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Abstracts
ICAR 2010

Italian Conference on AIDS and Retroviruses

Brescia, Italy

20 – 22 June 2010

Contents

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ICAR 2010

Italian Conference on AIDS and Retroviruses

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Sunday 20 June, 2010

Pre-Congress Courses
The pre-congress courses will take place at the Faculty of Medicine and Surgery at the following times: from 14.30 to 17.00

Antiretroviral treatment in pregnancy and children
Co-ordinators: *G.V. Zuccotti* (Milan), *M. Floridia* (Rome), *R. Badolato* (Brescia)
Teachers: *M. Floridia* (Rome), *E. Tamburini* (Rome), *M. Ravizza* (Milan), *R. Badolato* (Brescia), *V. Giacomet* (Milan), *A. Vigano* (Milan), *C. Cerini* (Milan), *D. Longhi* (Brescia)

Methodology of clinical trials in HIV (supported by NEAT)
Co-ordinators: *A. Cozzi Lepri* (Minneapolis), *A. Knellwolf* (Rome), *C.Terraroli* (Brescia)
Teachers: *A. Cozzi Lepri* (Minneapolis), *A. Knellwolf* (Rome), *C.Terraroli* (Brescia)

Key issues of the HIV disease management in resource limiting settings
Co-ordinators: *C. Giaquinto* (Padua), *V. Pietra* (Ouagadougou)
Teachers: *C. Giaquinto* (Padua), *M. Penazzato* (Padua), *V. Pietra* (Ouagadougou)

17.30 **OPENING OF THE CONGRESS WORK**
Opening Ceremony

Authorities welcome
Presentation: *E. Sagnelli* (Naples)
Introduction: *G. Carosi* (Brescia)

Lectures

18.15–18.45 **HIV 2010 Top Ten issues**
J. Lange (Amsterdam)

18.45–19.15 **Potency, adherence, and quality of life: can all these be achieved by current ART regimens? And how?**
A. Pozniak (London)

19.15–19.45 **Reports of ongoing projects**
Transplantation in HIV: *A. Nanni Costa* (Rome)
NEAT and ESTHER: *S. Vella* (Rome)

Monday 21 June, 2010

8.00–8.30 **Registration**

Lectures (ASSEMBLY HALL)
Chairmen : *B. Ensoli* (Rome), *G. Di Perri* (Turin)

8.30–9.00 **Defining optimal virological suppression during HAART**
A. M. Geretti (London)

9.00–9.30 **Single agent HAART as a new treatment paradigm**
J. Arribas (Madrid)

9.30–11.30 **SYMPOSIUM: Clinical Science / ARVT: Efficacy (ASSEMBLY HALL)**
Chairmen: *R. Esposito* (Modena), *V. Vullo* (Rome)

Up-dates in antiretroviral therapy efficacy
J. Gallant (Baltimore)

Weighting the treatment efficacy based on new information from the drug resistance field
F. Ceccherini Silberstein (Rome)

Do we need specific ART regimens for late presenter patients?
C. Mussini (Modena)

Emerging issues on ART adherence in patients achieving viral suppression
R. Murri (Rome)

- Supervisors: *A. Lazzarin* (Milan), *A. Antinori* (Rome)
- Coordinators/Discussants: *A. Ammassari* (Rome), *A. Castagna* (Milan), *A. De Luca* (Rome), *G. Marchetti* (Milan)

SYMPOSIUM: Basic Science / Virology (ROOM B)
Moderatori: *C. Mastroianni* (Rome),
F. Baldelli (Perugia)

Methodology and clinical relevance of genotypic tests for HIV tropism
V. Svicher (Rome)

Biology of HIV-1 strains resistant to integrase inhibitors
F. Canducci (Milan)

Prosequencing and intra-host analysis of infecting HIV populations
M. Capobianchi (Rome)

Characterization of intracellular HIV variants: implications for HAART management
O. Turriziani (Rome)

- Supervisors: *G. Angarano* (Foggia), *C.F. Perno* (Rome)
- Coordinators/Discussants: *G. Antonelli* (Rome), *M. Clementi* (Milan), *S. Rusconi* (Milan), *M. Zazzi* (Siena)

11.30–13.00 **SYMPOSIUM: Epidemiology and Social Science / Epidemiology and Prevention (ASSEMBLY HALL)**
Chairmen: *A. Orani* (Lecco), *M. Toti* (Grosseto)

HIV infection in drug addicted patients
G. Serpelloni (Verona)

Surveillance of new HIV diagnoses: implementation problems in the Italian Regions
C. Pasqualini (Alessandria)

New HIV infections: delayed diagnosis and characterization of risk populations
N. Orchi (Rome)

Phylogenesis and phylodynamic studies of HIV in Italy
M. Ciccozzi (Rome)

- Supervisors: *G. Ippolito* (Rome), *G. Rezza* (Rome)
- Coordinators/Discussants: *C. Mussini* (Modena), *P. Pezzetti* (Rome), *V. Puro* (Rome), *B. Suligoi* (Rome)

SYMPOSIUM: Basic Science / Immunopathogenesis (ROOM B)
Chairmen: *M. Mondelli* (Pavia), *M. Moroni* (Milan)

Nef-trafficking Intercellular highways for HIV evasion of antibody production
A. Cerutti (New York)

HIV-1 structural proteins: more than the driving force for virion assembly
S. Fiorentini (Brescia)

How viruses shaped the human genome
M. Sironi (Milan)

- Supervisors: V. Barnaba (Rome), M. Andreoni (Rome)
- Coordinators/Discussants: A. Caruso (Brescia), A. Cossarizza (Modena), M. Clerici (Milan), G. Poli (Milan)

13.00–14.00 **Lunch**

14.00–15.30 **ORAL COMMUNICATIONS (ASSEMBLY HALL)**
Session: Clinical Science / ARVT: Efficacy
President: *A. Scalzini* (Mantova)
Chairmen: *N. Abrescia* (Naples), *G. Carnevale* (Cremona), *G. Magnani* (Reggio Emilia)

CO 1 **Extended resistance to the historical antiretroviral drug classes: is it still a risk factor for HIV progression?**
M. Zaccarelli, P. Lorenzini, F. Forbici, V. Tozzi, C. Gori, P. Marconi, F. Ceccherini-Silberstein, A. Boumis, P. Narciso, C.F. Perno, A. Antinori

CO 2 **Efficient inhibition by Raltegravir of HIV-1 Infection in Human Primary Macrophages and in CD4+ T Lymphocytes and of the cellular Apoptosis HIV-1 correlated**
M. Pollicita, F. Scopelliti, A. Casabianca, C. Orlandi, R. Salpini, F. Di Santo, A. Bertoli, M. Magnani, S. Aquaro, F. Ceccherini Silberstein, C.F. Perno

CO 3 **Immunity and hormonal status in HIV-infected women: study of dendritic cells, CCR5 expression, IFN-α response and immune activation markers**
G. la Martire, R. Rossi, M. Lichtner, R. Marocco, C. Ajassa, G. d'Ettorre, C. M. Mastroianni, V. Vullo

CO 4 **Natural raltegravir-resistance is a rare event in integrase-inhibitors naïve patients, and when present, is confined to a restricted minority of secondary variants and is not associated with virological response to raltegravir**
D. Armenia, I. Vandenbroucke, L. Fabeni, R. D'Arrigo, K. Van Baelen, H. Van Marck, V. Micheli, L. Van Wesenbeeck, M.P. Trotta, S. Lo Caputo, B. Bruzzone, A. Capetti, G. Di Perri, P. Narciso, G. Rizzardini, A. Antinori, L. Stuyver, C.F. Perno, F. Ceccherini-Silberstein

CO 5 **Efficacy of Maraviroc (MVC) as intensification strategy in immunological non-responder (INR) HIV-1-infected patients treated with HAART**
S. Rusconi, P. Vitiello, F. Adorni, S. Ferramosca, E. Focà, A. Capetti, P. Meraviglia, T. Quirino, S. Bonora, M. D'Annunzio, A. Di Biagio, M. Di Pietro, L. Butini, G. Orofino, M. Colafigli, V. Vullo, D. Francisci, M. Andreoni, E. Merlini, G. Marchetti

