant, reasons for not wanting a child, partnership, HIV disclosure, physical and mental health, ART adherence, drug use. For the present analysis only women aged < 45 years and engaged in a partnership were included. Absence of motherhood desire was defined by a negative answer at the question whether the women at present would like to have a child. 178 women were included: mean age 39 (IQR, 33–42), HIV transmission heterosexual 75%, IVDU 11%, heterosexual/IVDU 2.5%, not known 7.5%; mean CD4 and HIV-RNA

were 552/mmc (+252) and 3.85 c/ml (+4.7), respectively. Absence of motherhood desire was found in 61% of women; 50% of women declared that HIV negatively affected motherhood desire, and 22% declared a decrease in desire after start of ART. The probability of vertical transmission was estimated higher than 50% by 19% of women, even when adopting all preventive measures. Not wanting a child was associated with: fear of vertical transmission ($p < 0.001$), fear of not being able to raise the child ($p < 0.001$), decline in motherhood desire after HIV ($p = 0.007$), unstable partnership ($p = 0.02$). At multivariable analysis, variables found to be significantly associated with negative pregnancy decision-making were: fear of vertical transmission (AOR 3.75; 95%CI 1.18–11.89), economic restrictions (AOR 0.28; 95% CI 0.10–0.76). In conclusion, absent motherhood desire in HIV-positive women with child-bearing potential is frequent and essential information on vertical HIV transmission is lacking. HIV-positive women of childbearing age may benefit from counseling interventions sensitive to factors that influence infected women's pregnancy decisions.

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P198

Pregnancy outcomes in HIV-infected women in a German cohort

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Background: To describe the findings of a German HIV-pregnancy cohort. To investigate factors associated with pregnancy complications and outcomes in HIV-infected women.
Methods: Retrospective analysis of HIV pregnancies from 2008 to 2010 in six German outpatient clinics specialized in HIV care.
Results: 230 mother-child pairs were included in the evaluation. In 25 cases, HIV infection was diagnosed during pregnancy (mean gestational age 17.5 weeks) with a mean CD4 cell count of 364 cells/μl and a median viral load (VL) of 6,660 copies/ml. 150 (65.2%) women were antiretroviral therapy (ART)-experienced prior to pregnancy; 112 (48.7%) received ART at conception; a further 97 (42.2%) started ART during pregnancy at an average gestational age of 25 weeks. Anemia was documented in 36.5% of the women with an average hemoglobin of 9.5 g/dl. Mean gestational age at delivery was 38 ± 2.41 weeks; range 24–42 weeks. 17 births (7.4%) were preterm. Average CD4 cell count at time of delivery was 447 cells/μl; in 162 (70.4%) cases, VL was <50 copies/ml. Mode of delivery was as follows: 70 (30.4%) vaginal, 131 (57%) primary and 29 (12.6%) secondary Caesarian (C)-section. Vaginal delivery was associated with a higher gestational age at delivery (39.1 vs 37.5 weeks, $p < 0.001$). Maternal CDC disease stage was found to be correlated with premature contractions ($p = 0.025$), shortened cervix ($p = 0.044$) and gestational age at delivery ($p = 0.042$). Further, healthier women, according to CDC classification, were more likely to deliver vaginally ($p < 0.001$). No vertical HIV transmission was documented. Mean birth weight was 2922 ± 580 g.
Conclusions: In this cohort, lower CD4 counts were associated with preterm contractions, shortened cervix, and a lower gestational age at delivery. In addition, women with less advanced disease were more likely to deliver vaginally.

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P199

Prevention of mother-to-child transmission of HIV in Latvia, 2008–2011

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Purpose of the study: The aim of this study was to describe trends in the management of pregnancies in HIV-infected women and their outcomes, over a 4-year period in Latvia on an Infectology Center of Latvia (LIC) basis.
Methods: The study of HIV-infected women in Latvia giving birth to one or more children between 1 Jan 2008 and 31 Dec 2011.
Results: We identified 199 HIV-infected women with 210 pregnancies. Mean age was 27 years, median baseline pregnancy CD4 count was 452 cells/mm^3, the baseline pregnancy plasma viral load (VL) was 53,066 copies/ml. Knowledge of HIV status before pregnancy was 60.5%, but 32.5% HIV-positive diagnosis was confirmed during pregnancy and 7.1% after delivery. One pregnant woman's HIV disease progressed to AIDS and death. Women on antiretroviral therapy (ART) were 82.3%. Maternal monotherapy with the zidovudine (ZDV) rate was 10.4%, dual therapy with nucleoside reverse-transcriptase inhibitor (NRTI) - 2.3%, triple therapy with the protease-inhibitor (PI) plus NRTI - 87.3%. Median VL at delivery was 1349. A greater proportion of cases 91.5% had a VL <1000 copies/ml, from them 47.4% <40 copies/ml. Vaginal deliveries range was 20.8% of pregnancies and elective cesarean delivery 68.6%. Preterm delivery occurred in 12.1%. Overall mother-to-child transmission (MTCT) of HIV rate was 4.3%. Among the 35.5% of mothers initiating ART at 14 weeks' gestation, MTCT was 1.4%, compared with 1.5% and 3.1% for those initiating ART at <14 weeks ($n = 67$, 31.9%) and >24 weeks ($n = 32$, 15.2%). Among 17.6% women, who did not receive prophylactic ART, MTCT rate was 16.2%. 7 of 9 women giving birth to an HIV-positive child were diagnosed with HIV before pregnancy, 1 of 9 during pregnancy, 1 of 9 after delivery. From women giving birth to an HIV-positive child 6 did not receive prophylactic ART, 1 started ART at week 14, 2 after week 14.
Conclusions: Women's low education, recurrent pregnancies, intravenous drug use, vaginal deliveries, not receiving and late initiation of prophylactic ART was independently ($p < 0.05$) associated with an increased risk of MTCT. Strategies are needed to facilitate earlier identification of HIV- infected women (also HIV status identification twice during pregnancy). Management of pregnancies in HIV-infected women according to the LIC guidelines, i.e. ART from week 14, intravenous ZDV during labour, elective cesarean delivery, neonatal ZDV during 6 weeks and no breastfeeding is effective to reduce risk for MTCT.

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P200

Prevention of HIV infection transmission from mother to child in Romania - a simultaneous objective and challenge

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The latest WHO data regarding HIV/AIDS infection have revealed the real dimension of this epidemic. In Romania, in 2011 out of 619 new detected cases, 19 represented children between 0–14 years. Vertical transmission was recorded for 16 (2.6%) of these cases. Within this epidemiological context, mother to child transmission continues to represent a top theme, which determined us to continue with the observations initiated in 2000 on this phenomenon.

Purpose of the study: The follow up of the evolution of a certain number of perinatally exposed children to HIV infection throughout 11 years, based on several risk factors: time of birth, time of the mother's and child's diagnosis; type of birth; type of nourishment for the newborn.

Methods: During 01.01.2000–31.12.2011, 435 children from all around the country were included in the study and assessed at I.N.B.I ''Prof. Dr. M. Bals'' in Bucharest, with ages between 0–18 months. They were clinically and biologically evaluated until the age of 18 months. Relevant data on the children were recorded: gender, age, time of diagnosis, ART prophylaxis (YES or NO), type of birth and nourishment, CD4 count, VL at the initial time and at the end of the surveillance period. For mothers we focused on: age, environment, level of education, occupation, time of HIV diagnosis, treatment/prophylaxis, type of birth, CD4 and VL at birth (data obtained from medical records or anamnesis).

Results: Out of the surveyed 435 children, 16% were considered infected with HIV. This rate decreased in stages, from 45% in 2005 to 17% in 2010. The main transmission causes were late HIV diagnosis in the mother, lack of prophylaxis/treatment for mothers, natural birth, breastfeeding, lack of prophylaxis in children or tardiness in initiating it.

Conclusions: The rate of HIV transmission is still very high. The elimination of this infection route is globally considered a realistic objective of public health policies. In this sense, the collaboration and active involvement of specialists from various medical and social domains is a necessity.

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P201

Outcome of pregnancy in the era of highly active antiretroviral: a 10-year experience in Southern Ireland

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Introduction: Since the introduction of HAART the desire to become a mother in women with HIV has become a viable option due to the drastic reduction in vertical transmission. The aim of this study was to look at the epidemiology, clinical characteristics, and safety of antiretroviral drugs and rate of vertical transmission in our cohort in the Munster region, Ireland.

Methods: We retrospectively reviewed all pregnant women with HIV who attended the ID clinic from January 2002 to April 2012. Patients' demographics, pertinent laboratory data, and pharmacy records were reviewed and statistically analysed.

Results: 105 HIV-positive women, with a total of 165 pregnancies, were seen from January 2002 to April 2012 at Cork University Hospital: 46 patients were previously known to be HIV-infected at their first pregnancy and 59 were diagnosed during antenatal screening (median of 32 week gestation at diagnosis). The median age at the time of pregnancy was 32 and the HIV transmission was 90% sexual: 39 women were from Europe/Asia and 66 were African; only two women were HCV co-infected and one was HBV co-infected. Of the patients diagnosed with HIV prior to pregnancy, 13 were on treatment, all of whom had no detectable virus at the start and during pregnancy. The median CD4+ at the start of pregnancy was 490 cells/μl. The median weeks of gestation at the start of HAART was 28 before 2006 and 20 after 2006, in accordance with National Guidelines. The HAART regime used was in line with current Guidelines. 18 pregnancies ended in miscarriage before week 12 gestation and 2 pregnancies resulted in intrauterine death at 28 weeks. 145 pregnancies progressed to delivery at full term but 10 infants were born before the 37th week, with one baby born at 23 weeks: 63 had SVD and 82 underwent C-section, of whom 12 emergency C-section due to prolonged membrane rupture. Most of the C-sections were planned due to obstetric reasons. 2 infants were born HIV+: in one case the mother was a late presenter at 38 of gestation; and in other the mother had poor compliance with viral load detectable at the time of labour. The overall number of pregnancies per year has been stable over the ten years (average of 14 pregnancies per year).

Conclusion: The use of cART with high level of adherence and a close clinical management during pregnancy has shown to dramatically reduce the vertical transmission of HIV in our cohort.

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P202

Use of efavirenz during the first trimester and resulting pregnancy outcome: experience of the Ambulatory Treatment Center of Brazzaville

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Background: The aim of this study is to report the experience of the Ambulatory Treatment Center of Brazzaville regarding the use of efavirenz (EFV) during pregnancy.

Methods: A retrospective cohort study of HIV-positive women was conducted at the Ambulatory Treatment Center of Brazzaville. The study examined the use of an anti-retroviral treatment containing EFV in women who reported being pregnant during follow-up between January 2009 and September 2011. Demographic, clinical and biological data, and adverse effects associated with exposure to EFV during pregnancy were assessed after each pregnancy from the register of pregnant women in terms of preterm delivery (birth occurring before 37 weeks of age) and spontaneous miscarriage (spontaneous expulsion of the fetus before 15 weeks of age).

Results: Of 220 patients on an anti-retroviral treatment who reported being pregnant during follow-up, 34 patients were administered combinations containing two nucleoside reverse transcriptase inhibitors (AZT/3TC = 27; d4T/3T = 4; TDF/FTC = 3) and EFV, with a median age of 31.95 years (IQR: 27.71–36.37) and median durations of exposure to EFV of 11.81 months (IQR: 5.46–21.22) and 35.14 weeks (IQR: 11–39.86) before and during pregnancy, respectively. In 13 patients who reported to be in their first trimester of pregnancy, a change from EFV to nevirapine was made in nine of these patients. The median CD4 count was 271.5 cells/mm^3 (IQR: 233.5 –414.5) and 305 cells/mm^3 (IQR: 205–408) in early pregnancy and at delivery, respectively; the viral load was undetectable in 90% and 85.7% of the patients, respectively. Twenty-three deliveries took place after 37 weeks gestation; additionally, five preterm deliveries, four spontaneous miscarriages, one terminated pregnancy, and one death in utero occurred.

Conclusions: EFV used during the first trimester of pregnancy offers security, but the number of fetal deaths is also important.

Reference

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P203

Pregnancy and treatment interruption enhances progression of HIV-infection if initial CD4$^+$ T-lymphocyte count is less than 700 cells/mm^3

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Purpose of the study: To determine velocity of immunological and virological progression of HIV-infection in respect to pregnancy and short-termed HAART.

Methods: Comparative retrospective study. Retrospective period - 4 years. All women had initial CD4$^+$ cell count in the range from 500 to 700 cells/mm^3 and viral load less then 5 $\log_{10}$ copies/ml. The study group - women having had pregnancy and short termed HAART (16 cases). The control group - women not having had pregnancy and episodes of HAART. 3 endpoints were determined: (i) average year CD4+ T-lymphocyte loss (cells/mm^3); (ii) average year% CD4+ T-lymphocyte loss; (iii) average year viral load elevation ($\log_{10}$ copies/ml). Endpoints were calculated by the least square regression.

Summary of results: Women in the study group showed higher progression rates of HIV infection, as shown in table 1 and figure 1 The difference in average year CD4$^+$ T-lymphocyte loss was 2,9 fold, average year% CD4$^+$ T-lymphocyte loss was 2,8 fold, average year viral load elevation - 4,5 fold. All differences were statistically significant.

There was no statistically significant difference between the groups in the age of women and initial viral load. If the initial CD4$^+$ counts were more the 700 cells/mm^3, pregnancy and HAART termination does not have significant effect on immunological progression, difference in viral load dynamics being still present (data not shown). The study does not allow to differentiate effects of pregnancy itself or of HAART termination. According to literature effect of pregnancy on HIV disease progression is not clear [1], that is why the most reliable hypothesis is the unfavourable influence of HAART termination on the course of HIV-infection. This provides a reliable evidence not to stop HAART after delivery if initial CD4$^+$ count is less then 700 cells/ml.

Conclusions: 1: Higher level of immunological progression is proved by elevated average year CD4$^+$ T-lymphocyte loss: in absolute count (cells/mm^3) and in% to the previous level. 2: Higher level of virological progression is proved by elevated average year viral load. 3: Enhancing progression of HIV-infection is due to changing level of HIV after HAART termination on the background of weakened and disbalanced cellular immunity.

Reference

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Table 1. analysis of HIV-disease progression indices in women having pregnancy and HAART termination and not

Average Year Index	Study group (with pregnancy)	Control group (without pregnancy)	t	Significance (two-tailed)
CD4+ T-lymphocyte loss (cells/mm^3)	79,6281	27,6484	2,404	0,019
% CD4+ T-lymphocyte loss	12,4350	4,5067	2,342	0,023
viral load elevation ($\log_{10}$ copies/ml)	,3830	,0854	2,710	0,009

Figure 1. 95% confidence intervals showing significant influence of pregnancy and HAART termination on HIV-disease progression.

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NEW TREATMENTS AND TARGETS

P204

Dolutegravir treatment response by baseline viral load and NRTI backbone in treatment-na ve HIV-infected individuals

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Background: In two 48-week studies in naïve subjects, dolutegravir with NRTI of choice has shown non-inferiority to raltegravir and, with ABC/3TC, superiority to Atripla. Factors that influenced choice of NRTIs included viral load, resistance and safety.
Methods: We analysed response rates and time to virologic failure by NRTI backbone and baseline viral load in the pivotal DTG-naïve studies. SPRING-2 randomized participants to DTG 50 mg QD or RAL 400 mg BID, each in combination with investigator-selected NRTIs (TDF/FTC or ABC/3TC). SINGLE randomised participants to DTG 50 mg + ABC/3TC QD or TDF/FTC/EFV (Atripla) QD. In SPRING-2, changes in serum creatinine were examined by INI and NRTI backbone.
Results: The two studies randomized and treated 1655 subjects, of whom 249 (15%) were female, 388 (23%) non-white, 495 (30%) had HIV-1 RNA >100,000 c/ml, and 224 (14%) had CD4+ count <200 cells/mm^3.
Primary analyses demonstrated non-inferiority of DTG to RAL in SPRING-2 ($\Delta = 2.5\%$; 95% CI: −2.2% to +7.1%, excluding −10%), and superiority of the DTG regimen in SINGLE (7.4%; +2.5% to +12.3%). In SPRING-2, response rates by NRTI backbone were comparable in each viral load stratum. In SINGLE, a 7% difference in response (favoring DTG + ABC/3TC) was observed in each viral load stratum. Exploratory analyses examining time-to-virologic failure showed no difference in response rates between the NRTIs irrespective of baseline viral load or study. Resistance to INIs or NRTIs was not demonstrated in any subject on DTG-based therapy through 48 weeks. Withdrawals due to AEs on DTG-based regimen were few (2%) in both studies. In SPRING-2, no significant differences were observed in serum creatinine change from baseline to Week 48 by NRTI backbones.
Conclusions: In SPRING-2 and SINGLE, DTG was effective with both ABC/3TC and TDF/FTC, and in subjects with high and low viral load. DTG was well tolerated in both studies. Renal safety also was similar by NRTI backbone. DTG is a once-daily, unboosted INI that can be used with either TDF/FTC or ABC/3TC backbone in treatment-naïve, HIV-infected individuals.

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P205

Enabling clinical development of an HIV attachment inhibitor through innovative pharmaceutical development: novel extended-release delivery of prodrug

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Background: HIV-1 attachment inhibitors are a new class of viral entry inhibitors which target viral gp120 preventing attachment of virus to its host cell receptor CD4. This class presents major challenges for development based upon low solubility and short half-lives. For progression into clinical studies, requirements include reliable and reproducible absorption from a tolerable and convenient oral dosing regimen.
Methods: A series of highly soluble prodrugs were designed to overcome the poor absorption caused by the low solubility of the active compounds. A regional absorption study was conducted to assess the uptake of active throughout the gastro-intestinal tract following oral prodrug delivery. An extended-release (ER) strategy was subsequently devised to optimise tolerability, decrease peak to trough ratios and reduce frequency of dosing. In silico absorption modelling was used to verify feasibility and drive in vitro testing leading to dosage form development and selection. The performance of the ER dosage form was verified in vivo prior to use in clinical studies.
Results: Phosphonooxymethyl prodrugs with aqueous solubilities in excess of 250 mg/mL were synthesised and shown to be readily converted to parent compound via alkaline phosphatase in vitro. Results of regional absorption studies for the selected compound, BMS-663068, confirmed the rapid absorption but short half-life of active following oral administration of prodrug. Delivery to specific regions throughout the GI tract showed absorption of active to be subject to regional variation with an extent of colonic absorption of approximately 40% of intestinal absorption. Incorporation of this data into an in silico model guided development of an ER tablet which releases prodrug over 24 hours and achieves the required exposure, pharmacokinetics and reproducibility in vivo.
Conclusions: The novel approach of combining prodrug synthesis and ER formulation has enabled clinical evaluation of a promising new class of therapeutic entity into Phase 2b studies.

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Abstract P204

Proportion of Subjects with Plasma HIV-1 RNA <50 c/mL at Week 48 (1° Endpoint)				
	SPRING-2		SINGLE	
	DTG	RAL	DTG	EFV
OVERALL	361/411 (88%)	351/411 (85%)	364/414 (88%)	338/419 (81%)
<100,000c/mL ABC/3TC	115/132 (87%)	110/125 (88%)	253/280 (90%)	
TDF/FTC	152/165 (92%)	154/170 (91%)		238/288 (83%)
>100,000c/mL ABC/3TC	30/37 (81%)	32/39 (82%)	111/134 (83%)	
TDF/FTC	64/77 (83%)	55/77 (71%)		100/131 (76%)

P206

The discovery of S/GSK1265744: a carbamoyl pyridone HIV-1 integrase inhibitor

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Background: HIV-1 integrase is a virally encoded enzyme essential for lentiviral replication. Assiduous medicinal chemistry efforts culminated in the discovery of raltegravir, the first marketed HIV-1 integrase inhibitor (INI). However, there is significant opportunity for improvement including overall dose burden, dosing interval and potency against resistant viruses. Our molecular design approach used a two-metal binding pharmacophore strategy and succeeded in identification of carbamoyl pyridone HIV-1 INIs. This enriched core scaffold has abundant structural features expanding the opportunity to control drug properties, leading to the discovery of S/GSK1265744.
Methods: The carbamoyl pyridone scaffold was derivatized and evaluated for antiviral activity against wild-type virus ($\pm$HSA) along with key INI-resistant mutants. Animal pharmacokinetic profiles including a key measure of the trough drug concentration over protein-adjusted antiviral potency (C24/PAIC$_{50}$) along with in vitro DMPK properties, were used along with the virological data for compound selection.
Results: The carbamoyl pyridone series inhibitors exhibited potent antiviral profiles with promising DMPK properties. S/GSK1265744 demonstrated good coverage of C24 over PAIC$_{50}$ predicting low mg unboosted once daily dosing, now validated in phase 2 clinical studies. These preclinical data along with a long human $T_{1/2}$ of ~30 hours in oral tablet study supports S/GSK1265744 as a long acting parenteral agent for once-monthly or less frequent dosing.
Conclusions: A medicinal chemistry approach utilizing key viral mutants in combination with C24/PAIC$_{50}$ has allowed for discovery of S/GSK1265744. This agent is currently in phase 2 development evaluating a novel, long-acting parenteral route of administration and may enable new approaches to HIV therapy and prevention.

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P207

Geno- and phenotypic correlates of virologic response to the attachment inhibitor BMS-626529 in an 8-day monotherapy study of its prodrug BMS-663068

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Background: Administered as monotherapy for 8 days, BMS-663068, the prodrug of the attachment inhibitor BMS-626529, demonstrated significant reductions in plasma HIV-1 RNA. Although baseline IC$_{50}$ $>$100 nM to BMS 626529 correlated with a poor virologic response, BMS-663068 did not appear to select for BMS-626529 resistance on population sequencing or phenotyping.
Methods: Genotypic population analyses of baseline samples from non-responders identified amino acid changes that could potentially encode for reduced susceptibility to BMS-626529. Reverse genetics of functional envelope clones confirmed changes responsible for this in phenotypic assays. Additional genotypic, phenotypic and reverse genetic assays were performed on samples from responders to probe the context dependence of the identified substitutions.
Results: The gp120 M426L substitution was the major change associated with reduced virologic response (present in 5 of 6 non-responders) and high BMS-626529 IC$_{50}$ (present in virus from 6 of 7 subjects with IC$_{50}$ $>$100 nM). The remaining non-responder virus sample contained a S375M substitution that encoded reduced susceptibility. However, the M426L substitution was also identified in two responders, one with reduced susceptibility (IC$_{50}$ 6300 nM) and another with low IC$_{50}$ (38 nM). A series of functional clones from 4 samples (including 2 responders with resistance mutations on population genotyping) were analyzed for susceptibility to BMS-626529. Variability of susceptibility of clones (37–246 fold) was higher than variability observed with other entry inhibitors (enfuvirtide, 6–9 fold; maraviroc, 3–9 fold). In the responder subject with M246L, all functional clones contained M426L and susceptibility varied by 246-fold, suggesting that susceptibility is highly context dependent. One of the responders contained viruses of either tropism. Clones of R5- or X4-tropic viruses from this individual exhibited the same variable range of susceptibility to BMS-626529.
Conclusions: gp120 substitutions M426L and S375M were found to be strongly, albeit not exclusively, associated with low susceptibility to BMS-626529 and a lack of virologic response to its prodrug, BMS-663068. Functional clones derived from single individuals exhibited 2-3 log$_{10}$ variability in susceptibility to the agent, regardless of tropism, suggesting that susceptibility can be highly context-dependent.

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NON-AIDS MORBIDITIES AND MORTALITY, AND AGEING

P209

Neurocognitive impairment, depression, and anxiety in HIV-1-infected patients across western Europe and Canada: the CRANIum study - ethnicity analysis

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Purpose of the study: The prevalence of neurocognitive impairment (NCI) in people living with HIV has previously been reported between 20–50%, with prevalence rates of depression reported between 12–71%. The primary objective of the CRANIum study was to describe the prevalence of a positive screen for NCI and depression/anxiety in an HIV-1-infected adult population, comparing ARV-naïve and -experienced patients. Here we present an ethnicity analysis of the CRANIum data.
Methods: The study was an epidemiologic, cross-sectional study that included HIV-1-infected patients $>$18 years old attending a routine clinic visit. One-third of patients were ART-naïve, one-third on a PI/r- and one-third on a NNRTI-based regimen. The Brief Neurocognitive Screen (BNCS) was used to screen for NCI. It consists of the Digit Symbol and Trailmaking A and B tests. A standard deviation of $>$1 on 2 tests or $>$2 on 1 test was considered a positive screen for NCI. The Hospital Anxiety and Depression Scale (HADS) was used to screen for anxiety (HADS-A) and depression (HADS-D). HADS is self-administered and consists of 14 items (7 HADS-A, 7 HADS-D) scored between 0 to 3. A score of $\geq$8 was considered as a positive screen for either condition.

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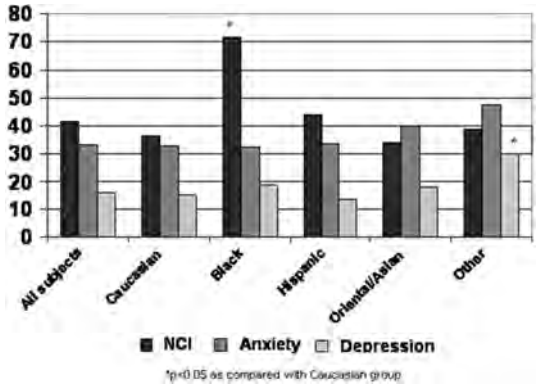
	All subjects	Caucasian	Black	Hispanic	Oriental/Asian	Other
Number of subjects (%)	2859	2254 (78.8)	387 (13.5)	127 (4.4)	50 (1.7)	41 (1.4)
Age - mean, years	42.95	43.80	39.79*	38.56*	40.57*	42.96
Gender - %						
- Male	61.7	67.3	26.9*	70.1	64.0	56.1
- Female	38.3	32.7	73.1*	29.9	36.0	43.9
Unemployed - %	33.1	32.8	35.7	26.0	30.0	51.2*
> Secondary school education - %	82.2	81.3	84.2	89.0*	90.0	78.0
HIV risk factor - %						
- Homosexual	42.5	48.5	4.1*	58.3*	36.0	31.7
- Heterosexual	44.8	37.3	89.4*	39.4*	46.0	51.2
- Other/ Not known	12.8	14.2	6.5*	2.4*	18.0	17.1
Duration of HIV infection - mean, months	98.10	103.22	73.46*	79.80*	82.16	113.84
Last recorded HIV-1 RNA level						
- ART-naïve- median, c/mL	22,390	23,539	11,483	32,241	23,112	12,660
- ART-experienced - median, c/mL	39.0	39.0	40.0	28.0	40.0	39.5
Last recorded CD4 count - mean, c/μL	586.02	598.70	527.57*	550.17	542.40	599.43
Previous AIDS diagnosis - %	17.5	17.7	16.6	17.3	16.0	19.5
Previous CNS infection - %	4.5	3.6	7.2*	6.3	6.0	17.1*
CD4 count nadir (mean, cells/μL)	295.02	302.65	255.01*	311.97	259.10	247.63
Hepatitis C co-infection - %	12.4	14.7	1.6*	3.9*	16.0	12.2
Previous psychiatric diagnosis - %	20.2	22.2	9.8*	15.9	20.0	17.1

Summary of results: 2859 evaluable patients were included from 15 countries. Baseline characteristics are shown in table 1 (*$p < 0.05$ as compared with Caucasian group). Overall, 41.4% of patients had a positive screen for NCI, 33.3% for anxiety and 15.7% for depression. Results by ethnicity are shown in figure 1.



Conclusions: In this large epidemiologic study, the overall prevalence of a positive screen for NCI was high. In particular, the rate in black patients was nearly double that of the overall study population. This finding needs to be interpreted in light of differences in demographics and disease characteristics between ethnic groups. The overall prevalence of a positive screen for depression in HIV-infected patients was nearly double what has previously been reported in the non-HIV-infected population in Europe when utilizing a similar screening tool, with no significant differences between identified ethnic groups. These results support a strategy of regular screening for, and clinical management of NCI, depression, and anxiety in all HIV-infected patients, with specific focus on NCI in the black population.

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P210

Determinants of medium and high VACS index in HIV-positive patients on effective HAART

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Non-AIDS events are the leading cause of death in HIV-positive patients (pts) on effective HAART. The VACS index, composed by HIV-RNA, CD4+, age, hemoglobin, FIB-4, eGFR and HCV co-infection, has been validated as 5-year mortality index in HIV- positive pts [1]. The aim of our study was to evaluate the prevalence and any possible predictive factors of medium-high VACS index in a cohort of HIV-positive pts; we also evaluated whether it relates with markers of systemic immune activation. 501 consecutive HIV-positive asymptomatic pts on effective HAART (HIV-RNA <40 cp/ml) were enrolled. T-cell activation (CD38+, CD8+45R0, CD8+38R0) and differentiation (CD127+) was assessed by flow cytometry; VACS index was calculated closest to the sample timepoint. Comparisons were assessed by Chi-square test. Factors associated with VACS index equal or greater than 10% (gender, time on HAART, CD4+nadir, AIDS diagnosis, previous or current IDU, immune-activation markers) in univariate model entered the multivariate logistic regression. Of the 501 patients enrolled, 350 (70%) had a low VACS index (VACS $<10\%$), 143 (28%) a medium index (VACS 10–30%) and 8 (1%) an high one (VACS $>30\%$). Groups (pts with low and medium-high VACS index) were comparable for CD4+ nadir, AIDS diagnosis, CD8+45RO%, CD8+38RO%, CD127+%. Females, active or previous IDU, pts with shorter HAART exposure showed more frequently medium-high VACS index (table 1). In the multivariable model, female sex (AOR 6.26, 95% CI 3.45-11.38, $p<0.000$), IDU history (AOR 2.409, 95% CI 1.31–4.422, $p=0.0045$) and current CD38+/CD8% (each% more: AOR 1.122, 95% CI 1.03-1.21, $p=0.004$) were all independent predictors of VACS $\geq 10\%$. Our data suggest that a persistently-activated immune profile despite

Abstract P210–Table 1. Variable associated with medium-high VACS index in univariate model

	Pts with low (<10%) VACS index (n = 350)	Pts with medium-high (>10%) VACS index (n = 151)	p
Female sex°	69 (19%)	66 (43%)	**0.0001**
AIDS°	75 (21%)	50 (33%)	0.38
Nadir CD4+ T cells/mmc*	211 (7–600)	183 (4–489)	0.75
HAART duration, years*	8.1 (1–21)	7.9 (1–20)	**0.01**
IDU°	74 (21%)	50 (33%)	**0.004**
CD127/CD4 + %*	35 (0–63)	35 (0–58)	0.81
CD127/CD8 + %*	44 (0–55)	45 (0–46)	0.70
CD8 + 45/RO%*	13 (0–43)	14 (0–61)	0.7
CD8 + 38/RO%*	1,5 (0–27)	1,6 (0–13)	0.85
CD8 + CD38 + %*	3.01 (0–23)	4.09 (0–23)	**0.004**

*Data are presented as mean (range).
°Data are presented as the number (percentage).

virologically-suppressive HAART may contribute to all-cause mortality risk, possibly through its role in accelerating degenerative disease. Possible determinants of gender differences in VACS index (such as hemoglobin) need to be further studied.

Reference

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P211

A five-year observance of changes in the cardiovascular risk profile in 505 HIV-positive individuals

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Purpose: Since the introduction of antiretroviral therapy (ART) and the extension of life expectancy, HIV-infected persons have shown an increasing number of cardiovascular events. The reduction of cardiovascular risk factors becomes a new challenge in HIV care. One of the main objectives of the HIV&HEART study is to examine the development of cardiovascular risk factors and treatment of cardiovascular diseases.
Methods: This study is an on-going, prospective, regional multicentre trial that was conducted to analyse the frequency and clinical course of cardiac disorders as well as cardiovascular risk factors in HIV-infected patients. 505 HIV-infected outpatients were recruited at baseline (BL) and re-examined during 5-year follow up (5YFU).
Results: 84% of 505 eligible HIV-infected patients were male. The average age was 44.3 ± 9.5 years at BL. The proportion of ART-treated patients increased from 85.7% at BL to 96.4% at 5YFU. During the 5-year observation period mean cardiovascular risk detected by Framingham score increased from 6% at BL to 10% at 5YFU. Even after adjusting for age there was a difference in the Framingham score of 2%. Between BL and 5YFU systolic blood pressure increased from 128.4 ± 19.8 mmHg to 138.3 ± 19.9 mmHg in spite of an intensified use of antihypertensive drugs, from 11.9% at BL to 24.0% at 5YFU. The rate of participants with adiposity, characterised by a BMI >30, increased from 7.9% at BL to 11.2% at 5YFU. Lipid-lowering therapy was applied in 10.3% of the patients at BL and in 13.9% at 5YFU. Triglycerides (TAG) ≥200 mg/dl reduced from 38.9% at BL to 36.8% at 5YFU; in contrast cholesterol values ≥200 mg/dl elevated from 57.8% to 61.8%. The same trend was observed in HDL ≤40 mg/dl. Here we found a change from 29.2% versus 31.3%. Doing regular sports elevated from 1.9% to 3.3%. The count of smokers increased for 2.8% and also mean pack-years changes from 24 to 26.5 pack-years.
Conclusion: During a 5-year period the cardiovascular risk in Framingham score increased disproportionately high in this HIV-infected cohort even after adjusting for age. There was an increasing blood pressure although an elevated use of antihypertensive therapy. There was also a tendency of elevating BMI and an increasing trend in smoking behavior. As protective facts, we found a tendency in doing sports and a decreasing TAG value during intensifying lipid-lowering therapy. Cardiovascular risk was increasing, in spite of interventions.

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P212

Comparison of screening tools for the detection of neurocognitive impairment in HAART-treated patients

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Background: Neurocognitive impairment (NCI) and HIV-associated neurocognitive disorders (HAND) remain prevalent despite HAART. We examined sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and correct classification rate (CCR) of screening tools for the detection of NCI and HAND in HAART treated patients.
Methods: We examined 101 unselected HAART-treated patients. Patients were administered the self-reported three questions (EACS Guidelines), the International HIV-Dementia Scale (IHDS), the Mini-Mental Status Examination (MMSE), and a comprehensive 6-domain (17-test) neuropsychological (NP) battery (120 minutes) that included, among others, the Digit Symbol (DS), the Trail Making Modalities (TM), and the Grooved Pegboard (GP) tests. NCI was

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	Sens, %	Spec, %	PPV, %	NPV, %	CCR, %	Time, min
Three questions	20.0	88.5	53.3	62.8	61.4	3
IHDS	55.0	82.0	66.7	73.5	71.3	4
MMSE	12.5	98.4	83.3	63.2	64.4	10
IHDS + TM	82.5	70.5	64.7	86.0	75.2	10
IHDS + DS	77.5	73.8	66.0	83.3	75.2	8
IHDS + GP	70.0	70.5	60.9	78.2	69.3	10
IHDS + TM + GP	85.0	60.7	58.6	86.1	70.3	16

defined according to the AAN criteria. HAND was diagnosed after exclusion of confounding conditions.

Results: Our cohort was relatively healthy (mean CD4 count: 575 cells/mm^3, undetectable plasma HIV RNA 85%). Prevalence of NCI and HAND were 39.6% (40 of 101) and 30.7% (31 of 101), respectively. Mean scores of IHDS (9.9 vs 10.8; $p < 0.001$) and MMSE (26.8 vs 28.2; $p = 0.004$) differed significantly between impaired and unimpaired patients, while mean three-questions scores (8.0 vs 7.0; $p = 0.23$) did not. The three questions showed also poor sensitivity for the detection of both NCI (20%) and HAND (22%). The IHDS showed fairly good sensitivity (55%) and NPV (73.5%). Adding to the IHDS some easy to administer NP tests, i.e. TM, DS, and GP, resulted in an increase in sensitivity and NPV for the detection of NCI (table). Similar results were obtained regarding the detection of HAND (not shown in table).

Conclusions: Both NCI and HAND are still very prevalent in HAART-treated patients. Among screening tools the self-reported three question show poor sensitivity. The IHDS performed better in terms of sensitivity, PPV, and NPV. Combinations of easy-to-administer NP tests with the IHDS resulted in increased sensitivity and NPV. Combining IHDS with one or two simple NP test may represent an improvement in the screening approach to the detection of both NCI and HAND.

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Clinical-epidemiological features of HIV-infected patients diagnosed at age of 50 years or older

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HIV/AIDS prevention and care efforts are directed to individuals of reproductive age (15–49 yrs). With the extension of sexual life of older people, they became a growing population at risk of HIV infection, usually not included in prevention strategies. In order to evaluate clinical profile of HIV/AIDS pts diagnosed at 50 yrs or older assisted in an HIV outpatient center in Buenos Aires, we retrospectively assessed clinical records of pts initiating care between Jan 1986 and Dec 2011. Age, CD4 cells and viral load (pVL) at HIV diagnosis and most recent value, opportunistic infections (OIs), co-morbidities and antiretroviral therapy (ARV) were recorded. Of 10,998 pts assisted in the 26-yr period, 495 (4.5%) were ≥ 50 yrs old at HIV diagnosis; median annual diagnoses: 18.5 (IQR 3.3–30.3) without significant changes in the last 20 yrs. Demographics: median age 54.7 yrs (IQR 51.8–59.2, rank 50–80), 76.6% male. Risk behavior: HTX 61.4%, MSM 34.1%, others 4.4%. 55.4% of HIV diagnoses occurred during hospitalization or simultaneously with acute OIs. One third (n = 176) had AIDS at diagnosis, 24% had history of STDs. HCV co-infection 5.7%, past HBV infection 28.1% and chronic HBV infection 5.1%. Median CD4 cells at HIV diagnosis: 223.5 (13.7%) (IQR 98.8–420.3), initial pVL 60,000 cp/mL (IQR 9,995.5–208,391). 69.3% of pts started ARV therapy during follow-up (FU), and the median time between diagnosis and treatment initiation was 3.4 mo (IQR 0.7–14); 56.9% of them started a non-nucleoside-based regimen (ZDV/3TC/EFV), 28.3% a PI-based regimen (ZDV/3TC/IDV) and 14.6% a nucleoside-based regimen (ZDV/ddI pre-HAART era). After a year ($\pm$6 mo), 63.8% pts achieved undetectable pVL and gained 136 CD4 cells from BSL (IQR 83–204). After 40.6 mo of FU (IQR 6.7-89.8), 66.3% are alive, 7.1% died (68.6% of HIV-related diseases) and 26.7% are lost to FU. Co-morbidities were present in 125 (25.3%), mainly hypertension, increased lipids, CVD and DBT. Among treated pts, 70.6% achieved pVL < 50 cp/mL, with a median increase of CD4 cells up to 410 (22%) (IQR 281.5–563.9) from BSL. 51% (176) changed ARV therapy due to toxicity/AE: 54.5%, ARV failure: 29.5% and simplification: 14.8%. Stable HIV epidemic in older people reinforce the need of specific prevention approaches, while growing age of HIV individuals in care highlights to consider risks associated to older age. Late presentation to care needs to be specifically addressed. Response to treatment is remarkable high in this population.

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High lifetime risk of cardiovascular disease vs low 10-year Framingham risk score in HIV-infected subjects under ART in Spain: the Coronator study

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Purpose: Due to the relative low age of HIV-infected patients, Framingham risk score (FRS) usually estimates a low CVD risk. Lifetime risk estimations use the risk of developing CVD over the course of an individual's remaining lifetime and may be useful in communicating the risk of CVD to young patients. Our aim is to estimate the lifetime risk of CVD in a representative sample of HIV patients under antiretroviral therapy in Spain.