CO 6 **Withdrawn**

CO 7 **Specific Genetic Signatures in V3 Base Can Modulate Co-receptor Usage in Vivo, the Interaction with Neutralizing Antibodies, and HIV-1 Cytopathic Effect**
C. Alteri, V. Svicher, A. Artese, F. Mercurio, R. D'Arrigo, S. Alcaro, F. Ceccherini, A. Giacometti, V. Vullo, A. D'Arminio Monforte, G. Di Perri, C. Mussini, R. Maserati, F. Maggiolo, C. Viscoli, R. Cauda, M.Borderi, A. Gori, A. De Luca, M. Andreoni, A. Antinori, M. Zazzi, S. Nozza, M. Clementi, G. Angarano, S. Parisi, A. Lazzarin, C.F. Perno

CO 8 **Comparative immunological response to efavirenz versus boosted protease inhibitors and to tenofovir versus zidovudine as first-line therapy in patients with advanced HIV infection**
L. Soavi, S. Leone, D. Valenti, G. Cologni, G. Gregis, G. Quinzan, D. Ripamonti, F. Suter, F. Maggiolo

CO 9 **Efficient Immune Reconstitution in Severely Immune Depressed HIV+ Naive Patients Starting a First Lopinavir/ritonavir-Containing Regimen**
G. Marchetti, E. Merlini, F. Bai, G. M. Bellistrì, G. Ancona, T. Bini, A. d'Arminio Monforte

ORAL COMMUNICATIONS (ROOM B)
Session: Basic Science / Virology
President: *A. Giacometti* (Ancona)
Chairmen: *F. Leoncini* (Florence), *P. Navarra* (Rome), *E. Raise* (Venice)

CO 10 **Genotypic Inhibitory Quotient and Historical Genotype predict the response to lopinavir and atazanavir therapy in HIV-1-infected patients**
M. Iannetta,C. D'Agostino, A. D'Abramo, L. Erario, F. Cristofano, G. Natoli, A.P. Massetti, V. Vullo

CO 11 **Modification of the abbott real-time HIV-1 assay to quantify minimal residual viraemia: standardization and performance evaluation**
A. Amendola, R. Sabatini, M. Bloisi, C. Angeletti, S. Belladonna, G. De Cunto, R. Moriconi, F.R. Pulvirenti, M.R. Capobianchi

CO 12 **Underestimation of viremia of HIV-1 variants by commercial Real Time PCR assays**
B. Foglieni, D. Candotti, I. Guarnori, L. Raffaele, A. Berzuini, M. Spreafico, A. Orani, R. Rossotti, D. Rossi, J.P. Allain, D. Prati

CO 13 **A Linear Trimannoside Mimic Inhibits DC-SIGN Mediated HIV Infection by Polyvalent Presentation**
A. Berzi, S. Sattin, M. Sanchez-Navarro, J.F Rojo, A. Bernardi, M. Clerici

CO 14 **High frequency of man having sex with man with unknown duration of infection in epidemiological networks involving primary resistance in HIV-1 naïve individuals**
A. Lai, M. Violin, E. Ebranati, M. Franzetti, A. Lo Presti , V. Rossini, A. Ranghiero, F. Simonetti, P. Meraviglia, G. Rizzardini, M.R. Gismondo, M. Galli, G. Zehender, C. Balotta

CO 15 **Clinical significance of JCV DNA replication in plasma and urine of PML patients**
A. Bestetti , S. Bossolasco, M. Testa, A. Granata, A. Pazzi, R. Formicola, A. Lazzarin, P. Cinque

CO 16 **JCV specific CTL responses against a novel HLA-A*02 restricted VP1 epitope**
M. Testa, A. Bestetti, S. Bossolasco, A. Pazzi, A.Granata, R. Formicola, A. Lazzarin, P. Cinque

CO 17 **Analysis of HIV-1 quasispecies by ultra-deep pyrosequencing in gut biopsies and plasma samples from acutely infected patients**
G. Rozera, I. Abbate, C. Vlassi, A. Bruselles, B. Bartolini, G. D'Offizi, P. Narciso, R. Lionetti, M.R. Capobianchi

CO 18 **Formal breaking of B tolerance to induce HIV blocking CCR5 Specific antibodies as new vaccinal strategies**
V. Asti, V. Merati, L. Diomede, F. Clemente, M.R. Parisi, C. Pastori, L. Lopalco

15.30–16.30 **ROUND TABLE (ASSEMBLY HALL)**
Determinants of sexual transmission of HIV
Chairman: *F. Brancati* (Milan)
Introduction: *A.M. Cattelan* (Rovigo)
Key points:

Behavioural determinants of sexual transmission of HIV
M.P. Carrieri (Marseille)

Viro-immunological determinants of sexual transmission of HIV
E. Girardi (Rome)

Controlling STIs to reduce sexual transmission of HIV: a worthwhile effort?
B. Suligoi (Rome)

ROUND TABLE (ROOM B)
HIV and access to drugs in disadvantaged populations
Chairman: *L. Monini* (Brescia)
Introduction: *M. Malena* (Verona)
Key points:

Drug addicts
A. Boschini (Coriano)

Inmates
*S. Babudier*i (Sassari)

Migrants
I. El-Hamad (Brescia) / *M.C. Pezzoli* (Brescia)

16.30–18.30 **ORAL COMMUNICATIONS (ASSEMBLY HALL)**
Session: Clinical Science / ARTV: Long-term Toxicity
President: *G. Pastore* (Bari)
Chairmen: *E. Francavilla* (Belluno), *L. Sighinolfi* (Ferrara), *E. Petrelli* (Pesaro)

CO 19 **Adiponectin and Osteoprotegerin in HIV-infected patients: an unespected association between protective and dangerosus factors for cardiovascular diseases**
G. Ceccarelli, G. d'Ettorre, S.T. Mewamba, MC. Rizza, S. Baroncelli, S. Vella, C.M. Mastroianni, V. Vullo

CO 20 **Anaemia in HIV pregnant women and their neonates exposed to non-ZDV-based HAART**
C. Pinnetti, S. Baroncelli, A. Molinari, K. Luzi, A. Degli Antoni, G. Guaraldi, E. Tamburrini, M. Floridia

CO 21 **People with intermediate level of adherence taking PI or NNRTI have different viro-immunological outcomes**
R. Murri, A. Cingolani, A. De Luca, S. Di Giambenedetto, G. Marasca, G. De Matteis, M. Fabbiani, C. Pinnetti, E. Tamburrini

CO 22 **The ritonavir pro-atherogenetic activity prevention by PPARα agonist in ApoE-/- mice is mediated by CD36**
S. Fiorucci, A. Mencarelli, S. Cipriani, D. Francisci, P. Giuseppe, B. Renga, F. Baldelli

CO 23 **Virological rebound after more than 6 months of follow-up in HIV-infected patients with residual viremia vs. <1 HIV RNA copy/mL**
N. Gianotti, L. Galli, S. Racca, F. Cossarini, V. Spagnuolo, B. Barda, F. Canducci, M. Clementi, A. Lazzarin, A. Castagna

CO 24 **Durability of a novel salvage therapy in R5 HIV-infected patients: maraviroc, raltegravir, etravirine**
S. Nozza, A. Bigoloni, L. Galli, N. Gianotti, M. Pogliaghi, F. Cossarini, S. Salpietro, A. Galli, L. Della Torre, G. Tambussi, A. Lazzarin, A. Castagna

CO 25 **Phase II study of intrathecal long acting liposomal cytarabine (Depocyte®) in the prophylaxis of lymphomatous meningitis in HIV-related non-hodgkin's lymphoma**
M. Spina, F. Martellotta, M. Berretta, E. Zanet, A. Lleshi, V. Canzonieri, P. Bulian, M. Bibas, A. Antinori, U. Tirelli

CO 26 **Long-term follow-up of rituximab and infusional cyclophosphamide, doxorubicin, and etoposide (CDE) in combination with HAART in HIV-related non-Hodgkin's lymphomas (NHL)**
M. Spina, U. Jaeger, J.A. Sparano, R. Talamini, G. Rossi, E. Vaccher, U. Tirelli

CO 27 **High prevalence of anal human papillomavirus infection among HIV-infected patients in the absence of anal intercourse**
G. d'Ettorre, G. Ceccarelli, A. Fiore, S. Stella, C. Rizza, S. Mewanda, S. Marcellini, C.M. Mastroianni, V. Vullo, M. Indinnimeo