Methods: Cross-sectional analysis in 10 HIV units across Spain, including information on demographics, HIV disease status, treatment history and cardiovascular risk factors of subject under ART. Lifetime CVD risk was calculated with the method of Berry et al, which classifies the lifetime risk in five mutually exclusive categories:

1. All risk factors are optimal; 2. At least one risk factor is not optimal; 3. At least one risk factor is elevated; 4. One major risk factor is present; and 5. Two or more major risk factors are present. Risk factors included are cholesterol level, blood pressure, diabetes and tobacco smoking. We grouped these five categories in two major groups, low-risk (groups 1+2+3) and high-risk category (groups 4+5). We calculated the prevalence of having a high lifetime risk, and its crude and aOR (adjusted by age, sex, place of origin, education level, transmission category, time since HIV diagnosis, CDC stage, current and nadir CD4 count, HCV coinfection, time on current and total ART, being on the first ART regimen, and PI vs. NNRTI regimen).

Results: We included 839 subjects free of previous CVD disease: 72% men, median age 45.6y, median CD4 count 598 cells, median time since HIV diagnosis 11y, median time on ART 6.3y, 87% had undetectable VL. Estimated 10-year CVD risk was low (<5%) in 78% of the patients, and intermediate (5–10%) in 20%. Lifetime risk estimation shows a high risk profile for 71.4% of the population studied (≥1 major risk factors). Factors significantly and independently associated with an increased lifetime risk were older age, non-Spanish origin and longer time on ART. Adjusted OR for patients on ART longer than 10 years (vs <5 years) was 2.2 [95% CI 1.13–4.34]. No relationship was found with current or nadir CD4 lymphocyte counts, CDC stage C, HCV confection or type of ART.

Conclusions: There are significant disparities between the low 10y CVD risk estimated with FRS and the elevated lifetime risk in HIV patients on ART. Prolonged ART is associated with an increased CVD lifetime risk.

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Prevalence of dyslipidemia in HIV-infected patients on combined antiretroviral treatment in Spain: a qualitative analysis

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Purpose: Among traditional cardiovascular risk factors, dyslipidemia could be particularly prevalent since virus, treatment and host factors may be involved in its development. Our analysis aimed to describe the prevalence of different types of dyslipidemia in a population of HIV-infected, treatment-experienced patients in Spain.

Methods: Cross-sectional analysis within 10 HIV units across Spain. We collected data on demographics and cardiovascular risk factors, including lipid profile as well as information on current use of lipid-lowering drugs. This analysis describes subjects under first-line ART as compared with others in more advanced lines of treatment.

Results: We included 860 patients (76.3% male) with no history of CVD, with median age 45.6 years. Median time since HIV diagnosis was 3 and 14 years (p = 0.000) and median time on ART was 22 and 136 months (p = 0.000) respectively. Lipid profile is described in the table.

n (%)	First line regimens, n = 219	Subsequent regimens, n = 641	p-value
Dyslipidemia			
Total cholesterol >240 mg/dL	17 (7.9)	70 (11.1)	0.180
LDL-cholesterol >160 mg/dL	19 (9.0)	49 (7.9)	0.636
HDL-cholesterol <40 mg/dL	85 (39.9)	188 (30.0)	0.008
Total cholesterol/HDL ratio >5	60 (28.2)	160 (25.5)	0.447
Triglycerides ≥200 mg/dL	43 (20.0)	136 (21.6)	0.616
Lipid-lowering drugs			
Statin use	10 (4.6)	101 (15.8)	0.000
Statin use AND Tcol/HDL >5	3 (33.3)	36 (36.0)	1.000
Fibrate use	7 (3.2)	12 (1.9)	0.286
Fibrate use AND TG ≥200 mg/dL	3 (42.9)	9 (75.0)	0.326

Conclusions: Dyslipidemia, especially low HDL and high TG, is highly prevalent in this population regardless being in their first or more advanced lines of treatment. The use of lipid-lowering drugs in our population is low and furthermore the control of dyslipidemia is not always achieved. Additional research is needed to understand how to achieve lipid goals in this population.

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Vascular dysfunction in HIV-infected patients

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Atherosclerotic cardiovascular disease is an increasing concern for patients with human immunodeficiency virus (HIV) infection. We investigated carotid intima-media thickness (IMT), flow-mediated dilation (FMD), pulse wave velocity (PWV) and the augmentation index (AIx), evaluated as indices of subclinical atherosclerosis, in HIV-infected patients compared to uninfected subjects. We enrolled 80 HIV-infected patients, 68 of whom treated with combined antiretroviral therapy (cART) and 12 therapy-naïve, matched with 82 healthy subjects for age, systolic and diastolic blood pressure. We investigated IMT, FMD, PWV, AIx, viro-immunological parameters, inflammatory markers, microalbuminuria and other biochemical parameters. Compared with uninfected subjects, HIV-infected subjects had higher IMT, PWV and AIx values (all P = 0.0001); and lower FMD (P = 0.001). In the HIV+ group, naïve patients had statistically lower levels of IMT (P = 0.02), and AIx (P = 0.042) and higher FMD (P = 0.032) compared with cART-treated patients. In the HIV+group, IMT values was significantly related to the number of CD4+ (r = −0.31, P = 0.008) and CD8+ cells (r = 0.261, P = 0.025), interleukin-6 (r = 0.284, P = 0.015) and endothelin-1 (r = 0.302, P = 0.009). Vascular dysfunction evaluated as IMT, FMD and arterial stiffness is increased in HIV-infected subjects than in healthy subjects. Furthermore, cART-treated patients showed higher IMT

and AIx and lower FMD values than naïve patients. Our data support the hypothesis that both HIV infection and cART treatment are risk factors for accelerated arteriosclerosis.

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Yield of annually performed routine physical examinations of HIV patients with stable disease

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Background: Adequate follow-up of HIV patients is essential in the cART era. Current guidelines advise regular assessment of the patient, yet the exact content and frequency are less clear and practices vary amongst different hospitals. The objective of this study was to determine the value of performing routine physical examination of patients with normal or near normal immune function, as part of adequate follow-up.
Methods: In a cohort of 300 HIV-1-infected patients monitored in a large teaching hospital we retrospectively analysed the outcome of routine physical examinations performed at annual check-ups in 2010. Only stable patients were eligible for inclusion (CD4 count >350 cells/mm^3 if not using cART, CD4 count >100 cells/mm^3 if using cART). Data was collected from the medical records. It was recorded whether or not the physical examination per se was the basis for establishing a new diagnosis.
Results: Of 300 stable HIV-1-infected patients (81% males) with a median age of 47 years old (range 21–79) 216 patients (72%) had physical abnormalities. Lipodystrophy (30%), lymphadenopathy (16%) and hypertension (8.3%) were the most common findings. Two-thirds of all findings were already known from the past medical history or could be related to current complaints. In 24 patients (8.0%), the physical examination was the basis for establishing a new diagnosis: 6/24 patients (25%) - all men who have sex with men (MSM) - had a concurrent sexually transmitted disease, 8/24 patients (33%) had hypertension. The other 10/24 (42%) patients had a large variety of diagnoses, of which a bradycardia due to a total atrioventricular block was clinically the most relevant diagnosis. Factors associated with the yield of the physical examination could not be identified.
Conclusion: Routine physical examination per se was the basis for establishing new diagnoses in only 8% of stable HIV infected patients. However, most diagnoses were of little clinical relevance, suggesting that the additional value of routine physical examination in stable HIV patients is limited. Based on our findings, the regular standard assessment could be restricted to measuring blood pressure and the performance of anogenital examination in MSM.

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P218

HIV infection does not contribute to increased cardiovascular risk as assessed by Framingham risk score

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HIV-1-infected patients are thought to be at higher risk of cardiovascular events. Measures of arterial stiffness are independently associated with cardiovascular risk [1]. The aim of our study was to determine if higher Framingham risk is associated with higher carotid femoral pulse wave velocity (cfPWV) in HIV-infected volunteers (HIV cohort) and to establish whether there is a difference in cfPWV between the HIV cohort and age- and gender-matched controls. We recruited 47 males (HIV cohort) on antiretroviral treatment, from a UK HIV clinic between October 2010 and March 2012 (31 low Framingham risk $<10\%$ and 16 high risk $>20\%$). This group was matched with 46 healthy subjects from a contemporaneous study performed by our group. The inclusion criteria were: age 35–75 years with Framingham risk $>20\%$ or $<10\%$, on antiretroviral treatment with undetectable viral load, no previous coronary heart disease, stroke or insulin therapy. Subjects underwent cfPWV measurement using Complior® (Artech, France). Student's t-test was used to evaluate differences between high- and low-risk groups and also between cases and controls. The mean age of the HIV cohort was 49.43 ± 9.35 years (mean $\pm$ SD) and in the control group 52.20 ± 8.80 years ($p = 0.15$). Mean duration of HIV infection was 13.83 ± 7.25 years, mean CD4 count was $728.81 \pm 312.62 \times 10^6$/L and all viral loads were undetectable. In the HIV cohort, cfPWV was 8.39 ± 1.09 m/s in the low-risk group and 10.43 ± 2.93 m/s in the high-risk group ($p = 0.02$). Multivariate analysis with cfPWV as dependent variable, and age, systolic blood pressure, cholesterol, smoking history, duration of HIV infection and antiretroviral therapy, zenith viral loads and nadir CD4 counts as independent variables was performed in the high- and low-risk groups. This showed age alone to be a significant predictive factor ($p = 0.002$). With Framingham risk as dependent variable and using the above factors as independent variables, no HIV-related factors were significant predictors. The overall mean cfPWV for the HIV cohort ($n = 47$) was 9.09 ± 2.13 m/s compared to 11.95 ± 2.37 m/s in the control group ($n = 46$)($p < 0.01$). HIV infection does not contribute to increased cardiovascular risk as assessed by Framingham risk score or carotid-femoral pulse wave velocity. This may be due to good control of traditional cardiovascular risk factors and a healthy lifestyle in this cohort.

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P219

Management of dyslipidaemia in an HIV-positive cohort

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Background: Dyslipidaemia, secondary to both HIV and the use of antiretroviral therapy (ART) is well recognised, with HIV replication and immune status also thought to contribute to the risk. Traditionally the HIV physician has looked after HIV with primary care physicians (GP) managing non-HIV-related medical issues. However with the ageing population and the effectiveness of ART the HIV physician is diversifying to focus management strategies on preventative measures also.
Method: 127 subjects were recruited. All subjects were HIV-positive males without any traditional cardiovascular disease symptoms or history. Details of patients demographics, family history, statin therapy, and primary care physician contact were collected. Baseline parameters were recorded and fasting bloods taken.
Results: 127 asymptomatic HIV-positive males were recruited. 74/127 (58.3%) met the EACS criteria for statin prescription. 33/74 (44.6%) were on a statin. There was no significant difference between the class of antiretroviral prescribed, (NNRTI v PI) and lipid abnormalities ($p = 0.628$). Hypertension and increased waist:hip ratio significantly

increased the chances of the patient being hyperlipidaemic. Patients were more likely to be prescribed a statin if they were older, had hypertension, an increased waist circumference, increased Framingham risk, increased brain natriuretic peptide (BNP), or were diagnosed HIV-positive for longer ($p < 0.05$). Pravastatin (21/33 [63.6%]), was most commonly prescribed statin. 24.2% received their statin prescription from their HIV physician, with 75.8% receiving their prescription from their GP. 5/21 (23.8%) on pravastatin met the target verses 7/7 (100%) on atorvastatin verses 2/2 (100%) on simvastatin versus 1/3 (33.3%) on rosuvastatin ($p = 0.02$). Meeting lipid targets was less successful in the protease inhibitor group (1/9) 11.1% versus 11/21 (52.4%) in the NNRTI group ($p = 0.16$).
Conclusion: The majority met criteria for lipid management but less than half of those were prescribed it. Of those, most received treatment from their GP. Nearly half of those on statins did not meet lipid targets. HIV physicians were most likely to prescribe pravastatin and those on pravastatin were the least likely to achieve lipid targets when compared to the other statins. HIV physicians need to diversify their knowledge base and have clearly defined management strategies for the management of dyslipidaemia.

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P220

Impaired neurocognitive function among HIV-infected Thais on stable antiretroviral therapy for more than 7 years

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Background: There are limited data on HIV-associated neurocognitive disorders (HANDs) from resource-constraint region and few studies have firm documentation of duration of treatment and suppression of plasma virus. This study aimed to estimate the prevalence of HIV-related cognitive deterioration among HIV-infected patients who were on stable ART and to describe the pattern of neurocognitive impairment (NCI), daily life disturbance and associated factors.
Methods: This was a cross-sectional evaluation of cognition in a sample of HIV adults at HIV-NAT, the Thai Red Cross AIDS Research Centre with data captured over a 6-month period. The Montreal Cognitive Assessment (MoCA), International HIV Dementia Scale (IHDS) and Activities of Daily Living Questionnaire (ADLQ) scale were administered. NCI was defined as a score of ≤ 10 on the IHDS or < 26 on the MoCA. The HIV-NAT Cohort Database was explored to retrieve sociodemographic data and clinical factors.
Results: Among the 162 patients evaluated, the mean ($\pm$SD) age was 42.8 ($\pm$7.3) years and 56.8% were male. HBV and HCV co-infection frequencies were 11.7% and 7.4%, respectively. The mean ($\pm$SD) duration of ART was 9.03 ($\pm$3.12) years. Of all, 59.3% were concurrently on protease inhibitor (PI) based regimens. 97.5% had virologic success with HIV-RNA load of less 200 copies/mL. The prevalence of NCI was 68.5% by MoCA and 75.8% by IHDS. Tests on visuospatial cognition, language and abstraction were most commonly poor scores (81.5%, 89.5% and 74.1%, respectively). Among these, 54.9% and 61.3%, respectively, were asymptomatic without overt daily functioning interference. Daily self-care and household care were the most commonly endorsed daily activity defects (16.7% and 12.3%, respectively). Remaining as a couple ($p = 0.001$), duration of education < 12 years ($p < 0.001$) and heterosexual risk ($p = 0.001$) were associated with NCI. The MoCA and IHDS scales correlated to each other ($r^2 = 0.177$, $p = 0.024$). Logistic regression demonstrated fewer years of education and remaining as a couple were associated with impaired MoCA scale ($P = 0.001$ and 0.008, respectively).
Conclusion: Impaired cognitive function is commonly detected among HIV-infected Thais on stable ART for over 7 years. The frequency of NCI is higher than that reported in other settings. However the performance characteristics of our screens have not been firmly established in this setting and the cut-off levels used may over-estimate NCI.

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P221

Prevalence and determinants of unemployment among ageing HIV-1-infected and HIV-uninfected individuals

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Purpose of the study: People living with HIV (PLWH) appear to be at increased risk for earlier onset of age-associated non-communicable co-morbidity (AANCC) and declines in physical and mental capacities, compared to the general population [1]. This earlier onset of AANCC in the setting of HIV infection is likely to negatively affect work participation and quality of life. Present study investigates prevalence and determinants of unemployment among older HIV-1-infected and HIV-uninfected participants of the AGEhIV Cohort Study.
Methods: Data were collected (Oct. 2010–Jan. 2012) within the ongoing prospective AGEhIV Cohort Study, recruiting HIV-1-infected patients > 45 years from a tertiary care HIV outpatient clinic, and HIV-uninfected Public Health Service attendants, comparable regarding age, gender and ethnicity. Data on socio-demographics, lifestyle, quality of life, AANCC and unemployment were collected, using a self-administered questionnaire and through medical examination. Current analysis was restricted to participants in the working age (45–65 years). Logistic regression analysis was used to study determinants of unemployment.
Summary of results: The majority from the first enrolled 277 HIV-1-infected and 251 HIV-uninfected subjects was male (88%), Dutch (76%) and homosexual (74%). About 50% was highly educated and the median age was 52 [IQR: 48–57]. Almost all (94%) HIV-1-infected individuals were on cART, median time since first ART was 11 years [IQR: 4–15], median time since HIV-diagnosis was 12 years [IQR: 7–18] and they had been diagnosed with more AANCC than HIV-uninfected individuals ($p < 0.01$). Unemployment was higher among HIV-1-infected (36.5%) compared to HIV-uninfected participants (21.9%) ($p < 0.01$). In multivariate analysis, being HIV-infected (OR_{adj} 2.0 [95% CI: 1.3–3.3]), experiencing > 2 AANCC (OR_{adj} 3.1 [95% CI: 1.4–6.8]), lower physical health status (OR_{adj} 2.0 [95% CI: 1.6–2.6]), being unmarried (OR_{adj} 2.1 [95% CI: 1.3–3.2]) and older age (OR_{adj} 60-65 yrs: 9.1 [95% CI: 4.5–18]) were independently associated with higher levels of unemployment.
Conclusions: Unemployment among HIV-1-infected individuals is higher compared to HIV-uninfected individuals, independent of socio-demographic characteristics, lifestyle, quality of life or number of concomitantly diagnosed AANCC. This suggests that, apart from these factors, specific HIV-related determinants, such as stage of HIV disease, but also experienced stigma, work related conditions, influence unemployment.

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P222

Gender differences in cardiovascular risk factors in HIV-infected patients on antiretroviral therapy: data from the Spanish Coronator study

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Purpose: HIV-infected patients present an increased cardiovascular risk (CVR) of multifactorial origin, usually lower in women than in men. Information by gender about prevalence of modifiable risk factors is scarce.
Methods: Coronator is a cross-sectional survey of a representative sample of HIV-infected patients on ART within 10 hospitals across Spain in 2011. Variables include sociodemographics, CVR factors and 10-year CV disease risk estimation (Regicor: Framingham score adapted to the Spanish population).
Results: We included 860 patients (76.3% male) with no history of CVD. Median age 45.6 years; 84.1% were Spaniards; 29.9% women were IDUs. Median time since HIV diagnosis for men and women was 10 and 13 years ($p = 0.001$), 28% had an AIDS diagnosis. Median CD4 cell count was 596 cells/mm^3, 88% had undetectable viral load. Median time on ART was 91 and 108 months ($p = 0.017$). There was a family history of early CVD in 113 men (17.9%) and 41 women (20.6%). Classical CVR factors are described in the table. Median (IQR) Regicor Score was 3% (2–5) for men and 2% (1–3) for women ($p = 0.000$), and the proportion of subjects with mid-high risk (>5%) was 26.1% for men and 9.4% for women ($p = 0.000$).
Conclusions: In this population of HIV-infected patients, women have lower cardiovascular risk than men, partly due to higher levels of HDL cholesterol. Of note is the high frequency of smoking, abdominal obesity and sedentary lifestyle in our population.

	Men n = 656	Women n = 204	P value
Age (men >55 y, women >65 y) n (%)	72 (11.0)	8 (3.9)	0.002
Smoking, n (%)	358 (54.9)	110 (53.9)	0.805
Waist >102 cm (men), >88 cm (women), n (%)	84 (12.9)	55 (27.4)	0.000
Hypertension, n (%)	208 (31.8)	45 (22.2)	0.009
Diabetes, n (%)	50 (7.8)	11 (5.4)	0.262
Total cholesterol >240 mg/dL, n (%)	63 (9.8)	24 (11.9)	0.399
HDL-cholesterol <40 mg/dL, n (%)	239 (37.5)	34 (16.8)	0.000
Total cholesterol/HDL >5, n (%)	197 (30.9)	23 (11.4)	0.000
Physical inactivity, n (%)	324 (56.7)	108 (69.2)	0.005

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P223

Prevalence of diabetes mellitus among Ethiopian-born HIV patients in Israel

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During the mid-1980s and early 1990s the majority of Ethiopian Jews immigrated to Israel. Diabetes mellitus (DM) rates were exceedingly low upon their arrival, reaching 0–0.4%, but rose to 16.6% at 10–16 years post-arrival. This may be a challenging factor in HIV patients, since metabolic abnormalities are a major concern in individuals receiving highly active antiretroviral therapy (HAART). In this study we assessed the prevalence of DM in HIV-positive Ethiopian immigrants. Data were retrospectively obtained from 245 HIV patients treated at the Clinic of Infectious Diseases at the Meir Medical Center, Kfar Saba, Israel. DM was determined according to the following: fasting glucose >127 mg/dl; hemoglobin A1C >6.5%; blood glucose >200 mg/dl; diagnosis of DM in patient problem list. Comparison between Ethiopian and non-Ethiopian Israelis was done by Student's t-test and $p < 0.05$ was considered as significant. The cohort included 176 Ethiopians and 69 other Israelis. The rate of DM in the Ethiopian group was remarkably high (22.9% vs. 4.3%, $p < 0.0001$). We therefore analyzed both conventional as well as HIV-related factors which may contribute to the development of DM. The data indicated that the mean age of the Ethiopian subjects was 5.5 years greater (47 ± 1.1 SD vs. 41.5 ± 1.4 SD, $p = 0.0056$). Surprisingly, body mass index (BMI) was not increased among the Ethiopians, as compared with other Israelis (24.2 ± 0.5 vs. 26.1 ± 1.1, $p = 0.057$). In terms of HIV-related features, both groups received similar rates of HAART and had comparable levels of viral loads. The Ethiopian group had lower CD4 levels (477.0 ± 18.0 /mm^3 vs. 550.1 ± 34.7/mm^3, $p = 0.046$), and disclosed longer periods of time elapsed from diagnosis of HIV (8.7 ± 0.4 years vs. 6.0 ± 0.6, $p = 0.0001$). In conclusion, we report a considerably high prevalence of DM among Ethiopian immigrants in Israel, who are HIV patients. Plausible risk factors are ethnic background and older age. Low CD4 levels and a longer HIV-carrier state were also noted, which had been proposed by others to increase insulin resistance by enhanced inflammation. The possibility of an exaggerated impact of HAART protocols on glucose levels in this cohort is currently being investigated. Intriguingly, BMI was not increased in the Ethiopian group, a finding that warrants further study, and implies a lower threshold to develop DM. Our data underscores the importance of defining HIV subpopulations with increased susceptibility to DM, especially among immigrants.

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P224

HIV infection stage at diagnosis and epidemiological features of late presentation

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Late presentation of HIV-infected individuals is gaining attention because of the negative impact on the patient and the society at a whole. In January 2011 the European Late Presenter Consensus working group published a consensus definition of ''late presentation'' and asked researchers to implement it. Objective: to identify presentation stage of HIV-infected individuals at diagnosis at the German Hospital in Buenos Aires, Argentina, and describe epidemiological features of them. The German Hospital is an acute care community hospital that assists around 600 000 out-patient consultations per year. We examine the clinical reports of all our

Abstract P224

1984–1999	1984–1999 No late	1984–1999 Late	1984–1999 % (Late/total)	1984–1999 Total	2000–2010 No late	2000–2010 Late	2000–2010 % (Late/total)	2000–2010 Total
Total	61	44	42	105	102	70	40,7	172
Age group								
<20	6	0	0	6	3	3	50	6
21–30	25	13	34,2	38	33	7	17,5	40
31–40	14	15	51,7	29	35	18	34	53
41–50	10	12	54,5	22	16	18	52,9	34
51–60	6	1	14,3	7	9	17	65,4	26
61–70	0	2	100	2	6	4	40	10
>71	0	1	100	1	0	3	100	3
Sex								
Female	18	6	25	24	8	8	38	21
Male	43	38	47	81	62	62	41	151

HIV patients, diagnosed 1984–2011, and grouped them as ''late'' or ''not late'' presentation according their status following the consensus definition criteria. We also looked for data, such as age, sex and year of diagnosis, that could differ between the groups. We reviewed 284 clinical records, 7 of which were excluded because of lack of data; 105 belonged to last century records. Median age for 1984–1999 group: 32 (16–73), for 2000–2010 group: 40 (180–78). 77% of the first group were men, and 88% of the second one.
In 55,5% of the 1984–1999 group diagnosis was due to an opportunistic infection, whereas the same applied to only 32,8% of the 2000–2010 group. In both groups there were a high proportion of male, due to the population profile of our hospital. The most frequent reason for testing was screening, but there is still a high number of late diagnosis and OI as first sign of the infection. Younger people are more aware of the need of testing. Female have the advantage of being tested when planning or becoming pregnant. We could not find statistical differences comparing data of both centuries. Forty percent of infections were diagnosed in a ''not late'' stage, but that was more evident in younger people. People in general and physicians in particular should be more aware of HIV in elderly people.

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P225

Screening for alcohol use disorders in HIV patients

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Many chronic health conditions have been linked to alcohol consumption, as well as excess morbidity, mortality and an increased financial burden on the National Health Service (NHS). The British HIV Association (BHIVA) recommends that HIV patients be asked about alcohol due to its effect on adherence to antiretroviral therapy. National Institute of Health and Clinical Excellence (NICE) guidelines recommend screening for alcohol use disorders in patients attending genitourinary medicine (GUM) clinics. In this study we looked at the use of a screening tool for alcohol use disorders in HIV patients in a metropolitan city. We assessed HIV patients over a 6-month period for alcohol use disorders using the AUDIT-C questionnaire. Patients with a score >4 were identified as higher risk and provided with brief advice about alcohol and offered written information and support. Demographic data was collected along with hepatitis B and C status, information on sexually transmitted infection (STI) testing and diagnosis. 352 patients were reviewed with a mean age of 41. 297 (84.4%) patients were male, 235 (66.8%) were white British and 251 (71.3%) were men who have sex with men (MSM). 277 (78.7%) patients were on antiretroviral therapy with 254 (91.7%) of these having an undetectable viral load. Alcohol use disorders were assessed using the AUDIT-C score in 332 (94.3%) patients with no patient declining assessment. 166 (50%) patients had an AUDIT-C score >4 signifying higher risk. Alcohol advice was provided to 161 (97%) of these patients and a Drink Smart guide offering advice on alcohol self help offered to 103 (64%) patients and accepted by 45 (43.7%). An opportunistic STI screen was offered to 258 (73.3%) patients on that visit in line with best practice guidelines and was accepted by 83 (32.2%). 25 infections were found in 20 patients, of which 13 (65%) had AUDIT-C scores >4. There were 8 active hepatitis C co-infected patients of which 3 had an AUDIT-C score >4 and 12 chronic hepatitis B co-infected patients with 3 having an AUDIT-C score >4. Our results show that screening for alcohol use disorders using the AUDIT-C questionnaire has high acceptability among HIV patients; however the data is biased to Caucasian MSM. Alcohol use has been shown to exacerbate liver damage in patients with chronic hepatitis, increase the likelihood of STI acquisition and compromise immunity. It is therefore important to screen for and quantify alcohol use as part of routine HIV clinical practice.

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P226

Non-communicable diseases among elderly patients with human immunodeficiency virus infection at an urban clinic in a resource-limited setting

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Purpose of the study: Following the introduction of highly-active antiretroviral therapy (HAART), there is improved survival of elderly persons infected with HIV, which may be complicated by multiple co-morbidities. There is limited data on non-communicable disease prevalence among HIV-infected elderly persons in developing

countries. The objective of the study was to estimate the prevalence of diabetes mellitus, hypertension and obesity among HIV-infected elderly persons above 60 years of age attending an urban clinic in Kampala, Uganda.
Methods: We retrospectively reviewed records from a program perspective of HIV-infected patients aged 60 years of age and above who were attending our clinic. The purpose was to assess prevalence of non-communicable diseases to improve clinical care.
Summary of results: During the period from April 2011 to March 2012 we reviewed records and identified 154 HIV-infected patients aged 60 years of age and above. Of these, 26 (16.9%) were aged 70 years and older while 128 (83.1%) were 60–69 years of age. The median age was 63 years (IQR: 61–68 years). Eighty-five (55.2%) were males while 69 (44.8%) were females. Only 10 participants (6.5%) had been diagnosed with diabetes mellitus while 42 participants (27.3%) had essential hypertension. On the contrary, only 6 patients (4%) had both essential hypertension and diabetes mellitus. There was evidence to show that 58.3% of the female participants with a BMI $\geq$25.00 kg/m^2 were significantly different from 38.7% of their male counterparts with a BMI of $\geq$25.00 kg/m^2 ($\chi^2 = 5.16$; 1 df; $p = 0.02$). There was strong evidence that hypertensive patients with BMI $<$25.00 kg/m^2 were significantly different from hypertensive patients with BMI $\geq$25.00 kg/m^2 ($\chi^2 = 9.55$; 1 df; $p = 0.002$).
Conclusion: Three in 10 elderly HIV positive persons aged 60 years and older had a non-communicable disease-either diabetes mellitus or essential hypertension. Thirty-one percent of patients were either overweight or obese. Almost 50% of patients were diabetic, hypertensive, overweight or obese. There is therefore need to incorporate diagnostic tests and management protocols of non-communicable disease control for elderly HIV-positive persons aged 60 years and older in resource-limited settings.

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P227

Rates of sexual violence among HIV-positive women: finding a way forward for a holistic service

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Rates of sexual violence are high, and several studies have suggested that rates are particularly high among HIV-positive women. Experience of sexual violence can lead to numerous physical and psychological co-morbidities as well as a wide range of social problems. On both a Scottish Government and an international level it has been suggested that routine questioning about sexual violence in vulnerable populations can help to ensure access to appropriate services. This study aimed to assess the level of engagement around sexual violence in one HIV centre looking specifically at how often it was discussed, rate of disclosure, advice given and the demographics of the population disclosing sexual violence. Through this the aim was to assess the prevalence of disclosed sexual violence, and how it was being dealt with, in order to improve service provision. This was achieved by undertaking a case note review of 50 female patients of 394 number being cared for by the genito-urinary physicians. Sexual violence was discussed at least once in 63% of cases, most commonly at time of diagnosis in a GUM clinic or other centre. 50% of those women disclosed experience of sexual violence, of while 60% ($n = 28$) were from sub-Saharan Africa and 44% ($n = 21$) had entered the country as asylum seekers or refugees. These results show that a large number of HIV-positive women within this city have experienced sexual violence, in particular in the asylum seeking population. As such, if services for HIV-positive women are to take account of the psychological and social needs of their service users they will need to be aware of this and make appropriate provisions. This could take the form of routine questioning around gender-based violence and/or providing good information about internal and external support services.

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P228

Clock-drawing test as a screening tool for HIV-associated neurocognitive disorder (HAND)

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Introduction: Current tests for diagnosing HIV-associated neurocognitive dysfunction (HAND) consume time and energy and are not very practical as a screening tool in the busy clinic. The clock-drawing test (CDT) was reported sensitive to subcortical pathology associated with periventricular and deep white matter. In addition, CDT has shown to be sensitive to executive dysfunction.
Aim: The aim of this study was to determine the value of a clock-drawing test as a screening tool for diagnosing HAND. Methods: The CDT that we used was largely based on Rouleau et al. (1992). The patient is asked to draw a clock, first the frame, than the numbers, and than the hands showing the time 10 to 2. The interpretation is based on the following criteria: frame, numbers, hands, center, general impression. If acceptable-2 points, non-acceptable-0, and acceptable but deviating-1 point. Other validated neurocognitive tests (e.g. TMA, TMB, DSST, etc) were used as the ''gold standard''.
Results: In the primary analysis 54 patients were included: 47 men and 7 women. Sensitivity was 77%, specificity 90%, positive predictive value 71.4%, negative predictive value 92.5%. In this preliminary study we found CDT to be a valid screening tool for HAND. It correlates highly with other well-established screening tools, but demands less resources (human and technological). It is especially good for ruling out the disease.

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P229

Aging-associated symptoms in the physician-patient dialogue in a group of long-term diagnosed HIV-infected individuals

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Background: The significant decrease in mortality has resulted in a large number of individuals aged over 50 living with HIV infection. Additionally, the coexistence of certain pathologies suggests premature aging. In this scenario, the presence of aging-associated symptoms in the physician-patient dialogue is yet to be explored.
Methods: Cross-sectional observational study to evaluate the presence of aging-associated symptoms in the physician-patient dialogue and to explore the possible differences between genders in a sample of 100 HIV-1 infected subjects diagnosed at least 15 years ago. The survey assessed questions/comments made by the patient, questions/comments made by the physician and patients' interest in obtaining more information than was provided. Number of patients and percentages were given and compared using the w2 or Fisher exact test (as appropriate).

Results: Participants were 60 men and 40 women, diagnosed with HIV infection a median (IQ) of 18 (15.7–21) years ago, who had a nadir CD4 and CD4 cell count at the study entry of 172 (95–272) and 543 (403–677), respectively. Eighty percent of the subjects had VL <25 copies and 42% were HCV/HIV co-infected (31 subjects with low fibrosis stage). The infection route had been mainly intravenous drug use (37%) and MSM (32%). Men and women had similar demographic and clinical characteristics. Sixty-two percent of the participants acknowledged asking their physicians about aging-associated symptoms (58% men vs 66% women; $p=0.50$), 48% reported that their physicians had provided information without having been asked (48% men vs 55% women; $p=0.51$) and 75% confirmed that they would like to have more information about aging-associated symptoms (22% men vs 80% women; $p<0.001$).
Conclusions: Around half of the men and women interviewed had discussed aging-associated symptoms with their physician. However, this seemed insufficient for four-fifths of the women, who would have liked to have obtained more information about aging.

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PRE- AND POST-EXPOSURE PROPHYLAXIS AND TREATMENT AS PREVENTION

P230

Raltegravir-based post-exposure prophylaxis (PEP): a safe, well-tolerated alternative regimen

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Three-drug regimens are routinely recommended in the UK for PEP after possible high-risk exposure to HIV. The current Department of Health and British Association for Sexual Health and HIV first-line regimen is lopinavir/ritonavir, tenofovir and emtricitabine (Truvada). Raltegravir-based regimens may be used as an alternative. This is a review of the use of raltegravir-containing PEP to identify why and when this is initiated and its tolerability and safety compared to first-line PEP. From February 2010 to April 2012, 509 courses of PEP were prescribed; 33 (6.5%) raltegravir-containing PEP. Pharmacy records identified eligible patients; these were compared to 33 courses of first-line PEP in the same time period. 18/33 (54%) of raltegravir-containing PEP were initiated due to potential drug-drug interactions with ritonavir, 3/33 (10%) due to the resistance profile of the contact and 12/33 (36%) due to intolerance of first-line regimen. All switches to raltegravir-based PEP occurred by day 3 of the course with 83% identified on day 1. All switches to raltegravir-containing PEP due to the resistance profile of the contact took place by day 3 of the course. Patients switching due to drug intolerance was largely due to gastrointestinal side effects between days 1 to 16; 2 cases were due to ALT changes. 19 courses of raltegravir-containing PEP were commenced on day one. Reported side effects in the raltegravir-containing PEP were lower than courses of first-line PEP: 10/19 (53%) patients reported no side effects by day 28 treatment compared to 5/33 (15%) patients on first-line PEP. 12/14 (79%) patients on first-line PEP who were switched to raltegravir-containing PEP reported improvement in their side effects. There were no significant liver or renal toxicities in the raltegravir group; 3 patients on first-line PEP had a significant ALT rise. One patient who started first-line PEP was found to be HIV-positive at baseline. An MSM who received raltegravir-containing PEP seroconverted 4.5 months after the course of PEP. He reported 3 episodes of unsafe sexual behaviour since PEP. Raltegravir-based regimens are safe and as well tolerated when compared to first-line regimen. Switching to raltegravir-based regimen is associated with a decrease in reported side effects. Self-reported adherence is better if patients are started on raltegravir. This study suggests that raltegravir-based PEP may be a preferred first-choice regimen.

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P231

Interest in the 'Test and Treat' strategy for HIV prevention among men who have sex with men living in Bangkok

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Background: The current HIV epidemic in Thailand is primarily driven by new cases among men who have sex with men (MSM). HPTN052 study demonstrated 96% efficacy of immediate antiretroviral therapy (ART) to reduce HIV transmission among serodiscordant heterosexual couples. As a result, universal HIV testing and immediate ART has emerged as a strategy to reduce HIV transmission in certain at-risk populations. The acceptability of this strategy, however, is unknown in MSM.
Methods: From August 2011-March 2012, we conducted a cross-sectional study using self-administered questionnaires to assess attitudes towards universal HIV testing and immediate ART among MSM VCT clients in Bangkok. Participants were asked to complete the questionnaires prior to and after knowing their HIV status. The study was approved by the Institutional Review Board of the Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand.
Results: Of 342 MSM, the median age (IQR) was 26 (22–31) years, and 34.2% had bachelor's degree or higher. Previous HIV testing was reported by 69.9%, 35.2% of which had HIV testing annually. The most common reasons for previous HIV testing included perceived risk behaviors (63.6%), annual health checkup (26.4%), and partner's request (13.8%). Prior to receiving pre-test counseling, 74.4% expressed interest to get regular HIV testing. Health benefits from testing (59.6%), free testing (36.5%), and speedy service (35.7%) were the most common persuasive reasons to come for regular HIV testing. Longevity (73.1%) and prevention of HIV transmission to others (58.4%) were reasons for interest in immediate ART (if tested positive) program while costs (37.0%) and life-long burden (36.7%) were cited as main barriers. Among MSM who tested HIV-positive ($n=45$, 13.2%), the interest to participate in immediate ART program was very high both before and after knowing their HIV status (86.7% vs 93.3%, $p=0.371$). Among HIV-negative MSM, the interest to participate in regular HIV testing program significantly increased after knowing HIV status (83.4% vs 77.0%, $p<0.001$).
Conclusions: MSM in Bangkok showed high level of interest in the ''Test and Treat'' strategy for HIV prevention. Knowing one's HIV status affected the interest to access regular HIV testing program.

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P232

Are we PREPared? Quality of information available to patients in the UK about PREP on the internet

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Professional bodies in the UK (BASHH/BHIVA) do not currently recommended pre-exposure prophylaxis (PREP) to prevent HIV aquisition for men who have sex with men (MSM) [1]. Conversely, although Federal Drug Administration approval is awaited, the Centers for Disease Control (CDC) have issued clinicians in the USA with interim guidance to facilitate PREP prescriptions [2]. Increasingly patients search the internet for information on HIV treatment, but disparate international policy can lead to confusing patient messages. This study was conducted to systematically assess the quality of internet information available to patients in the UK about PREP. More than 90% of internet searches in the UK are performed using 'Google.co.uk' and 'Bing' [3]. Using pre-specified criteria, we reviewed the first 100 hits retrieved from each search engine when the following searches were performed: ["HIV pre-exposure prophylaxis"]; ["HIV PREP"]; ["HIV PREP guidelines"]; ["HIV PREP guidelines UK"]; ["truvada prophylaxis HIV"]. Of 172 unique websites identified, 124 websites were active at the time of the review (July 2012). 33 websites were links to academic journals including commentaries and clinical trials, not intended to specifically provide patient information; 5 were internet portals directing users to alternative sites and 10 websites contained no information about PREP. Of the remaining 76 websites, 28 were written by medical professionals and 48 were written by journalists, where 7/48 (15%) were individual blogs. 64/76 (84%) contained a definition of PREP; 63/76 (83%) discussed the rationale and 58/76 (76%) reported efficacy data. Advantages and disadvantages of PREP were presented in 56/76 (74%) and 41/76 (54%) of websites respectively. Only 21/76 (28%) of sites referenced existing national guidelines (CDC/BASHH). A minority of sites described the current clinical practice in the UK (7/76, 9%) with an even smaller number presenting the contrast in clinical stance between the CDC and BASHH/BHIVA (3/76, 4%). The use of PREP is evolving, and the internet is an important patient resource. However, current clinical practice in the UK is seldom described in accessible websites. Avoiding ad hoc and unsupervised use of PREP is crucial to prevent future drug resistance and risky sexual behaviour. More should be done to engage at-risk groups and ensure patients in the UK have access to comprehensive information including the current UK PREP professional guidance.

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P233

2011 UK PEPSE guidelines: new incentive to document HIV-1 serum viral load of patients' HIV positive sexual partners

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The 2011 UK guidelines for the prescription of Post-Exposure Prophylaxis for the Prevention of HIV infection following Sexual Exposure (PEPSE) take account of the reduction in the risk of HIV transmission from an HIV-positive individual who has an undetectable serum HIV-1 viral load as a result of combination antiretroviral therapy (cART) [1]. Prescription of PEPSE is no longer routinely recommended for individuals who have had sex with a partner who is HIV-positive and is known to have an undetectable serum HIV-1 viral load on cART, unless unprotected receptive anal sex is reported. In this study we assessed how the application of the new UK PEPSE guidelines would alter PEPSE prescription in our region. We performed a retrospective case note-review of all PEPSE prescriptions occurring between the 1st of January 2011 and the 31st of December 2011 in 4 sexual health clinics in the Oxford deanery (Oxford, Banbury, Reading and Slough). 91/ 96 PEPSE prescriptions were available for review. The mean age of each PEPSE recipient was 30.3 years; 71/91 (78%) of recipients were male, of whom 54/71 (76%) were men who have sex with men (MSM). 63/91 (69%) of PEPSE recipients were of white UK ethnicity. In 32/91 (35%) of cases, the patient reported having sex with a partner was known to be HIV-positive. Of these, 10/32 (31%) reported that their partner was taking antiretroviral therapy, and 4/10 (40%) of this group reported that their partner had an undetectable serum HIV-1 viral load. Thus of 91 PEPSE prescriptions, 4 (4%) occurred in patients reporting sex with HIV-positive partners who were taking antiretroviral therapy and had an undetectable HIV-1 serum viral load: receptive anal sex was reported in 1 case, and vaginal sex in the remaining 3 cases. Despite a significant change in the UK PEPSE guidelines, in only 3/91 cases in which PEPSE was previously given would prescription no longer be recommended. 32/91 patients reported sex with an HIV-positive partner, and the HIV-1 viral load was either unknown or not documented in the majority of cases. It may not be possible to corroborate a patient's report of their partner's HIV-1 viral load in all cases; thus PEPSE will still be required. However, the new PEPSE guidelines increase the incentive for all clinicians to actively seek and accurately document the HIV-1 viral load of patients' HIV-positive sexual partners.

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P234

HIV-infection during treatment of a chronic hepatitis B virus infection: implications for PrEP?

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The protective effect of oral tenofovir disoproxil fumarate (TDF) with or without emtricitabine (FTC) as pre-exposure prophylaxis (PrEP) against HIV differed significantly among clinical studies and poor PrEP-adherence was closely associated with PrEP-failure. Despite HIV-infections during PrEP-exposure the development of resistance mutations against PrEP was rarely observed so far. As PrEP is an

emerging tool against HIV transmission, it is important to identify risk-factors for PrEP-failure and the induction of PrEP-associated resistance mutations against antiretroviral drugs. We here present the case of a 25-year old MSM who was successfully treated with TDF due to a chronic hepatitis B virus (HBV) infection (HBV-DNA always $<$357 IU/ml after ten months of treatment). As HIV tests were negative when the treatment was initiated and six months later, no routine HIV tests were performed although the patient repetitively acquired sexually transmitted infections (STI). After 30 months, an HIV infection (subtype B) was diagnosed during a syphilis re-infection. At this point, HIV was TDF-resistant (K65R and A62V mutations within the reverse transcriptase gene). Retrospective analysis of frozen serum samples revealed HIV-seroconversion 12 months prior to diagnosis and low HIV-RNA levels from seroconversion to diagnosis (always $<$400 copies/ml). The TDF-based therapy of the chronic HBV-infection resembles a TDF-HIV-PrEP. But here poor therapy adherence is an unlikely cause for the 'PrEP-failure' as the constantly suppressed HBV-DNA indicates therapeutic TDF-levels over years. Combining TDF with FTC might have augmented the prophylactic effect. However, TDF-levels in the rectal mucosa are high and should therefore protect MSM who practice receptive anal intercourse. On the other hand, the concomitant STI of our patient may have promoted HIV transmission (via compromising the mucosal barrier function and promoting inflammatory reactions) and therefore possibly counteracted TDF-effects. Finally, infection with a TDF-resistant virus strain might explain the lack of protection in this case. But K65R is a rarely transmitted drug resistance mutation and low level viremia for one year suggests considerable TDF effectiveness. In fact, we here rather present a K65R mutation induced by a PrEP-like TDF therapy. The development of the K65R mutation in a PrEP-like situation emphasizes the urgent need of regular HIV-tests during PrEP exposure.

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RESISTANCE

P236

Spatial-temporal analysis of HIV-1 PR and RT resistance-associated mutations of nucleotide sequences from Western Europe, using vircoTYPE™ HIV-1 assay

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Highly effective regimens have drastically improved HIV morbidity and mortality although anti-retro viral resistance remains a limiting factor in disease management. Therefore, analysis of large sequence datasets may provide better insight into drug resistance & assist policy makers to select optimized treatment strategies. Using a secure, web-based sequence submission tool (vircoNETTM, Janssen Diagnostics BVBA), centers within EU have been able to retrieve the CE-marked vircoTYPETM HIV-1 (VTY) genotyping reports for their patients. The purpose of this study is to perform a descriptive analysis of the prevalence of HIV-1 PR & RT resistance-associated mutations (RAMs) from submitted nucleotide sequences, collected during an 8 year period, from 5 West-European countries & Switzerland. From January 2005-June 2012, 27,262 sequences were submitted via vircoNETTM & analyzed using VTY. Approximately 50% of the sequences were submitted from Spain (n = 14120) & 24% from Italy (n = 6415). The remaining sequences were from UK (n = 2097), France (n = 1508), Germany (n = 1041) & Switzerland (n = 2081). The majority (80%, 21,647/27,262) of the sequences were Clade B. For NRTI RAMs, M184V was the most prevalent mutation (36%, n = 9944) followed by M41L (25%, n = 6701). For NNRTI RAMs, K103N mutation was most prevalent (24%, n = 6481) followed by Y181C (10% n = 2704). For PIs, L90M (16%, n = 4453) and M46I (12%, n = 3397) were the most prevalent. The overall RAM prevalence has declined over the 8 year period. 7602 (28%) sequences had no major RAMs and were sensitive to all 18 FDA & EMA-approved drugs present on VTY. In the PI class, VTY predicted 95% (20097/21243) of the sequences as sensitive & 5% (1146/21243) resistant to darunavir, followed by tipranavir, lopinavir & saquinavir with equal sensitivity rate (SR) of 81% & a resistance rate (RR) of 13%, 18% & 19% respectively. In the NNRTI class, etravirine had a better SR (81%, 8628/10683) & RR (19%, 2055/10683) when compared to nevirapine and efavirenz, with a SR of 59% & RR of 41% for both drugs. For NRTIs, the highest SR was found for stavudine (77%, 20889/27262) followed by tenofovir (67%, 18249/27262) with 23% (6499/27262) resistant sequences observed for stavudine & 33% (9114/27262) for tenofovir. The current analysis provides some preliminary insight into HIV mutation pattern prevalence and resistance within Western Europe, suggesting good therapeutic opportunities for regimens containing new generation PIs & NNRTIs.

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P237

High frequency of genotypic resistance in HIV-1-infected patients on highly active antiretroviral therapy with persistent low level viremia

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Background: Resistance is a major cause of virologic failure in HIV-1-infected patients; genotypic analyses optimize salvage therapy but technical constraints limit testing in plasma viral load (pVL) below 1000 copies/ml. Nevertheless a great amount of patients are failing therapy with a persistent low viral load, it is possible to obtain genotypic information at lower viremias although slight modifications are required during genotype standard procedures.
Objective: To assess genotypic resistance in HIV-1-infected patients with persistent low level viremia and virologic response after switching to genotype-guided salvage therapy. To evaluate viral selection of mutation when previous genotypic information were available.
Study design: Cohort prospective study in which eligible patients were at least 18 years old, provided informed consent, were on HAART for at least 12 months with two consecutive pVL between 200–999 copies/ml after achieving and maintaining viral suppression (two pVL $<$50 copies/ml). Modifications in genotype standard procedures included a larger volume of starting plasma, concentrating the sample by centrifugation and higher viral RNA input. Resistance was defined as the detection of any NRTI, NNRTI or PR major resistance mutations. Virologic response was assessed 12 weeks after salvage therapy.
Results: Eighteen patients, 50% male, median age 52, median CD4 405 cells/mm^3, median pVL 596 copies/ml, median of number of previous regimens 5, 17 (94%) with successful genotype. Resistance mutations were detected in 14 patients (77%). All patients had NRTI mutations, four patients had NNRTI mutations and ten patients had PR mutations, most common mutations were M41L, D67N, M184V, K103N, M46I, I47V, I54V and L90M. Of these fourteen patients, nine started a genotype-guided salvage regimen and presented a pVL $<$50 copies/ml after 12 weeks of follow up. For two patients there

was previous genotypic information highlighting the selection and accumulation of resistance mutation during persistent low level viremia.
Conclusion: In this group of heavily pretreated patients with persistent low viremia, a high frequency of genotypic resistance was observed; obtaining genotypic information may prevent further accumulation of resistance mutation and preserve future therapeutic options.

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P238

HIV-1 drug resistance testing at low viral load may help to differentiate between ongoing replication and release from reservoirs

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Purpose of the study: Low level viraemia in HIV-infected patients treated with anti-retroviral therapy (ART) is a phenomenon still not fully understood. If the observed viraemia is a result of ongoing replication or if virus is released from cellular reservoirs remains unclear. We analysed our database of genotypic resistance and interpretations to screen for an effect of viral load on frequency of detected drug resistance.
Methods: 1939 viral load and protease and reverse transcriptase sequence pairs from the years 2009 to 2011 were analysed. Drug resistance interpretation was performed by the HIV-GRADE resistance interpretation rule set. Pairs were split up into viral load categories of below 200 cop/ml, 200–400, 400–1000, 1000–10,000, 10,000–100,000 and more than 100,000 cop/ml. Resistance interpretation was stratified in the following categories: no resistance, resistance against one, two or three drug classes. The collected data were then analysed using chi-squared test (R Core Team; 2012; R: A language and environment for statistical computing).
Summary of results: 1390 sequences showed no relevant drug resistance, while 336 sequences showed resistance against one drug class (two classes: 145, three classes: 38). In 25 samples viral load was below 200 cop/ml (200–400: 29, 400–1000: 63, 1000–10,000: 275, 10,000–100,000: 526, above 100,000: 472). In both groups below 400 cop/ml no significant increase of resistant variants was observed compared to the mean distribution, while in the groups with 400–1000 cop/ml and 1000–10,000 cop/ml significant more resistant variants were found than expected ($p < 0.001$). This reverses above 100,000 cop/ml, where significantly ($p < 0.001$) more susceptible variants were observed.
Conclusions: As in most of the samples with a viral load below 400 cop/ml, no mutations leading to resistance could be found, we conclude that virus in these cases is released from cellular reservoirs. Viral loads between 400 cop/ml and 10,000 cop/ml under ART are a clear sign for ongoing replication, because in this group the highest rate of drug resistance was observed. Viral loads above 100,000 cop/ml seems here to be a sign of missing selective pressure due to incompliance of the patients and thus no drug resistance was observed.

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P239

HIV2EU: supporting standardized HIV-2 drug resistance interpretation in Europe

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Various items are complicating the treatment of HIV-2 infected patients. Compared to HIV-1 there is much less treatment experience, no evidence from randomized control trials, a reduced number of effective drugs and no broadly available test for viral load monitoring. In case of treatment failure there is only limited guidance and presently no easy accessible tool for nucleic acid sequence interpretation available. To solve this problem, we initiated an expert workshop to address some of these problems. A panel of experts from four different European countries voted on a rule set for interpretation of mutations in the HIV-2 protease, reverse transcriptase and integrase. Rules were proposed by each member and were then modified during discussion by considering data gained from HIV-1 and accumulated experience of the follow up of HIV-2-infected patients. Based on the HIV-GRADE internet-tool an online tool was developed to make the rule set easily accessible and usable. Rules were laid down for the interpretation of HIV-2 drug resistance to NRTIs, PIs and INIs (integrase inhibitors). Due to natural resistance of HIV-2, usage of NNRTIs and T-20 was not recommended as part of an antiretroviral regimen for HIV-2. These rules were then translated in a machine interpretable format (algorithm specification interface, ASI) and the HIV-GRADE tool was extended for usage of HIV-2 sequences. Further consensus sequences were generated from the reference sequence data set provided by Los Alamos National Laboratories. In contrast to HIV-1, mutations were compared to a group specific consensus sequence (Group A or Group B) and not to a consensus sequence from the most predominant HIV-2 Group A. This change was necessary due to significant differences between the various HIV-2 strains. We developed a rule set and an automated tool for HIV-2 drug resistance analyses. This tool and the rules will be freely available on the internet. Access to the pre-publication versions can be granted by each of the group members. To keep the algorithm rules up-to-date it will be actualized on a yearly basis.

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P240

HIV-1 primary drug resistance mutations in antiretroviral therapy-na ve patients in Istanbul, Turkey

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According to the official information of Turkish Ministry of Health of HIV/AIDS surveillance data, in the period 1985 to the end of 2011, there are 4826 HIV-1 infected cases in Turkey. However, there is no data available on the antiretroviral (ART) drug resistance.

The objective of this study was to determine primary drug resistance in HIV-1 infections in newly diagnosed, ART-naïve Turkish patients in Istanbul, Turkey. The study was carried out between June 2009 and June 2012 and 59 HIV-1-infected patients were included (gender; 52 male/7 female, age, median years (range); 37.9 (20–57), CD4+ T-cell count, median mm^3 (range); 280 (3–813), HIV-RNA load, median IU/ml (range); 4.1 +E5 (2.6+E3–2.9+E6)). For HIV-1 subtyping most widely known algorithm; the HIVdb-Stanford University genotypic resistance interpretation algorithm has been used. According to population-based sequencing of the reverse transcriptase and protease genes of HIV-1, the patients had pre-existing primary ART drug resistance mutations and were related to NRTIs (M41L, D67N, T215D, T215E, T215S), NNRTIs (V179D) and PIs (I54V, V82A). The prevalence of overall primary ART drug resistance were 11.8% (7/59) in Turkish patients and according to NRTIs, NNRTIs and PIs drug groups were 10% (6/59), 1.7% (1/59) and 1.7% (1/59), respectively (in one patient has been either NRTIs and PIs resistance detected). The high prevalence of HIV-1 primary drug resistance in ART-naïve patients suggested the resistance testing must be an integral part of the management of HIV infection and the choice of first-line therapy regime should be guided by genotypic resistance interpretation in Turkey.

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P241

Findings from the WHO/PAHO early warning indicators of HIV drug resistance monitoring system performed in Argentina

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Background: In the last years, WHO developed a Global Strategy for HIV Drug Resistance Prevention and Assessment using a public health approach. This strategy supports optimal functioning of treatment programs to minimize emergence of preventable HIV drug resistance and to maintain effectiveness of first- and second-line ART regimens. Since 2011, Argentina has been monitoring some of the indicators of this strategy (called early warning indicators [EWIs]). The aim of this study was to analyze the outcomes measured during the mentioned year.
Methods: Based on the availability of information in the hospitals' pharmacies, where the data collection took place, and on the relevance for Argentina, some of the EWIs proposed by WHO were selected and adapted. The information is being collected since beginning of 2011, and a first analysis was performed at the end of that year. Since this was a pilot phase, 6 representative hospitals' pharmacies participated.
Results: Data are available for 4 of the sites. The data produced the following indicators: EWI 1a: Percentage of adult patients initiating ART who are prescribed a non-recommended first-line ART regimen (goal 0%). Site A: 22.5%; Site B: 11.1%; Site C: 0%; Site D: 2.7%. EWI 1b: Percentage of adult patients initiating ART who withdraw a non-recommended first-line ART regimen (goal 0%). Site A: 22.5%; Site B: 25.8%; Site C: 15.5%; Site D: 16.1%. EWI 2: Percentage of patients lost to follow-up 12 months after ART initiation (goal less than 20%): Site A: 41.6%; Site B: 9.3%; Site C: 22.2%; Site D: 0%. EWI 4: percentage of patients who picked up prescribed ARV drugs on time (goal: >90%): Site A: 39.1%; Site B: 72.4%; Site C: 44.5%; Site D: N/D.
Conclusions: There is a high proportion of patients in Argentina which are prescribed non-recommended regimens, and a higher proportion withdraw these regimens from pharmacies: 75% of sites do NOT reach the goal of EWI 1a; 100% do NOT reach the goal for EWI 1b. There is also a high proportion of patients lost to follow up during the first year after treatment initiation: 50% of sites reach the goal of EWI 2. A very high proportion of patients do NOT pick-up ART on time: none of the sites reach EWI 4 goal. The use of these indicators allowed us to visualize that there is a high proportion of patients that would be nonadherent. With these data the Directorate of AIDS will improve efforts to know better the situation, understand the causes and implement strategies to increase adherence.

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P242

Integrase resistance variants among integrase inhibitor treatment-na ve and treated patients from Northwestern Poland

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Purpose of the study: HIV integrase inhibitor use is limited by low genetic barrier to resistance and possible cross-resistance among representatives of the class. The aim of this study was to analyse the sequence variability in the integrase region in treatment-naïve and experienced patients with no prior integrase inhibitor (InI) exposure and to investigate the development of the InI drug resistance mutations following the virologic failure of the raltegravir (RAL)-containing regimen.
Methods: Sequencing of HIV-1 integrase region (866 base pair, HXB2 genome location: positions 4230–5096) from plasma samples of 80 integrase treatment-naïve patients and treatment failing subjects from a group of the 46 RAL-treated patients were analysed. Drug resistance mutations were called with Stanford DB database and grouped into major and minor mutations. For subtyping, bootstrapped phylogenetic analysis (1000 replicates) with under the GTR +I+gamma model with reference sequences.
Results: Majority of the integrase region sequences were classified as subtype B; the remaining ones being subtype D, C, G, and CRF01_AE, CRF02_AG and CRF13_cpx recombinants. No major integrase drug resistance mutations have been observed in InI-treatment naïve patients. In 30 (38.5%) cases polymorphic variation, with predominance of the E157Q mutation was observed. This mutation was more common among subtype B (26 cases, 54.2%) than non-B sequences (5 cases, 16.7%), $p = 0.00099$, OR: 5.91 (95% CI: 1.77–22.63)] (Figure 1a, 1b). Other variants included L68V, L74IL, T97A, E138D, V151I, R263. Of the RAL-treated patients in 12 cases (26.1%) treatment failure was observed. In 4 cases major the following InI drug resistance mutations were found: N155H, V151I, E92EQ, V151I, G163R (3 cases) and Q148H, G140S mutant (one case). Time to the development of drug resistance ranged from 2.6 to 16.3 months with mean increase of HIV viral load of 4.34 (95% CI: 1.86–6.84) log HIV-RNA copies/ml at the time of emergence of the major mutations. Baseline polymorphisms, including E157Q were not associated with the virologic failure on RAL ($p = 0.5$).
Conclusions: In InI treatment-naïve patients polymorphic integrase sequence variation was common, with no major resistance mutants observed. In the failing patients selection of drug resistance occur rapidly, and follows the typical drug resistance pathways accumulation of mutations. Pre-existing integrase polymorphisms were not associated with the treatment failure.

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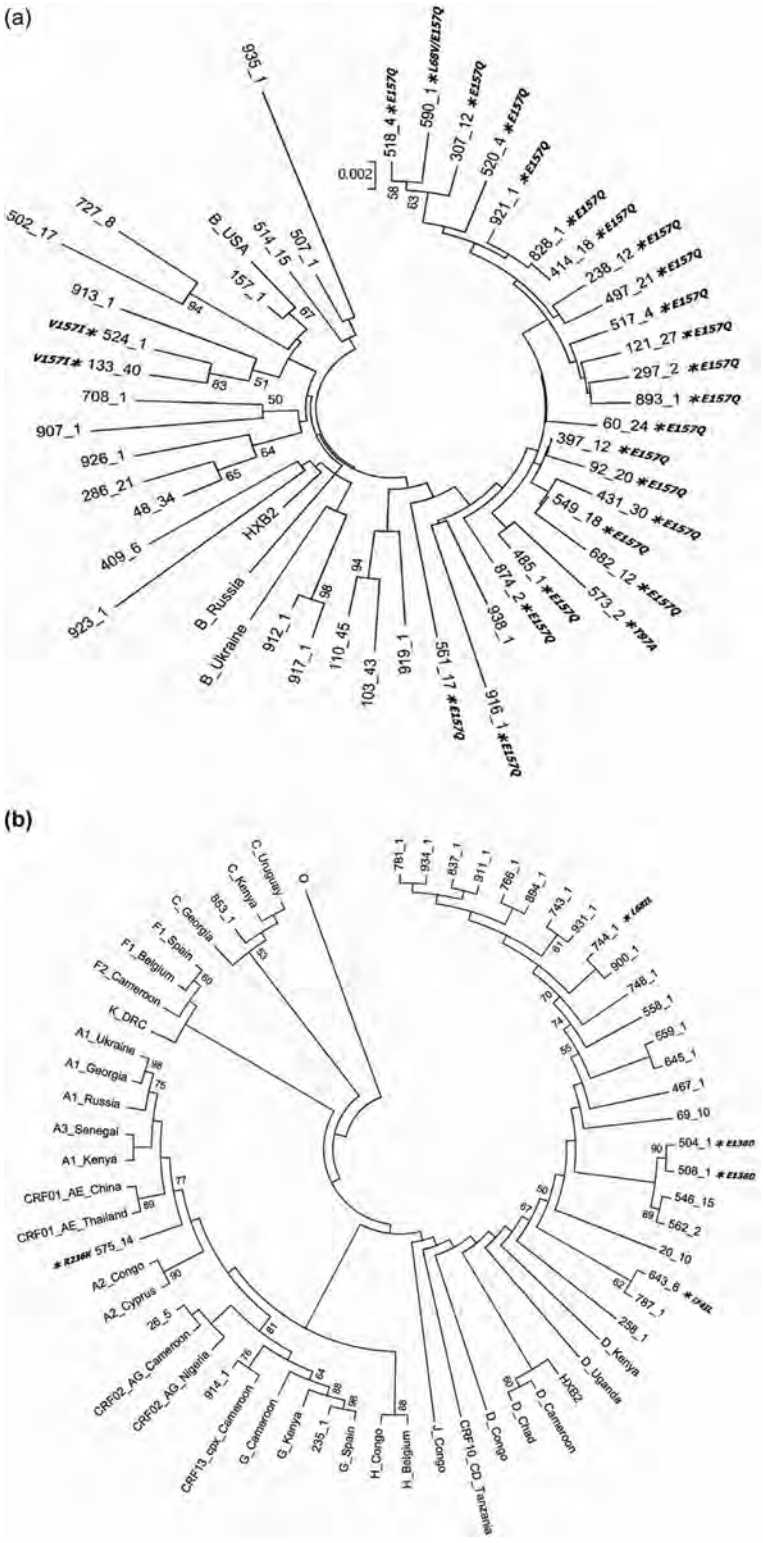
Abstract P242



P243

Antiretroviral drug resistance in HIV-1 therapy-na ve patients in Cuba, 2006–2011

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In 2009, genotypic drug resistance testing was introduced for HIV-1 patients failing antiviral therapy in Cuba. The high prevalence of drug resistance in this population indicated the need for surveillance of

transmitted drug resistance (TDR) in therapy-naïve patients. Therefore, the objectives of this study were to analyze the level and patterns of TDR and subtype in therapy-naïve HIV-1 patients in Cuba from 2006 to 2011, and to compare it with reported data from 2004 that indicated 4% TDR, solely restricted to NRTI. 153 plasma from HIV-1 therapy-naïve patients were collected between June 2006 and December 2011 and subsequently extracted, amplified and sequenced. Drug resistance was interpreted according to HIVdb v.6.1.1 and WHO list for TDR surveillance (2009) using the CPR tool v.6.0. Phylogenetic analysis was performed using Neighbour Joining (Kimura 2) in Mega 4. The majority of patients was male (82.4%), MSM (68.6%) and originated from Havana province (68.1%). 8.4% were recent infections. Subtype B was the most prevalent subtype (31.3%) followed by CRF20-23-24_BG (28.1%), CRF19 (18.3%) and CRF18 (13.0%). The prevalence of subtype B declined from 43.7% in the 2004 study to 31.3% in the present study, whereas BG recombinants increased from 14.4% to 28.1%. Overall, 12.4% (19/154) had evidence of TDR. 3.9% carried at least one NRTI, 1.9% at least one NNRTI and 1.9% at least one PI mutation. Drug resistance mutations against both NRTI and NNRTI were observed in 3.9%, whereas triple class resistance was found in only 0.6%. The most frequent NRTI mutations were M184V (55.5%), T215F/Y/rev (16.6%) and K70R (16.6%). The most frequent NNRTI mutations were K103N (61.1%) and G190A (22.2%). The most common PI mutation was L90M (5.5%). From the 19 patients with TDR, 13 (68.4%) were diagnosed with a recent HIV-1 infection. AZT/D4T +3TC+NVP may be effective in 6 of the patients with TDR (31.5%), partially effective in 6 (31.5%) and ineffective in 7 (36.8%). AZT/D4T+3TC+IDV would be effective in 9 of the patients with TDR (47.3%), partially effective in 8 (42.1%) and ineffective in 2 (10.5%). This analysis confirmed the further expansion of BG recombinants in Cuba and revealed that antiretroviral drug resistance in HIV-1 therapy-naïve patients has increased to 12.4% in 2006–2011. The current study emphasizes the need to perform surveillance studies for TDR in therapy-naïve patients, as the extent of TDR might jeopardize the effectiveness of first-line regimens prescribed in Cuba.

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P244

Antiviral drug resistance in Cuban children infected with HIV-1

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Between 1986 and 2011, 100 children have been diagnosed with HIV-1 in Cuba. 38 have acquired HIV-1 by vertical transmission, 6 by blood transfusion and 56 by sexual contacts (teenager). Currently, AZT/D4T +3TC+NVP/KALETRA are available for the treatment of pediatric patients. The aim of the study was to monitor the subtype distribution and emergence of drug resistance in pediatric HIV-1 infections. Plasma from 46 HIV-1-infected children were collected from November 2005 to November 2011, subsequently extracted, amplified and sequenced. Phylogenetic analysis was performed using Mega 4 (Neighbour joining, Kimura 2). The CPR tool v6.0 (WHO list 2009) was used to interpret transmitted drug resistance (TDR). In addition, acquired drug resistance was interpreted according to HIVdb v6.1.1. Experiments were successful for 28 samples from 20 patients (5 patients with multiple samples). At the moment of analysis, 17 children were receiving ART. The median age at diagnosis was 1.9 years, whereas the median age at sampling was 4.5 years. Ten children were male (50%), 16 (80%) were infected by vertical transmission, 1 by blood transfusion (5%) and 3 by sexual route (15%). The subtypes were CRF18_cpx (25%), CRF19_cpx (25%), B (20%), CRF20_BG (10%), G (10%), CRF24_BG (5%) and C (5%). 82.3% of the children who were receiving ART at sampling (14/17) displayed at least one drug resistance mutation. The most common NRTI and NNRT mutations were: M184V (55.5%), T215FY (16.6%) and K70R (16.6%); and K103NS (61.1%) and G190A (22.0%). In contrast, only one PI mutation, L90M (5.5%), was observed. 5.8% of these children displayed single NRTI class resistance, 17.4% single NNRTI class resistance, 59% double NRTI+NNRTI class resistance and 5.8% triple NRTI+NNRTI+PI class resistance. According to HIVdb, NRTI, NNRTI and PI resistance was present in respectively 42.8%, 58.7% and 8.08% of the treated children. High-level NVP and EFV resistance was observed in 76.5% and 58.8%, respectively. 35.2% displayed already low-level resistance to ETR/RPV. For NRTI, high-level resistance to 3TC/FTC was detected in 50%. High-level resistance to NFV was detected in only one sample. No NNRTI TDR was observed, while one patient displayed PI TDR (L90M) and another NRTI TDR (D67N, T215S and K219Q) (2/11) (18.1%). At this moment, insufficient data is available whether resistance is associated with TDR, poor adherence to treatment or poor efficacy of ART regimens in use. The present study reinforces the usefulness of resistance tests for the correct management of ART.

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P245

HIV-1 drug resistance among antiretroviral treatment-na ve Ethiopian patients

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Background: In many African countries, access to antiretroviral treatment (ART) has been significantly scaled up over the last five years. Nevertheless, data on drug resistance mutation are scarce. The objective of the current study was to determine the predominant subtypes of HIV-1 as well as to identify baseline mutations with potential drug resistance among ART-naïve patients from Ethiopia.
Methods: Genotypic drug resistance on the entire protease and partial reverse transcriptase (codons 1–335) regions of the pol gene was determined by an in-house protocol in 160 ART-naïve patients. Genotypic drug resistance was defined as the presence of one or more resistance-related mutations, as specified by the consensus of the Stanford University HIV drug resistance database (HIVDB) available at http://hivdb.stanford.edu/ and the 2011 International AIDS Society (IAS) mutation list (http://www.iasusa.org/resistance-mutations/).
Results: A predominance of HIV-1 subtype C (98.7%) was observed. According to the IAS mutation list, antiretroviral drug resistance mutations were detected in 20 patients (13%). However, the level of drug resistance is 5.2% (8/155) when the most conservative method, HIVDB algorithms were applied. In both algorithms, none had major PI mutation and mutation-conferring resistance to NRTI and NNRTI were not overlapping.
Conclusions: There is strong evidence for clade homogeneity in Ethiopia and low influx of other subtypes to the country. The level of transmitted drug resistance exceeds that of WHO estimates and indicates that many HIV-infected individuals on ART are practicing risk-related behaviours. The results also show that HIV drug resistance testing should be installed in resource limited settings.

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P246

Low emergence of secondary antiretroviral drug resistance mutations among HIV-1 subtype C-infected Ethiopian patients

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Background: The emergence of HIV-1 drug resistance mutations has been mainly linked to the duration and composition of antiretroviral treatment (ART) as well as the level of adherence. In Ethiopia, first-line ART with NRTI and NNRTI was introduced in 2005 and PI in limited access was available since 2009. This study reports the emergence and pattern of secondary antiretroviral drug resistance mutations and long-term outcomes of ART.
Methods: 127 HIV-infected treatment-naïve patients initiating ART at AIDS clinic of University of Gondar, Ethiopia were enrolled and followed for up to 36 months on ART. HIV viral load and drug resistance mutations were determined at baseline and after a median time of 30 months on ART using Abbott qRealTime HIV-1 assay and an in-house protocol, respectively. Genotypic drug resistance mutations were interpreted according the Stanford University drug resistance database [http://hivdb.stanford.edu] and to the IAS mutation list [http://iasusa.org/resistance-mutation].
Results: The mean baseline HIV viral load was 4.30 ± 1.03 $\log_{10}$ copies/ml. Viral suppression rate (HIV RNA levels <2.60 $\log_{10}$ copies/ml) after a median time of 30 months (range: 21–37) was found to be 88.2% (112/127). Of the patients with viral load >2.60 $\log_{10}$ copies/ml, six had harboured one or more drug-resistant associated mutation on RT region. The observed NRTI resistance associated mutations were the lamivudine-induced M184V mutation ($n = 4$) and tenofovir-associated mutation K65R ($n = 1$). The NNRTI resistance-associated mutations were K103N ($n = 2$), V106M, Y181S, Y188L, V90I, K101E and G190A ($n = 1$ each). Thymidine analogue mutations and major drug resistance mutation on PR region were not yet detected. Most of the patients with virologic failure and accumulated drug resistance mutations had not met the WHO clinicoimmunologic failure criteria and continued the failing regimen.
Conclusions: The incidence and pattern of secondary antiretroviral drug resistance mutation is low and less complex than has been previously reported in sub-Saharan Africa. However, the data suggest the need for virological monitoring and resistance testing for early detection of ART failure.

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P247

Surveillance of transmitted drug resistance in untreated HIV-infected patients in Cuba

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Background: Knowledge of transmitted drug resistance (TDR) in untreated HIV-infected patients is fundamental in the epidemiological surveillance programs, because it is associated with suboptimal virological outcome of first-line HAART. The aim of this study was to evaluate the epidemiology of TDR in newly diagnosed Cuban patients.
Methods: 250 HIV-1-infected patients diagnosed between 2009 and 2011 were included in the study. RNA was isolated from plasma and used as target to amplify the pol gen by RT-nested PCR. PCR products were sequenced and the data generated used to determine the viral subtype by phylogenetic analyses. The TDR were detected by means of Stanford University calibrated population resistance tool, using the 2009 surveillance drug resistance mutations list.
Results: Baseline characteristic were as follows: 78.4% of the cases were males, mean age was 35.5 years, 66.3% of infections were acquired by homosexual transmission and the median viral load was 4.6 log. The 39.2% of the analyzed samples corresponded to the subtype B and 60.8% for non-B genetic forms, with prevalence of CRF 19_cpx, CRF 20 BG and CRF 23 BG [1]. The overall prevalence of TDR increased in comparison with previous studies (19.2% versus 5.2%) [2]. The majority of mutations were seen within the group of nucleoside reverse transcriptase (NRTI) (8.5%) and non-NRTI (9.7%). TDR was less common in the group of protease inhibitors (1.7%). The most common mutations were M184V and K103N for the NRTIs and NNRTIs, respectively. The prevalence of TDR in samples of the subtype G was significant ($p = 0.005$) in comparison with other genetic forms.
Conclusions: This study confirms an increase in the transmission of resistance-associated mutations, which indicates the importance of maintaining a constant epidemiological surveillance of the TDR in newly diagnosed Cuban patients.

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P248

Transmission of primary resistance mutation K103N in a cluster of Belgian young patients from different risk groups

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Background: We analysed the distribution of an HIV-1 subtype B strain resistant to efavirenz and nevirapine among incident infections in the Belgian population.
Method: The Belgian AIDS reference laboratories searched their databases for HIV-1 subtype B sequences harbouring the K103N mutation in the reverse transcriptase (RT) or the C67S and V77I mutations in the protease (PR). We included the earliest RT sequence available of drug-naïve patients as well as sequences related to treatment failure. Fifty sequences were aligned omitting the codon 103 and submitted to phylogenetic analysis. Epidemiological data were collected through the Institute of Public Health national database. In addition, three sequences from the cluster were analysed by deep sequencing using the Roche GS Junior platform.
Results: Phylogenetic analysis revealed the presence of a 24 virus sequences cluster. All except one of those sequences resulted from patients who were ARV-naïve at the time of sampling, and 21 had the K103N mutation. Two thirds of the clustered patients were infected through homosexual or bisexual contacts while the others were heterosexuals. No case was related to migrants contaminated abroad. Fifteen of the clustered patients were diagnosed between January 2011 and June 2012; 87% of them were

aged between 20 and 29 at the time of diagnosis. Interestingly, 60% of them reside in the province of Namur. Deep sequencing analysis of 3 individuals sampled near seroconversion revealed no other resistance mutations at a frequency >1% than those already picked up by Sanger sequencing (RT A98S, K103N; PR V77I), except the RT V90I.

Conclusion: We identified a transmission cluster of drug resistant HIV-1 variants mainly including homo- and heterosexual young adults. Most individuals are of Belgian origin and are living around the city of Namur (Belgium). The K103N mutation had no apparent impact on transmission fitness as its spread raised during the last years. These observations may impact on local prevention and ARV prophylaxis strategies.

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P249

HIV-1 drug resistance-associated mutations among antiretroviral-na ve Thai patients with chronic HIV-1 infection

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Purpose of study: Antiretroviral therapy (ART) has been scaled up in resource-limited settings. This study aimed to determine the prevalence of HIV-1 drug resistance-associated mutations (DRAMs) among patients with chronic HIV-1 infection and to compare DRAMs between CRF01_AE and B subtypes.

Methods: ART-naïve Thai patients who were indicated for ART initiation between 2010 and 2011 were prospectively enrolled. Genotypic assays of reverse transcriptase and protease genes were performed within 4 weeks prior to ART. DRAMs were assessed using International AIDS Society USA 2011 list.

Summary of results: A total of 330 patients were included. HIV-1 subtypes included CRF01_AE (241, 73.0%), B (79, 23.9%), and others (10, 3.1%). Median (IQR) CD4 was 66 (23–172) cells/mm^3 and median (IQR) HIV-1 RNA was 5.2 (4.6–5.8) log copies/mL. The prevalence of patients with ≥1 DRAMs to any antiretroviral agents was 17.6%; 17.0% to NNRTIs, 0.6% to NRTIs, and 0.6% to protease inhibitors (PIs). V106I (23, 7.0%), V179D (14, 4.2%), V179T (6, 1.8%), E138A (5, 1.5%), V90I (4, 1.2%), K103N (3, 0.9%), Y181C (3, 0.9%), and P225H (1, 0.3%) were DRAMs to NNRTIs. M184V (1, 0.3%) and T215S (1, 0.3%) were DRAMs to NRTIs. M46L (2, 0.6%) was the only major DRAM to PI. Minor DRAMs to PIs including I13V, M36I, H69K, and L89M were more frequently observed in CRF_01 AE but A71V/T and V77I were more common in subtype B ($P < 0.05$). By multivariate analysis, the factors 'HIV-1 subtype B' and 'low pretreated CD4 cell count' were associated with higher rate of DRAMs.

Conclusion: HIV-1 DRAMs, especially to NNRTIs, is emerging in a middle-income country after a widespread use of NNRTI-based ART. HIV genotypic assay prior to ART initiation in patients with chronic HIV-1 infection should be considered.

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P250

The prevalence and economic burden of 1st-generation NNRTI resistance

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The prevalence of NNRTI resistance in the community and costs associated with HIV disease and treatment failure are examined. NNRTI-based HAART therapy using EFV is recommended as a 1st-line treatment choice in international guidelines, and it is the most common component of initial therapy. Resistance to NNRTIs is common in the community (treated or untreated) and may impact economic burden. Published articles and conference abstracts detailing the epidemiology of NNRTI resistance, the economic burden of HIV disease progression, or the costs associated with treatment failure were located using PubMed/MEDLINE and Embase. NNRTI resistance data sources included randomized or observational trials, or cohort studies of European, US, or Canadian patients, published between years 2005–2011 in English. Inclusion criteria for cost data were studies reporting total direct medical costs of HIV disease in the US. Prevalence of NNRTI resistance early in infection (generally pre-antibody response) was reported in 6 European studies and in 3 US studies. Among chronically-infected treatment-naïve patients, 13 studies reported prevalence of NNRTI resistance in Europe, 2 in US, and 2 in Canada. All studies collected data from 2009 and earlier, when 2nd-generation NNRTIs were not available. The reported prevalence was generally higher in US/Canada than it was in Europe (range = 7–10% vs. 2–10%). The prevalence of resistance among patients was similar in early vs. later infection for both regions (range = 2.0–6.7% [median = 3.7%] vs. 1.7–10.2% [3.0%] in Europe and 7.0–13.0% [8.8%] vs. 3.8–11.5% [7.6%] in US/Canada, respectively). Using UDS, the prevalence of NNRTI resistance in treatment-naïve patients was reported at 24% (intra-quasi-species prevalences 0.34–98.8%). The most recent time-based trends suggest that NNRTI-resistance prevalence may be stable or reducing. Annual HIV medical costs increased 1) as CD4 cells decreased, driven in part by hospitalization at lower CD4 cell counts; 2) for treatment changes (cost of 3rd line 1.5-fold higher than 1st or 2nd line), and 3) for each virologic failure. The economic burden of regimen failure and disease progression underlines the importance of ensuring optimal initial therapy choices and regimen succession. The possible erosion of efficacy or of therapy choices through resistance transmission or selection, even when present in an individual as a 1% minority, may become a barrier to the use of 1st generation NNRTIs.