CO 28 **Monitoring the toxicity related to HAART from 2001 to 2009 in Burkina Faso: clinical adverse events vs. laboratory adverse events: prevalence, grading and outcome**
E. Focà, S. Odolini, F. Buelli, V. Pietra, J. Semporé, K. Sanogo, P. Rodari, S. Pignatelli, J. Simporé, G. Carosi, F. Castelli

CO 29 **Early markers of mitochondrial tubular injury in patients treated with tenofovir vs abacavir-including backbones**
C. Bellacosa, P. Maggi, V. Montinaro, A. Volpe, G. Trillo, G. Angarano

CO 30 **APRI and FIB-4 for the evaluation of liver fibrosis: concordance analysis, evolution and predictors in a cohort of HIV patients without HCV or HBV infection: results from the EPOKA-a MASTER Cohort**
M. Mendeni, D. Gotti, N. Ladisa, E. Quiros-Roldan, E. Focà, F. Castelnuovo, G. Carosi, G. Angarano, C. Torti

ORAL COMMUNICATIONS (ROOM B)
Session: Epidemiology and Social Science / Epidemiology and Prevention
President: *F. De Rosa* (Rome)
Chairmen: *C. Cellesi* (Siena), *A. Chiodera* (Macerata),

CO 31 **HIV incidence estimate in Lazio Region combining HIV/AIDS surveillance with data about testing history and biomarker HIV test results to identify recent infections**
A. Mammone, P. Pezzotti, C. Angeletti, N. Orchi, A. Carboni, A. Navarra, M.R. Sciarrone, M. Selleri, C. Sias, V. Puro, E. Girardi

CO 32 **Potential impact of routine testing of patients with HIV ID in preventing late HIV diagnosis**
G. Chiaradaia, P. Scognamiglio, A.Navarra, S. Pittalis, G. De Carli, M. Giuliani, S. Aviani, L. Tacconi, S. Schito, A. De Filippis, S. Grisetti, A. Sampaolesi, A. Corpolongo, V. Puro, N. Orchi, G. Ippolito, E. Girardi

CO 33 **Main features of newly diagnosed HIV patients**
S. Casari, R. Allegri, S. Costarelli, S. Compostella, G. Paraninfo, C. Muscio, C. Facchi, A. Tenchini, F. Castelli, G. Cristini, G. Carosi

CO 34 **Characteristics trends of AIDS and tuberculosis cases in Italy: 1993-2009**
L. Camoni, S. Boros, V. Regine, M. Raimondo, M.C. Salfa, G. Rezza, B. Suligoi

CO 35 **Temporal trend of HIV incidence among patients with sexually transmitted infections in Italy, 1991-2007**
V. Regine, M.C. Salfa, M. Dorrucci, M. Giuliani, L. Camoni, M. Raimondo, B. Suligoi and the Italian STI Surveillance Working Group

CO 36 **Alternative and not-invasive screening to implement hiv prevention program: easy test performed in street-lab**
M.R. Parisi, L. Soldini, D. Colzani, S. Negri, F.B.Lillo, A. Lazzarin

CO 37 **Molecular epidemiology and prevalence of Human Immunodeficiency Virus infection in adult cases of Acute Hepatitis A in the Rome metropolitan area, 2002-2008**
P. Scognamiglio, L. Bordi, G. Rozera, M. R. Sciarrone, G. Antonucci, A. Rianda, A. Corpolongo, P. Noto, S. Grisetti, C. Gnesivo, M. R. Loffredo, G.Ippolito, M. R. Capobianchi, E. Girardi

CO 38 **The migration project in Veneto Region: evaluation of epidemiological impact of Tubercolosis, HIV, HBV, HCV infections and syphilis**
E. Morelli, M. Disegna, N. Gennaro, C. Gallo, E. Raise

CO 39 **The necessary surveillance of screening of HIV infection in pregnant women: not a matter taken for granted**
F. Cervi, B. Guerra, C. Puccetti, M. Contoli, F. Bellussi, A. Pedrazzi, M. Masi, N. Rizzo

CO 40 **Causes of death in persons infected with the Human Immunodeficiency Virus**
S. Leone, C. Torti, S. Di Giambenedetto, S. Lo Caputo, N. Ladisa, L. Sighinolfi, E. Quiros-Roldan, M. Airoldi, A. Pan, M. Fabbiani, F. Castelnuovo, F. Suter, F. Maggiolo

CO 41 **Antiretroviral prophylaxis following sexual HIV exposure in Italy**
V. Puro, G. De Carli, E. Schifano, P. Piselli, A. Franco, F. Niero, L. Signorini, G. Ippolito

CO 42 **Acceptability of the Contact Tracing (CT) & Partner Notification (PN) procedures**
M. Permiani, O. Bosco, E. Baccaglino, P. Di Ruscio, U. Galvan, M. Malena, G. Serpelloni

Tuesday 22 June, 2010

Lectures (ASSEMBLY HALL)
Chairmen: *P.L. Viale* (Bologna), *C. Viscoli* (Genua)

8.30–9.00 **Horizon scanning: new drugs**
C. Flexner (Baltimore)

9.00–9.30 **Neuropenetration/neuroactivity of ARV drugs and impact on neuropsychological aspects of HIV disease**
S. Letendre (San Diego)

9.30–11.30 **SYMPOSIUM: Clinical Science / Co-infections and co-morbidities (ASSEMBLY HALL)**
Chairmen: *G.B. Gaeta* (Naples), *G. Taliani* (Rome)

HIV-related tuberculosis: prevention and management
R. Chaisson (Baltimore)

Towards a decline in hepatitis related mortality in HIV infected patients
V. Soriano (Madrid)

Emergent diseases of the CNS: pathogenesis and possibile treatments
P. Cinque (Milan)

The impact of "behavioural, environmental" and HIV-related factors on the risk of neoplasias in HIV
M. Spina (Aviano)

- Supervisors: *R. Cauda* (Rome), *F. Mazzotta* (Florence)
- Coordinators/Discussants: *R. Bruno* (Pavia), *A. Gori* (Monza), *A. Matteelli* (Brescia), *P. Nasta* (Brescia)

SYMPOSIUM: Epidemiology and Social Science / Pharmacoeconomics, Access to Care and Quality of Life (ROOM B)
Chairmen: *E. Concia* (Verona), *G. Scalise* (Ancona)

HAART today: quality and sustainability
M. Moroni/G. Rizzardini (Milan)

How to measure the HAART costs?
A. Tramarin (Vicenza)

What does hamper access and retention into care of HIV patients? How could we overcome?
M. Oldrini (Milan)

Quality of life of HIV-infected people: implications for research and clinical practice
R. Bucciardini (Rome)

- Supervisors: *A. Cerioli* (Bologna), *F. von Schloesser* (Rome)
- Coordinators/Discussants: *S. Bonora* (Turin), *E. Girardi* (Rome), *S. Marcotullio* (Rome), *S. Vella* (Rome)

11.30–12.30 **ORAL COMMUNICATIONS (ASSEMBLY HALL)**
Session: Clinical Science / Co-infections and Co-morbidities
President: *G. Filice* (Pavia)
Chairmen: *G. Antonucci* (Rome), *F. Ghinelli* (Ferrara), *N. Petrosillo* (Rome)

CO 43 **Detection of IgG against JC Viral Protein-1 (VP1) for management of patients with Progressive Multifocal Leukoencephalopathy (PML)**
S. Bossolasco, K. Simon, M. Testa, A. Bestetti, H. Hasson, A. Lazzarin, L. Gorelnik, P. Cinque

CO 44 **Neurosyphilis incidence and screening practices among HIV infected patients**
V. Bergamaschi, A.C. Carvalho, I. El-Hamad, S. Bigoni, F. Castelnuovo, C. Fornabaio, V. Del Punta, S. Casari, S. Caligaris, G. Cristini, G. Carosi, A. Matteelli

CO 45 **Cervico-vaginal HIV shedding is not related to cervical HPV infection**
C. Fornabaio, F. Lillo, J.R. Fiore, A.C. Carvalho, V. Bergamaschi, S. Bigoni, A. Calabresi, F. Castelnuovo, I. El-Hamad, M. Comelli, M.R. Parisi, G. Carosi, A. Matteelli

CO 46 **Longitudinal assessment of pre-transplant mortality risk among HIV-infected and uninfected patients with end-stage liver disease: the role of delta-meld score**
S. Cocchi, S. Zona, R. Montalti, F. Di Benedetto, M. Codeluppi, G.E. Gerunda, R. Esposito, G. Guaraldi

CO 47 **Measurement of endothelial function in HIV-infected pregnant women: a case-control study**
K. Luzi, S. Zona, A. Lattanzi, R. Bruno, F. Facchinetti, R. Esposito, G. Guaraldi

CO 48 **HBV Evolution and Drug Resistance Emergence in HIV-HBV Co-infected Patients depends upon the Synergistic Interaction between Immunological and Pharmacological Selective Pressure**
V. Cento, R. Salpini, A. Lo Presti, C. Gori, A. Bertoli, F. Marcuccilli, M. Arlotti, M. Puoti, N. Ladisa, G. Rizzardini, M. Ciccozzi, A. D'Arminio Monforte, C.F. Perno, V. Svicher

ORAL COMMUNICATIONS (ROOM B)
Session: Epidemiology and Social Science / Pharmacoeconomics, Access to Care and Quality of Life
President: *M.S. Mura* (Sassari)
Chairmen: *L. Minoli* (Pavia), *P. Patané* (Catania), *G. Stagni* (Perugia)

CO 49 **Health care expenditure for HIV-patients by Health States**
P. Bonfanti, U. Restelli, E. Ricci, S. Melzi, E. Porazzi, L. Carenzi, M. Coen, G. Orlando, L. Casartelli, E. Foglia, G. Rizzardini, D. Croce

CO 50 **Analysis of HAART combinations and costs in first line treatment in HIV-positive naïve patients at the Hospital-University Center "L. Sacco" in Milan**
R. Curcio, M.G. Piacenza, S. Vimercati, S. Melzi, M. Coen, P. Zucchi, A. Muscatello, A. Capetti, G. Rizzardini, M. Medaglia

CO 51 **Drug-specific risk of adverse events onset related to HAART in a resource-limited setting from 2001 to 2009: the experience of 3 Medical Centers in Burkina Faso**
E. Focà, F. Buelli, S. Odolini, V. Pietra, J. Semporé, K. Sanogo, M. Rosina, S. Pignatelli, J. Simporé, G. Carosi, F. Castelli

CO 52 **Arterial stiffness assessment in Tanzania by Pulse Wave Velocity: a case-control study of a HIV-infected cohort**
G. Guaraldi, L. Kalolo, S. Zona, A. Bianchi, C. Sola, M. Calmieri, C. Broglia, S. Bettonte, P. Salvi, P. Raggi

CO 53 **Learning from the past: the possible impact of migration, late HAART initiation and prescription of non-HAART regimens on the risk of positive HIV-RNA at delivery**
I. Izzo, M.A. Forleo, S. Casari, A. Calabresi, E. Quiros-Roldan, M. Magoni, G. Carosi, C. Torti

CO 54 **The ISS-HIV-symptom scale: the routine evaluation of health related quality of life**
R. Bucciardini, G. D'Ettorre, G. Ceccarelli, M. Lauriola, V. Fragola, M. Mirra, R. Murri

Lectures (ASSEMBLY HALL)
Chairmen: *O. Armignacco* (Viterbo), *P. Grossi* (Varese)

12.30–13.00 **HIV Host Genomics**
P. Tarr (Basilea)

13.00–13.30 **Timing to start HAART: towards earlier interventions**
J. Gallant (Baltimore)

13.30–14.30 **Lunch**

14.30–15.30 **ORAL COMMUNICATIONS (ASSEMBLY HALL)**
Session: Basic Science / Immunopathogenesis
President: *E. Pizzigallo* (Chieti)
Chairmen: *Borgia* (Naples), *G. Raineri* (Cuneo), *G. Parruti* (Pescara)

CO 55 **Carotid artery intima-media thickness and arterial stiffness in HIV infected patients**
C. Ucciferri, K. Falasca, P. Mancino, R. Tommasi, A. Tatasciore, E. Pizzigallo, J. Vecchiet

CO 56 **Naturally C-Terminally truncated STAT5 (STAT5Δ): a novel negative controller of HIV-1 transcription and expression**
G. Della Chiara, A. Crotti, M. Giacca, G. Poli, M. Lusic

CO 57 **HIV-1 infection of cervico-vaginal tissue ex vivo**
E. Saba, J.C. Grivel, C. Vanpouille, A. Lisco, L. Margolis

CO 58 **Effect of envelope cholesterol withdrawal on HIV ability to induce type I interferon production and pDC activation**
B. Tavano, C.M. Royle, S. Doumazos, D.R. Graham, V.N. Aquino, L. Piacentini, M. Biasin, M. Clerici, A. Boasso

CO 59 **The mucosae-associated epithelial chemokine (CCL28) modulates mucosal immunity in balb/c mice immunized with hiv-1 virus like particles**
V. Rainone, K. Überla, V. Temchura, D. Trabattoni, A. Clivio, F. Veas, M. Nebuloni, M. Clerici

CO 60 **Emergence of exhausted B and T cells in asymptomatic HIV-1-infected patients naïve for HAART is related to reduced immune surveillance**
M. Fogli, F. Malacarne, C. Torti, S. Fiorentini, I. Izzo, F. Maggi, G. Carosi, A. Caruso

ORAL COMMUNICATIONS (ROOM B)
Session: Clinical Science / Co-infections and Co-morbidities
President: *A. Chirianni (Naples)*
Chairmen*: T. Santantonio (Bari), G. Todaro (Catania), M. Tavio (Ancona)*

CO 61 **Predictors of complete early virological response (cEVR) and sustained virological response (SVR) in HIV-HCV co-infected subjects treated with Pegilated interferon/ribavirin (PEG/RBV)**
F. Gatti, P. Nasta, E. Ragazzoni, P. Navarra, M. Puoti, K. Prestini, F. Borghi, G Carosi

CO 62 **Association between hepatitis C viremia and serum triglyceride in Italian national cohort observational study (OPERA)**
P. Nasta, F. Gatti, F. Suter, I. Maida, A Chirianni, G. Golotta, A. De Bona, A. Manini, P. Sacchi, C. Iannacone, G. Carosi

CO 63 **Raltegravir and enfuvirtide as a "bridge" antiretroviral therapy in kidney-transplanted patients with HIV infection receiving everolimus and low-dose cyclosporine: a case-control study**
S. Cocchi, D. Bonucchi, R. Pulizzi, G. Ghiandai, G. Mori, C. Americo, S. Zona, M. Codeluppi, R. Esposito, G. Cappelli, G. Guaraldi

CO 64 **High prevalence of HPV infection in genital and oral sites in HIV-infected patients: predictors of oncogenic genotypes and abnormal genital cytology**
L. Comi, F. Bai, M. Rovati, A. Pandolfo, M. Tarozzi, B. Cassani, S. Rossi, M. Moneta, G. Marchetti, A. Carrassi, M. Ravizza, S. Bosari, T. Bini, A. d'Arminio Monforte

CO 65 **HIV-1 and HPV: high risk of cervical cancer**
A. Busto, A. Maddaloni, M.G. Guida, M. D'Abbraccio, M. De Marco, M. Figoni, A. De Rosa, M. Talamo, N. Abrescia

CO 66 **Haemostatic markers and cardiovascular risk in HIV naïve patients**
P. Corsi, C. Martinelli, A. Carocci, V. Mastronardi, F. Cesari, R. Abbate, A. Rogolino, F. Leoncini

15.30–17.00 **SYMPOSIUM: Clinical Science / ARTV: Long-term Toxicity (ASSEMBLY HALL)**
Chairmen: *F. Piccinino* (Naples), *R. Russo* (Catania)

Osteopenia/osteoporosis
F. Vescini (Gorizia), *M. Borderi* (Bologna)

Diabetes and renal diseases
M. Bevilacqua (Milan), *A. Castagna* (Milan)

- *Supervisors: A. d'Arminio Monforte* (Milan), *M. Galli* (Milan)
- *Coordinators/Discussants: C. Gervasoni* (Milan), *G. Guaraldi* (Modena), *P. Maggi* (Bari), *R. Maserati* (Pavia)

15.30–17.00 **ORAL COMMUNICATIONS (ROOM B)**
Session: "Late Breakers"
Chairmen: *P. Di Gregorio* (Catania), *M. Mazzeo* (Salerno), *R. Pempinello* (Naples)

Please see pages *94-97.*

17.00–17.15 **PRIZE-GIVING CEREMONY FOR THE BEST CONTRIBUTIONS FROM YOUNG RESEARCHERS (ASSEMBLY HALL)**

17.15–17.45 **INTO THE FUTURE (ASSEMBLY HALL)**
IX Congresso SIMIT, Roma 2010
A. Antinori (Rome), *G. Ippolito* (Rome)

III° ICAR, Firenze 2011
F. Mazzotta (Florence)

XIX IAS, Roma 2011
S. Vella (Rome)

CONCLUSIONS
G. Carosi

CO 1

Infection 2010; 38 (Suppl. I): 11

Extended resistance to the historical antiretroviral drug classes: is it still a risk factor for HIV progression?