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P251

Is there a relationship between HIV tropism and historical genotypic resistance in treatment-experienced patients?

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Purpose of the study: Since X4/DM HIV-1 tropism is associated with poorer prognosis and worse response to treatment, the aim of this study was to assess whether X4/DM HIV-1 tropism is also related with a higher accumulation of resistance in patients experiencing treatment failure.

Methods: HIV protease (PR) and reverse transcriptase (RT) resistance mutations and tropism test results were extracted from a national database. Viral tropism data included enhanced sensitivity Trofile assay (ESTA) and geno2pheno results at 10% false positive rate. Historical resistance mutations (HRM) for PI, NRTI and NNRTI, detected in all genotypic tests performed during patient treatment history, were selected according to IAS-USA indications.
Summary of results: Overall, 1280 patients were included: males 65%, median age 45 years (IQR: 40–50), median CD4 nadir 116 (IQR: 34–272), median past regimens 7 (IQR: 3–12), median previous NRTI used 5 (IQR: 4–7), median previous NNRTI used 1 (IQR 1–2) and median previous PI used 3 (IQR 1–5). HIV tropism was assessed by ESTA in 271 patients (21.2%) and by geno2pheno in 1009 patients (78.8%). Four hundred and fifteen patients (32.4%) carried X4/DM virus and 321 (25.1%) had ≥ 1 HRM for each antiretroviral class. The mean number of HRM was higher in patients harboring X4/DM virus than in patients harboring R5 virus (5.1 ± 6.4 vs. 4.3 ± 5.9, $p = 0.02$ at ANOVA test). X4/DM strains also harbored a higher mean number of PI-related HRM (1.8 ± 2.8 vs. 1.5 ± 2.6, $p = 0.003$) and NNRTI-related HRM (1.2 ± 1.6 vs. 0.9 ± 1.4, $p = 0.001$), but not of NRTI-related HRM (2.2 ± 2.6 vs. 2.0 ± 2.6). At logistic regression, patients with HRM for all the 3 classes had a significant higher risk of also harboring X4/DM virus (OR: 1.6, 95% CI: 1.0–2.4, $p = 0.04$). Moreover, X4/DM virus was found to be associated with previous use of NNRTI-containing regimens (OR: 1.4, 95% CI: 1.1–1–9, $p = 0.03$) and lower CD4 nadir (OR: 0.9, 95% CI: 0.9–1.0, $p = 0.001$, per 50-CD4 increase). The analysis was adjusted by number of genotypic tests, number of treatment lines, age and HV subtype. Single mutations significantly associated with X4/DM tropism were: for PI, V32I and L76V; for NRTI: M41L, K70R, L74V and T215Y and for NNRTI: E138G and V179T.
Conclusions: Our data suggest that X4/DM tropism is associated with accumulation of resistance mutations during treatment history. X4/DM tropism is also confirmed to be a marker of a more compromised clinical and immune-virological condition.

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P252

Genotypic susceptibility to etravirine-assessment in a population of NNRTI-experienced patients

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Background: With the availability of the 2nd-generation non-nucleoside reverse transcriptase inhibitor (NNRTI) etravirine (ETR), it is possible to obtain undetectable plasma viral load in HIV-1-infected treatment experienced patients with resistance mutations to NNRTIs. The purpose of this study is to determine the proportion of patients with prior exposure to NNRTIs who may benefit from a therapeutic regimen including ETR.
Patients and methods: Analysis of the genotypic resistance tests of patients having failed efavirenz (EFV) or nevirapine (NVP) antiretroviral-based regimens, in a 5-year period (2007–2011). Susceptibility to ETR was assessed using four different algorithms: HIVdb Stanford University HIV Drug Resistance Database, ANRS score, REGA score and Tibotec weighted genotypic score.
Results: Of 170 patients with a history of failure or abandonment of regimens containing EFV or NVP, 68 (40%) had mutations conferring resistance to these NNRTIs (RAMs). Resistance tests were carried out from seven months before to 3 years after ($X = 48 \pm 207$ days) the NNRTIs discontinuation. Of the HIV-1 subtypes identified ($n = 67$), most were were subtype B (53.7%) and G (34.3%) RAMs found in the 68 samples successfuly genotyped: V90I ($n = 2$), A98G ($n = 1$), L100I ($n = 7$), K101E ($n = 5$), K103N ($n = 38$), K103S ($n = 2$), V106A ($n = 1$), V106M ($n = 1$), V108I ($n = 4$), V179D ($n = 4$), Y181C ($n = 18$), Y188C ($n = 1$), Y188H ($n = 1$), G190A ($n = 11$), G190E ($n = 1$), G190S ($n = 1$), H221Y ($n = 6$), P225H ($n = 1$), F227L ($n = 3$) and K238T ($n = 2$). In 27 (39.7%) patients only one RAM was detected, 30 (44.1%) had 2, 6 had three mutations and 5 other patients had more than three RAMs to NNRTIs. Susceptibility to ETR varied depending on the used algorithm:

	Susceptible	Intermediate resistance	Resistant
ANRS	60 (88.2%)	3 (4.4%)	5 (7.4%)
HIVdb	49 (72.0%)	17 (25.0%)	2 (3.0%)
REGA	40 (58.8%)	27 (39.7%)	1 (1.5%)
Tibotec	44 (64.7%)	23 (33.8%)	1 (1.5%)

Conclusion: In this population with resistant virus to EFV and NVP, we found a low frequency of mutations conditioning severely impacting on susceptibility to ETR. Based on these results, ETR could be a useful component of effective treatment regimens for the majority of these patients with prior exposure to 1st-generation NNRTIs.

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P253

Analysis of HIV-1 primary drug resistance in Kazakhstan

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Purpose of the study: Monitoring of primary resistance in HIV-1 variants circulating in Russia and FSU countries is the important task of HIV infection molecular epidemiology. The data of HIV molecular epidemiology are absent or limited in many FSU countries. IDU-A variant of HIV-1 subtype A has been dominating in Russia ($>90\%$) and other FSU countries since 1996. Additionally, the Central Asian region (e.g. Kazakhstan and Uzbekistan) is characterized by relatively wide spread of CRF02_AG recombinant. The aim of our study was the analysis of HIV primary drug resistance in HIV-1 variants from Kazakhstan.
Methods: Blood collection from the HIV-infected naïve patients was carried out by local specialists. The study was performed with the informed consent of patients. All sequences of *pol* gene were analyzed by COMETv0.1 and HIVdb on-line programs. The phylogenetic analysis and tropism testing were carried out by MEGA4.0 and geno2pheno.
Summary of results: 51 PBMC samples were analyzed. According to *pol* gene phylogenetic analysis and genotyping 24 (47.0%) samples belonged to recombinant CRF02_AG; 25 (49.0%)-to subtype A1; 2 (3.9%)-to CRF03_AB circulating in Russia and some FSU countries. Only one subtype A1 sample had D30N mutation in Pro-region that cause high-level resistance to NFV. All AG-samples had K20I substitution which is characteristic for HIV-1 subtype A and G and is believed to be associated with resistance to LPV and NFV. In addition, we found that 2 AG-samples had L10V and L76I substitutions, accordingly. Two A1-subtype samples studied had L10I and K43T, accordingly. A62V characteristic mutation in RT-region was found in 12 (48%) subtype A1-samples. One of them had M184I mutation as well. Besides, we found 3 A1-samples harboring NNRTIs resistance mutations-K103N, G190S, K238N, accordingly.

Further we analyzed IN region of *pol*-gene in 16 and *env*-gene in 23 samples studied. We found only one E157Q mutation (in CRF03_AB sample) in IN region. As to tropism, only two subtype A1 and 1 CRF03_AB samples belonged to X4/X4R5 variant, all these A1-subtype samples harbored A62V and one of them-G190S in RT region of *pol*-gene; the other samples were treated as R5 variants.

Conclusions: Our data demonstrated the low level of HIV primary drug resistance in Kazakhstan. HIV-1 subtype A variant dominates on this territory, but CRF02_AG recombinant is rather widespread as well. CRF02_AG variant studied has characteristic features in Pro region compared with IDU-A.

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P254

Community viral load in patients harboring HIV drug-resistant strains and new cases of TDR in Northern Greece - a retrospective cohort study

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Purpose of the study: Recent studies suggest an association between community viral load and new diagnoses of HIV infection. Aim of our study was to explore a potential association between the pattern of new cases of transmitted drug resistance (TDR) in Northern Greece and the community viral load in the subset of patients who harbored HIV drug-resistant strains during 2000–2007.

Methods: Data on viral load measurements and genotypic HIV drug resistance were extracted from the respective databases of the Infectious Diseases Division of the AHEPA University Hospital and the National Reference Laboratory for AIDS of Northern Greece which provide healthcare services free of charge for the majority of HIV-positive individuals in Northern Greece. Patients who had undergone at least once genotypic resistance testing were included in the study. The 2009 SDRM list was used to categorize patients in subsets with regard to genotypic resistance results. Community viral load (CVL) was calculated as follows: The per-year weighed mean viral load was calculated for each individual patient and the median value of this set was defined as the community viral load. Poisson log-linear regression models with robust estimators were employed to examine the association between new cases of TDR and CVL of patients with genotypic drug resistance, patient number and year.

Results: 512 patients out of 701 ever recorded had undergone genotypic HIV drug resistance testing at least once (73%). Overall, 202 out of 512 patients (39.4%) were identified with at least one resistance mutation (106/512 NNRTI, 175/512 NRTI, 104/512 PI). Poisson log-linear multivariate models correlated new cases of TDR with either log CVL ($p = 0.068$, RR: 7.59, 95% CI: 0.863–66.71) and year ($p = 0.013$, RR: 2.19, 95% CI: 1.18–4.08) or log CVL ($p = 0.030$, RR: 5.08, 95% CI: 1.17–22.06) and number of patients with drug resistance ($p = 0.0001$, RR: 1.03, 95% CI: 1.01–1.06).

Conclusions: Our results indicate that the community viral load of patients with HIV drug resistance may affect the number of new patients with TDR, underline the need for successful viral suppression in patients with resistant HIV strains from a public health standpoint and, should they be supported by further studies, suggest that community viral load could be used as a biomarker for TDR surveillance.

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P255

First-line antiretroviral treatment outcome in a patient presenting an HIV-1/2 multiclass drug resistant infection

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Background: With the expansion of HIV-2 epidemic beyond African countries, co-infection with HIV-1 becomes a global challenge. We have recently identified an HIV-1/2 dual infection with both viruses bearing multiclass drug resistance in an untreated patient [1]. We now present the patient's combined antiretroviral treatment (cART) outcome after 6 months follow-up.

Patient and Methods: Clinical samples were obtained upon informed consent from a 23-year-old man living in Guinea-Bissau until March 2011 when he moved to Switzerland. As previously reported [1], HIV-1/2 co-infection was confirmed by HIV-1 PCR (21.000 copies/ml) and total HIV-1/2 viremia (4.351 nU/ml) by product-enhanced reverse transcriptase (PERT) assay. The patient denied previous HIV testing or exposure to antiretroviral drugs. Dual infection consisted of HIV-1 CRF02_AG bearing resistance mutations M184V/V90I and HIV-2 clade A, harboring K65R/D67N mutations as amplified from proviral-DNA. Baseline CD4 +T-cell count was 408 cell/mm^3. We initiated cART in accordance to drug resistance mutations (see below). Treatment compliance was assessed with an electronic pillbox device and drug-plasma concentrations. Clinical and laboratory follow up were done at weeks 2, 4, 9, 12 and 24.

Results: cART was initiated with tenofovir/emtricitabine (TDF/FTC), boosted-darunavir (DRV/r) and raltegravir(RAL). Treatment compliance was fluctuant during the first 3 months after which it remained stable with an average monthly intake of 92%. Antiretroviral drug-plasma concentrations were traced at percentile 25th. HIV-1 viremia became undetectable at week 12. Additionally, HIV-2 viremia was retrospectively assessed by real-time RT-PCR at two independent laboratories showing undetectable values across the study period including baseline. Thus, baseline viremia, as assessed by the PERT test for particle-associated reverse transcriptase activity was due to HIV-1 alone. CD4+T-cell count was 559 cell/mm^3 at week 24. Laboratory assessments showed a neutrophile drop to 0.96 at week 4, fully restored at week 9.

Conclusion: This case of HIV-1/2 dual infection underscores the importance of assessing genotypic analysis of both viruses ahead to treatment choice. It also highlights viral load platforms constraints when it comes to clinical monitoring of HIV-1/2 co-infection in western settings. Overall, first-line salvage treatment was well tolerated and suppressed HIV-1 resistant clade allowing recovery of CD4+ T-cell count.

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P256

Trends in transmitted HIV drug resistance in Iran from 2010 to 2011

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Background: Drug-resistant (DR) HIV emerges during antiretroviral treatment (ART), creating concern about widespread transmission of DR-HIV as ART is expanded in resource-limited countries. The aim of this study was to determine the predominant HIV-1 subtypes and prevalence of drug-resistance mutations among antiretroviral-naïve patients in Iran.
Design and methods: For this HIV DR threshold surveillance study, blood samples were collected from 50 antiretroviral-naïve HIV-1-infected patients. Antiretroviral-resistant mutations were determined by sequencing HIV-1 protease (PR), reverse transcriptase (RT) and integrase (INT) regions. The HIV-1 subtype of each sample was determined by sequencing the p17 and C2-V5 regions of the gag and env genes, respectively.
Results: The PR, RT and INT regions were successfully sequenced in 47 samples (94.0%). Phylogenetic analyses of these regions revealed that 45 (95.7%) cases were CRF35_AD. The remaining two cases were subtype B (2.1%) and CRF01_AE (2.1%). Consistent results were obtained also by Env and Gag sequences. Regarding prevalence of transmitted drug-resistant viruses, two cases were found to harbor RT-inhibitor mutations. In addition, nine amino acid differences compared to that of HXB2 were found in protease region as compared to that of HXB2, though none matched with the mutations shown in the WHO list for surveillance of transmitted mutations. No drug-resistant mutations were found in the INT region.
Conclusion: Our study clarified that CRF35_AD is the major HIV-1 subtype among Iranian HIV-1-infected patients. According to the WHO surveillance algorithm, the prevalence of transmitted drug resistance in Iran was estimated as moderate (5–15%).

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P257

Analysis of enfuvirtide resistance mutations prevalence among HIV-1 variants circulating in Russia and CIS countries

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Background: Enfuvirtide (ENF/Fuzeon/T-20) was the first member of the class 'fusion inhibitors'. This was approved for the treatment of HIV infection in the year 2003 in Europe and the USA. Fuzeon has not yet approved in Russia but in the near future his introduction expected. Resistance to ENF has been associated with mutations in the HR1 domain at codons 36–45. Mutations outside of this region and in the HR2 domain may also serve as secondary mutations. Unique and highly homogeneous HIV-1 subtype A variant-IDU-A is the most prevailing in Russia and CIS countries. HIV-1 genetic variants circulating in Russia and CIS countries and, in particular, variant IDU-A are poorly studied on resistance mutations to enfuvirtide. The aim of this work was to study the prevalence of mutations associated to HIV fusion inhibitor enfuvirtide resistance in Russia and CIS countries.
Methods: We used 40 proviral DNA samples (12 IDU-A sequences, 8 subtype B sequences, 6 subtype G sequences, 8 CRF03_AB recombinant sequences and 6 CRF02_AG recombinant sequences) isolated from peripheral blood mononuclear cells of HIV-infected patients. All the samples belonged to enfuvirtide-naïve patients. Fragments of env gene with coordinates 7754–8342 (corresponding to strain HXB2) were sequenced. Phylogenetic analysis was carried out using DNASTAR program package.
Results: Enfuvirtide resistance mutations were not found among viruses studied in Russia and CIS countries. The frequencies of natural polymorphism mutations associated with enfuvirtide hypersusceptibility were found to consist up to 35%, and the frequencies of accessory mutations N126K and E137K in the HR2 region-up to 27.5%.
Conclusions: Enfuvirtide resistance mutations are rare in Russia and CIS countries. HIV-1 genetic variants circulating in Russia and CIS countries should be sensitive to enfuvirtide. However, accessory mutations in HR2 the case of HR1 resistance mutations may contribute to resistance development by improving viral fitness.

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P258

HIV-1 genetic variants in Kyrgyzstan

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Objectives: During the last two decades, HIV-1 has been spreading rapidly in former Soviet Union republics including Kyrgyzstan. The current molecular monitoring of HIV-infection epidemic is carried out in Russia only with no or limited data from the other FSU countries. The aim of this work was to investigate the prevalence of HIV-1 genetic variants circulating in Kyrgyzstan.
Methods: Blood collection from the HIV-infected patients was carried out by local specialists with the informed consent and the questionnaire was answered by each of the patients. The total number of samples was 100. The washed cell pellets were transferred to Moscow following with proviral DNA extraction, PCR amplification and gag, pol and env genes sequencing. The phylogenetic analysis of nucleotide sequences using neighbor-joining method was carried out by MEGA 3 program. The preliminary data were obtained in 22 samples isolated from PBMC of HIV-infected patients from Kyrgyzstan.
Results: Among the samples studied 6 (27.3%) samples belonged to a subtype CRF02_AG, 16 samples - to subtype A (A1). One of the samples belonging to CRF02_AG, probably, is a recombinant between CRF02_AG and A1. There was no major drug resistance mutations in the samples studied. The minor mutations were presented in small proportions: 1 in PR (L10I), 6 in RT (A62V - in 3 samples, V108G, E138A, Y181F, M184I, L210M - on one sample) and 1 in IN (L74M). It was impossible to associate the distribution of mutations with HIV-1 genetic variant. The V3 loop (env gene) in 17

samples was analyzed for tropism using geno2pheno program; all samples were found to be R5-viruses.
Conclusion: The HIV-1 subtype A seems to dominate in Kyrgyzstan like in other FSU countries. The recombinant CRF02_AG epidemiologically linked to Uzbekistan is quite widespread. The rest of Kyrgyzstan collection is under investigation and the data will be refined soon.

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TREATMENT OF CHILDREN

P259

High prevalence of CXCR4-using viruses in vertically HIV-1-infected infants in Thailand

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Purpose of the study: Previous studies evaluating the frequency of CXCR4-using strains in HIV-1 vertically infected children restricted mainly to patients infected with subtype B or C strains. However, the coreceptor use by non-B or non-C subtypes remains little known, especially in infants. In this study, we determined the HIV-1 coreceptor usage in infants with vertically-acquired HIV-1 infection in Thailand, where the predominant circulating HIV-1 strains are CRF01_AE and the minority are subtype B.
Methods: C2-V3-C3 gp120 was amplified in a triplicate nested-PCR and sequenced. Coreceptor usage was predicted using the geno2-pheno [coreceptor] algorithm and analyzed with a false positive rate (FRP) of 10%.
Summary of results: A total of 255 sequences were obtained from viral isolates of 85 HIV-1-infected infants (34 male and 51 female) participating in the National AIDS Program (NAP) of the National Health Security Office (NHSO) of Thailand. All children were received ARV prophylaxis according to the Thai national guidelines. The median age was 84 days (range: 33–308). Seventy-four children (87.1%) were infected with CRF01_AE strain and 11 (12.9%) were infected with subtype B strain. Concordance in tropism prediction for the triplicates was observed in all samples. CXCR4 coreceptor-using strains were found in 44.7% (38 of 85) and CCR5 coreceptor-using strains were found in 55.3% (47 of 85). No significant difference in age ($p = 0.34$) and clinical signs of AIDS ($p = 0.47$) were observed between these populations. CCR5Delta32 and CCR5m303 mutation genotypes that may contribute to a selective pressure of viruses to alternatively use CXCR4 as a coreceptor were not found.
Conclusions: A high prevalence of HIV-1 CXCR4-using variants was found among HIV-1 vertically infected infants in Thailand, indicating that a direct vertical transmission of CXCR4-using variants or a rapid switch from CCR5-using to CXCR4-using viruses shortly after transmission. These observations may have implications for clinical and therapeutic aspects, especially in the early stage of HIV-1 infection in infants and may benefits for using of CCR5-antagonists in this population.

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P260

Cholecalciferol supplementation, vitamin D status and T-cell immune phenotype in HIV-infected children: a randomised controlled trial

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Purpose of the study: Besides its known effects on bone metabolism, vitamin D may regulate immune function. We performed a randomized controlled trial (RCT) to test whether cholecalciferol supplementation can improve vitamin D status and modulate immune responses in HIV-infected children and youth.
Methods: Caucasian vertically HIV-infected patients (aged 8 to 26 years) with vitamin D deficiency and normal parathormone (PTH) levels were randomized into an experimental ($n = 25$) and control ($n = 25$) group to receive 100,000 IU of oral cholecalciferol every 3 months for a total of 4 doses, or placebo. A pre-randomization period (−3 months) was also taken into account to better model within-individual variability. Mixed linear regression models were used to evaluate the between-group changes in the outcomes of interest. The analysis was intention to treat.
Summary of results: 47 subjects completed the RCT. Cholecalciferol supplementation produced an early decrease in PTH levels (3 months) and a later concomitant increase in 25(OH)D and 1,25(OH)2D levels (6 months), both persisting up to 12 months.
The supplementation had no effect on CD4+T-cell numbers or percentage while was associated with a decreased loge Th1, an increased loge Th2 (*$p < 0.05$), an increased loge Treg (**$p < 0.01$), and and a decreased loge Th17:Treg(*$p < 0.05$).
Conclusions: In our cohort, supplementation with oral cholecalciferol was effective in increasing serum 25(OH)D and 1–25$(OH)_2$D while decreasing serum PTH levels, had no effect on CD4+T-cell count, but was associated with T-cell phenotype changes mainly favoring Tregulatory subset.

Reference

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Abstract P260

	Loge VDR	Loge Th1	Loge Th2	Loge (Th1:Th2)	Loge Th17	Loge Treg	Loge (Th17:Treg)
Month 3	0.5	−1.6	−0.1	−1.4	−1.5	0.6	−2.5
	(−0.1 to 1.2)	(−3.6 to 0.5)	(−0.6 to 0.5)	(−3.5 to 0.7)	(−3.2 to 0.2)	(−0.3 to 1.6)	(−4.5 to −0.4)*
Month 12	0.7	−0.7	1.1*	−1.6	0.3	1.7**	−1.3
	(−3.0 to 1.7)	(−2.5 to 1.1)	(0.02 to 2.1)	(−3.7 to 0.5)	(−1.2 to 1.8)	(0.6 to 2.7)	(−3.3 to 0.7)

TREATMENT STRATEGIES

Naive Patients

P261

Maraviroc 150 mg QD plus lopinavir/ritonavir, a NRTI-sparing regimen for HIV-infected na ve patients: 48-weeks final results

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Novel strategies with NRTIs-sparing regimen in antiretroviral naïve HIV-infected patients are currently used in clinical trials [1]. We previously presented preliminary results of this study [2] and here we present the 48-weeks final results. Prospective, open-label, randomised (1:1), multicenter, proof-of-concept trial. HIV-infected naïve patients were assigned to once daily maraviroc (MVC) plus lopinavir/ritonavir (LPV/r) or to tenofovir/emtricitabine (TDF/FTC) plus LPV/r. Objectives of the study were the 48-weeks virological and immunological efficacy. Data were collected at baseline (BL) and at 4, 12, 24, 36 and 48 weeks. T cell subsets from frozen peripheral blood mononuclear cells collected at BL, 4 and 48 weeks were also evaluated. ANOVA for repeated measures performed and Greenhouse-Geisser probabilities calculated. Results reported as median (Q1–Q3) or frequency (%). Fifty patients (26 in MVC group and 24 in TDF/FTC group) were enrolled and reached week 48. Similar BL characteristics were observed in the two study groups; age: 39.1 (34.2–44) years, 2/50 (4%) females, infected since 2.9 (0.8–5.3) years, CD4+ nadir 266 (242–315) cells/μL, BL CD4+ 295 (260–369) cells/μL; CD4% 18.6 (14.6–23), HIV-RNA 4.4 (3.9–4.8) log_{10} copies/

		Baseline	Week 12	Week 24	Week 36	Week 48	p-value[a]
CD4+ cells/mm^3	MVC+LPV/r	292 (261–359)	438 (381–500)	517 (432–620)	533 (457–682)	614 (455–709)	0.046
	TDF/FTC+LPV/r	297 (257–373)	450 (354–511)	496 (367–568)	470 (402–568)	505 (419–705)	
CD4%	MVC+LPV/r	19.5 (16.3–24.3)	24 (18–29.5)	26.2 (22.2–29)	28.2 (21.3–32.2)	27.7 (21.6–33)	0.718
	TDF/FTC+LPV/r	18.8 (14.3–22.3)	24.7 (18.4–26.2)	25.2 (21.3–30.1)	24.9 (21.5–31.6)	25.7 (22.1–30.2)	
CD4/CD8 ratio	MVC+LPV/r	0.35 (0.25–0.48)	0.45 (0.3–0.62)	0.54 (0.4–0.67)	0.66 (0.4–0.82)	0.72 (0.47–0.93)	0.316
	TDF/FTC+LPV/r	0.33 (0.26–0.4)	0.44 (0.33–0.55)	0.51 (0.39–0.66)	0.52 (0.48–0.7)	0.54 (0.49–0.72)	
HIV-RNA log_{10} copies/ml	MVC+LPV/r	4.42 (4.07–4.84)	1.56 (1.56–1.56)	1.56 (1.56–1.56)	1.56 (1.56–1.56)	1.56 (1.56–1.56)	0.188
	TDF/FTC+LPV/r	4.41 (3.84–4.76)	1.56 (1.56–1.56)	1.56 (1.56–1.56)	1.56 (1.56–1.56)	1.56 (1.56–1.56)	
Haemoglobin (g/dL)	MVC+LPV/r	14.7 (13.7–15.1)	14 (13.5–14.6)	14.3 (13.7–14.9)	14.1 (13.3–15.1)	14.5 (13.6–15.2)	0.357
	TDF/FTC+LPV/r	14.1 (13.8–14.9)	14.4 (13.5–15.1)	14.8 (13.5–15.3)	14.7 (13.7–15.3)	14.7 (13.6–15.2)	
White blood cell (10^9/mm^3)	MVC+LPV/r	5 (4.6–5.6)	5.6 (5.2–6.9)	5.8 (4.8–7.2)	5.9 (5–7.7)	5.9 (5–7.5)	0.806
	TDF/FTC+LPV/r	4.5 (3.9–5.2)	4.3 (4.3–6.5)	5.1 (4.5–7.1)	5.1 (4.3–6.8)	5.5 (4.4–6.7)	
Cholesterol (mg/dl)	MVC+LPV/r	178 (149–204)	–	202 (177–233)	–	218 (167–260)	0.794
	TDF/FTC+LPV/r	160 (144–194)	–	189 (157–239)	–	199 (164–239)	
Tryglicerides (mg/dl)	MVC+LPV/r	91 (64–126)	–	193 (113–254)	–	170 (105–270)	0.825
	TDF/FTC+LPV/r	91 (66–148)	–	159 (106–203)	–	147 (110-187)	
Glucose (mg/dl)	MVC+LPV/r	84 (78–91)	–	86 (75–89)	–	84 (76–93)	0.200
	TDF/FTC+LPV/r	81 (75–89)	–	85 (79–92)	–	82 (77–88)	
Insulin (U/L)	MVC+LPV/r	5.7 (4–10.2)	–	7 (5.1–8.4)	–	6.8 (5.8–10.8)	0.554
	TDF/FTC+LPV/r	7.2 (5.7–14.6)	–	6.8 (5.7–10)	–	5.8 (5.3–9.3)	
Creatinine (mg/dl)	MVC+LPV/r	0.83 (0.77–0.95)	0.79 (0.72–0.85)	0.78 (0.69–0.87)	0.78 (0.71–0.86)	0.81 (0.75–0.87)	0.149
	TDF/FTC+LPV/r	0.83 (0.78–0.98)	0.88 (0.79–1)	0.85 (0.75–0.93)	0.85 (0.77–0.92)	0.85 (0.74–0.95)	

mL. At W48, all patients in MVC group and 22/24 (96%) in TDF/FTC group had HIV-RNA <50 copies/ml (p = 0.225). CD4+ trend during follow-up was different between the two groups (p = 0.046) with a higher CD4 gain of 286 (183–343) vs 199 (125–285) cells/mL in MVC and TDF/FTC, respectively (p = 0.033). In MVC vs TDF/FTC group, we observed a higher expression of CCR5+CD4+ T cells [W48 change: +7.5% (−4.5/11) vs −5.4 (−15.1/ −0.5), p = 0.016] and a higher increase of CD4+ effector memory [W48 change: +1.6% (0.7/4.8) vs -4.4 (−13.5/ −0.2), p = 0.007]. No significant variations in naïve and central memory CD4+ T cells. Treatment was well tolerated, without grade 3 or 4 adverse events. No significant difference between the two groups as for the 48-weeks trend of bone marrow function, AST, ALT and CPK values, creatinine value, glicyde profile (fasting glucose, fasting insuline) and lipid profile (total cholesterol, LDL and HDL cholesterol, tryglicerides). Results are shown in Table 1. In naïve-patients, virological efficacy and tolerability of a NRTIs-sparing regimen with maraviroc and lopinavir/ritonavir was similar to conventional treatment in addition to a better immunological recovery, in particular of the Effector Memory CD4+ cells subset.

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P262

Impact of antiretroviral dosing frequency and daily pill burden on virological success rates in patients of the ICoNA cohort starting their first ART

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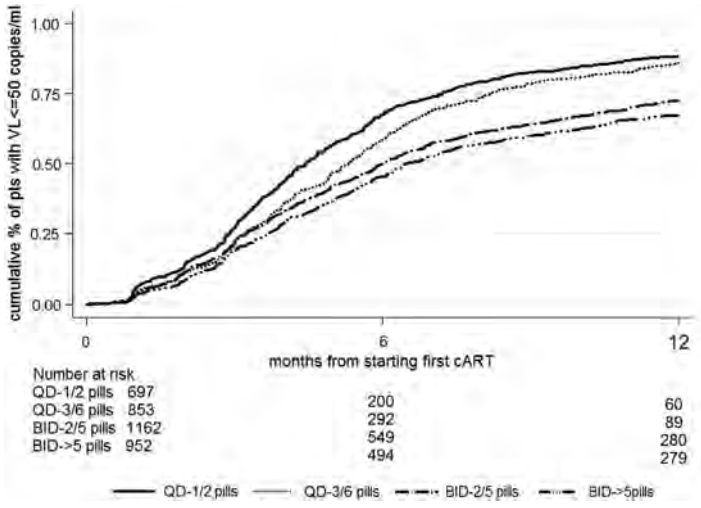
Complexity of antiretroviral treatment (ART) is a reason for non-adherence and may impact treatment outcome. The association between daily dosing and pill burden and chance of virological success (VS) of first ART has been rarely assessed. 3,674 naïve patients who started treatment after January 2000 were identified from the ICoNA cohort. Number of daily doses and pills were estimated on the basis of the drugs used to rank first ART complexity: 1–2 daily pills once a day (low-pills QD [lpQD]); 3–6 daily pills QD (high-pills QD [hpQD]); 2–5 daily pills BID (low-pills BID [lpBID]); >6 daily pills BID (high-pills BID [hpBID]). VS was the date of first HIV RNA <50 cp/ml. Follow-up was censored at the date of VS or last available HIV RNA. Kaplan-Meier curves estimated probability of achieving VS according to ART complexity. Univariable and multivariable Cox regression stratified by clinical site was used to identify variables associated with VS. ITT principle was applied, using competing risk approach for death. Population: male 75%; median age 37 y (IQR, 32–44); HIV transmission heterosexual 43%, homosexual 33%, drug use 16%; Italian origin 86%; CDC group C 17%; median pre-ART CD4 and log HIV-RNA were 271/mm^3 (range, 0–1672) and 4.84 cp/ml (1.70–6.38), respectively. Regimens were started in '00–'02 24%,'03–'05 17%,'06–'08 17%,'09–'12 42% and based on NNRTI in 40%, PI/r 43%, PI 8%, other ART 10%. Frequencies in complexity ranks were: 19% lpQD, 23% hpQD, 32% lpBID, 26% hpBID. VS was achieved by 85% of patients with an overall median time to VS of 5.6 months (95% CI: 5.4–5.8). Median months to VS were shorter with decreasing complexity: hpBID 6.5; lpBID 6.0; hpQD 5.3, lpQD 4.5. Kaplan-Meier curves are shown (Figure).
After stratifying for clinical site and adjusting for age, gender, origin, transmission route, CDC group C, HCV/HBV infection, years of HIV, pre-cART CD4 and HIV-RNA, type of regimen a significantly reduced likelihood of achieving VS was found for ART complexity (hpQD: HR 0.76 95% CI 60–0.96; lpBID: 0.74, 0.59–0.94) when compared with lpQD. The chance of VS was higher in people starting ART more recently (RH 1.28 [95% CI 1.09–1.51] for '03–'05; RH 1.64 [1.27–2.10] for '09–'12; vs. '00–'02) and was lower in people with previous AIDS (RH 0.85 [0.73–0.98]). Once-a-day dosing of ART, especially



when combined with low daily pill burden, seems to be one of main factors contributing to the higher rate of success of ART in recent years.

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P263

Effectiveness of first-line antiretroviral therapy based on NNRTIs vs ritonavir-boosted PIs in HIV-1 infected patients with high plasma viral load

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Purpose of the study: Few clinical trials have compared non-nucleoside reverse transcriptase inhibitors (NNRTI) and ritonavir-boosted protease inhibitors (PI/r) as initial combined antiretroviral therapy (cART) for HIV-1-infected patients with high plasma viral load (pVL), and non-conclusive results have been reported. We compared the effectiveness between NNRTI and PI/r as first-line cART for HIV-1-infected patients with high pVL.
Methods: Observational retrospective study of 664 consecutive treatment-naïve HIV-1-infected patients with pVL (HIV-1 RNA) $>100{,}000$ copies/mL who initiated NNRTI or PI/r-based cART between 2000–2010 in three University hospitals. Only currently preferred or alternative regimens in clinical guidelines were included. Primary endpoint: percentage of therapeutic failures at week 48. Virologic failure was defined as: a) lack of virologic response (<1 log RNA HIV-1 decrease in first 3 months); b) RNA HIV-1 >50 c/mL at week 48; c) confirmed rebound >50 c/ml after a previous value <50 c/mL. Intent-to-treat (ITT noncompleter = failure) and on-treatment (OT) analyses were performed.
Results: 62% of patients initiated NNRTI-regimens (83% efavirenz) and 38% PI/r-regimens (62% lopinavir/). Baseline characteristics: male 83%; median age 39 yrs; median CD4 count: 212/μL (NNRTI 232 vs PI/r 177, $p=0.028$); pVL 5.83 $\log_{10}$ c/mL (NNRTI 5.43 vs PI/r 5.55, $p=0.007$); AIDS 24% (NNRTI 21% vs PI/r 29%, $p=0.015$). NRTI backbones were tenofovir plus 3TC or FTC in 72%. The percentage of therapeutic failure was higher in the PI/r group (ITT NC = F 26% vs 18%, $p=0.012$) with no differences in virologic failures (PI/r 5%, NNRTI 6%, $p=0.688$). The rate of treatment changes due to toxicity and/or voluntary discontinuations was higher in the PI/r group (15% vs 8%, $p=0.008$). A multivariate analysis adjusted for age, gender, CD4 count, VL and AIDS showed NNRTI vs PI/r as the only variable associated with treatment response (OR 0.61, 95% CI 0.41–0.88). Median pVL and rate of resistance at virologic failure were higher in patients receiving NNRTI (3.97 vs 2.49 log copies/mL, $p<0.001$ and 62% vs 12%, $p=0.004$, respectively).
Conclusions: Initial NNRTI-regimens showed higher effectiveness compared with PI/r-regimens in HIV-1-infected patients with high pVL, although virologic failure rates were low and comparable. Resistance emergence was more frequent and pVL higher in patients failing NNRTI. However, more patients initiating PI/r-based regimens changed or discontinued therapy.

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P264

VERxVE 144 week results: nevirapine extended-release (NVP XR) QD versus NVP immediate-release (IR) BID with FTC/TDF in treatment-na ve HIV-1 patients

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Background: Here we report 96- and 144-week follow-up data from VERxVE, which demonstrated that NVP XR (400 mg QD) was non-inferior to NVP IR (200 mg BID), each on a backbone of emtricitabine/tenofovir at 48 weeks.
Methods: VERxVE was a double-blind, double-dummy, non-inferiority study in adults with screening viral-load (VL) >1000 copies/mL and CD4+ cell count <400 cells/mm^3 (males) and <250 cells/mm^3 (females). Randomization was stratified by baseline VL (copies/mL), $\leq 100{,}000$ or $>100{,}000$. Primary endpoint was confirmed virologic response (<50 copies/mL) at Week 48. Cochran's statistic incorporating baseline-VL strata tested non-inferiority of XR efficacy to IR. Secondary endpoints included 144-week sustained virologic response and safety.
Results: 1011 patients were randomized and treated; 736 (NVP XR: 378, NVP IR: 358) completed 144 weeks. Virologic response was 63.6% for NVP XR and 58.5% for NVP IR (adjusted difference of 4.8% [95% CI: −1.1%, 10.8%] favoring NVP XR). No significant differences were seen in changes in CD4+ T cell counts from baseline, virologic failures, and total discontinuation rates between treatment arms regardless of demographic or baseline characteristics.
Conclusions: NVP XR continued to demonstrate non-inferior virologic efficacy to NVP IR in prior treatment-naïve HIV infected patients out to week 144. NVP XR continued to be well-tolerated with a safety profile similar to NVP IR.

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	48 Weeks		96 Weeks		144 Weeks	
	NVP IR 200 mg BID	NVP XR 400 mg QD	NVP IR 200 mg BID	NVP XR 400 mg QD	NVP IR 200 mg BID	NVP XR 400 mg QD
% Virologic response	75.9	81.0	66.6	69.3	58.5	63.6
Change from baseline in CD4+ Count (cells/mm^3)	207	213	257	275	286	317
Virologic failures (%)	5.9	3.2	10.7	11.1	15.8	15.1
Discontinuation rate (%)	19.2	16.6	26.1	23.6	29.2	25.1
Discontinuations due to AEs	8.3	6.3	9.5	8.3	10.7	8.5

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Indirect treatment comparison of efficacy, safety and resistance of EVG/COBI/FTC/TDF (Quad) vs. RAL + FTC/TDF in treatment-na ve HIV patients

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Purpose: To compare the efficacy, tolerability and resistance profile at week 48 of elvitegravir 150 mg/ cobicistat 150 mg/ emtricitabine 200 mg/ tenofovir DF 300 mg qd (QUAD) relative to raltegravir 400 mg bid + emtricitabine 200 mg/ tenofovir DF 300 mg qd (RAL + FTC/TDF) in treatment-naïve, HIV-1-infected adults based on an indirect treatment comparison.
Methods: Using the phase 3 studies GS-US-236-0102 (102) and STARTMRK, outcomes examined were viral suppression (HIV RNA < 50 cps/mL), mean CD4+ cell count (cells/μL) change from baseline, discontinuation due to any reason and due to adverse events (AE) and resistance to EVG and RAL. Efavirenz/emtricitabine/tenofovir DF was used as the common comparator. A Bayesian generalized linear model framework for indirect treatment comparison was adopted to estimate relative and absolute treatment effects, using QUAD as baseline value.
Results: The odds ratio (OR) of viral suppression with QUAD relative to RAL + FTC/TDF was 0.98 (CI: 0.52; 1.86). Discontinuations due to any reason or AE were comparable. The OR of resistance with QUAD relative to RAL + FTC/TDF was 0.63 (CI: 0.09; 4.21). The estimated probability of viral suppression was 88.8% (CI: 85.3%; 91.9%) for QUAD; 88.8% (CI: 82.7%; 93.4%) for RAL + FTC/TDF. Mean CD4+ cell count change from baseline was estimated at 239.0 cells/μL (CI: 220.9; 257.1) for QUAD and 232.0 cells/μL (CI: 204.9; 259.2) for RAL + FTC/TDF. The estimated probability of discontinuation due to any reason is 10.6% (CI: 7.6%; 14.1%) for QUAD and 9.2% (CI: 4.9%; 15.4%) for RAL + FTC/TDF and due to AE 3.7% (CI: 2.0%; 6.0%) for QUAD and 2.9% (CI: 1.0%; 6.4%) for RAL + FTC/TDF. Integrase resistance is estimated at 2.0% (CI: 1.0%; 4.0%) for QUAD and 4.3% (CI: 1.0%; 16.0%) for RAL + FTC/TDF.
Conclusion: Comparable results were found between QUAD and RAL + FTC/TDF for the studied outcomes analyzed at week 48, in treatment-naïve, HIV-1-infected patients.

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P266

Increasing subject compliance in pivotal phase III clinical trials of dolutegravir (DTG, S/GSK1349572) in HIV-infected, ART-na ve subjects

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To maximise the application of results of large-scale clinical trials, recruitment and retention of a diverse subject population is key. With commonly used algorithms (Snapshot, TLOVR, missing = failure), all withdrawals in HIV studies, regardless of reason, are classed as failures in efficacy analyses. Good subject compliance therefore improves statistical power and the quality of trial results. In four recent GSK/ViiV-sponsored phase IIIB/IV HIV ART-naïve studies (HEAT, KLEAN, APV109141 and ARIES), 24% of subjects withdrew and approximately 2/3 of these withdrawals (16%) potentially were avoidable (i.e. not treatment related) [1]. To increase subject compliance in the phase III, treatment-naïve studies of DTG (ING113086 ''SPRING-2'' and ING114467 ''SINGLE''), a more robust subject compliance program focussing on understanding subject needs and building sponsor-site and site-subject relationships was implemented. The compliance program included opt-in study visit reminders, late study visit tracking, subject compliance support materials, subject transportation support, on-going site training, relationship management and presentations on prior withdrawal rates and associated risk factors for attrition at investigator meetings. Week 48 withdrawals, both overall and for potentially avoidable reasons, were considerably lower in SPRING-2 and SINGLE than historical HIV trials. Comparison of withdrawal rates prior to, and after implementation of robust patient compliance program. Addressing individual study subject needs with a customized approach in SPRING-2 and SINGLE contributed to considerably lower percentages of withdrawals than in historical HIV studies. Identifying the specific impact of a single subject compliance initiative is difficult as study compliance can be influenced by overall study design, investigational product tolerability profile, current standard of care and treatment access for the disease under study. However, consistently reducing the number of avoidable withdrawals has the potential to lead to improved quality of trial results and smaller, quicker studies in the future, benefitting the whole HIV population.

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Study	N	Week	Withdrawals from study n (%)	Withdrawals for unavoidable reasons*	Withdrawals for potentially avoidable reasons[#]
HEAT/KLEAN/APV109141/ARIES[~]	2290	36–96	552 (24%)	179 (8%)	373 (16%)[&]
SPRING-2	822	48	103 (13%)	57 (7%)	46 (6%)
SINGLE	833	48	135 (16%)	79 (9%)	56 (7%)

*Due to adverse events, lack of efficacy, protocol-defined stopping criteria.
[#]Due to lost to follow-up, withdrew consent, protocol deviation, investigator discretion.
[~]Pooled data from HEAT (EPZ104057), KLEAN (ESS100732), APV109141, ARIES (EPZ108859).
[&]Week 48 Kaplan-Meier estimates = 15%, 13% and 9% respectively for HEAT, KLEAN and APV109141.

P267

Compliance with HIV treatment guidelines in the Spanish CoRIS cohort: impact on mortality and immunovirological response

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There is little evidence assessing compliance with clinical practice guidelines for antiretroviral treatment and its impact on clinical outcomes. The Spanish national guidelines for antiretroviral treatment are published by the Spanish AIDS Study Group (GeSIDA). The aim of this study was to assess compliance with national guidelines for the treatment of naïve patients from a multicentre Spanish cohort (CoRIS). The specific aims were to evaluate the proportion of patients treated according to the guidelines' recommendations, to investigate factors associated with the prescription of a non-recommended treatment, and to assess the impact of non-recommended treatments on mortality and on virological and immunological response (defined as undetectable viral load and increase of 100 CD4/ml, respectively, after 1 year). Drug combinations were classified as recommended, alternative, or not recommended, according to the guidelines' ''what to start with'' recommendations. 6225 naïve patients were included between the years 2004 and 2010. Among 4516 patients who started treatment, 3592 (79.5%), 540 (12%), and 384 (8.5%) started with a recommended, alternative and not-recommended treatment, respectively. The use of a not-recommended treatment was significantly associated with CD4 count >500/ml (OR: 2.03, 95% CI: 1.14–3.59), hepatitis B infection (OR: 2.23, 95% CI: 1.50–3.33), treatment in a hospital with <500 beds, and starting treatment in the years 2004 to 2006. There was no significant association of having a not-recommended treatment with gender, route of transmission, hepatitis C infection, country of origin, education, or viral load. The use of a not-recommended regimen was significantly associated with mortality (HR: 1.61, 95% CI: 1.03–2.52, $p=0.035$) and lack of virological response (OR: 0.65, 95% CI: 0.45–0.93, $p=0.019$), but it was not associated with immunological response (OR: 0.90, 95% CI: 0.75–1.08, $p=0.273$). In conclusion, compliance with ''what to start with'' recommendations of Spanish national guidelines was high. The use of not-recommended regimens was more likely in patients with >500 CD4/ml, hepatitis B infection, and starting treatment in the years 2004–2006 and in small hospitals. Not-recommended regimens were associated with higher mortality and lack of virological response.

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P268

Long-term efficacy and safety of atazanavir/ritonavir treatment in a cohort of treatment-na ve HIV patients: an interim analysis of the REMAIN study

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Purpose: Combined antiretroviral therapy has dramatically improved HIV-infected individuals survival. Long-term strategies are currently needed to achieve the goal of durable virologic suppression. However, long-term available data for specific antiretrovirals (ARV) are limited. In clinical trials, boosted atazanavir (ATV/r) regimens has shown good efficacy and tolerability in ARV-naïve patients for up to 4 years. The REMAIN study aimed to evaluate the long-term outcomes of ATV/r regimens in ARV-naïve patients in a real life setting.
Methods: Non-comparative, observational study conducted in Germany, Portugal and Spain. Historical and longitudinal follow-up data was extracted six monthly from the medical record of HIV-infected, treatment-naïve patients, who initiated an ATV/r-regimen between 2008 and 2010. The primary endpoint was the proportion of patients remaining on ATV treatment over time. Secondary endpoints included virologic response (HIV-1 RNA <50 c/mL and <500 c/mL), reasons for discontinuation and long-term safety. The duration of treatment and time to virologic failure (VF) were analyzed using the Kaplan-Meier method. Data from an interim analysis including patients with at least one year of follow-up are reported here.
Results: A total of 411 patients were included in this interim analysis [median (Q1, Q3) follow-up: 23.42 (16.25, 32.24) months]: 77% male; median age 40 years [min, max: 19, 78]; 16% IDUs; 18% CDC C; 18% hepatitis C. TDF/FTC was the most common backbone (85%). At baseline, median (Q1, Q3) HIV-RNA and CD4 cell count were 4.91 (4.34, 5.34) $\log_{10}$ c/mL and 256 (139, 353) cells/mm^3, respectively. The probability of remaining on treatment was 0.84 (95% CI: 0.80, 0.87) and 0.72 (95% CI: 0.67, 0.76) for the first and second year, respectively. After 2 years of follow-up, 84% (95% CI: 0.79, 0.88) of patients were virologically suppressed (<50 c/mL). No major protease inhibitors mutations were observed at VF. Overall, 125 patients (30%) discontinued ATV therapy [median (Q1, Q3) time to discontinuation: 11.14 (6.24, 19.35) months]. Adverse events (AEs) were the main reason for discontinuation ($n=47$, 11%). Hyperbilirubinaemia was the most common AE leading to discontinuation (14 patients). No unexpected AEs were reported.
Conclusions: In a real life clinical setting, ATV/r regimens showed durable virologic efficacy with good tolerability in an ARV-naïve population. Data from longer follow-up will provide additional valuable information.

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P269

Four-drug induction regimen for patients with high baseline viral load

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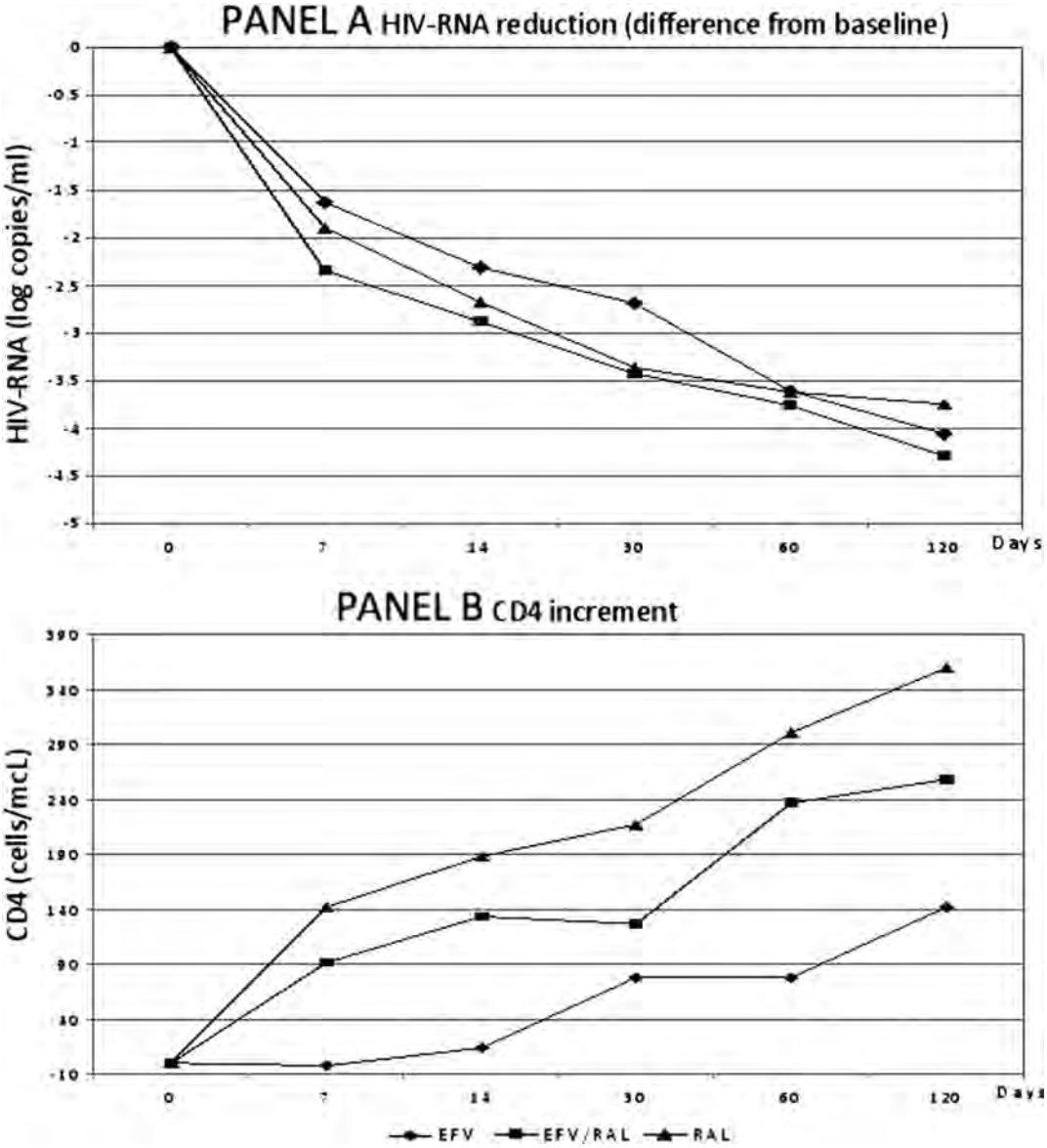
Early virologic changes after treatment have been associated with long-term virologic success. The objective of this pilot, randomised, prospective study is to evaluate the effect of an induction, 4-drug HAART regimen in patients with high baseline viral load. Twenty-one naïve patients with HIV-RNA $>100{,}000$ copies/ml were randomised to TDF + FTC + EFV (1); TDF + FTC + EFV + RAL (2), TDF + FTC + RAL (3). Viral load, CD4 and immune activation markers were evaluated at days 7, 14, 30, 60, 120 from the start of therapy. Mean age was 38.2 years, 19 (90.5%) were male, and the main risk factor for HIV infection was heterosexual contacts in 52.4% of patients. The mean



baseline viral load was 265,266 copies/ml and the mean CD4 cell count was 314 cell/mm^3. CD8+CD38+HLA-DR+ cells mean was 38%. No difference was observed among the three groups. Early HIV-RNA reduction was significantly higher in group 2 at day 7 ($P = 0.007$), 14 ($P = 0.018$), 30 ($P = 0.046$) after HAART start, thereafter HIV-RNA values were comparable among the groups. No significant differences were observed at any time-point between group 1 and group 3. The viral decay (delta VL), evaluated as reduction of viral load, was faster and higher in group 2 at any time-point; the reduction was statistically significant (compared to group 1 and 3) after 7 days ($P = 0.006$), but not thereafter. No differences were observed between group 1 and 3 (Figure, panel A). At the end of follow-up (120 days) only patients in group 2 reduced HIV-RNA below <3 copies/ml in 30% of cases. Although not statistically significant (probably because of the small sample) immune recovery, as measured by the increment of CD4 cells, was greater in the two groups receiving RAL (Figure, panel B). At the end of the follow up the mean increment was 142 cells/mm^3 in group 1; 258 cells/mm^3 in group 2 and 360 cells/mm^3 in group 3. No difference was observed as far as the reduction of immune activation is concerned. A 4-drug regimen in naïve patients with high pre-therapy viral load improves early virologic response, that has been proved to be a prognostic marker for sustained virologic response. CD4 cell recovery is much higher in patients receiving RAL compared to those treated with EFV. This study highlights the importance of a personalised therapy especially in high-risk patients. Further studies are necessary to define the best therapeutic regimen in patients with high baseline viral load.

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P270

Rilpivirine efficacy, virology and safety in ARV treatment-na ve patients with viral load $\leq$100,000 HIV-1 RNA c/mL: ECHO and THRIVE 96-week results

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	RPV N = 368			EFV N = 329		
	All	**Up to Week 48**	**Weeks 48–96**	**All**	**Up to Week 48**	**Weeks 48–96**
Resistance at time of failure						
VF_{res}, n (%)	28 (7.6)	20 (5.4)	7 (1.9)	20 (6.1)	14 (4.3)	6 (1.8)
VF_{res} with genotypic data	**N' = 27**	**N' = 19**	**N' = 7**	**N' = 17**	**N' = 11**	**N' = 6**
developing NNRTI RAMs, n	10	7	2	6	5	1
developing N(t)RTI RAMs, n	12	8	3	2	2	0
Safety						
AEs leading to discontinuation, n (%)	18 (4.9)	13 (3.5)	3 (0.8)	22 (6.7)	18 (5.5)	2 (0.6)
Grade 2–4 AEs at least possibility related to treatment, n (%)	66 (17.9)	56 (15.2)	5 (1.4)	104 (32)	97 (29.5)	12 (3.6)
AEs of interest at least possibly related to treatment, n (%)						
Any neurological AE	70 (19.0)	67 (18.2)	1 (0.3)	135 (41.0)	132 (40.1)	2 (0.6)
Dizziness	35 (9.5)	35 (9.5)	0	97 (29.5)	97 (29.5)	1 (0.3)
Any psychiatric AE	61 (16.6)	54 (14.7)	2 (0.5)	75 (22.8)	68 (20.7)	5 (1.5)
Abnormal dreams/nightmares	27 (7.3)	25 (6.8)	0	38 (11.6)	36 (10.9)	1 (0.3)
Rash (grouped term)	9 (2.4)	8 (2.2)	1 (0.3)	43 (13.1)	43 (13.1)	0

Background: In the ECHO and THRIVE Phase III, randomised, double-blind trials, rilpivirine (RPV, TMC278, EDURANT) 25 mg qd showed non-inferiority compared to efavirenz (EFV) 600 mg qd in antiretroviral (ARV) treatment-naïve, HIV-1-infected adults at Weeks 48 and 96. In Europe, RPV combined with other ARVs is approved for the treatment of ARV-naïve adults with a viral load (VL) $\leq$100,000 c/mL. We present results from a pooled analysis of Week 96 data from this patient subgroup.
Methods: Patients received RPV 25 mg qd or EFV 600 mg qd, both with TDF/FTC (ECHO) or TDF/FTC, AZT/3TC or ABC/3TC (THRIVE). Response rate (% VL $<$ 50 c/mL, intent-to-treat-time-to-loss-of-virologic response [ITT-TLOVR]), virologic failure in the resistance analysis (VF_{res}) and resistance development, as well as safety and tolerability were evaluated.
Results: Baseline characteristics were similar between the 368 RPV and 329 EFV patients with baseline VL $\leq$100,000 c/mL. At Week 96, response rates (RPV 84% vs EFV 80%; difference 4.0% [95% CI: $-$1.7%, 9.7%]) and VF_{res} percentages (8% vs 6%, respectively; p = 0.46) (Table) were similar in each treatment group. A comparable proportion of VF_{res} developed NNRTI resistance-associated mutations (RAMs) in each group. More RPV than EFV VF_{res} developed N(t)RTI RAMs (p = 0.02). The increase in mean (95% CI) CD4+ cell count from baseline to Week 96 was 224 (208; 240) cells/mm^3 for RPV and 206 (188; 225) cells/mm^3 for EFV. Treatment-related grade 2–4 overall AEs, any rash, and neurologic AEs, including dizziness were less frequent for RPV than EFV (all p $<$ 0.0001, Fisher's Exact test) (Table).
Conclusions: At Week 96, in ARV treatment-naïve adults with baseline VL $\leq$100,000 c/mL, RPV demonstrated sustained antiviral efficacy similar to EFV. There were similar frequencies of RPV and EFV VF_{res}, and RPV had a more favourable safety/tolerability profile than EFV.

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P271

Causes for switch-infected patients: the NEXT study

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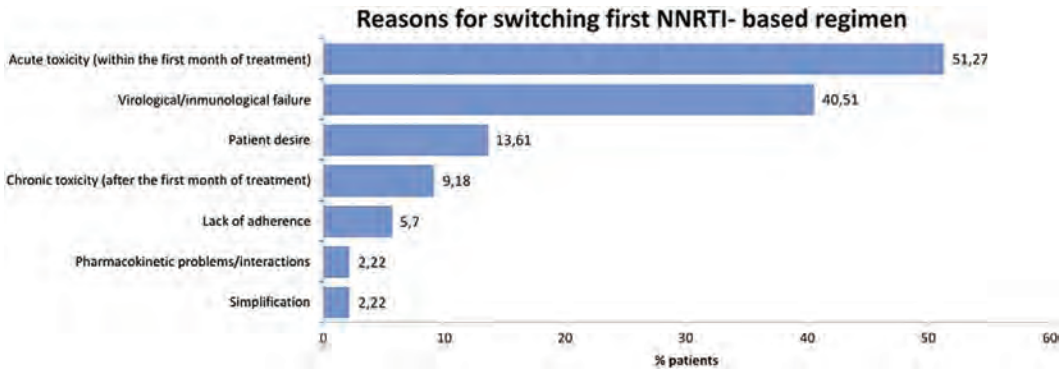
Purpose of the study: NNRTIs are commonly used to initiate HAART. Despite their demonstrated efficacy, tolerability and resistance issues could lead to a treatment change. The objective of the NEXT study was to evaluate the reasons for switching an initial non-nucleoside based regimen in the clinical setting, and the alternative regimen selected.
Methods: A retrospective multicentre study was undertaken between April and October 2009. Patients from 38 Spanish centres who had changed the initial EFV or NVP-based regimen in the previous six-month period were included. Social-demographic and HIV-related data was collected from medical records. Responsible physicians were interviewed about reasons for switching the non-nucleoside and the alternative regimen of choice.
Summary of results: A total of 391 HIV-1 infected patients had changed the initial EFV or NVP-based regimen in the previous six months. Data were available for 316 (80.8%) of them. 245/316 patients received EFV as first line (77.5%). Median time to switch the NNRTI regimen was 16.9 months, shorter in case of EFV-based regimen, 15.4 months, than NVP-based regimen, 20.8 months. Most of changes were observed in the first month after initiation, representing 51.3% of the discontinuations, especially in case of EFV (57.1% EFV; 31% NVP). 9.2% of the patients switched due to chronic toxicity (after the first month of treatment). CNS toxicity was the most common reason for switching therapy in the acute term in 63% of the patients. Other tolerability issues that led to treatment discontinuation in the short term were lipid abnormalities due to EFV (4.1%) and liver enzyme elevations related to NVP (7%). Rash led to a similar rate discontinuation with both NNRTIs (12%). The second reason to discontinue the first-generation NNRTI was virological/immunological failure in 40.5% of the patients (128/316). The new regimen selected was a boosted PI regimen in 52% of the cases, and was another NNRTI based regimen in 62.3%. Physicians marked safety/tolerability as the main reason for switching in 58.5% of cases (185/316).
Conclusions: In the clinical setting, both acute and chronic intolerance/toxicity represents the main cause of the first line treatment change based on a first generation NNRTI, mainly EFV. CNS toxicity

Abstract P271



was the most common reason for switching therapy in the acute term. Therefore, the tolerability profile of the alternative regimen played a relevant role when switching regimens.

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P272

Open-label study of maraviroc + lamivudine/zidovudine in treatment-na ve adults infected with HIV-1, predominantly subtype A, by population genotyping

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HIV-1 subtype A infection predominates in Russia; however, little experience of response to maraviroc in this subtype exists and population genotyping in this setting requires further exploration. One hundred and twenty-one treatment-naïve HIV-1-infected individuals from seven centres in Russia were screened using V3 loop population genotyping with a false-positive rate of 10% (geno2pheno); 75% of patients were confirmed to have CCR5 (R5)-tropic HIV-1, 21% of patients had non-R5 HIV-1, and 4% of tests were non-reportable. Seventy-seven patients met the inclusion criteria and were treated with maraviroc 300 mg twice daily (BID) in combination with lamivudine/zidovudine. Virologic and immunologic responses were assessed in this 24-week planned interim analysis. Fifty-one male (66.2%) and 26 (33.8%) female patients were enrolled. In total, 76.3% of patients had subtype A infection, and 28.6% were co-infected with hepatitis C virus. At baseline, the mean ($\pm$ standard deviation [SD]) CD4 count was 404 ± 122 cells/mm^3, and the mean viral load was 4.77 ± 0.74 $\log_{10}$ copies/mL, with 38% of patients having viral loads $\geq$100,000 copies/mL. At Week 24, 80.5% of patients had viral loads $<$50 copies/mL and the mean ($\pm$SD) CD4 cell count was 411 ± 124 cells/mm^3. No treatment-emergent adverse events were attributed to maraviroc, and three patients experienced Grade 4 anaemia associated with lamivudine/zidovudine. Seven patients discontinued from the study, but only one of these discontinuations was due to an insufficient clinical response. Two patients had 3TC resistance at the time of discontinuation. Virologic responses to a maraviroc-based regimen in patients infected with R5-tropic HIV-1 subtype A, determined using population genotyping, were confirmed.

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P273

Retention on third agents in HAART regimens at the Maple Leaf Clinic in Toronto, Ontario, Canada

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This study evaluated the 12-month retention rate of third agents in HAART (highly active anti-retroviral therapy) regimens in routine clinical practice in a Canadian HIV clinic. This is a descriptive retrospective database analysis of HIV-positive patients naïve to antiretroviral therapy (ART). The study included male and female HIV patients $\geq$18 years of age at HAART initiation date, seen in routine consultation at the Maple Leaf Medical Clinic (MLMC), Toronto, Ontario, Canada. Data were extracted from the MLMC database for the period of September 1st, 2003 to August 31st, 2010 for patients who commenced a protease inhibitor (PI), a non-nucleoside reverse-transcriptase inhibitor (NNRTI), or an integrase inhibitor (II) -based regimen in combination with two nucleoside reverse transcriptase inhibitors (NRTI). Demographic and baseline disease characteristics were extracted and include age, gender, disease duration, baseline HIV-1 RNA count, CD4 cell count, and hepatitis B and C co-infection status at baseline. A total of 722 patients were included in the analysis. The primary outcome of the study was the proportion of HIV patients remaining on their initial third agent (PI, NNRTI, or II) at one year post-treatment initiation. For therapies used by more than 10% of patients (efavirenz [EFV] = 315, atazanavir [ATV] = 104, lopinavir [LPV] = 162, as other agents were used but in limited numbers), the percentage of patients still on the initial third agents at one year was 77%, 64% and 62%, respectively. In addition, viral load (VL) was less than 50 copies/mL in 95% of EFV, 79% of ATV and 76% of LPV patients at one year. The rate of discontinuation at 12 months from EFV, ATV, and LPV due to efficacy (i.e. lack of virologic suppression) or safety (i.e. adverse events) were 15.56%, 19.23%, and 19.75% respectively. In a clinical practice setting, the majority of patients treated with HAART regimens were maintained on therapy at one year and were able to suppress their viral load consistently. Of those reported here, EFV resulted in the best retention rate and viral suppression overall.

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P274

Low plasma zinc level and response to zinc supplement in HIV-infected patients who have immunological discordance after antiretroviral therapy

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Purpose of the study: Immunological discordance in HIV-infected patients is associated with the higher risk of mortality

and disease progression. Zinc is an essential micronutrient for immune function. We aimed to determine plasma zinc level and immunological response after zinc supplementation in HIV-infected patients with immunological discordance after antiretroviral therapy (ART).

Methods: A pilot study of 2 phases including a cross-sectional study to determine plasma zinc level in patients with immunological discordance and a prospective, randomized, open-label, placebo-controlled trial was conducted in HIV-infected patients with immunological discordance in a medical-school hospital. Immunological discordance was defined as patients who received ART, had complete virological response (HIV RNA <40 copies/ml), and had immunological response with CD4 cell count <200 cell/mm^3 and increased less than 30% from baseline after ART with undetectable HIV RNA for at least 6 months. Plasma zinc level was measured and stratified into low (<75 μg/dL) and normal plasma zinc level. Patients were randomly assigned to receive zinc or placebo supplementation for 6 months. CD4 cell count was monitored every 3 months.

Summary of results: Of 31 patients, median (IQR) plasma zinc level was 76 (66–88) μg/dL (IQR) and 12 (38.7%) patients had low plasma zinc level. Five of 12 patients with low plasma zinc level and 8 of 19 patients with normal plasma zinc level were randomized to receive zinc supplementation. Median (IQR) change of plasma zinc level after zinc supplementation in patients with low and normal plasma zinc level were 29 (-2–50) and -8 (-17–10) μg/dL, respectively. Significant increase of CD4 cell count after zinc supplementation was observed in patients with low plasma zinc level. Median (IQR) CD4 cell count at baseline and after zinc supplementation were 176 (161–200) and 250 (192–262) cells/mm^3. The effect of zinc supplementation compared to placebo on the rising of CD4 cell count was not significantly different in both patients with low and normal plasma zinc level.

Conclusions: Low plasma zinc level is observed over one-third of patients with immunological discordance. Zinc supplementation increases plasma zinc level and CD4 cell count in patients with low zinc level but the effect was not significant different from placebo. Further large-scale study to determine long-term benefit of zinc supplementation in patients with immunological discordance is needed.

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P275

First line etravirine use in na ve patients: real-world data in a UK centre

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Etravirine (ETV) is licensed in the UK for treatment-experienced patients and existing data suggest ETV is an effective switch for patients intolerant of efavirenz (EFV). ETV has a favourable tolerability profile and therefore may be an attractive non-nucleoside reverse transcriptase inhibitor (NNRTI) option in first line therapy. We present data of ETV use as a once-daily first-line treatment option in naïve patients. 26 treatment-naïve patients commenced on ETV were identified through pharmacy records up until May 2012. Demographic data were collected with information on hepatitis B and C status, CD4, viral load (VL), liver function and lipids. Patients were followed for 6-monthly intervals and outcomes recorded. Of the 26 patients identified 25 were male and one female. 19 identified as men who have sex with men (MSM), 4 heterosexual and 3 bisexual. 19 were white British and 3 black African. There were no hepatitis B or C co-infections. ETV was prescribed as 400 mg once daily, co-prescribed with Truvada in 24 (92.3%) patients, Kivexa in one patient, and tenofovir/abacavir combination in one patient. 3 (11.5%) patients discontinued ETV therapy, 2 due to erythematous rashes in the first 16 days and one after 5 months due to reports of unpalatability. 10 (38.5%) patients chose to dissolve ETV. Median CD4 count at ETV initiation was 326 and median VL was 30,000c/ml. 6 (23.1%) patients had a starting VL $>100,000$. 6-month follow-up data for 19 (73.1%) patients showed a median CD4 of 461 and 18 (94.7%) patients had a VL <40c/mL. One patient had a viral load of 53c/ml with a reduction from a baseline of $>1,000,000$c/ml. 12-month data for 17 (65.4%) patients revealed a median CD4 count of 518 and all with VLs <40c/ml at a year. 18-month follow-up data of 11 (42.3%) patients showed a median CD4 of 587 and 9 with a VL <40c/ml. 2 patients had a detectable VL due to documented poor adherence. There was no significant change in median alanine transaminase (ALT), bilirubin, total cholesterol, high density lipoprotein or triglycerides from baseline to 6-, 12- or 18-month levels. Patient preference was towards a once-daily treatment for ETV. The availability of 200mg tablets and the ease of dissolvability have further increased acceptability. VL suppression was excellent with 100% <40c/ml at 12 months without any virological failures or significant adverse events. This data has shown that ETV is a highly acceptable, effective and well tolerated first-line treatment option.

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P276

Antiretroviral therapy in HIV-infected patients with tuberculosis and chronic viral hepatitis

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Background: The purpose of the study was to determine the influence of an HIV infection with tuberculosis or chronic viral hepatitis on efficiency and safety during 48 weeks of HAART.

Methods: HAART was received by 327 naïve HIV patients (pts). Clinical symptoms of an HIV infection had 273 pts (83.5%). The 1st group - 59 HIV pts with tuberculosis, the 2nd group - 217 HIV pts with chronic viral hepatitis, the 3rd group - 51 HIV-monoinfected pts. All pts were treated with 2 NRTI +EFV/PI. Evaluation of HAART efficacy based on the change of amount CD4 cells and RNA HIV level after 24 and 48 weeks therapy. Safety of HAART was evaluated on the frequency of adverse events and the change of laboratory abnormalities.

Results: After 24 weeks 61–72% of patients had undetectable RNA HIV level. CD4 cells increased in all groups. The percentage of pts with low CD4 cells (<200 cells/mm^3) decreased from 40–55% to 26–30%. After 48 weeks HAART CD4 cells increased by 90–127 cells/mm^3 (vs baseline) in all pts, however 17.4–26.7% pts saved low CD4 cells. Undetectable RNA HIV level registered in 75.6% pts with tuberculosis and 87.5–88.8% other pts. The proportion of pts who had adverse events was more among 1st and 2nd groups as compared as HIV-monoinfected pts (33–35% and 19%, $p<0.05$) after 24 weeks of therapy. After 48 weeks HAART the frequency of adverse events and laboratory abnormalities decreased to 20–28%

in 1st and 2nd groups and to 2% in 3rd group. The most frequent we observed CNS disorders (grade 1) due to EFV and gastrointestinal symptoms due to PI or Combivir (CBV). In pts with accompanying diseases the frequent increase of ALT level was observed in 30–40%, in HIV-monoinfected pts - 4–10%. The frequency of interruption HAART was greatest among patients with tuberculosis - 14.3% (vs 5% and 5.8% in patients with hepatitis and monoinfected patients). In general, the interrupt has been associated with the combination of side effects of antiretroviral and antituberculosis drugs.
Conclusions: Availability of chronic liver disease or tuberculosis almost have no influence on the HAART efficacy. However, essential increase the frequency of adverse events HAART that leads to change HAART regimen or interruption it.

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P277

Long-term durability of nevirapine-based ART in a cohort of 82 patients after induction with protease inhibitor treatment

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Purpose of the study: There is still an open question how to start antiretro-viral therapy (ART). This retrospective study shows results of a de-escalation strategy starting with a protease inhibitor (PI), followed by a nevirapine-based regimen over a period of five years.
Methods: All patients were ART-naïve and received PI in combination with two NRTIs. The PI was changed to nevirapine, when viral load (VL) stayed at least 12 months below the detection limit (50 or 40 copies/ml plasma). The median time to negative VL was measured. CD4, VL and liver tests were followed in 82 patients over at least 5 years before ART, during PI phase and over a median of 48 months after change to nevirapine. Resistance tests were performed - if possible - in patients before initiating ART.
Summary of results: 20 female and 62 male patients were treated for an average of 28 months with PI (43 × lopinavir, 5 × indinavir, 6 × invirase/r and 3 × fortovase/r, 8 × nelfinavir, 14 × atazanavir/r, 3 × norvir-mono plus two backbone NRTI in various combinations). There were 2 cases of hepatitis B and 5 HCV positives in the cohort. The mean CD4 before starting ART was 246/μl and the average VL was 421,038 copies/ml plasma (ranging from 1,050–9,000,000 copies/ml plasma). The median time to negative VL was 188 days. CD4 cells were rising by 364/μl during PI treatment to 610/μl. This was followed by a steady increase of another 70 cells/μl during the first year after changing to nevirapine. The median follow up after de-escalation to nevirapine was 48 months. Although the median CD4 was above 400/μl in all patients when changed to nevirapine, no severe liver toxicity was seen in the cohort. Change to NNRTI was safe in the group of 20 women with CD4 cells above 400/μl. Allergic skin reactions where seen in 7 out of 82 patients during the first 3 months after changing to nevirapine. No events of resistancies were seen in the group of 82 patients before and under treatment.
Conclusions: Long-term durability of nevirapine containing ART regimens following an induction phase with PIs is very high. No risk of treatment failure by resistance mutations was seen in a follow up of more than 48 months. Liver toxicity was not seen when ART was changed to nevirapine neither in female nor in male patients. The study was supported by Boehringer Ingelheim Pharma GmbH.

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P278

Antiretroviral therapy in na ve Romanian HIV patients

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Background: The peculiarity of Romanian HIV epidemic is the high number of long-time survivors, nosocomially infected with F subtype during early childhood. Although ART is provided for free, patients from certain regions are difficult to attain viral load (VL) and HIV resistance tests.
Objectives: To assess the durability of first-line antiretroviral therapy (1st ART) in Romanian HIV patients.
Methods: Retrospective assessment of new HIV diagnosed patients during 2005–2010, monitored every 24 weeks (wk) in HIV clinic from Galati - Romania, considering demographic data, HIV transmission pattern, immunity, HIV-RNA blood levels, co-morbidities, 1st ART regimen and adherence according to the national protocol. The endpoint was term on loss to follow-up, death or 96 wk of ART.
Results: 100 new diagnosed HIV patients since 2005 received 1st ART. Characteristics of naïve patients: median age on HIV diagnostic = 22.5 years old; sex ratio M/F = 53/47; living area rural/urban = 55/45; low literacy 26%; HIV infection pattern paediatric/sexual/ unknown = 29/61/10; advanced late presenters 51%; TB as HIV indicator 22%; VHB co-infection 22%; baseline av. CD4Ly = 171/mm^3. Experience of 1st ART: 2 NRTI + EFV 38% or LPV 27% or other protease inhibitor 35%. The reasons for 58% interrupting 1st ART: 9% dead, 17% abandoned, 18% failed, 12% developed adverse events and 2% drug-drug interactions. While 53% patients were adherent previous to endpoint, no more than 42% kept on 1st ART > 96 wk and recovered immunity with av. CD4Ly = 213/mm^3. Poor recovery of CD4Ly < 100/mm^3 was acquired by 13/48 patients with available HIV-RNA < 50 c/ml in 48 wk. The main risks below 24 weeks of 1st ART are the death ($p = 0.005$; OR = 36) and the adverse events ($p = 0.018$; OR = 24). Abandon rate ($p = 0.016$; OR = 5.14) is higher over 48 weeks. Regardless of 1st ARV regimen, adherence behaviour, immunologic benefits and ART durability were comparable. Viral failure is related to non-adherence ($p = 0.03$; OR = 4.5) and low literacy situation ($p < 0.001$; OR = 7.5). Mortality is 4.6 times higher in TB and 2 times in HBV co-morbidities.
Conclusions: Over a half of naïve HIV patients continued 1st ART less than 96 wk. 26% patients with low literacy are a vulnerable group and require individualised educational and adherence programmes. To improve the sustainability of the 1st ART in HIV patients from Galati needs to intensify the support for earlier HIV diagnostic and current virology follow-up.

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Experienced Patients

P279

Sustained virological response on second-line antiretroviral therapy following virological failure in HIV-infected patients in rural South Africa

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Purpose of the study: Over the last decade, a massive roll-out of antiretroviral drugs in resource-limited settings has taken place. In general, good virological responses on first-line antiretroviral therapy (ART) are achieved in most HIV-infected patients residing there. Still, a growing number of patients experience virological failure over time, resulting in an increasing need for second-line regimens [1]. This study describes the clinical, immunological and virological efficacy of protease inhibitor (PI)-based second-line ART in a clinic in rural South Africa.
Methods: An observational cohort study was performed on 210 patients (including 39 children) who initiated PI-based second-line ART at least 12 months prior to data collection. Biannual clinical, immunological and virological monitoring was performed. Primary endpoints were adequate virological response (HIV-RNA <400 copies/ml), full virological suppression (HIV-RNA <50 copies/ml), virological failure (HIV-RNA >1000 after initial virological response) and on-going viremia (HIV-RNA never <400 copies/ml for more than six months). Data were analyzed by an on-treatment (OT) and intention-to-treat (ITT) approach.
Results: Median duration of follow-up after switch to second-line treatment was 21 months [IQR 14–37]. 150/210 patients (71%, ITT) were in care and on treatment at the end of follow-up and 16/210 (8%, ITT) had died. After twelve months, an adequate virological response was seen in 106/143 patients (74%, OT), of which 86/143 (60%, OT) experienced full virological suppression and 20/143 (14%, OT) showed persisting low-level viremia (HIV-RNA between 50 and 400 copies/ml). Furthermore, virological responses remained stable after 24 months of second-line ART. Virological efficacy was similar amongst adult and pediatric patients. Median increase in CD4 counts from switch until end of follow-up was 145 cells/mm3 [IQR 1–397] in adults. As in first-line ART, we observed a lack of correlation between virological treatment failure and WHO-defined immunological failure in PI-based therapy.
Conclusions: Promising virological outcomes are achieved with PI-based, second-line antiretroviral therapy in adult and pediatric patients in rural South Africa. Results were sustainable during the two-year follow-up period with a high retention rate, although persisting low-level viremia occurred in a subset of patients. The observed viro-immunological dissociation emphasizes the need for virological monitoring.