M. Zaccarelli[1], P. Lorenzini[1], F. Forbici[1], V. Tozzi[1], C. Gori[1], P. Marconi[1], F. Ceccherini-Silberstein[2], A. Boumis[1], P. Narciso[1], C.F. Perno[2], A. Antinori[1]
[1]National Institute for Infectious Diseases "Lazzaro Spallanzani", Rome, [2]Department of Experimental Medicine, University of "Tor Vergata", Rome, Italy.

Background: Recent observations from our research group demonstrated that extended resistance to all the three main antiretroviral classes (NRTI, NNRTI, PI), calculated using the IAS-USA criteria for multi-class resistance, is a marker of disease progression up to six years of follow-up from failure. However, in the past five years an extraordinary number of new drugs and three new drug classes were approved and entered in the current clinical use.
Therefore, the aim of the present analysis is to evaluate if extended resistance to the main historical drug classes is a risk factor for HIV progression in recently cART-failing patients.
Methods: Patients undergoing genotypic resistance test after treatment failure in the period 1999-2008 were included. The risk of progression was calculated with survival analysis separately for patients who failed between 1999-2003 and 2004-2008. To identify the independent effect of resistance on HIV progression, demographic, behavioral and clinical factors were considered as covariates. Class resistance for the three historical drug classes was assessed using Rega interpretation system (v. 8.0.1) when no fully active drug in each class was present. Darunavir was not considered in the analysis since the drug resulted fully active in all patients.
Follow-up was carried out up to December 2009: new AIDS event or death were considered study end-point.
Results: Overall, 1360 patients were included, of whom 693 in the 1999-2003 and 667 in the 2004-2008 group; during follow-up, 151 and 58 new AIDS/death were observed in the two groups, respectively. At survival analysis, the proportion of patients who achieved the study end-point after 5 years of observation were 24% in the 1999-2003 and 11% in the 2004-2008 group.
In the 1999-2003 group, the use of the latest Rega system confirmed a higher risk of progression related to resistance to all the three main classes: 44% vs. 23% in patients with resistance to <3 classes, (p=0.06). In contrast, the risks of progression were considerably lower in the 2003-2008 group and without significant differences by number of class resistance (10% in patients with resistance to all 3 classes vs. 9% for resistance to <3 classes).
At multivariable analysis, factors related to higher risk of progression in patients enrolled from 2004 were: lower CD4 count, higher HIV-RNA, previous AIDS diagnosis and intravenous drug-use as risk factor for HIV.
Conclusions: The availability for current use of new drugs, belonging to old classes but with different resistance pattern and to new classes: entry inhibitors, integrase inhibitors and CCR5 inhibitors, completely changed the scenario of antiretroviral therapy, particularly in multi-experienced patients. Indeed, our data suggest that the new drugs allow to overcome extended resistance to the historical drug classes, contributing to reduce the onset of AIDS and to improve survival on short/medium period of observation.

CO 2

Infection 2010; 38 (Suppl. I): 11

Efficient inhibition by Raltegravir of HIV-1 Infection in Human Primary Macrophages and in CD4+ T Lymphocytes and of the cellular Apoptosis HIV-1 correlated

M. Pollicita[1], F. Scopelliti[1], A. Casabianca[2], C. Orlandi[2], R. Salpini[1], F. Di Santo[1], A. Bertoli[1], M. Magnani[2], S. Aquaro[1, 3], F. Ceccherini Silberstein[1], C.F. Perno[1]
[1]Dept of Experimental Medicine and Biochemical Sciences, University of Rome, Tor Vergata, Italy; [2]Dept of Biomolecular Sciences, University of Urbino, Italy; [3]Dept of Pharmaco-Biology, University of Calabria, Rende (CS), Italy.

Background: Raltegravir (RAL) is the first integrase strand transfer inhibitor (INSTI) approved for the treatment of HIV-1 infection. Consistent evidences show an unusually drop of viral load in the first weeks of treatment. The reason of this effect is still not clarified, and could be due to the effect on HIV-reservoirs, as monocytes-macrophages (M/M). Aim of our study is to investigate the anti-HIV-1 activity of RAL in CD4+ T Lymphocytes and in M/M, and evaluate the ability of such compounds in preventing the HIV-1 related apoptosis.
Methods: CD4+ primary T lymphocytes and M/M were infected with R5- or X4-using HIV-1 strains in presence of RAL and coreceptors inhibitors (AMD and Maraviroc). HIV-1 p24 production was assessed by immunoenzymatic test. Apoptosis of T cells was evaluated by propidium iodide. The quantification of viral DNA (integrated and extracromosomic forms) was performed on HIV-1 infected CD4+T lymphocytes by Real time PCR. Student T test was used for statistical analysis.
Results: The values of EC50 and EC90 for RAL in HIV-1 Bal infected M/M were, respectively, 0.3 and 6.9 nM respectively, comparable to values in PBMC (0.1 and 6.5 nM, respectively).
At day 6 the HIV-1 p24 Ag gag-production was completely negative for all the RAL (120 nM) treated samples ($p<0.001$). In addition, after 3 days (and confirmed at 6 days) of HIV-1 Bal and IIIB infection, we observed that integration inhibition by RAL led to the increase of the extrachromosomic forms (HIV-1 IIIB 80±22%, HIV-1 Bal 100%) compared to what observed in absence of RAL (HIV-1 IIIB 12 ±7%, HIV-1 Bal 47%) or in presence of RT-inhibitor AZT (HIV-1 IIIB 40±38%, HIV-1 Bal 5%).
This phenomenon was highly reduced in presence of RAL (more than 90%of apoptosis reduction; $p<0.001$).
Conclusions: These results showed that RAL strongly reduces HIV-1 production similarly in two different cellular systems, such as M/M and CD4+T lymphocytes, increases the viral extrachromosomial HIV-1 DNA forms, and prevents the HIV-1 related T cellular apoptosis.

CO 3

Infection 2010; 38 (Suppl. I): 11

Immunity and hormonal status in HIV-infected women: study of dendritic cells, CCR5 expression, IFN-α response and immune activation markers

G. la Martire[1], R. Rossi[1], M. Lichtner[2], R. Marocco[2], C. Ajassa[1], G. d'Ettorre[1], C. M. Mastroianni[2], V. Vullo[1]
[1]Sapienza Univ, Rome and [2]Sapienza Univ, Polo Pontino, Latina, Italy

Background: Women have more chances to get infected with HIV and have an increased risk of developing AIDS compared to men at the same level of viral replication. Recent studies suggest that there are sex differences in the innate immune response with women experiencing higher TLR–mediated response of plasmacytoid dendritic cells

(pDC) and IFN-α production. Sexual hormones were found to influence CCR5 expression even if results are controversial.
Objectives: To study circulating pDC and mDC, CCR5 expression, immune activation and IFN-α production in women and men with HIV infection and if hormonal status (menopause, follicular phase, luteal phase) have an influence on immunological parameters.
Methods: Circulating mDCs and pDCs were assessed in whole blood samples from 183 HIV infected patients (58 women, 125 men) and 66 healthy donors using TruCOUNT assay and monoclonal antibodies. In a subgroup of patients CCR5 expression, HLA-DR + and CD38 + CD4 and CD8. IFN-α production were tested in whole blood stimulated by imiquimod.
Results: Women had lower levels of mDCs than men in HIV patients (median: 6420 cells/ml in women vs 8869 of men; p=0,002) and in controls (median: 13059 cell/ml in women vs 14505 cells/ml of men; p=0,04). mDC count was still significant in antiretroviral-treated patients (48 females/94 males) with viral load suppression (median: 6420 cells/ml in women vs 9402 cells/ml in men; p<0,001), while no differences were found in antiretroviral-naïve viremic patients. There were no significant differences in circulating pDC and CD4 count between men and women. The analysis of IFN-α production showed that women had significantly higher production in controls (median: 229 pg/ml in women vs 5 pg/ml in men) while there were no differences in both HIV + women and men. Premenopausal women tended to have a higher degree of CCR5 expression compared to men and postmenopausal women, while the levels of immune activation markers on CD8 T lymphocytes seem to be higher in menopausal women but the results aren't uniform.
Conclusions: The study suggests that innate immunity could play an important role in driving the differences in immune activation and disease progression in HIV-infected women and men. Our study also suggest that sexual hormones are responsible of immune differences between women and men and between women in different hormonal status. This could explain at least in part the different patterns of HIV infection and disease progression and could open to the possibility of different therapeutic strategies in the various phases of women life.

CO 4

Infection 2010; 38 (Suppl. I): 12

Natural raltegravir-resistance is a rare event in integrase-inhibitors naïve patients, and when present, is confined to a restricted minority of secondary variants and is not associated with virological response to raltegravir

D. Armenia[1], I. Vandenbroucke[2], L. Fabeni[1,3], R. D'Arrigo[3], K. Van Baelen[2], H. Van Marck[2], V. Micheli[4], L. Van Wesenbeeck[2], M.P. Trotta[3], S. Lo Caputo[5], B. Bruzzone[6], A. Capetti[4], G. Di Perri[7], P. Narciso[3], G. Rizzardini[4], A. Antinori[3], L. Stuyver[2], C.F. Perno[1, 3], F. Ceccherini-Silberstein[1]
[1]Department of Experimental Medicine and Biochemical Science, University of Rome "Tor Vergata", Rome; [2]Virco BVBA, Mechelen, Belgium; [3]Antiviral Drugs Monitoring Unit & Infectious Disease Divisions, INMI "L. Spallanzani", Rome; [4]Infectious Disease Division, L. Sacco Hospital, Milan; [5]Infectious Disease Division, SM Annunziata Hospital, Florence; [6]Microbiology and Virology Laboratory, San Martino Hospital, Genoa; [7]Department of Infectious Diseases "Amedeo di Savoia Hospital", University of Turin, Turin.

Background: Raltegravir (RAL) is a very potent and effective strand-transfer integrase-inhibitor (INSTI), recently FDA-approved for use in first-line HAART regimen. At today it is unclear if minor variants resistant to RAL are associated with virological response to RAL and might emerge during failure. Therefore the aim of this study is to analyze the prevalence and evolution (by Sanger- and ultra-deep sequencing) of mutations associated with resistance to RAL among HIV-infected patients starting RAL-treatment.
Methods: 111 multi-experienced patients received RAL plus optimized-background-therapy for at least 24 weeks. Integrase (IN) genotyping was performed on plasma HIV-RNA of 111 patients by Sanger-sequencing, while 454-pyrosequencing was done in 23 (14 failing patients and 9 with virological success). Stanford RAL-resistance mutations (primary: 155H-148HRK-143RC; secondary: 74M-92Q-97A-121Y-138AK-140AS-143H-147G-151I-155S-157Q-163R) detected at levels >0.1% (with >10 reads) have been analyzed. IN phenotyping was also performed at baseline and during treatment for failing patients.
Results: At baseline (BL), median HIV-RNA was 5.1log cps/ml; HIV-RNA reached <50 cps/ml in 90/111 patients (67.8%). BL Sanger-sequencing showed no primary and very rare secondary RAL mutations (only T97A, G140A, V151I, G163R, in 1 patient each). At BL pyrosequencing, among >200,000 IN sequences analyzed, no minor variants of primary RAL mutations with a prevalence of >0.1% were found. Secondary F121Y mutation was found with a low frequency (0.6% of sequences) in 1 failing patient. T97A, E138K and V151I mutations were also found at BL, in both failing- and success-group of patients, with a frequency ranging from 0.25 to 98% of viral species. Independently of the sequencing method, the presence of secondary-resistant species at BL was not associated, at failure, with evolution at the same amino acid position or to specific primary RAL-resistance mutations. RAL phenotypic-resistance has never been observed at baseline. At failure, all patients carrying primary mutations N155H, Q148H/R or Y143R, in presence of secondary mutations showed fold changes on susceptibility to RAL >30-100. Interestingly, in 1 patient, we found the combination of two primary mutations, Y143C and N155H, by both Sanger-sequencing and 454-pyrosequencing. These mutations appeared at failure for more than 80% on same haplotypes, and showed a very high phenotypic resistance, particularly for RAL (FC RAL = 493.2; FC elvitegravir = 114.4).
Conclusions: Overall data confirm that pre-existing RAL-resistance is a rare event in INI-naïve patients, and when present, is confined to a restricted minority of secondary variants only. Based on this evidence, IN genotyping in all patients before RAL treatment may not be cost effective and should not be recommended today, at least until evidence of transmitted drug resistance to INIs, or the clinical relevance of IN minor-variants/polymorphisms will be determined.

CO 5

Infection 2010; 38 (Suppl. I): 13

Efficacy of Maraviroc (MVC) as intensification strategy in immunological non-responder (INR) HIV-1-infected patients treated with HAART

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[1]Dipartimento di Scienze Cliniche "Luigi Sacco", Sezione di Malattie Infettive-Immunopatologia, Università degli Studi di Milano, [2]ITB-CNR, Segrate (MI), [3]Clinica Malattie Infettive, Università degli Studi di Brescia, Spedali Civili, Brescia, [4]1a Div. Malattie Infettive, Ospedale Luigi Sacco, Milano, [5]2a Div. Malattie Infettive, Ospedale Luigi Sacco, Milano, [6]Div. Malattie Infettive, Ospedale di Circolo, Busto Arsizio, [7]Clinica Malattie Infettive, Università degli Studi di Torino, [8]Clinica di Malattie Infettive, Ospedale Policlinico di Bari, [9]Clinica Malattie Infettive, Università degli Studi di Genova, Ospedale San Martino, Genova, [10]Div. Malattie Infettive, Ospedale S. Maria Annunziata, Antella-Firenze, [11]Div. Malattie Infettive, Ospedale di Ancona, [12]Div. A Malattie Infettive, Ospedale Amedeo di Savoia, Torino, [13]Istituto di Clinica Malattie Infettive, Università Cattolica del Sacro Cuore, Roma, [14]Div. Malattie Infettive, Ospedale Policlinico Umberto I, Roma, [15]Clinica di Malattie Infettive, Ospedale Policlinico Monteluce, Perugia, [16]Clinica Malattie Infettive, Università Tor Vergata, Roma, [17]Clinica Malattie Infettive e Tropicali, Università degli Studi di Milano, Ospedale San Paolo, Milano.

Background: Under HAART, 7-39% of HIV-infected patients (pts) fail to exhibit a recovery in CD4 cells despite full suppression of viral replication. In MOTIVATE trials, MVC was superior to OBT in increasing CD4 cells in ARV-experienced pts. This study evaluated the clinical efficacy of MVC in terms of CD4 cells recovery, viral replication and tolerability in INR pts.

Methods: Randomised, multicentre, proof of concept study enrolling 100 pts divided into 2 arms: A HAART+MVC, B HAART. Planned F-U is 1 year. Ultrasensitive HIV-RNA was quantified via Amplicor HIV-1 Monitor Kit v1.5, followed by RT-PCR for quantifying 1-50 cp/mL. Naive CDRA+62L+, memory CD45RA-, activated HLA-DR+CD38+, proliferating Ki67+ were measured by flow cytometry. T-test was used for intra and inter-group comparisons. ANCOVA was used to adjust the baseline values.