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P280

Effectiveness of ritonavir-boosted protease inhibitor monotherapy in routine practice

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Backround: Recent trials have shown the potential benefits of ritonavir-boosted protease inhibitor (PI/r) monotherapy. As this alternative strategy has recently been included in European HIV treatment guidelines, its effectiveness needs to be assessed in routine practice.
Methods: From 1st January to 31 December 2011, we identified all patients receiving a current PI/r monotherapy at a university-based hospital setting using the Diamm database system. Antiretroviral-naïve patients who directly initiated PI/r monotherapy were excluded. Patients who continued PI/r monotherapy after ending participation in a clinical trial were also included. We performed a retrospective, descriptive analysis of demographic, clinical and therapeutic characteristics of these patients. For biological variables, the last available value in 2011 was retained.
Results: In 2011, among 3140 antiretroviral-treated patients in our department, 107 (3.4%) received PI/r monotherapy (lopinavir/r n $=58$, darunavir/r n $=$ 49). Of them, 30 (28%) started during 2011 and 31 (29%) continued after a prior trial. Two patients switched to DRV/r due to intolerance. Eighty-eight percent were male and median age at initiation was 45 years. The median time from starting multitherapy and switching to monotherapy was 30 months (range 2–117). At PI/r monotherapy initiation, median CD4 count was 567 cells/mm^3 and HIV RNA was below 50 copies/mL in 90% of patients. The median duration under PI/r monotherapy was 25.4 months (range 0.5–93). At the end of follow-up, median CD4 count was 643 cells/mm^3 and HIV RNA was below 50 copies/mL in 89% of cases. During 2011, 11 patients discontinued PI/r monotherapy, of whom 8 presented viral rebound. Only one patient exhibited major protease mutations. All these 8 patients achieved an undetectable viral load 3 months after therapeutic intensification.
Conclusion: This descriptive analysis shows that PI/r monotherapy in routine practice could be considered as an alternative and successful maintenance strategy, especially among patients who achieved an undetectable viral load while undergoing prior multitherapy.

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P281

Etravirine in protease inhibitor-free antiretroviral combination therapies

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Etravirine (ETR) is a next generation non-nucleoside reverse transcriptase inhibitor (NNRTI). The studies for ETR EMA approval were almost exclusively performed together with the protease inhibitor (PI) darunavir. However the fact that ETR can be active against NNRTI-pretreated HIV variants and that it is well tolerated suggests its application in PI-free antiretroviral combination therapies. Although approved only for PI-containing therapies, a number of ETR treatments without PIs are performed currently. To evaluate the performance of ETR in PI-free regimens, we analyzed the EURESIST database. We observed a total of 70 therapy switches to a PI-free, ETR containing antiretroviral combination with detectable baseline viral load. 50/70 switches were in male patients and 20/70 in females. The median of previous treatments was 10. The following combinations were detected in the EURESIST database: ETR + MVC + RAL (20.0%); ETR + FTC + TDF (18.6%); 3TC + ETR + RAL (7.1%); 3TC + ABC + ETR (5.7%); other combinations (31.4%). A switch was defined as successful when either $\leq$50 copies/mL or a decline of the viral load of 2 $\log_{10}$, both at week 24 (range 18–30) were achieved. The overall success rate (SR) was 77% (54/70), and for the different combinations: ETR + MVC + RAL = 78.6% (11/14); ETR + FTC + TDF = 92.3% (12/13); 3TC + ETR + RAL = 80.0% (4/5), 3TC + ABC + ETR = 100% (SR 4/4); and for other combinations = 67.6% (23/34). These SR values are comparable to those for other therapy combinations in such pretreated patients.

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P282

Use of maraviroc in clinical practice: a multicenter observational study

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Purpose of the study: Promising research suggest that maraviroc (MVC) has favourable clinical outcome in HIV-infected patients (pts). Aim of the study is to assess: durability, safety profile and immunovirological recovery in a large MVC-based cohort.
Methods: All HIV pts treated with antiretroviral therapy (ART) containing MVC for at least 6 months (all viruses CCR-5 tropic analyzed by genotypic and phenotypic test) were recruited in an observational multicenter study. Eight Infectious Diseases Centers in Liguria and Piedmont (Italy) collected at baseline and every 3 months demographics, clinical and immunovirological data on a web-based system (by MedinfoDist, University of Genoa). We used SPSS for Pearson Chi square test and for generalized estimating equation (GEE); in this model for longitudinal data and frequency analysis we considered altered: TCD4 + $\leq$350/mmc, HIVRNA > 50 cp/ml, total cholesterol > 200 mg/dl, triglycerides > 160 mg/dl, transaminase > 40 mg/dl, creatinine > 1.3 mg/dl and we divided data in 5 time periods: baseline, 1–6, 9–12, 15–24 and 24–45 months.
Summary of results: We enrolled 55 pts: 36 (65%) males, median age 49.6 years (yrs) (range [r] 18.2–76.6, IQR 44.5–53.3), 11 (20%) HCVRNA-positive, 4 (7%) HBsAg-positive, 1 both infection. Twenty-four (44%) pts were classified as CDC C stage, median nadir TCD4 + was 219/mmc (r 11-529, IQR 125–317), median duration of ART was 15.3 yrs (r 1.3–27.3, IQR 12–16.8), median duration of treatment with MVC was 23 months (r 6–47, IQR 14–36). At baseline 42 (76%) pts had HIVRNA > 50 cp/ml, 11 (20%) HIVRNA $\leq$50 cp/ml, 2 (4%) pts no data; on treatment at the last examination 53 pts (96%) had HIVRNA $\leq$50 cp/ml, 2 pts still had HIVRNA > 50 cp/ml (CCR5 tropic) and median TCD4 + count was 469/mmc (r 73–1802, IQR 302–592). One pt died and only 2 pts shifted to X4. Chi square test at 9–12 months showed p = 0.0001 and the 80% of pts had TCD4 + > 350/mmc; at the same observation time 83.3% of pts had HIVRNA $\leq$50 cp/ml (p = 0.0001). About cholesterol, triglycerides, transaminase and creatinine no significative differences were found and the median value showed no changes.
Conclusions: In our study a majority of pts treated with ART containing MVC achieved a count of TCD4 > 350/mmc and HIVRNA undetectable within 9–12 months. This regimen is a safe, feasible option and in pts with a poor immunological stage, MVC offered a remarkable TCD4 + count gain with limited X4 strains onset.

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P283

A phase 4, single-arm, open-label, pilot study of maraviroc, raltegravir and darunavir/r in HIV-1 adults with triple class failure: TERCETO study

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The purpose of this phase 4, single-arm, open-label study was to evaluate the safety, tolerability, efficacy, antiviral and immunological activity of maraviroc (MVC) in combination with raltegravir (RGV) and darunavir/r (DRV/r) in adult HIV-1 infected patients (pts) with limited treatment options. HIV-1 pts with documented virologic triple class failure or multi-drug class resistance defined as the presence of Q151 complex, 69 insertion complex and/or $\geq$3 TAMs for NRTIs and K103N, G190S + Y181C or Y188L mutants for NNRTIs and $\geq$3 RAMs (L10F/I/R/V; M46I/L; I54V/M/L; V82A/F/T/S; I84V; L90M) for protease inhibitors (PIs) were offered a triple drug regimen consisting of MVC 150 mg BID, RGV 400 mg BID and DRV/r 600/100 mg BID. Safety, lipid profile and virologic efficacy were evaluated at week 4, 12, 24, 36 and 48. Between January 2010 and March 2012, 27 pts were enrolled. Screening failure rate was 52% due to undetectable viral load (pVL) or non R5 tropism type (Trofile)™. Despite being heavily pre-treated pts, only 26% had negative tropism test at SCR. Baseline characteristics of 13 included pts were: 77% male, median age 43 years (IQR: 40.1–48.6), 38% had a prior AIDS-defining condition. Median BSL pVL was 23,350 cps/mL (4.4 $\log_{10}$) (IQR: 11,236–55,785) and median CD4 was 222 cells/mm^3 (IQR: 179–318). Median time on NRTIs, NNRTIs and PIs were 10.7 (8.6–13.7), 1.7 (1.3–7.6) and 5.4 (4.7–10) years respectively. Pts had received a median of 2 PIs (IQR: 2–3). 8/13 pts showed thymidine analogue-associated mutations (TAMs), and $\geq$2 were present in 5/13. Detectable NNRTI resistance-associated mutations (RAMs) were

present in 10/13 patients. 9/13 had ≥4 primary PI RAMs. At 48 weeks, 2 pts had discontinued therapy (OIs related death (cryptococcal meningitis) = 1, withdrawn from the study on W36 due to blips despite not achieving criteria for virologic failure = 1) and the remaining pts (11/13) achieved undetectable pVL and increased CD4 in 133 cell/mm^3 from BSL (IQR: 81–174.5). Median total cholesterol levels increased from 162 mg/dL (IQR: 135-188) to 215 mg/dL (IQR: 182–237) between BSL/W48; median change in cholesterol levels: 40 mg/dL (IQR: 6.5-66). Salvage therapy including MVC, RGV and DRV/r achieved sustained reductions in pVL (<50 copies/mL) through 48 weeks of therapy in this pilot study with no treatment limiting toxicity.

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P284

High viral load, previous fosamprenavir use and more recent HIV diagnosis correlate with darunavir failure in salvage therapy in Sao Paulo, Brazil

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Purpose of the study: Efficacy of DRV-containing regimen in antiretroviral-experienced patients in Brazil is unknown. The aim of this study was to evaluate the prevalence and risk factors associated with virologic failure (VF) to DRV containing salvage regimen in experienced HIV-infected patients in Sao Paulo and also determine the prevalence of DRV resistance associated mutations (RAM) in this population.

Methods: Retrospective study of 131 patients who started a DRV-containing salvage regimen between 12/2007 to 12/2009 in 2 centers in Sao Paulo. Protease resistance mutations listed by 2011 IAS-USA panel update were considered. Genotypic sensitivity score (GSS) was calculated for the proposed regimen using the 2008 Rega algorithm. We have assessed VF during 48 weeks of follow up and VF was defined as the failure to achieve viral suppression in 48 weeks or viral rebound after suppression. Stopping the use of DRV for any reason was also considered VF.

Summary of results: We analysed 131 patients, 71% male, median age 44y. More than half of the patients had a baseline CD4 cell count <200/mm^3 (58,9%) although only 21,4% presented a VL ≥100.000 copies/ml. 78,6% had previous used more than 2 PI and more than half of the patients harbored viruses with at least 11 IAS PI resistance mutations (59,5%) The majority of patients had less than 2 DRV RAM (84,7%) and the most prevalent major and minor DRV RAM were respectively I84V (24,4%) and L33F (34,3%). Most patients (79,4%) have received more than 2 active drugs in their regimen. Twenty patients (15,3%) have failure in achieving VL <50copies/ml at 48 weeks. Ten patients were lost of follow up and the remaining 10 were treatment failure. In multivariate analysis, VL ≥ 100.000 copies/mL (p = 0,002), less than 15 years of HIV diagnosis (p = 0,013) and previous fosamprenavir use (p = 0,027) were independently predictive of VF.

Conclusions: This study, conducted in routine clinical conditions, is probably the large cohort to evaluate risk factors to VF with DRV containing regimen worldwide and is the first one to evaluate prevalence of VF with DRV containing regimen in Brazil. We found an elevated response rate in this population (84,7%) which couples with the low number of DRV RAM despite the elevated number of previous PI used and by the high GSS. The factors associated with VF were similar to previous reports except for the time of HIV diagnosis, and one can speculate that this correlates with lower adherence in this group.

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Switch Studies

P285

SPIRIT: switching to emtricitabine/rilpivirine/tenofovir DF single-tablet regimen from boosted protease inhibitor maintains HIV suppression at week 48

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Antiretroviral regimen simplification improves quality of life and medication adherence while reducing the risk of HIV virologic failure (VF) and long-term drug-related toxicities. Emtricitabine/rilpivirine/tenofovir disoproxil fumarate (FTC/RPV/TDF) is a well-tolerated and efficacious once-daily single-tablet regimen (STR) treatment option. Here we report the Week 48 safety and efficacy results of SPIRIT, the first study to evaluate switching from boosted protease inhibitor (PI + RTV)-based HAART to a simplified regimen of FTC/RPV/TDF STR. SPIRIT is a phase 3b, randomized, open-label, multi-center, international, 48-week study to evaluate the safety and efficacy of switching from PI + RTV regimens to FTC/RPV/TDF in virologically-suppressed HIV-1 infected participants. Participants were randomized 2:1 to switch to FTC/RPV/TDF at baseline or maintain their current PI + RTV regimen with a delayed switch to FTC/RPV/TDF at Week 24. The primary endpoint was non-inferiority (12% margin) of FTC/RPV/TDF relative to PI + RTV regimens in maintaining plasma HIV-1 RNA <50 copies/mL at Week 24 by FDA snapshot analysis. Plasma HIV-1 RNA levels were assessed at screening, baseline, and at Weeks 4, 8, 12, 24, (28 and 32 for delayed switch participants), 36, and 48 or early termination. A total of 476 participants were randomized and received at least 1 dose of study drug (317 FTC/RPV/TDF; 159 PI + RTV + 2NRTIs). Baseline characteristics were similar across treatment arms. The primary endpoint of non-inferiority at Week 24 was met (HIV-1 RNA <50 copies/mL by FDA snapshot analysis 93.7% FTC/RPV/TDF vs. 89.9% PI + RTV + 2NRTIs; difference 3.8%, 95% CI: −1.6 to 9.1]). Through Week 48, 88.3% of subjects switching to FTC/RPV/TDF at baseline maintained virologic suppression (HIV-1 RNA <50 copies/mL by FDA snapshot analysis). The rate of virologic suppression at Week 48 for the 152 participants who switched to FTC/RPV/TDF at Week 24 was

comparable to the rate of virologic suppression at Week 24 for those who switched to FTC/RPV/TDF at baseline (delayed switch to FTC/RPV/TDF 92.1%; baseline switch to FTC/RPV/TDF 93.7%). In the Week 48 analysis of SPIRIT, the first study to evaluate switching to FTC/RPV/TDF STR from a PI + RTV-based regimen in virologically-suppressed, HIV-1-infected participants, virologic suppression was maintained regardless of whether participants switched to FTC/RPV/TDF at baseline or at Week 24.

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P286

A randomized pilot study of tenofovir/emtricitabine (TDF/FTC) + boosted atazanavir (ATV/r) vs. raltegravir (RAL BID) + ATV/r vs. RAL BID + ATV BID

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Patients virologically suppressed on TDF/FTC + ATV/r may require alternative regimens that maintain suppression while addressing some drug-related side effects. We explored two alternative regimens that replace RTV and/or TDF/FTC. This open-label exploratory pilot trial enrolled 43 patients on TDF/FTC + ATV/r. Subjects were randomized to one of three arms. Arm 1 (n = 15) replaced TDF/FTC with RAL 400 mg BID while continuing ATV/r. Arm 2 (n = 14) made two changes: TDF/FTC was stopped and RAL BID was used instead; ritonavir was stopped and ATV 300 mg BID was used. Arm CTL (n = 14) continued the baseline (BL) regimen. The week 48 final endpoint is summarized. The primary endpoint was maintaining virologic suppression (< 40 c/mL); secondary endpoints compared safety measures. Overall mean age was 46, with 74% Caucasian, 21% black race and 12% female; similar characteristics noted across arms. Through week 48, all but two patients maintained virologic suppression; both virologic failures (> 200 c/mL on two consecutive tests) were on arm 2; both reported adherence problems and no resistance mutations were detected. Overall CD4 counts were 534/mm^3 at BL and 555/mm^3 at week 48. There was a significant CD4 cell count difference favoring CTL (+52/mm^3) vs. arm 2 (−14/mm^3), p = 0.03. No significant differences across arms were noted in lipid fractions or other lab tests. There were no clinically significant EKG changes across arms. Among AEs of interest through week 48, there were more neurologic AEs on arm 1 (n = 7) and 2 (n = 6) vs. CTL (n = 1), and more musculoskeletal events noted on arm 2 (n = 7) vs. arm 1 (n = 3) and CTL (n = 1). Quality of life was measured with a self-assessment Likert scale. Scores were similar across arms despite the BID dosing in two arms. Self-reported adherence using 3-day recall was > 95% in all three arms at both baseline and week 48. In this randomized pilot study, two of the three arms maintained virologic suppression in all subjects; there were two virologic rebounds in arm 2. No resistance mutations were detected in either, and adherence issues were noted for both subjects. We also noted that the CD4 cell change was significantly less on arm 2, and there were more neurologic and musculoskeletal AEs on arm 2 vs. CTL. In this study, the use of ATV/r with either TDF/FTC or RAL was successful over 48 weeks, but unboosted BID ATV 300 mg + BID RAL 400 mg as an alternative in virologically suppressed patients should be used with caution.

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P287

Effects of switching to PI monotherapy on measures of lipoatrophy: meta-analysis of six randomized HIV clinical trials

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Background: Switching from triple combination treatment to protease inhibitor (PI) monotherapy may prevent or reverse adverse events related to long-term nucleoside analogues. Lipoatrophy is associated with long-term use of thymidine analogues (zidovudine and stavudine).
Methods: A detailed MEDLINE search was conducted to identify randomised clinical trials of triple combination treatment versus PI monotherapy. Summary results from analysis of changes in body composition (DEXA analysis) were collected: the mean change in limb fat and trunk fat to Week 48 or 96, and the percentage of patients with lipoatrophy (20% reduction from baseline in limb fat) or lipohypertrophy (20% rise from baseline in trunk fat).
Results: Six randomised trials of PI monotherapy versus triple therapy with data on body composition changes, measured by DEXA scanning at baseline and Week 48 or 96, were identified: Abbott-613 (LPV/r vs ZDV/3TC/EFV, induction-maintenance trial, n = 105), Monark (LPV/r vs ZDV/3TC/LPV/r, first-line trial, n = 63), Kalesolo (LPV/r vs LPV/r + 2NRTIs, switch trial, n = 42), MONOI (DRV/r vs DRV/r + 2NRTIs, switch trial, n = 156), MONARCH (DRV/r vs DRV/r + 2NRTIs, switch trial, n = 30) and KRETA (LPV/r vs LPV/r + ABC/3TC, switch trial, n = 74). In the meta-analysis, there were greater rises in limb fat in the PI monotherapy arms than the triple therapy arms (mean difference = 277g, 95% CI = +36 to +517g, p = 0.024). The percentage of patients with lipoatrophy was significantly lower in the PI monotherapy arms (4%) than the triple therapy arms (20%), (p = 0.0005). There was no difference between PI monotherapy and triple therapy for mean change in trunk fat (mean difference = −73g, 95% CI = −621 to +475g, p = ns). There was also no significant difference in the risk of lipohypertrophy between the PI monotherapy arms (32%) and the triple therapy arms (27%) (p = ns). In each of the four analyses, there was no evidence for heterogeneity of treatment effects between the trials (Cochran's Q tests, p = ns for each comparison).
Conclusions: In this meta-analysis, the risk of lipoatrophy was significantly lower for patients taking PI monotherapy, compared to triple therapy. There was no significant difference between the arms for lipohypertrophy. However, several of the trials included zidovudine in the control arm, which carries a higher risk of lipoatrophy than tenofovir and abacavir, which are now more widely used.

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P288

Novel Kivexa-based regimens in early courses of treatment for HIV infection

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Background: As the long-term efficacy of antiretroviral therapy regimens is confirmed, we need to identify additional combinations

with long-term safety and potency, while also favoring simplicity of administration. In this light, we have undertaken a review of the use of abacavir/lamivudine (Kivexa, KVX)-based regimens using integrase or CCR5 inhibitors as the third agent.

Methods: A retrospective chart review was undertaken, with informed patient consent. We identified all the patients in whom KVX was prescribed (following appropriate HLA-B5701 screening) with either raltegravir (RGV) or maraviroc (MVC) as initial therapy or as a switch from another regimen for reasons other than virologic failure. Virologic efficacy over 48 weeks was evaluated, along with specific drug-associated toxicity, adherence, and regimen modifications.

Results: A total of 38 patients (5 women) were evaluated, 24 on KVX/RGV, 13 on KVX/MVC, 1 on KVX/RGV/MVC. This was used as initial therapy in drug-naïve subjects in three cases, and was selected as a modification of previous (current or not) therapy in 35 cases. Switches included replacement of the third agent with RGV or MVC (n = 13), replacement of the NRTI backbone with KVX (n = 13) or both. In all cases, the change was implemented to address a current or previous medication-associated toxicity, most commonly to address jaundice (n = 8), diarrhea (n = 5) or reduced renal function (n = 5). Patients were predominantly MSMs (n = 17) or IDUs (n = 13) with a mean baseline CD4 cell count of 363 cells/mm^3, and plasma viral load of 46407 copies/mL (20 with full suppression at time of study entry). At 48 weeks, 34/38 (89%) achieved or maintained full suppression, with a mean CD4 count of 553 cells/mm^3. Virologic failure with the development of the M184V mutation was observed in 3/4 non-suppressed patients, and a loss of CCR5 tropism and RGV resistance were observed in one case each, all in the context of reduced adherence. There were no treatment discontinuations for toxicity and no medication-associated serious adverse events.

Conclusion: KVX-based regimens are safe and effective alternatives to more commonly used regimens in clinical practice, and offer the benefit of good long-term tolerability and little or no need to enhance follow-up for laboratory-based abnormalities. Consideration should be given to non-NNRTI and non-PI-based regimens to address issues of toxicity and simplification without apparent loss of efficacy.

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P289

Etravirine with 2 NRTIs: an effective switch option for ARV simplification and side effect management

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Etravirine (ETV) has been approved for use in treatment-experienced patients based on results of the Duet clinical trials [1]. Less experience exists with ETV in earlier stages of treatment. ETV has a favorable genetic barrier, lipid profile, and little associated CNS toxicity. These characteristics make ETV attractive as a switch strategy for simplification and/or management of side effects. A retrospective chart review was conducted at a large urban HIV clinic in Toronto. All patients who were switched to ETV plus 2 nucleosides and whose viral load (VL) was <200 copies/ml at the time of switch were included. Maintenance of viral suppression, CD4 and lipid changes at 24 weeks and reason for switch to ETV are reported. Seventy-three patients (67 male) were identified. Mean age was 46 ± 10 and mean duration of HIV infection was 11.7 ± 7.4 years. Switches were from efavirenz = 29, atazanavir = 23, lopinavir = 16, other = 5. Duration of prior regimen was long; median 195 weeks. CNS and GI intolerance were the most common reasons for switches. At the time of analysis, 63 patients had reached week 24. Three patients had discontinued ETV prior to week 24, 3 LTF/U, 4 had <24 weeks follow-up. 92% (67/73) maintained VL suppression (ITT); failures were 6 patients who stopped/lost-to-follow-up prior to week 24. On treatment, CD4 increased and lipid decreased changes as seen below. All patients who switched due to CNS side effects had subjective improvement.

	Baseline	Change from baseline to week 24 (OT, n = 63)	P value
CD4 (cells/mm^3)	632 ± 269	$+49 \pm 137$	<0.01
Total cholesterol (mmol/L)	4.76 ± 1.11	-0.57 ± 0.77	<0.01
HDL (mmol/L)	1.20 ± 0.36	-0.05 ± 0.21	0.06
LDL (mmol/L)	2.71 ± 1086	-0.40 ± 0.73	<0.01
Triglycerides (mmol/L)	2.06 ± 1.86	-0.55 ± 1.76	0.02

Switch to ETV plus 2 nucleosides maintained viral suppression, improved lipid profiles and improved side effect profile in this selected group of patients. 48 week f/u will be presented.

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P290

Effectiveness and tolerability of abacavir-lamivudine-nevirapine (ABC/3TC/NVP) in a multicenter cohort of HIV-infected ARV-experienced patients

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Purpose of the study: Very scarce information has been published to date with the combination of ABC/3TC/NVP but it is currently being used in clinical practice in many centers in Spain. Our aim was to present the clinical experience with this regimen in a cohort of adult HIV-infected pts.

Methods: Retrospective, multicenter, cohort study. Consecutive adult HIV-infected ARV-experienced pts, HLA-B*5701-negative, who started ABC/3TC/NVP between 2005–2010, with at least one follow-up visit, were included. Demographic, clinical and laboratory variables were assessed at baseline, month 1, and every 3–4 months thereafter. The primary end point was HIV-1 viral load (VL) <40 c/mL at 48 weeks. Data were analyzed by intent-to-treat (ITT) (non-completer = failure) and on treatment (OT).

Summary of results: 227 pts were included and followed up for a median of 30 (0.5–76) months. 75% male, 47 (24–83) years, 21% AIDS, 13% HCV+, baseline CD4 570 (32–1404) cells/μL and VL undetectable in 90% with a median of <1.59 (<1.59–5.1) log. Most pts were receiving NVP (63%), ABC (25%) or both (4%) in the previous regimen. ABC/3TC/NVP was initiated due to toxicity (42%), simplification (35%) or other reasons (22%) including to reduce drug

cost. After 48 weeks, VL was <40 c/mL in 82% (ITT) and 94% (OT), and in 94% (OT) after 96 weeks. CD4 increased $+63$ ($p<0.001$) and $+77$ ($p<0.001$) cells/μL after 48 and 96 weeks, respectively. One or more drugs of the regimen were discontinued in 18% of pts during follow up: toxicity (7%), virologic failure (3%), lost to follow-up (3%), unrelated death (0.4%) or other reasons (4%). No significant differences were observed in ALT, AST, or triglyceride changes during follow up. A significant increase of 7%, 10% and 14% was observed in total cholesterol, LDLc and HDLc, and a significant decrease in TC/HDL ratio (-5%, $p=0.004$) after 96 weeks, respectively.
Conclusions: In this particular cohort of ARV-experienced pts previously receiving NVP or ABC, a combination of ABC/3TC/NVP was safe and mantained virologic suppression in the vast majority of pts, with rates similar to other switch strategies. A favourable lipid profile was observed after 96 weeks of follow up.

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P291

TRANxITION 144-week results: switching virologically stable HIV patients from immediate-release nevirapine (NVP IR) to extended-release NVP (XR)

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Purpose of the study: TRANxITION compared the efficacy and safety of switching virologically suppressed patients from NVP IR (200 mg BID) to NVP XR (400 mg QD) and demonstrated the non-inferior efficacy of NVP XR in virologically suppressed patients. Here, post-48-week safety and efficacy results of patients initially randomized to NVP IR and allowed to switch to NVP XR after 48 weeks, were compared to patients on NVP XR throughout the study.
Methods: TRANxITION was an open-label, parallel-group, non-inferiority clinical trial where adult HIV-1 patients receiving NVP IR plus a fixed-dose NRTI combination of lamivudine (3TC)/abacavir (ABC), tenofovir (TDF)/emtricitabine (FTC) or 3TC/zidovudine (ZDV), with undetectable viral loads (VL) were initially randomized (2:1) to NVP XR or NVP IR. After week 48, patients initially randomized to NVP IR were allowed to switch to NVP XR. Primary endpoint was continued virologic suppression (VL <50 copies/mL) at week 24. Secondary endpoints included long-term follow-up at 48 and 144 weeks.
Summary of results: At week 48, proportions of patients with virologic response (LLOQ $=$ 50 copies/mL TaqMan, FAS) were 88.5% (131/148) NVP IR BID arm, and 88.8% (262/295) NVP XR QD, with an observed difference of 0.3% (95% CI -6.1, 6.7). Division of Acquired Immunodeficiency Syndrome (DAIDS) grade 3 and 4 events were similar for the NVP XR and NVP IR groups at week 48, 6.4% (19/295) vs. 6.1% (9/148) respectively, although serious AEs were slightly higher in the NVP XR group (10.2%, 30/295, vs. 8.1%, 12/148 for the NVP-IR group). After week 48, all but 13 patients in the NVP IR arm switched to NVP XR. At week 144, proportions of patients with virologic response were 115/121 (95.0%, patients switching from IR to XR after week 48 [IRpost48XR]), and 238/250 (95.2%, patients on XR throughout [XRpost48]). DAIDS grade 3 and 4 events were similar for both post-week-48 XR groups at week 144, with (10/130, 7.7%, [IRpost48XR] vs. (31/276, 11.2% [XRpost48]), while serious AEs were higher in the XRpost48 patients (54/276, 19.6% vs. 17/130, 13.1% for the IRpost48XR group).
Conclusions: NVP XR QD resulted in continued virologic suppression at weeks 48 and 144. While fewer patients remained in the study post-week 48, both XR groups had high virologic response rates. Rates of serious AEs were modestly higher than seen at week 24 in both post-week-48 XR arms up to week 144, most likely due to the open-label design of the study.

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P292

Reasons for antiretroviral treatment changes in Spanish HIV 1 patients in 2011: SWITCH AUDIT study

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Background: Until the past decade, immune/viral failure was the main reason for antiretroviral treatment changes. After HAART generalization the management of antiretroviral treatment toxicities was the most prevalent reason for treatment modification. Today, with the advent of new more potent and less toxic drugs as well as more convenient combinations may have changed the situation. We aim to describe the main reasons that today leads to ART changes in HIV+ patients in Spain in the current clinical practice.
Methods: Multicentre, national, cross-sectional epidemiological study. Eligible patients had to be HIV+, >18 years old and under current ART that was going to be changed by any reason. Patients did sign inform consent. The study consisted in a single visit (change of treatment) in which data on social and demographic characteristics, HIV disease and ARV treatment were collected.
Results: 349 patients were included; mean age: 43.7 ± 8.9 y, 70.5% male and 89.1% Caucasian. Main transmission categories were IVDU (36.4%) and heterosexual (36.4%). Mean time from HIV diagnosis was 11.3 ± 7.6 y. 59.5% were CDC C category. Median CD4 nadir was: 155 cells/mm^3 and median CD4 at the time of switching was 467 cells/mm^3. 64.1% had undetectable viral load (<50 copies/ml); 40.1% had HCV or HBV co-infection. Main reasons for treatment change were simplification (40.2%), treatment toxicities (29.2%) and immune/viral failure (20.1%). No significant correlations were found between reason for changing treatment and age, gender, race, nationality and level of education. Simplification was significantly the main reason both in employed and unemployed patients ($p<0.01$).
Conclusions: Currently, treatment simplification was the most prevalent reason for a change of treatment even in advanced lines of treatment. This is so probably because of the advent of ARV drugs that are more potent and effective, with less toxicity and more convenient. Treatment simplification was significantly the first cause of treatment change in those patients who are currently working or seeking for a job. This highlights the need for simpler regimens that can adapt to an active life.

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P293

Switch from efavirenz to nevirapine, with full dose after one week: efficacy, safety and pharmacokinetics

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Purpose of the study: In a prior study in patients switching from efavirenz (EFV) due to neurologic side effects, we compared nevirapine (NVP) full dose (200 mg twice-daily) from the beginning to the standard dosage (200 mg once-daily for two weeks and then increase to 200 mg twice-daily) [1]. Adequate concentrations were seen with the experimental arm but with a trend towards higher toxicity, with 25% of patients having to stop NVP due to rash or hepatitis. Our hypothesis is that NVP 200 mg daily for 1 week and then increasing it to 200 mg twice-daily will achieve adequate plasmatic concentrations with better tolerability.
Methods: Patients taking an EFV-based regimen were offered to switch to NVP without changing the backbone. Patients received NVP 200 mg once-daily for 1 week and 200 mg twice-daily thereafter. EFV and NVP plasma trough levels were determined at days 0, 3, 7, 14, 30 and 90. Blood tests were performed at each visit and AE recorded. Chi-squared and Fisher exact test were used for qualitative variables and Mann-Whitney U and Wilcoxon signed rank tests for quantitative variables.
Summary of results: 22 patients were included, 73% male, median age 48 years, median CD4 569 cell/mm^3, all with CV <25 copies/mL and 41% had HCV co-infection. Reasons for switch were CNS symptoms in 50%, dyslipidemia in 46% and pregnancy desire in 4%. Backbone was TDF + FTC in 73% and ABC + 3TC in 27%. Median NVP trough concentrations were 2.2, 2.7, 4.3, 4.5 and 5.5 μg/mL at 3, 7, 14, 30 and 90 days, respectively. 35% of patients had NVP plasma trough levels >3 μg/mL at day 7 and 88% at day 14. EFV concentrations were subtherapeutic (<1 μg/mL) at day 7 and undetectable in all but one patient at day 14. There was a significant increase in GGT ($+22$ mg/dL, $p = .013$) and significant decreases in total cholesterol (-16 mg/dL, $p = .035$) and triglycerides (-50 mg/dL, $p = .005$) after 3 months. In the first month, two patients had to stop NVP due to rash and one due to rash and hepatitis. There was no correlation between plasma concentrations and rash or hepatitis. There were no virologic failures.
Conclusions: Nevirapine concentrations were adequate when dose was increased to 200 mg twice daily after one week, maintaining virologic efficacy and with good tolerability.

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P294

Study to determine the improvement in neuropsychiatric symptoms after changing the responsible antiretroviral drug to nevirapine: the RELAX study

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Objectives: Primary - evaluate the improvement in psychiatric symptoms attributable to changing the antiretroviral drug responsible for such symptoms to nevirapine (NVP). The tools used were a sleep test (the Pittsburgh Sleep Quality Index [PSQI]) and the Hospital Anxiety and Depression Scale (HADS). Secondary - determine the neuropsychiatric disorders and evaluate adherence to treatment and quality of life.
Methods: Prospective, observational post-authorisation study that included HIV-1 patients from 36 Spanish hospitals who satisfied the following criteria: age over 18 years; change of antiretroviral treatment to NVP due to CNS side-effects; a PSQI score >5 (significant sleep disturbance); a HADS score ≥ 10 on the day of starting NVP treatment; and no psychoactive drug treatment initiated during the 6 weeks prior to starting treatment with NVP. Other data gathered from the patients included clinical and demographic details and administration of the Epworth somnolence scale, the Medical Outcomes Study-short form 30 items (MOS-SF-30) quality of life scale and the Simplified Medication Adherence Questionnaire (SMAQ). Evaluations were performed at baseline, 1 and 3 months after the change.
Results: 129 patients were included (73.6% men; mean age, 43.2 $\pm$ 9.8 years; 36.5% homosexual, 30.2% heterosexual; 28.7% drug users; 38% AIDS; 33.3% co-infection). The drug changed was efavirenz in 89.9% of cases. The reason for the change was sleep disturbances in 75.2%, anxiety in 65.1%, other psychiatric disturbances in 38.7%, attention disturbances in 31%, and other reasons in 31%; a mean of 2.4 neuropsychiatric disturbances were detected in each patient. CD4 rose from 582 $\pm$ 261 to 619 $\pm$ 299 (non-significant difference). Only three patients had developed an HIV viral load at the end of the study. The differences produced by the change are shown in Table 1. 29 patients withdrew from the study, for the following reasons: 9 for NVP-related toxicity (7 cases of rash and 2 of hepatitis); 7 for loss to follow-up; 4 for voluntary withdrawal; 9 for other reasons.
Discussion: The study shows that the change to NVP from a drug that is causing neuropsychiatric disturbances (principally, efavirenz) is effective in resolving those disturbances, with an improvement in all the parameters studied (quality of sleep, anxiety/depression and

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	Baseline (n = 129)	1 month (n = 100)	3 months (n = 100)	p value, baseline-1 mo	p value, baseline-3 mo
Percentage of patients with a PSQI score >5, suggestive of a significant alteration of sleep	96.9%	60.7%	44%	<0.001	<0.001
Percentage of patients with clinical problems of anxiety and depression, HADS	86.8%	46.4%	32%	<0.001	<0.001
Mean score and percentage of patients with normal somnolence, Epworth scale	8.3 $\pm$ 4.7/(65.9%)	6 $\pm$ 4 (89.3%)	5.5 $\pm$ 3.6 (91%)	<0.001/0.001	<0.001/0.001
Percentage of compliant patients, SMAQ	65.9%	75.9%	81%	0.036	0.013
Percentage of patients with a good quality of life, MOS-SF-30	57.5 $\pm$ 18.9%	69.8 $\pm$ 19.7%	73.6 $\pm$ 16.8%	<0.001	<0.001

somnolence). This leads to better adherence and a better quality of life with no detriment to their immunological and virological control.

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P295

Switching to darunavir/ritonavir monotherapy (DRV/r mx): effect on kidney function and lipid profile

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Purpose of the study: DRV/r mx is proposed as a therapeutic option for patients with NNRTI toxicity. We aimed to evaluate the impact of switching to DRV/r mx in kidney function and lipid profile.
Methods: From March 2009 to June 2012 we conducted an observational, retrospective multicenter study evaluating patients switching to DRV/r mx. Kidney function and lipid levels were measured at baseline and at 48 weeks of DRV/r mx. Renal function was estimated by MDRD GFR. Comparative analyzes were performed using Student's t test for paired samples.
Summary of results: We identified 147 patients: women 30.6%, age 49 ± 7yr, 45% IDU, 27.9% heterosexuals, AIDS 41.5%, Caucasian 58.5%, HCV-coinfected 48%, baseline HIV-RNA < 1.7 log 93.2%, nadir and baseline CD4 count 180 ± 150 and 663 ± 297 cells/mm^3, length of antiretroviral therapy 12.83 ± 4.6 years and of HIV-RNA < 1.7 62 ± 43 months. The rate of HIV-RNA < 1.7 at week 48 were 78.9% ITT; 92.6% OTT. Improvement was observed in kidney function after 48 w of DRV/r mx, mean 0 w vs 48 w MDRD (84.43 ± 22.32 vs. 87.88 ± 23.24; p = 0.001). Subgroup analysis demonstrated significantly higher increases in MDRD in patients with a prior tenofovir-based regimen (TDF), 83.14 ± 21.86 and 48 w 88.97 ± 21.23; p = 0.000, and those with a protease inhibitor plus TDF-based regimen (mean 0 w vs 48 w MDRD 80.66 ± 22.53 87.09 ± 23.37; p = 0.002). Lipid profile improved significantly in terms of reduction in total cholesterol (mean 0 w col: 192.47 ± 42.44 vs mean 48 w col 170.48 ± 70.79; p = 0.013) with an improvement in the ratio total cholesterol/ HDL (0 w 4.46 ± 1.62 vs 48 w ratio 3.97 ± 2.12; p = 0.000). There were no significant changes in lipid profile in subgroup analysis according to previous antiretroviral treatment change.
Conclusions: Patients switching to DRV/r monotherapy showed significant improvement in kidney function and lipid profile at 48 w, both implied on cardiovascular risk.