Results: 100 pts have been randomized (50 pts/arm). 59 pts reached week 12: 30 in arm A and 29 in arm B. 2 HIV-unrelated clinical events were registered in arm B and 2 in arm A (not known the correlation with MVC administration) as well as 9 drop-outs at baseline (withdrawal of the informed consent). No grade 3-4 lab toxicity were reported. At baseline, CD4/CD8 and immune-phenotype was comparable in arm A and B. At week 12, no significant changes in mean CD4 recovery were seen between pts in arm A and B (+41,2 vs -11,6/µl; p=.12). A statistically significant change was observed in mean CD8+ count between pts in arm A and B (+99,3 vs -126,1/µl, p=.025)

At baseline and week 12 an immunological study performed by flow cytometry was carried out in 24 out of 61 pts (13 in arm A, 11 in arm B): at week 12, while B pts experienced a progressive contraction of naive CD4 (81 to 67%, p=.02) and CD8 (81 to 77%, p=.04) with a parallel rise in memory CD4 (16 to 30%, p=.02) and CD8 (13 to 17%, p=.06), no significant loss of naive CD4 (70 to 57%, p=.18) and CD8 (69 to 66%, p=.42) was displayed by A pts with a tendency to higher gain in memory CD4 (24 to 40%, p=.06) and CD8 (11 to 25%, p=.008). By week 12, a similar reduction in activated HLA-DR+CD38+ CD8 and CD4 was shown in B (p=.05) and A pts (p=.03 and p=.02 for CD8 and CD4). No changes were shown in proliferating Ki67+CD4 in A (p=.42) and B pts (p=.47), while a tendency to Ki67+CD8 reduction was shown in A (p=.06) and not in B pts (p=.45). HIV-RNA quantification evidenced a trend to higher median values (BL vs week 12) in B pts: 2 vs 5 cp/mL (p=.37). No changes occurred in arm A.

Conclusions: we can consider the use of MVC as intensification strategy that seems to impact T-cell peripheral immune-phenotype after examining the significant change in CD8* cells count and the evidence of not significant CD4 gain in arm A.Our findings of reduced loss of naive T-cells with a parallel robust rise in the memory pool suggest a role of MVC in reducing peripheral antigen-driven T-cell death, possibly preserving new T-cell production. However, further data are needed to confirm our results.

CO 6

Withdrawn

CO 7

Infection 2010; 38 (Suppl. I): 14

Specific Genetic Signatures in V3 Base Can Modulate Co-receptor Usage in Vivo, the Interaction with Neutralizing Antibodies, and HIV-1 Cytopathic Effect

C. Alteri[1], V. Svicher[1], A. Artese[2], F. Mercurio[1], R. D'Arrigo[3], S. Alcaro[2], F. Ceccherini[1], A. Giacometti[4], V. Vullo[5], A. D'Arminio Monforte[6], G. Di Perri[7], C. Mussini[8], R. Maserati[9], F. Maggiolo[10], C. Viscoli[11], R. Cauda[12], M.Borderi[13], A. Gori[14], A. De Luca[12], M. Andreoni[1], A. Antinori[2], M. Zazzi[15], S. Nozza[16], M. Clementi[16], G. Angarano[17], S. Parisi1[8], A. Lazzarin[16], C.F. Perno[1] on behalf of OSCAR group.
[1]Università degli Studi di Roma "Tor Vergata"; [2]Università di Catanzaro "Magna Graecia"; [3]Istituto Nazionale per le Malattie Infettive "Lazzaro Spallanzani", Roma; [4]Azienda Ospedaliero Universitaria Ospedali Riuniti di Ancona; [5]Policlinico "Umberto I", Roma; [6]Ospedale "S. Paolo", Milano; [7]Università degli Studi di Torino; [8]Policlinico di Modena; [9]IRCCS Policlinico S. Matteo, Pavia; [10]Ospedali Riuniti Bergamo; [11]Azienda Ospedaliera Universitaria San Martino, Genova; [12]Università Cattolica "Sacro Cuore"; [13]Policlinico "S. Orsola-Malpighi", Bologna; [14]Ospedale "S. Gerardo", Monza; [15]Ospedale "S.M. Annunziata", Firenze; [16]IRCCS "San Raffaele"; [17]Università degli Studi di Foggia; [18]Università degli Studi di Padova.

Background: Here, we investigate the correlation of V3-determinants correlated with different coreceptor-usage with viro-immunological parameters, and how they affect the interaction with CCR5 N-terminus, crucial for R5-viruses entry, and neutralizing antibody-412d.
Methods: HIV-1 coreceptor-usage was assessed in 544 HIV-1 B-subtype infected patients by V3-sequencing+tropism-prediction using geno2pheno-algorithm (false-positive rate=10%). The enhanced sensitivity version of Trofile (ESTA) was available for 324 patients. The gp120-interaction with CCR5 N-terminus/antibody-412d was evaluated by docking-analysis starting from the model described in Huang, Science 2007.
Results: Genotypic test identified 410 R5-viruses and 134 X4-viruses. Concordance with ESTA was 81.8%, specificity and sensitivity were 92.3% and 59.2%, respectively.
Genotypic analysis shows additional V3 determinants (beyond V3-positions 11/25) significantly correlated with CCR5- or CXCR4-usage. Those, associated with CXCR4-usage and localized in V3-base, modulate gp120 binding-affinity for both CCR5 N-terminus and antibody-412d. This is the case of N5Y and N7K absent in R5-viruses and present in 4.5% and 6% of X4-viruses (P<0.005 after multiple-comparison correction), respectively, and of Q32K, occurring in 28.4% of X4-viruses and 14.9% of R5-viruses (P=0.004 after multiple-comparison correction). Their presence determines a decreased-affinity for CCR5 N-terminus equal or stronger than that already known and observed in presence of positive-charges at the well-known positions 11 or 25 (N5Y:-6.60Kcal/mol; N7K:-5.40Kcal/mol; Q32K:-6.70Kcal/mol; E25R=S11R:-6.70Kcal/mol; WT:-6.90Kcal/mol). N7K alone increases the distance between V3-position 7 and the sulphotyrosine at CCR5-position 14 (crucial for binding to gp120), thus abrogating the interaction between these two important residues. Conversely, N5Y and N7K (but not Q32K) determine an increased affinity for the neutralizing-antibody-412d, again stronger than in presence of S11R (N5Y:-6.50Kcal/mol; N7K:-6.60Kcal/mol; S11R:-6.30Kcal/mol; WT:-5.50Kcal/mol), supporting that specific determinants in V3-base can enhance HIV-1 sensitivity to neutralizing-antibodies.
In addition, among all V3-determinants associated with CXCR4-usage, only the presence of N5Y and T8A/I, even in X4-viruses from drug-naive patients, correlate with lower CD4-count, (without any correlation with viremia) (37±24cells/ul with T8A/I versus 302±175cells/ul without T8A/I, P=0.02, and 103±115cells/ul with N5Y versus 349±188cells/ul without N5Y, P=0.03, after multiple-comparison correction), thus suggesting their ability to interfere with HIV-cytopathicity
Discussion: This study provides a snapshot of mechanisms underlying HIV-1 entry and sensitivity to neutralizing-antibodies. This study supports genotype-use for a finer tuning of CCR5-antagonists efficacy, and can also have molecular-implication for vaccine and new entry-inhibitors design.