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P296

Switching to unboosted atazanavir combined with tenofovir and emtricitabine is effective as maintenance therapy

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Purpose of the study: Due to a pharmacokinetic interaction leading to reduced serum levels of atazanavir (ATV) when combined with tenofovir (TDF), it is recommended to add ritonavir (r) as a booster for atazanavir when combined with TDF. However, ATV is also licensed for use as an unboosted drug. In our clinic many patients switched to unboosted ATV after viral suppression was achieved, mostly for simplification. We report on the efficacy of unboosted ATV with TDF and emtricitabine (FTC) in our clinic cohort.
Methods: File review of all patients with no history of virological failure commencing unboosted ATV (400 mg) + TDF + FTC with a HIV-1-RNA of < 400 copies/ml. Virological failure was defined as two consecutive HIV-1-RNA measurements > 400 copies/ml.
Summary of results: 178 patients (pts) were observed for 1-81 months (mean 21.9, median 18.5) totalling 325 patient-years. Mean age was 44 years, mean weight 76 kg, mean CD4 516 cells/mm^3. Duration of preceding viral suppression was 0-177 (mean 32.4, median 20) months. Most common preceding regimen was ATV/r + TDF + FTC (89 pts). Most common reasons given for switching to ATV + TDF + FTC were simplification (83 pts), dyslipidemia (17), gastrointestinal toxicity (10), coronary risk (10), CNS toxicity (10), hyperbilirubinemia (6). No virological failure was observed. 113, 86 and 62 pts were observed for at least 12, 18 and 24 months; with 95% CI for virological failure 0-2.6%, 0-3.4% and 0-4.7% respectively. 118 pts are still on the regimen. Most frequent reasons for discontinuing were: elevated creatinine (11 pts) viral load blips < 200 copies/ml (7), death (5), pregnancy (4), pts' own decision (4), gastrointestinal intolerance (3).
Conclusions: Switching to unboosted ATV combined with TDF and FTC is effective as maintenance therapy in patients with viral suppression and no prior treatment failure.

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Efficacy and safety of switching double-boosted protease inhibitors to boosted darunavir in HIV-infected patients with virologic suppression

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Purpose of the study: Switching to ritonavir-boosted darunavir (DRV/r) in patients treated with double ritonavir-boosted protease inhibitors (PI/r) may result in better tolerability, less pill burden, better lipid profile and a lower cost, while maintaining virologic efficacy.
Methods: Multicentre, concurrent cohort observational study. HIV-infected adults with HIV RNA < 50 copies/mL for at least the previous 12 months on a double PI/r-based therapy were offered to switch to DRV/r (DRV group) or to continue on the same regimen (control group). Visits (including blood tests, adherence and side effects assessment) were performed every 3 months, with a follow-up of at least one year. Descriptive values are described as n (%) or median (interquartile range). Changes from baseline in quantitative variables have been calculated with the Wilcoxon Signed Ranks Test and comparisons between groups have been performed with the Mann-Whitney test, using SPSS 20.0 statistical package.
Summary of results: 65 patients were included (35 DRV group and 30 control group); median age was 46 (40–49) years, 76% were male. At baseline, double-boosted PI regimens were lopinavir-atazanavir/r

24%, lopinavir-saquinavir/r 46%, lopinavir-fosamprenavir/r 8%, atazanavir-saquinavir/r 18% and others 4%. There were no significant differences between groups in baseline characteristics, except for patients who switched to DRV had a higher number of prior antiretroviral regimens [6 (3–8) vs 2 (1–4), p = .002]. Of the patients who switched to DRV/r, 46% received DRV/r once-daily and 54% twice-daily. After 48 weeks, one patient in each arm had virologic failure and one patient in the DRV arm stopped treatment due to side effects (depressive syndrome); there were no episodes of rash or clinical hepatitis. Efficacy (HIV RNA <50 copies/mL) was similar in the DRV and control groups by intention-to-treat analysis (94 vs. 97%, p = NS). There were no significant differences in laboratory parameters between treatment groups except for a decrease in total bilirrubin in patients who switched to DRV/r (−0.69 vs +0.28 mg/dL, p = .028). Treatment switch represented a median saving of 157 (32–264) euros per patient per month.

Conclusions: Switching from a double-boosted PI regimen to DRV maintains virologic efficacy, with good tolerability and a lower cost.

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P298

Rilpivirine/tenofovir/emtricitabine fixed-dose combination is an efficacious and well-tolerated ''switch'' regimen for patients on therapy

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The rilpivirine/tenofovir/emtricitabine fixed-dose combination (RTE FDC) (Complera, Eviplera) is a potent convenient, well-tolerated antiretroviral regimen. While it is officially indicated only for treatment-naïve patients, it is attractive for use as a regimen to switch to for patients experiencing toxicities or side effects, or who simply want a regimen with fewer pills. This is a retrospective review of patients who switched to RTE FDC from other antiretroviral regimens in a large HIV specialty private practice. 111 patients were identified who switched to RFE FDC from other regimens who had at least six months follow-up (median 8 months). 44 were previously taking the efavirenz/tenofovir/emtricitabine fixed-dose combination (ETE FDC) (Atripla), 24 nevirapine with NRTIs, 16 protease-based regimens, 10 on raltegravir with NRTIs, and 17 on various other regimens. Patients had been on therapy for a median of 6.25 years. 86 patients had an HIV PCR <20 at the time of switch, 21 had low grade positive PCRs (<400) and 4 patients switched after an interruption in therapy with viral loads of 5880–88,000. Median CD4 cell count at the time of switch was 663 (range 142–2244). 14 patients had previously failed treatment and had resistance mutations; 4 with M184V, 5 with K103N, but none with rilpivirine nor tenofovir-specific resistance mutations. One patient discontinued RFE FDC after a single PCR of 520; all others have remained undetectable at most recent visit (91 <20, 19 <400). Median CD4 cell count on the most recent visit is 656. Creatinine (first visit after switch) increased by a mean of 0.04 mg/dl (0.05 in those switching from a non-tenofovir containing regimen, 0.04 in those switching from a tenofovir containing regimen). There was no significant change in LFTs. Mean cholesterol decreased by 18 mg/dl (23 in those switching from ETE FDC, 12 from protease inhibitors, 27 from nevirapine and 2 from raltegravir). Six patients co-infected with hepatitis B remain with an undetectable hepatitis B PCR. Patients were asked to complete a questionnaire, rating their new and old regimens on a scale of one (bad) to ten (good) (Table). For appropriate patients wishing to switch their treatment regimen for toxicity, side-effects or even just pill burden, RTE FDC is an efficacious, well tolerated, convenient alternative.

	RTE FDC	Old regimen
No side effects	9.6	8.3
Ease of administration	9.5	8.6
No problem with food requirement	8.9	
	8.7	

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P299

ATV/r-based regimens: durable virological suppression and good tolerability as switch strategy from NNRTI-containing regimens in a real-life cohort

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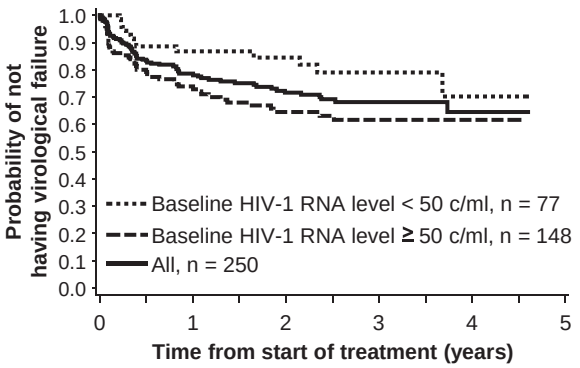
Current therapeutic options for the treatment of HIV provide high rates of virological suppression and good tolerability. However, as long-term treatment success has become a realistic goal, data evaluating the long-term efficacy and safety of switching strategies become more needed. The purpose of this sub-analysis is to describe the long-term outcomes of ATV/r regimens after switching from combinations containing non-nucleoside reverse transcriptase inhibitor (NNRTI) in a clinical setting. Non-comparative, retrospective study including data from 3 European databases (France – DatAids, Germany-KompNet, Sweden-InfCare). Data from antiretroviral (ARV)-experienced adults starting an ATV/r-regimen between October 2004-March 2007 were extracted every 6-months (maximum follow-up 5 years). Time to virological failure (VF) was analysed by the Kaplan-Meier method. Reasons for discontinuation and safety data were also collected. Of 1294 patients analysed, 250 switched from a NNRTI-based regimen. Patients were predominantly male (74%); median age 42 years (min, max: 23, 85); prior ARV exposure: median 5.0 years. At baseline (BL), 56% of patients had HIV-1 RNA <500 c/mL and 31% had <50 c/mL; median (min, max) CD4 cell count: 388 (6, 1299) cells/mm3. After 3-year follow-up, the probability of not having VF was



Number at risk

<50:	77	61	48	41	35	22	15	11	6	1	0
≥50:	148	97	80	64	54	41	29	10	3	1	0
All:	250	178	144	118	100	71	51	26	12	2	0

Figure 1. Time to virological failure (2 consecutive HIV-1 RNA ≥50 c/mL or 1 HIIV-1 RNA ≥50 c/mL followed by discontinuation).

79% (95% CI 65–88%) and 62% (95% CI 52%–70%) for patients with BL HIV-1 RNA <or ≥50 c/mL, respectively. The most frequent reasons for discontinuation were ''unknown'' (18%) and adverse events (8%). Hyperbilirubinemia was reported as reason for discontinuation in only 2 patients. In a clinical setting, switching from NNRTI to ATV/r-based regimen is associated with sustained virological suppression and good tolerability.

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P300

Safety and efficacy of a raltegravir-based dual antiretroviral therapy in clinical practice

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Background: HAART has revolutionized HIV disease management and increased life expectancy for most HIV-infected individuals on treatment. A nucleoside/tide reverse transcriptase (NRTI) inhibitor backbone is a recommended component of standard first-line HAART. Nevertheless, NRTI-sparing alternatives are warranted in order to reduce long-term toxicities in many patients (pts). Aim of the study was to evaluate safety of raltegravir-based dual antiretroviral therapy (DUAL) in a clinical practice setting.
Methods: All pts on DUAL regimen followed at our outpatient HIV service on May 31st 2012 were recruited. Their clinical files were retrospectively studied. Collected data included: demographics, CDC staging, reason to DUAL switching, cholesterol (total and HDL), creatinine, CK, CD4+ count and HIV RNA were recorded at switch and every six months after for the first year. Change in CD4 count after the switch was evaluated by Student t-test.
Results: The cohort included 55 pts (27 M); mean age was 54 years (38–72). HIV infection was acquired through: injective drug abuse (25), unprotected homosexual (24) and heterosexual (16) intercourse. CDC staging was: A = 16, B = 26, C = 13. Mean previous treatment regimens were 4. At time of study pts had been on DUAL regimen for 23 months. They had been switched to DUAL therapy for: drug resistance (14; 25.5%) (DRR) or drug toxicity (41; 74.5%). The most frequently associated drug was darunavir/rtv (19; 34.5%), followed by atazanavir (13; 23.6%; 5 were unboosted); lopinavir/rtv (12; 21.8%), and NVP (11; 20%). DRR pts presented at baseline a mean viral load of 40,153 copies of HIV-RNA/ml; after at 12 months all but 3 showed undetectable (<40 copies) viral load and a mean CD4 gain of 142 cells/ml. Pts switched to DUAL for toxicity presented persistent undetectable viral load and a mean CD4+ gain of 94 cells/ml. The observed CD4+ increase in both groups (DRR and toxicity) presented a statistical significance ($p < 0.01$). Total and HDL cholesterol, and creatinine did not present significant variations. CK remained stable and no toxicity episode was observed.
Conclusion: DUAL approach showed good safety and also remarkable results in terms of viral suppression and immunological recovery. Notwithstanding the potential low genetic barrier of some combinations (e.g. NVP+RAL) this strategy demonstrated to be effective. The long term reliability of DUAL should be confirmed by studies with a longer follow up and a wider sample.

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Simplification

P301

Predictors of long-term HIV RNA suppression on darunavir/ritonavir monotherapy in the MONET trial

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Background: In previous studies of protease inhibitor (PI) monotherapy, patients with higher nadir CD4 counts, baseline HIV RNA <1 copy/mL and high adherence to treatment have been most likely to show sustained HIV RNA suppression <50 copies/mL.
Methods: In the MONET trial, 256 patients with HIV RNA <50 copies/mL at screening switched to DRV/r 800/100 mg once daily, either as monotherapy (n = 127) or with 2 NRTIs (n = 129). HIV RNA results were classified as either <5 (no detection), 5–49 (virus detected under quantification limit) or >50 copies/mL. Treatment failure was defined as two consecutive HIV RNA levels >50 copies/mL (TLOVR) by Week 144, or discontinuation of study drugs. Additional analyses were conducted (i) excluding discontinuations for adverse events or other reasons (ii) including patients who intensified with NRTIs. Multivariate logistic regression was used to identify factors predictive of treatment failure by Week 144.
Results: By Week 144, the percentage of patients with HIV RNA <50 copies/mL (ITT, TLOVR, Switch = Failure) was 69% versus 75% in the DRV/r monotherapy and triple therapy arms respectively. In the Switch Included analysis, HIV RNA <50 copies/mL was 84.0% versus 83.5% in the DRV/r monotherapy and triple therapy arms respectively. In the multivariate analysis for the TLOVR endpoint, positive HCV serology correlated with treatment failure (odds ratio [OR] = 2.44, 95% CI 1.20–5.00). In the analysis including only virological endpoints, both positive HCV serology (OR = 2.77, 95% CI 1.18-6.67) and baseline HIV RNA >5 copies/mL (OR = 2.71, 95% CI 1.21-6.08) predicted treatment failure. In the Switch Included analysis, only HIV RNA >5 copies/mL was predictive of treatment failure (OR = 2.78, 95% CI 1.28–6.01). Nadir CD4 count and prior PI use were not predictive of treatment failure in any analysis. In the ITT TLOVR analysis, the response rates in the DRV/r monotherapy arm at Week 144 were 79% (66/84) for HCV-ve patients with baseline HIV RNA <5 copies/mL, 63% (12/19) for HCV-ve patients with baseline HIV RNA >5 copies/mL, 47% (9/19) for HCV+ve patients with baseline HIV RNA <5 copies/mL and 20% (1/5) for HCV+ve patients with baseline HIV RNA >5 copies/mL.
Conclusions: In the MONET trial, patients without HCV co-infection (based on serology), and with baseline HIV RNA <5 copies/mL by the Roche Amplicor assay (i.e. no virus detected) were most likely to show sustained HIV RNA suppression <50 copies/mL on DRV/r monotherapy.

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P302

A clinical trial to compare the quality of life of HIV+ patients who start monotherapy with LPV/r versus continuing triple therapy with a boosted PI

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Purpose of the study: Efficacy, toxicity and complexity of antiretroviral (ARV) regimens may impact the quality of life (QoL). Since over the past years the simplification approach of lopinavir/ritonavir (LPV/r) as monotherapy (MT) has been shown to be non-inferior to triple therapy (TT) in virological and immunological efficacy, the objective of this study was to compare several health- and treatment-related outcomes between both ARV strategies with LPV/r.
Methods: A phase IV national, multicenter, controlled, randomized (2:1), open label, parallel-group clinical trial to compare the QoL in patients on ARV TT containing any boosted protease inhibitor (PI), undetectable viral load (VL < 50 cop/mL) in the past 6 months and a CD4 nadir > 100 cells/μL, versus those who were simplified to LPV/r MT, for 24 weeks. QoL and health outcomes were evaluated by the Medical Outcomes Study HIV Health Survey (MOS-HIV) and the five-dimensional EuroQol questionnaire (EQ-5D). Treatment satisfaction was assessed by the Spanish Questionnaire of Satisfaction with ARV Treatment (CESTA). Treatment adherence was assessed by the Spanish Multifactorial Adherence questionnaire (GEEMA) and a visual analog scale (VAS). Tolerability, safety and virological and immunological efficacy at week 24 were also analyzed.
Summary of results: 225 patients from 29 sites were enrolled (MT: 146, 64.5%; TT: 79, 35.1%). Mean age (years) was 44.5 in MT and 45.2 in TT ($p = 0.745$); mean duration (years) from HIV infection was 13.4 in MT and 12.8 in TT ($p = 0.587$) and 71% were male in both arms. 87.6% of patients completed correctly the study (MT: 88.4%; TT: 86.1%; $p = 0.674$). Health and treatment outcomes evaluated at final study visit are shown in figure 1. At study end, 84.1% in MT and 89.6% in TT had undetectable VL ($p = 0.313$) and mean CD4 count were 742.8 cells/μL in MT and 646.5 cells/μL in TT ($p = 0.060$). There were no significant differences in the percentage of patients with virological failure at week 24 as VL >50 cop/mL (MT: 8.2%; TT: 3.9%; $p = 0.271$) and as VL >200 cop/mL (MT: 3.4%; TT: 0%; $p = 0.167$).
Conclusions: The MT simplification strategy with LPV/r maintains comparable virological and immunological efficacy, as well as the tolerability profile, than the TT. The saving resulting from NRTIs withdrawal from the ARV regimen and the good results on QoL and patients treatment satisfaction make MT strategy with LPV/r be taken into account in clinical practice.

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P303

STRike - characteristics of HIV-1-infected patients treated with a single-tablet regimen in daily clinical practice

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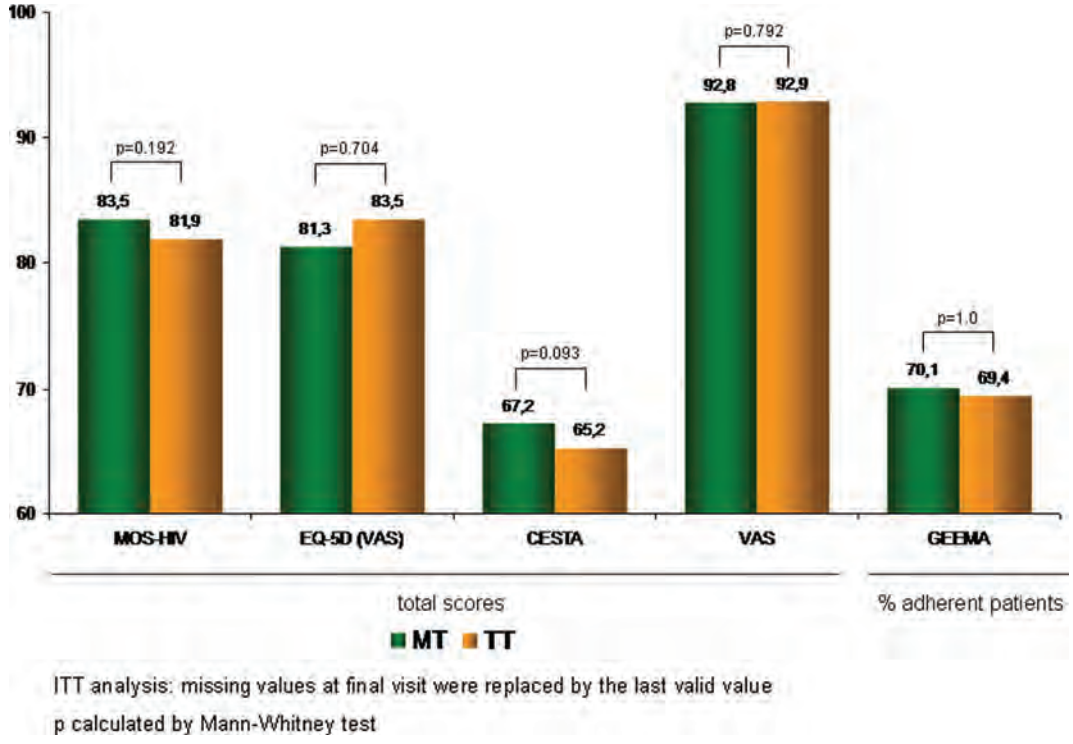
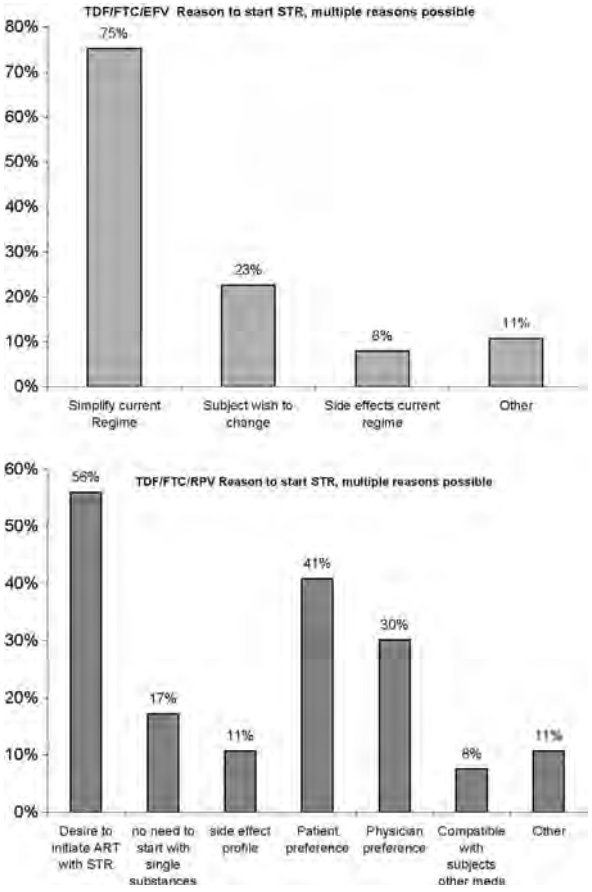
The life-long antiretroviral treatment of HIV-1 infection requires effective and well tolerated medications complemented by high rates of adherence in order to achieve viral suppression, immunologic reconstitution and to prevent the development of resistance. Single-tablet regimens (STRs), combining a full antiretroviral regimen in one tablet taken once daily, have been designed to achieve high adherence and better long-term outcomes. ''STRike'' is the first cohort study, describing the use of various STRs in routine clinical practice in Germany. In this observational cohort study 800 participants will be included in 4 treatment arms, treated with the STRs of TDF/FTC/EFV (a retrospective and prospective arm), TDF/FTC/RPV or TDF/FTC/COBI/EVG after regulatory approval. Patients are followed for at least two years, and reasons for choice of medications and treatment satisfac-



Abstract P302–Figure 1. 'Quality of life' impact: monotherapy vs triple therapy.

tion will be collected, in addition to safety, demographic, effectiveness data. To date 344 patients on TDF/FTC/EFV and 123 patients on TDF/FTC/RPV are being followed. In general, the spectrum of patients in the study reflects the German HIV-1 infected population with regards to gender (88%/89% male), age (median 40/38 years of age) and mode of infection (71%/63% MSM). However, patients starting TDF/FTC/RPV are less progressed in their disease according to their CDC stage compared with patients on TDF/FTC/EFV (74.5% stage ''A'' vs. 53.2%). Patients starting TDF/FTC/RPV show less comorbidities (54% vs. 82%) with a spectrum different from patients on TDF/FTC/EFV. Pre-existing neuropsychiatric comorbidities are relatively more common (10% more) among patients starting TDF/FTC/RPV than TDF/FTC/EFV. The decision to use an STR is mostly driven by patient preference to start with a more convenient ART regimen (56%) or to simplify their current ART regimen (75%). STRs aim to make treatment of HIV more convenient, more efficacious and more durable and by that allowing for earlier initiation of treatment. Different STRs may meet the requirements of distinct patient populations. TDF/FTC/RPV in this early review of our data, is utilized by younger patients with fewer overall comorbidities, but is selected more frequently for patients with pre-existing neuropsychiatric comorbidities presumably to avoid the known neuropsychiatric complications of TDF/FTC/EFV. TDF/FTC/RPV appears to fit into the concept of early HIV treatment initiation as recommended by national and international guidelines.



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P304

Monotherapy with boosted protease inhibitors as antiretroviral treatment simplification strategy in the clinical setting

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Antiretroviral treatment simplification with darunavir/ritonavir or lopinavir/ritonavir monotherapy maintains sustained HIV viremia suppression in clinical trials. However, data about the efficacy of this strategy in routine clinical practice is still limited, and no direct comparison between darunavir/ritonavir and lopinavir/ritonavir has been performed to date. We retrospectively studied all HIV-1-infected subjects who initiated monotherapy with darunavir/ritonavir or lopinavir/ritonavir while having plasma VL <50 c/mL, and had at least 1 subsequent follow-up visit in our clinic. When two consecutive PI-monotherapy regimens were used, each regimen was considered separately. The primary endpoint was the percentage of patients who maintained virological suppression (HIV-1 VL <50 c/mL) through follow-up. Virological failure was defined as at least two consecutive HIV-1 VL >50 c/mL. We also evaluated other reasons for treatment discontinuation. Analyses were performed considering all regimens (full dataset analysis) either as ''on treatment'' or as ''treatment switch equals failure''. Five hundred and seventy-three PI-monotherapy regimens corresponding to 520 subjects were included, 262 with darunavir/ritonavir and 311 with lopinavir/ritonavir. Medians (IQR) follow-up were 50 (26.3–107.6) and 85.6 (36.9–179.1) weeks for subjects on darunavir/ritonavir and lopinavir/ritonavir, respectively ($p<0.001$). Overall, 67 (11.7%) subjects experienced virological failure, 23 (8.7%) were on darunavir/ritonavir and 42 (13.5%) were on lopinavir/ritonavir ($p=0.796$). Two hundred and three (77.5%) patients on darunavir/ritonavir and 154 (49.5%) on lopinavir/ritonavir maintained virological suppression in the ''treatment switch equals failure'' ($p=0.002$). Other reasons for treatment discontinuation were gastrointestinal toxicity and dyslipidemia in 7.2% and 5.9% of cases, respectively. Gastrointestinal toxicities and dyslipidemia leading to treatment discontinuation were more frequent in patients on lopinavir/ritonavir (10.6% and 10.3%, respectively) than in patients on darunavir/ritonavir (3.1% and 0.8%, respectively). Monotherapy with darunavir/ritonavir or lopinavir/ritonavir as simplification strategy appears to be effective and safe in subjects with virological suppression in clinical practice. Virological efficacy seems to be similar between regimens. However, rates of discontinuation due to toxicities were higher in subjects on lopinavir/ritonavir than darunavir/ritonavir.

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P305

Durability of lopinavir/r monotherapy in people with viral load $\leq$50 copies/Ml

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There is debate about whether lopinavir/r mono-therapy (LPV/r-MT) is a valid treatment option for HIV-infected patients who have shown perfect adherence to therapy. The objective was to evaluate the durability of LPV/r-MT in terms of time to virological rebound (VR), time to discontinuation/intensification or a composite endpoint considering both (= treatment failure). We also identified factors associated with faster progression to treatment failure and estimated the median CD4 count over time while people were still on LPV/r-MT. Patients enrolled in 10 clinical sites in Italy who ever started LPV/r-MT with a viral load $\leq$50 copies/mL (baseline) are included. Patients' follow-up accrued from baseline to the date of the event of interest (VR, defined using the thresholds of 50 and 200 copies/mL, or discontinuation/intensification) or at the date of last available visit/VL measurement. Standard survival analysis employing Kaplan-Meier curves was used. We studied 139 patients starting LPV/r-MT on average in 2010 (IQR: 2009–2011) with a VL $\leq$50 copies/mL already for a median of 1 month (range: 1–17). Median age 45 years (IQR: 39–50), 35% females, 32% IDU. Median time from first initiation of ART was 33 months (16–58) with no history of virological failure. Median (IQR) marker values at baseline were 611 (432–741) CD4 count cells/mm^3, 937 (655–1254) CD8 count and 28 (19–47) IU/L of ALT. Median CD4 count were 519 cells/mm^3 at 3 months, 660 at 6 months, 603 at 9 months and 467 at 12 months. The table shows the Kaplan-Meier estimates by 1 year and 2 years for a number of endpoints examined. There was a wide range of estimates depending on the endpoint used. Of those stopping/intensifying, 6 people (4%) added Truvada (n = 4), Kivexa (n = 1) and darunavir (n = 1), the remaining 8 restarted cART.

Abstract P305

End point	No. events	1 year		2 years	
		Point estimate	95% CI	Point estimate	95% CI
Stop/ intensification	14	4.6%	0.7–8.5	14.0%	6.2–21.8
Single VL > 50	32	19.3%	11.1–26.8	29.7%	19.2–38.8
Confirmed VL > 50	8	5.7%	1.8–9.6	7.4%	1.5–13.3
Single VL > 200	10	7.5%	1.6–13.4	11.1%	3.2–18.8
Single VL > 200 or stop / intensification	18	10.5%	4.6–16.4	19.1%	9.2–28.8

In our 'real-life' setting, by 2 years of starting LPV/r-MT, 70% of patients remained persistently suppressed $\leq$50 copies/mL. This percentage was >80% when considering only confirmed virological failures while people still remaining on the drug. Our results, though lacking precision because of the small number of events, are consistent with those of recent clinical trials.

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P306

Switching to an etravirine regimen in virologically suppressed patients with previous virological failures and presence of resistance mutations

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Background: Simplification of antiretroviral therapy (ART) may be an option for virologically suppressed patients for a variety of reasons. Etravirine (ETV) 400 mg qd has a good safety profile and retains activity against viruses resistant to nevirapine or efavirenz. Our objective was to evaluate the efficacy of ETV plus two nucleoside reverse transcriptase inhibitors (NRTIs) as a simplification strategy in treatment-experienced virologically suppressed individuals with prior episodes of virological failure (VF) and presence of genotypic resistance mutations (GRM).

Methods: Eligible subjects were followed for $\geq$6 mo. Primary endpoint was proportion of patients remaining virologically suppressed using an ITT analysis. Genotypic sensitivity score (GSS) to new regimen was calculated according to Stanford resistance database.

Results: Fourteen (10%) of 145 subjects switching to ETV + 2NRTIs while virologically suppressed had a documented prior VF and presence of GRM and were included in the analysis. Median (range) number of previous episodes of VF to ART, NRTI-containing regimen, to a NNRTI-containing regimen and to a PI-containing regimen were 4 (1–6), 2 (1–5), 1 (0–2) and 1 (0–2) respectively. Median duration of virological suppression before switching therapy was 22.5 months (1–65). All patients switched from an effective PI-containing regimen (8 LPV/r, 5 ATV/r and 1 DRV/r) to a qd regimen with ETV 400 mg plus Truvada® (n = 12) or Kivexa® (2). 11/14 patients (79%) remained virologically suppressed at $\geq$6 mo. All of them had a GSS >1.5 to the new regimen and none had resistance to etravirine. Conversely 3/14 (21%) developed a VF at 1, 3 and 6 months respectively. All these 3 patients had a GSS $\leq$1.5 to the new regimen and 2 of them intermediate resistance to ETV (Y181C). No side effects were reported.

Conclusions: Our results suggest that ETV plus 2NRTI could be a good strategy for simplification in virologically suppressed patients despite previous episodes of VF if the GSS to the new regimen is $\geq$1.5 and ETV remains active.

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P307

Raltegravir 800 mg once-daily is efficacious in already virologically suppressed patients

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Raltegravir is a potent, extremely well tolerated antiretroviral, and is a component of a preferred regimen in many treatment guidelines. Despite its indication as a twice-daily (400 mg BID) drug, there has always been interest in once-daily (800 mg QD) use of raltegravir (RTG). The ''QD Merck'', however, showed a higher rate of virologic failure in subjects taking RTG QD with Truvada as opposed to twice daily (BID). This trial, however, was in treatment-naïve patients, and the majority of virologic failures were in those with high viral loads. In patients already virologically suppressed on antiretroviral therapy a regimen including QD raltegravir is more convenient, and may still be effective for virologic suppression. This is a retrospective review of patients in a large HIV-specialty private practice. 105 patients were identified who have been on QD RTG for at least 6 months (median 23, range 6–55 months). 70 patients were also on Truvada, 10 on Epzicom, 7 on atazanavir, and 18 on more than two additional drugs.

All patients had undetectable (<200) viral loads when starting QD RTG, and had been on other treatment for a median of 117 months (range 13–276). Median CD4 count on starting QD RTG was 606 (range 154–1358). 50 patients had been previously on BID RTG for a median of 12 months; 55 started directly on a QD RTG regimen. 32 patients had a history of previous treatment failure/resistance, although mostly to drugs not included in the current regimen. All patients remain undetectable (PCR <200 copies/ml) with no treatment failures seen. In clinically stable patients already suppressed on antiretroviral therapy, including BID RTG regimens, a switch to QD RTG appears to be effective at maintaining long-term virologic control. QD dosing is certainly more convenient, and may improve adherence.

Reference

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P309

Lamivudine plus a boosted-protease inhibitor as simplification strategy in HIV-infected patients with toxicity to nucleoside analogues

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Purpose of the study: Dual therapy with lamivudine plus a PI boosted with ritonavir (PI/r) could be an alternative to standard triple therapy or PI/r monotherapy as a simplification strategy in patients with toxicity to nucleoside analogues (NA).
Methods: Retrospective cohort study of 44 HIV-infected patients on suppressive HAART, with no chronic HBV, who simplified to this dual therapy since 2008. Virological and immunological outcome, lipids and renal changes were evaluated.
Summary of results: Mean age was 50 years (38-70), 66% were male, and the median time of HIV infection was 18.6 years. The median nadir CD4+ count was 150 cells/ml (2–407). At inclusion, patients were receiving therapy with lamivudine plus atazanavir/r in 5 cases, lopinavir/r in 12, and darunavir/r in 27, and they had an HIV RNA level <50 copies/ml for a median time of 794 days (129–2344, 90% >6 months). The NA discontinued was tenofovir (27), didanosine (12), AZT (3), and d4T (2). The reasons for changing were toxicity in 76% of cases, especially renal impairment. They had received a mean of 8 regimens before (2–20), and 55% were in CDC-stage C. In 11 cases, history of resistance was available (to NA in 7 cases, including the 210W mutation in four). The mutations 184V was not observed, but four patients (9%) had a previous failure to therapy including 3tC. Mutations in the protease gene were observed in 8 patients (2 to 7 mutations, the most frequent 77I and 93L), without resistance to the current PI/r. During 62.8 patient-years of follow-up (median, 802 days), only 2 patients failed (4.5%), due to incomplete adherence, at 27 and 141 days. Of note, these two patients had no previous failed with 3tC or PI. Overall, CD4+ count increased for 55 cells/ml. No new adverse events were observed, but total cholesterol (from 180 to 246 mg/dl, $p=0.007$) and triglycerides (from 166 to 195, $p=0.01$) increased during the first 24 weeks with improvement at 48 weeks. On the other hand, estimated glomerular filtration rate improved during follow up (from 74.2 ml/min to 83.08 ml/min after 48 weeks, $p=0.1$).
Conclusions: Dual therapy with lamivudine plus a boosted PI is safe and effective as simplification strategy in patients with toxicity to NA. This combination could be an alternative to mono or triple therapy in hard to treat patients, although an initial increase in lipid parameters could be observed.

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P310

Effectiveness and safety of a single-tablet regimen of emtricitabine/efavirenz/tenofovir in HIV-1-infected patients in infectious diseases department

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Objective: Evaluate the effectiveness and safety of simplification of tenofovir/emtricitabine/efavirenz (TDF/FTC/EFV) in selected treatment-experienced HIV-1-infected patients who have been virologically suppressed for >3 months on their current regimen.
Methods: We selected patients who started the simplified regimen between December 1st 2008 and March 31st 2012. Exclusion criteria: prior therapeutic failure, presence of resistance mutations to any component of TDF/FTC/EFV and patients previously observed in other centers. Efficacy and safety assessments were performed at baseline, 4 weeks after switch and then every 12–24 weeks. Statistical analysis was performed with SPSS version 20.0.
Results: 384 patients were evaluated; 302 (79%) male; mean age 47 (SD = 10) years; median CD4 cells count was 504 cells/mm^3 (367–710). Baseline median glomerular filtration rate (eGFR; Cockcroft-Gault equation) was 100 mL/min (86–116) and median ALT was 33 U/L (21–47). Median total cholesterol (TC) was 205 mg/dL (176-236), high-density lipoproteins (HDL) 45 mg/dL (38–54); low-density lipoproteins (LDL) 130 mg/dL (108–151); triglycerides (TG) 125 mg/dL (84–176). Prior NNRTI-based regimen in 327 (85%) patients (TDF/FTC and EFV in 76%); protease inhibitor in 52 (14%) and integrase inhibitor in 5 (1%). Discontinuation of treatment occurred

Abstract P310

	CD4	AST	ALT	TC	HDL	LDL	TG	eGFR
Baseline								
Median	501	27	32	203	46	130	123	100
Percentiles 25	358	22	22	174	39	108	84	85
Percentiles 75	712	36	45	236	54	151	179	113
Follow-up								
Median	541	28	32	196	49	123	115	111
Percentiles 25	397	22	22	174	41	101	80	96
Percentiles 75	734	36	46	223	57	141	155	133
p-value	<0.001	0.395	0.513	<0.001	<0.001	<0.001	<0.001	<0.001

in 49 patients (13%) after a mean time of 1.1 years (SD = 1.1) of follow-up: nervous system symptoms (n = 11), decreased eGFR (n = 5), virological failure (n = 5), pregnancy (n = 5), gastrointestinal symptoms (n = 3), rash (n = 1), other reasons (n = 2); 12 patients dropped out the treatment and 5 died. Occurrence of blips (transient increase in VL ≤200 copies/mL) was documented in 98 (26%) patients; in 70, VL decreased to <20 copies/mL after the blips and in 28 VL is not yet available. 317 patients (83%) achieved ≥48 weeks of follow-up after simplification. Compared with baseline, significantly higher levels of CD4 cells count, HDL and eGFR were found and lower levels of TC, LDL and TG.
Conclusion: Simplification to TDF/FTC/EFV was shown to be an efficient and safe option in virologically suppressed patients and without a previous virological failure.

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Other

P311

Intensification with maraviroc in HIV-infected individuals (with or without liver cirrhosis) with a discordant CD4 response to cART

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Background: Patients with a discordant response to cART, defined as persistent CD4+T-cell counts <200 cells/mm^3 and lack CD4 increase despite virologic suppression on HAART, have an increased risk of morbidity and mortality. Several studies have suggested a potential benefit of intensification with maraviroc (MVC) on CD4+T-cell recovery.
Methods: A 24-week prospective, open-label, randomized, controlled study. Subjects on cART, plasma HIV RNA <37 copies/mL for at least 12 months, and CD4 < 200 cells/L, with CD4-gain in the previous 12 months <50 cells/μL, were randomized to add MVC (A) or continuing same cART (B). Randomisation was stratified by the presence of liver cirrhosis (CH) (n = 10) and non-CH (n = 28). We measured by flow cytometry changes in the following parameters of CD4+and CD8+T-cell subsets: activation (CD38, HLA-DR), senescence (CD28, CD57, CD45RA and RO), coreceptors (CCR5 and CXCR4) and apoptosis (Annexin-V).
Results: Thirty-eight subjects were included at the final analysis. Median values were: age 51 years (IQR, 44–57), time with VL <37 copies/mL before entry 43 months (IQR 24–62 months), baseline CD4+T-cell count 144 cells/μL (IQR 106–181). Four subjects were lost of follow-up (3 in A, 1 in B). One subject from group B experienced confirmed virologic failure at week 24. Adverse events were similar in both arms. Median increase in CD4+T-cell count from baseline to weeks 2,4 and 24 in both groups were +15.5 vs -1 (p = 0.025); +16.5 vs -2.5 (p = 0.158); +46.5 vs+6.50 (p = 0.190). Similar trend towards a higher CD4 increase were seen in both CH and non-CH individuals. At W24, 8 subjects from arm A vs 1 subject from arm B achieved a CD4+T-cell count above 200 cells/μL (p <0.05). Markers of immune activation (CD38 and HLA-DR) decreased during MVC intensification, especially in CD8+ T cells (p <0.01) whereas apoptosis did not. Additionally CCR5 expression tended to increase (p = 0.051) in CD8 T cells from arm A subjects. No significant differences were found in the immunological assay between cirrhotic and non cirrhotic individuals.
Conclusions: MVC intensification was safe and was associated with a significant a trend towards increasing CD4+T-cell counts both in cirrhotic as well as non-cirrhotic patients with discordant response. The addition of MVC was associated with a decrease in markers of immune activation in both groups.

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P312

Safety and efficacy of once-daily single generic fixed-drug combination tablet of tenofovir, lamivudine and efavirenz among HIV-infected Thais

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Background: Generic fixed dose combinations (FDCs) of nucleoside reverse transcriptase inhibitors (NRTIs) and non-nucleoside reverse transcriptase inhibitors (NNRTIs) is commonly used in resource-limited settings to increase adherence to lifelong treatment. However, the cumulative evidence of the long-term complications, particularly mitochondrial toxicity of NRTIs, especially stavudine (or zidovudine), brings about widespread use of tenofovir (TDF). This study was aimed to assess the efficacy and safety of a FDC comprising 300 mg tenofovir (TDF), 300 mg LAM and 600 mg efavirenz (EFV).
Methods: A Phase II open-label clinical trial was conducted at HIV-NAT, Thai AIDS Research Center, Thai Red Cross from April 2010 to December 2011. Patients were eligible to enroll if they were either: 1) on TDF, LAM and EFV as separate tablets, for at least 6 months with an undetectable viral load (= switch arm) or 2) treatment-naïve. Safety profiles, including liver and renal functions, were assessed at baseline, weeks 4, 12, 24 and 48. In switch group, mid-dose TDF plasma concentrations were measured by HPLC at baseline and week 4 after a switch to single FDC tablet.
Results: A total of 100 patients were enrolled (51 naïve). Median age was 34 years and 30% were female. The median baseline CD4 cell count (IQR) was 512 (395–620) cells/L and 232 (164–284) cells/L for the switch arm and ARV-naïve group, respectively. The median (IQR) $\log_{10}$ HIV-1 RNA for ARV-naïve group was 4.9 (4.2–5.3) copies/mL. By ITT analysis, the proportion of cases with HIV RNA <50 copies/mL was 93% and 92% at week 24 and 48, respectively. Only 1 confirmed virological failure at week 12 with NNRTI-resistant mutations (A98G, K103N, V118I, E138Q, Y181C). The reported 3 SAEs (severe headache, infective endocarditis, cervical dysplasia) were found and one was possibly related to the study drug. There were 49 mild to moderate efavirenz-related central nervous system events, occurring in first few days-weeks. There were no statistically significant changes on renal function and liver enzymes. Mean plasma concentrations of all three drugs in FDC met the acceptable target levels.
Conclusion: The generic FDC of TDF/3TC/EFV was well tolerated and efficacious. Our findings lend support to the use of this generic FDC as first-line antiretroviral therapy in resource limited settings.

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P313

Predictive factors of therapeutic success of a HAART regimen including atazanavir with or without ritonavir in HIV-infected patients

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To evaluate the factors that may influence the persistence and the virological failure of an atazanavir (ATV)-containing antiretroviral regimen. We conducted a retrospective cohort study in HIV-positive patients (pts) who were being followed at the Infectious Diseases Division, University of Milan. Data regarding viral load, CD4 lymphocytes and the blood chemistry parameters were collected at 1st, 3rd, 6th months from the beginning of therapy and then every six months. Factors related to persistence of therapy with ATV and virological failure (HIV-RNA $>$ 50cp/mL after six months) were evaluated with Kaplan-Meier curve, Cox model and logistic regression. 574 pts were evaluated: 480 experienced therapy with ATV with ritonavir (ATV/r) (80 naïve), 218 with unboosted ATV (5 naïve) and 124 with both regimens. At baseline: median age of 43 years (IQR 39–48), CD4+ median count 418 cell/mm^3 (IQR 277–606), VL $<$ 50cp/mL in 370 pts (54.4%), and median duration of infection 12 years (IQR 6–18). The median duration of therapy was 21 months (IQR 7–49) in pts treated with ATV/r and 22 months (IQR 8–44) with unboosted ATV. We observed a borderline significant difference for the persistence of the regimen between the two groups ($p = 0.05$) that disappears after removing the suspensions for simplification. Pts treated with ritonavir (OR = 1.563; 95% CI 1.058–2.308, $p = 0.025$) and with a backbone containing AZT-ddI-d4T (OR = 3.34; 95% CI 1.873–5.956, $p < 0.001$) had an increased risk of therapy suspension, whereas starting therapy with ATV in recent years resulted protective (OR = 0.741; 95% CI 0.678–0.809, $p < 0.001$). The suspension for toxicity was not significantly different between pts treated with ATV/r and unboosted ATV. No significant difference between the two therapies was observed regarding virological failure. Of note, pts with an elevated VL at baseline (OR 1.234; 95% CI 1.065–1.429, $p = 0.005$) and male gender (OR 1.667; 95% CI 1.06–2.621, $p = 0.027$) were at elevated risk of failure, whereas a backbone containing AZT-ddI-d4T (OR 0.356; 95% CI 0.196–0.638, $p = 0.001$) and a recent year of starting ATV (OR 0.64; 95% CI 0.579–0.71, $p < 0.001$) are protective factors. No significant difference between pts treated with ATV/r or unboosted was observed regarding the induction of hyperbilirubinemia of ACTG grade III and IV. Treatment with unboosted ATV can last longer than that with ATV/r without an increased risk of therapeutic failure. A comparable safety profile was seen for pts who received ATV/r or unboosted ATV.

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P314

Impact of lamivudine monotherapy in failing patients with multidrug-resistant HIV: final 48 weeks results (MONO-AIFA FARM7PAZS3)

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Purpose of the study: To assess the impact of lamivudine (3TC) monotherapy in failing patients with multidrug-resistant HIV and limited therapeutic options.
Methods: Prospective, open-label, multicenter, randomised (1:1), pilot study. HIV-1 failing pts with M184V mutation, HBsAg negative were assigned to 3TC 300mg QD for 24 weeks followed by a new regimen for 24 weeks (Arm A) or to a new regimen for 48 weeks (Arm B). The new HAART regimen was decided before randomisation in both groups, based on clinical history, genotype and viral tropism.

Table 1. Virological success according to Nadir CD4+, screening HIVRNA and GSS of the new regimen

ITT ANALYSIS					
Characteristic	**Strata**	**Percent of patients with HIV-RNA $<$50 copies/mL at week 48 in Arm A**	**Percent of patients with HIV-RNA $<$50 copies/mL at week 48 in Arm B**	**P-value**	**Breslow-Day Test P-value**
Nadir Cd4+(cells/μL)	$<$200	10/24 42%	10/24 42%	0.999	0.173
	$\geq$200	5/14 (36%)	7/10 (70%)	0.214	
Screening HIV-RNA (copies/mL)	51–10000	15/26 (58%)	15/26 (58%)	0.999	0.092
	$>$10000	0/12	2/8 (25%)	0.147	
New Regimen GSS	$<$2	3/7 (43%)	3/8 (38%)	0.999	0.479
	$\geq$2	12/31 (39%)	14/26 (54%)	0.294	
OT Analysis					
Characteristic	**Strata**	**Percent of patients with HIV-RNA $<$50 copies/mL at week 48 in** Arm A	**Percent of patients with HIV-RNA $<$50 copies/mL at week 48 in Arm B**	**P-value**	**Breslow-Day Test P-value**
Nadir Cd4+(cells/μL)	$<$200	10/12 (83%)	10/19 (53%)	0.128	0.027
	$\geq$200	5/9 (56%)	7/8 (88%)	0.294	
Screening HIV-RNA (copies/mL)	51–10000	15/17 (88%)	15/22 (68%)	0.251	0.052
	$>$10000	0/4 (0%)	2/5 (40%)	0.444	
New Regimen GSS	$<$2	3/4 (75%)	3/5 (60%)	0.999	0.816
	$\geq$2	12/17 (71%)	14/22 (64%)	0.740	

Primary endpoint was the proportion of pts with HIV-RNA <50 copies/mL (VS) at week 48 (W48). ITT and OT analysis performed. Results described by median (IQR).

Summary of results: 109 screened, 34 screening failures, 75 randomised, 72 initiated the assigned treatment [38 and 34 pts in Arm A and B, respectively]: 69% males; age: 47.4 (43.2–51.9) years; years of HIV infection: 17 (14–23); nadir CD4+: 150 (47–231) cells/μL. Similar baseline demographic and clinical characteristics were found in Arm A vs Arm B [CD4+: 413 (294–550) vs 377 227–520) cells/μL; HIV-RNA: 3.94 (2.89–4.43) vs 3.66 (2.78–4.20) log_{10}copies/mL; number of mutations: 9 (5–13) vs 9 (3–19); R5-virus: 67% vs 50%; new regimen GSS: 2 (2–3) vs 2 (2–2); 60% vs 56% pts included in the new regimen at least two of the following drugs: DRV/r, MVC, RAL, ETR, T-20]. At W48, pts with VS were 15/38 (39%) vs 17/34 (50%) in Arm A and B, respectively (ITT: P = 0.477). In Arm A, 25/38 (66%) completed the 24-weeks of monotherapy and 21 reached week 48 vs 27 pts in Arm B (P = 0.045). Pts with VS were 15/21 (71%) vs 17/27 (63%) in Arm A and B, respectively (OT: P = 0.758). VS according to nadir CD4+, screening HIVRNA and GSS of the new regimen shown in Table 1. SAEs occurred in 4 (11%) and 2 (6%) in Arm A and B, respectively; all but 1 in Arm A unrelated to the regimen; 4 CDC events: 3 oral candidiasis and 1 recurrence of CMV infection in Arm A; 1 oral candidiasis in Arm B. W48 CD4 change from baseline was: ITT: −4 (−108/+56) and 53 (−37/+110) cells/L (P = 0.735); OT: 8 (−62/+58) and 68 (−24/+148) cells/L in arm A and B, respectively (P = 0.500). Mutations associated with resistance at W48 were 4 (0–7) and 7 (2–13) in Arm A and B, respectively (P = 0.031). R5 virus at W48: Arm A = 55% vs Arm B = 29% (P = 0.124).

Conclusions: Use of 3TC monotherapy was associated with greater discontinuation. It may be considered in patients without effective therapeutic options to favour virological efficacy of the subsequent regimen.

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P315

Safety and efficacy of fixed-dose combination rilpivirine-tenofovir-emtricitabine (RPV/TDF/FTC) in treatment-experienced patients infected with HIV-1

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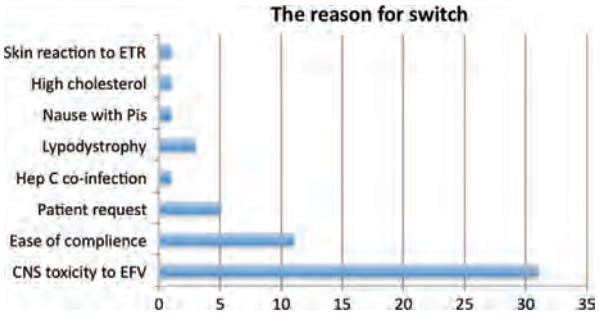
Purpose of the study: Rilpivirine (RPV) is a new non-nucleoside reverse transcriptase inhibitor (NNRTI) which has shown non-inferiority to efavirenz (EFV) in terms of efficacy and safety profiles. The vast majority of clinical data has been performed in the treatment naïve population and has not been studied in depth in treatment-experienced patients. We sought to explore the safety and efficacy of RPV/TDF/FTC in treatment-experienced patients attending our clinics.

Methods: HIV-infected individuals commenced on RPV/TDF/FTC from December 2011 to June 2012 were retrospectively identified from a patient database. Patient demographics were extracted. Biochemical, virological and immunological parameters were collated. At baseline, 1 month and 3 month time points the following laboratory results were compared using the Kruskal-Wallis test: CD4 count, HIV viral load, amino transferase (ALT), cholesterol, triglyceride and HDL/cholesterol ratio.

Summary of results: Sixty-five patients (4 female) were identified. Median age was 38 years (range: 25–73). Fifty-six patients were treatment experienced (2 re-start); 39 on NNRTI-based (33 on EFV), 10 on PI-based and 4 on other regimens. 9 patients were naïve to treatment. The reasons for switch are illustrated in Fig. 1.



Fifty-four patients had HIV-RNA-1 <40 copies/mL at the time of switch and all remained undetectable at 3 months. At baseline, the median CD4 count was 555 cells/mm^3 (range: 209–1586) in the switch group, which increased significantly to 638 cells/mm^3 (p <0.005) 3 months after switch. Switch to RPV/TDF/FTC had a favorable effect on lipid profile. At baseline the median cholesterol, triglyceride and HDL/cholesterol ratio levels were 4.8 mmol/L, 1.78 mmol/L and 4.37 respectively. At 1 month post-switch this decreased to 4.5 mmol/L, 1.65 mmol/L and 4.24 and at 3 months post-switch decreased to 4.1 mmol/L, 1.44 mmol/L and 4.04. Median HIV-RNA-1 in treatment-naïve patients (n = 9) at baseline was 50298 copies/mL, at 1 month four patients had HIV-RNA-1 <40 copies/mL and at 3 months eight patients had HIV-RNA-1 <40 copies/mL. RPV/TDF/FTC had no favourable effect on lipid profile in treatment-naïve group and had no effect on ALT levels in either the switch or the treatment-naïve group.

Conclusion: In this cohort, RPV/TDF/FTC has been shown to have a safe virological efficacy and safety profile as a switch therapy for patients suppressed on their current standard of care and are experiencing adverse events.

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P316

Persistence of antiretroviral treatment in emtricitabine/tenofovir (FTC/TDF) users vs other NRTI in ART-na ve patients >50 years: TRIP study

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The major antiretroviral guidelines recommend starting ART in patients >50 y of age, regardless of CD4 cell count. However, no references to the preferred cART for these patients have been described. The combination FTC/TDF is one of the cornerstones of combined antiretroviral therapy (cART) in naïve patients. We studied the persistence of coformulated FTC/TDF in this scenario. National, retrospective cohort analysis of HIV-infected patients >50 y at the time they began the first cART regimen (January 1, 2006 – December 31, 2009). Patients were selected in a proportion 2:1 to FTC/TDF vs. other NRTI regimens (no-TDF). We compared the persistence of treatment in FTC/TDF users vs. no-TDF (main groups). Among TDF users, we compared the persistence in PI vs. NNRTI users and in

lopinavir/r vs. efavirenz users. Persistence was defined as the duration of the initial treatment; we analyzed time to any change or discontinuation according to initial regimen. We included 161 patients: median age: 54.6 y, 83% males, median CD4 count 191 cells/μl, median viral load 4.7 log, follow up: median 19 months, max 48 months. Of them, 112 started with FTC/TDF (53 with PIs, 57 with NNRTIs); and 49 with other NRTIs (no-TDF) (22 with PI, 23 NNRTI). During the follow-up period 79 patients (49%) modified their treatment, with statistically significant differences among groups, as shown in Table 1.

Abstract P316–Table 1. Proportion and hazard ratio of non-persistence (any change or discontinuation of any component of initial cART), aOR adjusted by age, sex, transmission category and baseline CD4 count and viral load

Initial cART	Non-persistence, N (%)	Log rank	Crude HR (95% CI)	Adjusted HR* (95% CI)
No-TDF vs. TDF	35/49 (71.4) vs. 44/112 (38.6)	0.001	2.04 (1.31, 3.18)	2.10 (1.34, 3.29)
Among TDF users:				
PI vs. NNRTI	26/53 (49.1) vs. 18/57 (31.6)	0.108	1.63 (0.89, 2.97)	1.63 (0.87, 3.06)
Lopinavir/r vs. efavirenz	19/35 (54.3) vs. 16/52 (30.8)	0.033	2.03 (1.04, 3.96)	2.05 (1.05, 3.99)

*Adjusted by age, sex, transmission category and baseline CD4 count and viral load.

In our study (antiretroviral-naïve patients >50 y), the persistence of FTC/TDF regimens was significantly higher than other NRTI regimens. According to the third agent, there was a trend to a higher persistence with NNRTI vs. PI. This reaches statistical significance when we compare EFV vs. LPV/r. In the absence of randomized clinical trials, our data may contribute to a better understanding on how cART works in this ageing population, which is progressively increasing.

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P317

Activation and inflammation markers in HIV-1-infected patients in dependency of treatment strategies

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Purpose of the study: HIV-1-infected patients have elevated levels of immune activation and systemic inflammatory markers which are partially strong predictors of disease progression or are associated with increased cardiovascular risk. The dependency of anti-retroviral treatment (ART), the usage of NNRTI or PI-based and the application of non-nuc regimens is analysed here on the basis of a dataset (Chronic Inflammation Dependency on TREatment: CIDRE cohort) from 1500 patients in Berlin.
Methods: In a retrospective analysis we compared relative CD4+ cell counts, viral load, relative CD8+CD38+DR-and CD3+DR+cells, concentration of high-sensitivity C-reactive protein (hsCRP) and interleukin-6 (IL-6) in therapy-naïve or treated patients dependent on usage or non-usage of NUCs, PI or NNRTI. Statistics were performed with R (R Core Team; 2012; R: A language and environment for statistical computing) using Wilcoxon rank sum test in two-sided analysis.
Summary of results: As to expect, ART-naïve patients (n=190) had significantly higher viral loads and lower CD4+cell counts (p: both <0.05) and showed higher activation levels than treated patient (CD8+CD38+DR- and CD3+DR+both <0.05). But no significant difference was calculated for hsCRP or IL-6. Nuc-sparing regimen (n=46) did not show any distinction compared to nuc-containing therapies (n=1249) for the analysed parameters. Significant differences were detected for PI-regimen (n=711) with lower CD4+ cell counts and higher activation (CD8+38+DR-, CD3+DR+) and IL-6 (p: all <0.05) but not for hsCRP (p=0.39). The opposite was true for NNRTI-based therapies (n=445) with higher CD4+ cell percentages and lower activation and inflammation markers (p: all <0.05) and as well no difference in hsCRP (p=0.97) compared with all other treated patients.
Conclusions: The lack of differences between therapy-naïve patients and patients on ART for inflammation markers may be due to the relative good immunological state of the first group, which could be one of the reasons why they are not treated so far. The number of nuc-sparing regimen is perhaps too low and too undifferentiated to find diverse inflammation states. Although the differences in activation status can be attributed to different treatment strata, there is no clear explanation for this outcome. A possible reason could be a pre-selection bias either for NNRTI-based or PI-based regimens. Additional data is acquired to perform longitudinal analysis to gain further insight.

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P318

Pregnant . . . pause? Is there a difference in the long-term outcome of women starting ART for the first time in pregnancy?

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Purpose of the study: The guidelines on the initial choice of antiretroviral therapy (ART) in women starting ART for the first time in pregnancy have changed considerably over the past 13 years [1,2]. We sought to determine whether these different ART strategies have influenced subsequent clinical, immunological or virological outcomes in our population. Women in our cohort received either zidovudine (AZT) monotherapy, short course antiretroviral therapy (SCART) or continued ART post-partum. AZT monotherapy in pregnancy was common a decade ago, but its use declined amidst concerns about efficacy and the potential development of resistance with monotherapy. SCART more effectively suppresses viral load (VL) but avoids unnecessary treatment post-partum in those considered at low risk of disease progression. This is used less now the benefits of starting ART at better-conserved CD4 counts and the risks of treatment interruption are known.
Method: 30 women who commenced ART during a pregnancy which resulted in a live birth between 1999 and 2004 were identified from a departmental database. Women already on ART or who had previously received AZT monotherapy or SCART were excluded, as were women with less than 2 years follow up post-partum. Outcomes included time to starting ART, CD4 count and VL on starting ART and at last follow up.

Summary of results: 12 women received AZT monotherapy, 7 SCART and 11 continued ART post-partum. In total there were 269 years of patient follow up (mean 9, range 2–13).
None of the women who received AZT monotherapy or SCART experienced clinical disease progression during their time off therapy, which was considerable (mean 4–5 years). All achieved virological suppression and good CD4 recovery on commencing ART. None of the available genotypes in these patients showed resistance mutations. Of the women who continued ART, more than half modified their regimen and a significant number experienced transient VL rebounds.
Conclusions: The clinical choices made a decade ago do not appear to have been detrimental to the longer-term treatment responses in this group of women. However, the effects of treatment interruption remain unclear and we suggest a cautious approach.

(mean)	AZT monotherapy	SCART	Continued ART
Baseline CD4	409	359	190
Baseline VL	1,950	6,799	59,566
Time to starting ART	5.2 years*	4.6 years**	
CD4 on starting ART	254	178	
CD4 <350 on starting ART	3/12	3/7	
CD4 at last follow up	519	451	543

*1 still not on ART at last follow up; **2 not on ART at last follow up.

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LATE PRESENTERS

P319

Treatment response to LPV/r-based HAART in HIV-infected patients aged >60 years - data from the STAR/STELLA cohorts

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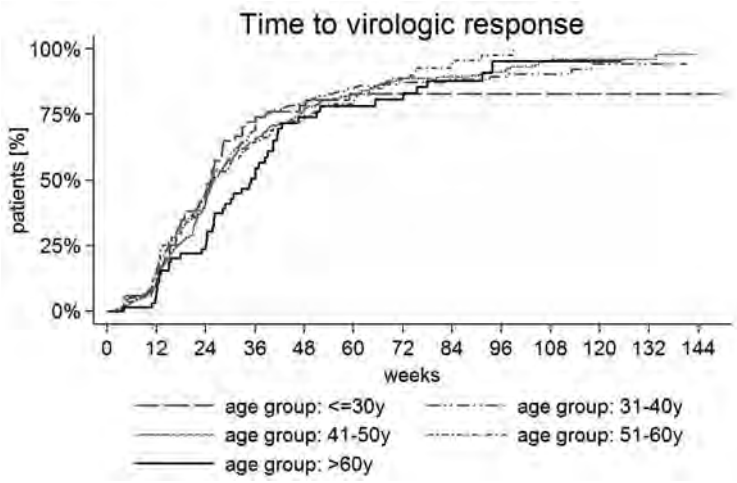
Age, y	≤30	>30–40	>40–50	>50–60	>60	P value	Statistical tests*
N	68	321	411	144	67		
Male, %	69	80	89	89	88	P <0.001	χ^2
Median time since diagnosis, y (IQR)	0.79 (0.21–2.98)	0.67 (0.09–3.23)	0.32 (0.06–3.24)	0.35 (0.06–2.27)	0.10 (0.05–0.69)	P =0.015	Kruskal-Wallis
BL HIV1-RNA >100,000 c/mL, %	43	49	56	60	48	P =0.038	χ^2
BL median CD4 count, cells/μL	256	208	203	212	121	P =0.001*	Kruskal-Wallis
BL CD4 count <200/μL, %	31	47	49	48	64		
BL CD4 count200–350/μL, %	47	36	33	31	31		
BL CD4 count >350/μL, %	22	17	18	21	5		
Median CD4 count at wk 48, 1/μL	446	416	412	392	361	P =0.033*	Kruskal-Wallis
Median time to+100/μL CD4 increase, wk	11.1	12.1	12.1	12.9	15.3	P =0.754	log-rank
Median change in CD4 at wk 48, 1/μL	234	214	214	180	165	P =0.113*	Kruskal-Wallis
Median time to HIV1-RNA <50 c/mL, wk	25.1	25.6	25.9	25.1	35.0	P =0.496	log-rank
Wk 48 HIV1-RNA <50 c/mL, % ITT	63.2	69.8	69.6	68.1	61.2	P =0.556	χ^2
Wk 48 HIV1-RNA <50 c/mL, % AT	75.4	82.1	80.1	77.8	78.9	P =0.755	χ^2

Abstract P319



Purpose of the study: In Germany, older age is described as a risk factor for late presentation of HIV disease (defined as <200 CD4/μL or AIDS at diagnosis). We describe treatment outcomes with respect to age distribution at the time of antiretroviral therapy (ART) initiation in the multicentre, observational, ongoing STAR and STELLA cohorts, which included patients (pts) initiated on LPV/r-based ART.

Methods: This analysis included ART-naïve HIV+ pts with a minimum of 48 weeks follow-up. Time to virologic response (defined as HIV1-RNA <50 c/mL) and time to CD4 cell increase of at least 100/μL were calculated using Kaplan-Meier analyses. Virologic response rates at week 48 were evaluated using 2 approaches: i) defining discontinuations for virologic or immunologic failure, side effects, noncompliance, or death as failures (ITT) and ii) as-treated (AT) analysis excluding discontinuations for reasons other than virologic failure.

Summary of results: 1011 ART-naïve pts were included (85% men; median age 43 years [y]). Baseline (BL) characteristics and treatment response rates are shown in Table 1. The overall prevalence of advanced immunodeficiency with <200 CD4/μL at ART initiation was 48%: 64% in pts aged >60 y and 31%–49% in the younger age groups (see Table 1). Across age groups, 43%–60% of pts had pretreatment HIV1-RNA levels $>100{,}000$ c/mL. Median times to virologic response (Figure 1) and response rates at week 48 did not differ across age groups in either analysis, nor did immunologic outcomes. Median times to +100/μL CD4 increase were between 11.1 and 15.3 weeks. CD4 increase at week 48 was lower in pts >60 y compared to patients of younger age categories (165/μL vs 211/μL; P = ns). However, these differences between age groups did not reach statistical significance, even when stratified by baseline CD4 count $<$ vs $=200$/μL.

Over the first 48 weeks of therapy, clinical and laboratory adverse events (AEs) of grade 3 or 4 were spontaneously reported in 9.6% of pts in the $=60$ y group and 4.5% of pts in the >60 y group ($P=0.194$). In addition, 11.3 % of pts $=60$ and 14.9% of pts >60 y discontinued therapy prior to week 48 due to treatment related AEs ($P=0.427$).

Conclusions: In the STAR/STELLA cohorts, pts aged >60 y had high rates of late presentation, with two-thirds of patients with CD4 cell counts <200/μL. Nevertheless, older pts did not differ significantly from younger pts regarding immunologic and virologic response after initiation of LPV/r-based therapy.

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P320

Observational epidemiological study to identify the clinical profile of na ve patients starting antiretroviral (ARV) therapy in Spain

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Purpose of the study: To identify the proportion of patients starting ARV treatment with NNRTIs or with a PI/r and to explore and compare their clinical profile establishing different factors whereby physicians select the initial ARV treatment in a Spanish clinical setting.

Methods: An observational study was conducted in two different phases. In Phase I a cross-sectional registration was conducted for patients who initiated ARV treatment in a 6-month period in 65 Spanish hospitals. In Phase II clinical and social-demographic features were collected retrospectively of patients who visited HIV clinics between August and November 2010 who had started ARV treatment containing an NNRTIs or a PI/r in Phase I.

Summary of results: In Phase I, 1,687 subjects who initiated ARV treatment were registered, of which 53% started with an NNRTI-based regimen whereas 42% started with a PI/r-based regimen. Two percent of the treatment initiations occurred in a clinical trial. In Phase II, 642 patients were paired consecutively and retrospectively. The group of patients was composed of predominantly male subjects (81% vs 19%). The median time between diagnosis and the start of ARV treatment was 3.6 ± 5.3 years. At the initiation of treatment, 72% of patients had a CD4 count below 350 cells/μl. Although treatment based on NNRTIs in naïve patients is the most frequent option in Spain, the analysis of clinical profiles shows that PI/r-based therapy is more often used than NNRTIs with statistical significance in patients with high viral load, Fig. A ($\geq$100.000 copies/ml) (58% vs 42%; OR:1,75; 95% CI: 1,26–2,43; $p<0{,}01$), with CD4 cell counts <200 cells/μl, Fig. B (68% vs 31%; OR: 2,92; 95% CI: 1,99–4,27; $p<0{,}01$), and in patients at CDC stage C (65% vs 35%; OR: 2,05; CI: 1,27–3,31; $p<0{,}01$).

Conclusions: In Spain, HIV is still diagnosed late (as measured by CD4 count <350 cells/μl). Treatment based on NNRTIs are more frequently used in naïve patients, although PIs/r-based regimens play an important role being the preferred option in patients with high viral load ($\geq$100.000 copies/ml) and low CD4 cell count (<200 cells/μl).

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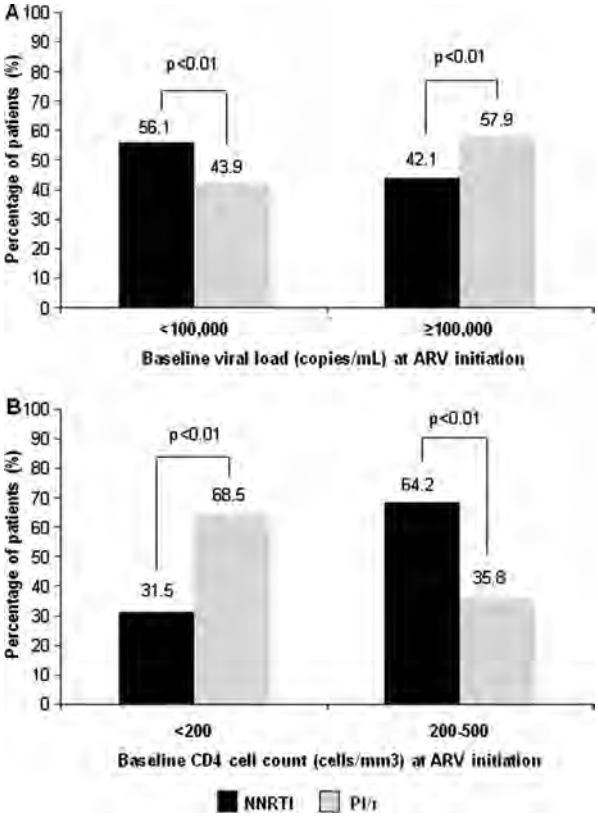

P321

HIV2 late presenters in an infectious disease ward: six years' experience

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Purpose of the study: About a third of HIV-infected patients in Europe present for care late in their disease. In 2010 a consensus was reached for a definition of late presentation, providing a new tool for research and acting. With regard to HIV2 infection this population has never been characterized.

Methods: Retrospective analysis of the clinical records of all the HIV2-infected patients who meet the inclusion criteria (those defined by the European Late Presenter Consensus working group: Late presentation of HIV infection: a consensus definition [1]) admitted to our ward between January 2006 and December 2011. The patients were characterized according to epidemiological, clinical and immunologic status and outcome.

Summary of results: During the period analyzed, 15 HIV2 patients were late presenters. The mean age of the patients was 48 years old (although 53% were older than 50 years); 8 (53%) were men; 11 (73%) were of African origin. Heterosexual transmission was reported in three of the patients, in the remainder the transmission mode was not available. The mean TCD4 cell was 188 (range 27–339), with 8 (53%) with a CD4 count below 200 cells. Twelve (80%) of the patients fulfilled AIDS criteria. There were 3 deaths, corresponding to a mortality rate of 20%. The cause of death was disseminated tuberculosis in two cases and non-Hodgkin's lymphoma in the third case.

Conclusions: Most late presenters with HIV2 infection are of African origin, there is an even distribution between genders, their mean age is around 50 years old, more than half had a CD4 cell count below 200 and there was a 20% mortality rate. These patients pose challenges at various levels: their mortality rate is much higher than in the general HIV-infected population and they are diagnosed very late, leading to a disproportionate increase in risk of transmission, morbidity and mortality.

Reference

1. Antinori A, Coenen T, Costagiola D, Dedes N, Ellefson M, Gatell J, et al. European Late Presenter Consensus working group. Late presentation of HIV infection: a consensus definition. HIV Med. 2011;12:61–4.

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P322

Women in Serbia as late presenters-an issue of concern

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Most of the clinical trials looking at the efficacy and side effects of highly active antiretroviral therapy (HAART) have been conducted primarily on HIV-infected males. So, we conducted a study to determine the factors influencing prognosis of HIV/AIDS and outcome in HIV/AIDS women on HAART, in a resource-limited settings. A cross-sectional study was performed on women, with HIV infection, who initiated HAART between 1st January 1998 and 31st December 2010, at the HIV/AIDS Center of the University Hospital for Infectious and Tropical Diseases in Belgrade, Serbia, with regular clinical and laboratory check-ups. SPSS-version-11.0 software, Univariate and stepwise Multivariate logistic regression analysis together, with the Kaplan-Meier analysis, were used to estimate risk factors influencing prognosis and outcome in HIV/AIDS women. Written consent was obtained. A total of 230 women were followed for 8.2 ± 3.4 years (range 1–12). Durring the follow-up, 26 patients died. The mean age of the patients at HAART initiation was 37 ± 9.7 years. Clinical AIDS at presentation was observed in 43.9% of the patients, while 80% of them had CD4 cell counts below 200 cell/mm^3. Univariate and stepwise multivariate analysis have shown that the progression to death was associated with basal CD4 counts below 100 cells/μL (OR 3.0 95% CI 1.7–8.4, $P = 0.02$) and HCV co-infection (OR 2.6 95% CI 1.0–6.6, $P = 0.03$). However the NNRTI based regimens and good adherence to HAART (OR 0.2, 95% CI 0.09–0.6, $P = 0.005$ and OR 0.3, 95% CI 0.1–0.66, $P = 0.03$, respectively), all prevented death. Although in patients with sustained viral suppression the CD4 counts varied significantly, these did not affect overall survival ($p = 0.21$, log rank) If HIV infected women with advanced HIV-related immunodeficiency reach and maintain optimal viral suppression during HAART, regardless of the level of immune recovery, and if they continue to maintain this achievement up to a mean 8 years of treatment, their prognosis may be fairly good even in a resource limited settings.

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P323

Retrospective evaluation of late presentation and retention in care in a monocentric cohort of HIV-patients in 2006–2011

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Almost 1/3 of HIV-infected individuals enter health care late in the course of infection, worsening their prognosis and costs of care. According to the recent European consensus definitions, late presenters are persons presenting with CD4 counts $<350/\mu L$, and presenters with advanced HIV disease have CD4 $<200/\mu L$ or an AIDS-event. These latter, in particular, are at high risk of further opportunistic infections or death despite of HAART. We included all patients newly diagnosed with HIV infection at the Infectious Diseases Unit of Pescara from 2006 to present, registered for at least one day of observation. The duration of follow up was plotted for all enrolled patients up to 31/12/2011. Demographic, clinical, virological and immunological data, lines of therapy and outcome of HAART were collected for each patient. We included 140 consecutive patients, 18.6% in 2006, 17.9% in 2011; 76.4% were male, while the average age was 39.3 ± 10.2y. AIDS diagnosis at presentation was for 39.7% (50% in 2006, 41.7% in 2011); 52.7% had advanced HIV disease (CD4 $<200/\mu L$, 53.8% in 2006, 70.8% in 2011), 67.2 % were late presenters (CD4 $<350/\mu L$, 73.1% in 2006, 79.2% in 2011). The average CD4 counts at enrollment were 313.8 ± 294.1 in 2006, 361.3 ± 263.1 in 2007, 281.8 ± 295.5 in 2008, 238.4 ± 201.6 in 2009, 394.1 ± 183.9 in 2010, 225.7 ± 245.2 in 2011. Eight per cent of patients were HCV coinfected. Heterosexual exposure occurred in 54% of patients, homosexual in 36%; drug addiction in 7.5%. Among enrollees, 71.4% were Italian, 18.6% from sub-Saharan Africa, 5.7% from South America and 4.2% from Eastern Europe. With a median follow up of 2.5 years, 105 patients (75%) were still being treated as of November 30th, 2011; among these 104 (99.1%) were in virological suppression. Among the 35 patients no longer followed, 15 (11.4%) died during the first 6 months of treatment, 20 (14.3%) were lost in the first 6 months of follow-up. All 15 deaths occurred in patients enrolled with CD4 $<200/\mu L$. After initiation of HAART only 1 patient (0.7%) switched for virological failure, 19 (13.6%) for toxicity or simplification. The proportion of late presenters at our center is high (67.2%) in the absence of appropriate local screening measures. Early mortality after diagnosis is similarly high, concentrated in patients with late presentation. Retention in care after 6 months and virological success of treated patients appear very promising, much more than recently reported in North America.

Reference

1. Antinori A, Coenen T, Costagiola D, Dedes N, Ellefson M, Gatell J, et al. Late presentation of HIV infection: a consensus definition. HIV Med. 2011;12:61–4.

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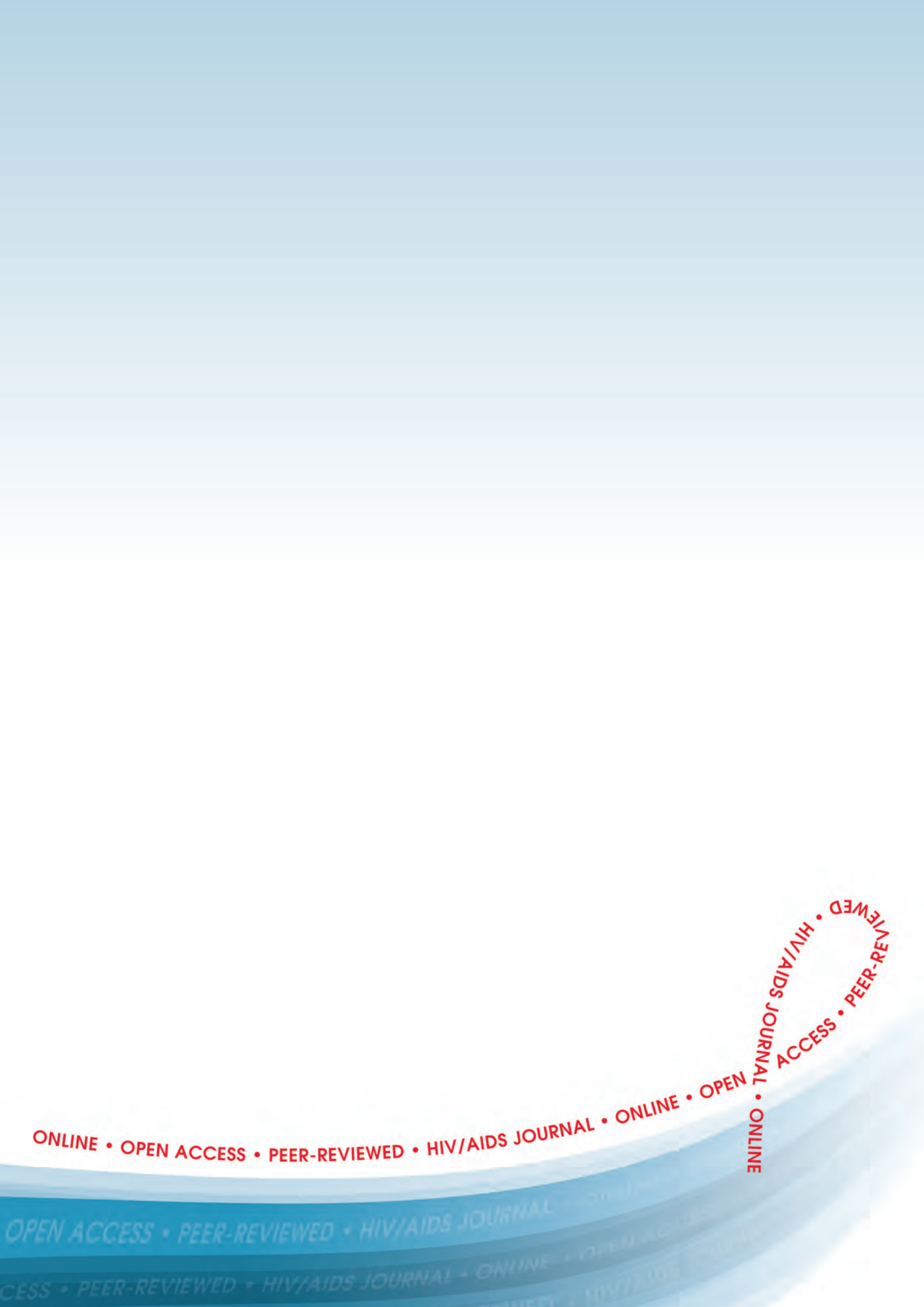
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