CO 8

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Comparative immunological response to efavirenz versus boosted protease inhibitors and to tenofovir versus zidovudine as first-line therapy in patients with advanced HIV infection

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Background: Efavirenz (EFV) and protease inhibitors boosted with ritonavir (PI/r) are both recommended as first-line therapies for patients with HIV when combined with two nucleoside reverse transcriptase inhibitors (NRTIs), mainly tenofovir (TDF) plus lamivudine (3TC)/emtricitabine (FTC) while zidovudine (AZT) plus 3TC was a formerly preferred regimen. It is uncertain which therapy is more effective for severely immunodepressed patients. Aim of this study is to compare the immune recovery of different therapeutic regimens.
Methods: Adult, antiretroviral naïve patients with advanced HIV-1 infection (CD4+ T-cells nadir < 350 cells/mmc) were identified in the database of our centre. Data collected included CD4+ T-cells count at baseline and every 6 months thereafter for 60 months. Intention-to-treat (ITT), last observation carried-forward (LOCF) and as treated (AT) analysis were performed.
Results: Overall, 763 patients (79.2% male; mean age 39 years, SD ± 8.8) met the eligibility criteria. By AT analysis PI/r-based regimen at 48 months achieved a better CD4+ T cells recovery than EFV-based regimen (p=0.041), but patients on PI/r dropped out significantly earlier than patients on EFV (mean follow-up: 675 days versus 1014 days, p < 0.0001). Therefore, the immunologic response to EFV and PI/r-based regimen did not significantly differ by either ITT or LOCF analysis. Regarding NRTIs, LOCF analysis showed that patients treated with TDF had a better immunologic response than patients treated with AZT throughout the study period (p < 0.0001), whereas the less stringent AT and ITT analysis detected this difference only in the first HAART period until the 36 follow-up months (Fig. 1). During the whole study period the risk of remaining below the threshold of 350 CD4+ T cells was significantly higher among patients treated with AZT compared with those who received TDF: OR 2.79 (95% CI 1.7-4.4, p < 0.0001) at 6 months and OR 1.55 (95% CI 0.9-2.4, p = 0.056) at 60 months, while there was no difference between EFV and PI/r based regimens when this endpoint was considered. Sub-analysis on specific regimens (AZT+3TC+PI/r, AZT+3TC+EFV, TDF+3TC/FTC+PI/r, TDF+3TC/FTC+EFV) showed a similar immunologic response in all cases but with AZT+3TC+EFV. Differences were not significantly different, probably due to the small sample size of each regimen.
Conclusions: Our study suggests that the immunological efficacy of EFV does not differ from that of PI/r as first-line therapy for HIV infection. AZT, when used as a part of the backbone, negatively influences immunological responses. Conversely, the immunological efficacy of TDF-based regimens seems to be superior to that of AZT-based regimens. TDF+3TC/FTC appears to be the best companion for EFV.

CO 9

Infection 2010; 38 (Suppl. I): 15

Efficient Immune Reconstitution in Severely Immune Depressed HIV+ Naive Patients Starting a First Lopinavir/ritonavir-Containing Regimen

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Background: A substantial number of HIV+ patients (pts) present for care with advanced immunodepression. Lopinavir/ritonavir (LPV/r)-containing regimens resulted in high immune recovery in large randomised trials. The aim of our study was to investigate immune restoration profile, T-cell activation and microbial translocation in HIV+ naïve pts starting a first LPV/r-containing regimen with severe immune depression.
Methods: 20 HIV+ naïve pts starting a first tenofovir/emtricitabine + LPV/r-containing ART with CD4 count<100 were followed for 12 months (T12). At T12 all pts displayed HIV-RNA<50cp/mL. Based on T12 CD4 recovery, pts were: Low Responders –LRs- (T12 CD4 gain <30% and/or CD4 <250/μL), and High Responders –HRs- (T12 CD4 gain ≥30% and/or CD4≥250/μL). Microbial translocation by plasma lipopolysaccharide (LPS) and sCD14 (LAL assay and ELISA), activated CD38+CD8, primed activated CD45R0+38+CD8, central memory CD127+, apoptotic CD95+ CD4 and CD8 (flow cytometry), and plasma IL-7 (ELISA) were tested at baseline (T0) and T12. T0 and T12 differences in each parameter were analyzed by T test.
Results: By T12, all pts showed a significant rise in median CD4 count (p<.0001), central memory CD127+CD4 (p<.0001) and a significant reduction in activated CD38+CD8+ (p=.004). No significant changes in the other immune-phenotypes and microbial translocation parameters were shown. At T12, 8/20 (40%) pts were LRs and 12/20 (60%) HRs. No T0 differences were shown in all parameters between HRs and LRs. T12 changes for HRs and LRs are shown in the table.
At T12, despite both HRs and LRs presented a trend towards reduction in plasma levels of IL-7, only HRs displayed a raise in central memory CD127+CD4. Despite no reduction in translocation parameters was shown in LRs, activated CD38+ CD8 significantly decreased with no differences between the 2 groups. No differences were observed in the others immune parameters between HRs and LRs.
Discussion: In pts with very severe immune depression, LPV/r-containing regimens resulted in adequate immune restoration and reduction of peripheral T-cell activation. Even if pts with lower CD4 recovery failed to efficiently control microbial translocation, LPV/r-based treatment was still able to significantly control peripheral T-cell hyperactivation. Given the predictive significance of T-cell activation on clinical events, our data advocate the efficacy of LPV/r regimens in a broad immune reconstitution even in pts with advanced CD4 T-lymphopenia.

	HRs (n=12)		LRs (n=8)	
	T0	T12	T0	T12
CD4 (n) (Median, IQR*)	56[a] (40,5-69,2)	293(259-354)	55[b] (44-84,5)	133(87–176)
CD95+CD4+ (%) (Median, IQR)	2(1,5-2)	1(0–1)	0(0-1)	1(1–1,75)
CD95+CD8+ (%) (Median, IQR)	3(2,5-9)	1(1–2)	1(1-1)	2,5(2–3)
CD127+CD4 (%) (Median, IQR)	3[a] (3,5-7)	10(7–12)	4(3–4)	4,5(3–8,25)
CD127+CD8 (%) (Median, IQR)	7(7-9)	8(6–10)	8(4—9)	6,5(6–10)
CD38+CD8+ (%) (Median, IQR)	16[a] (14,5-19)	2(2–2)	4[c] (3–8)	1(0,25–1)
CD45R0+CD38+CD8+ (%)(Median,IQR)	8(8-11,5)	8(8–8)	11(7–15)	8,5(5–13,5)
IL-7 (pg/mL)(Median, IQR)	4,8(2-7)	3,7(2–5,5)	11,5(9,5–16)	9(7,1-16)
LPS (pg/mL) (Median, IQR)	75 (53,5-78,6)	75(66–112)	75(60,2–93,8)	77,2(74–129)
sCD14 (μg/mL) (Median, IQR)	3(2,8-4,4)	2,5(2,4–2,9)	3,26[b] (2,9–3,5)	10,6(4,4–14,4)

*IQR (Interquartile Range): [a]p<0,001 T0 vs T12 in HRs; [b]p<0,01 T0 vs T12 in LRs; [c]p<0,05 T0 vs T12 in LRs.

CO 10

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Genotypic Inhibitory Quotient and Historical Genotype predict the response to lopinavir and atazanavir therapy in HIV-1-infected patients

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Background: Resistance to Protease Inhibitor (PI) is correlated to an increase in the drug concentration needed to suppress viral replication. The Genotypic Inhibitory Quotient (GIQ) is the ratio between drug concentration and the number of resistance mutations. The aim of our study was to evaluate the predictive value of historical GIQ (hGIQ) on atazanavir and lopinavir response in HIV-1-infected patients.
Patients and Methods: Forty-seven patients, 26 receiving atazanavir and 21 receiving lopinavir, were enrolled in this study. Drug trough concentrations (Ctrough) were measured at baseline by a high performance liquid chromatography method with ultraviolet detection. HIV RNA was determined at baseline and after 3 months. Virologic response was defined as a viral load < 50 copies/ml or a decrease >1 log10. hGIQ was calculated as the ratio of the PI Ctrough to the number of atazanavir or lopinavir specific mutations in the historical genotype.
Results: In the group of patients receiving lopinavir, 67% were male, mean age was 49 years, mean CD4 count was 536 cells/mm3, mean value of number of previous regimens was 3 and mean Ctrough was 6356 ng/ml. In the group of patients receiving atazanavir, 62% were male, mean age was 42 years, mean CD4 count was 496 cells/mm3, mean value of number of previous regimens was 5 and mean Ctrough was 1118 ng/ml. The cutoff value estimated for the lopinavir hGIQ was 4720 (receiver operating characteristic curve test: 75% specificity, 72% sensitivity, AUC: 0,691). In the group of patients receiving atazanavir the cutoff value of the hGIQ was 222 (receiver operating characteristic curve test: 82% specificity, 80% sensitivity, AUC: 0,812). Virologic response was achieved in 86% of patients with lopinavir hGIQ > 4720, compared with only 50% of patients with hGIQ < 4720; furthermore virologic response was achieved in 93% of patients with atazanavir hGIQ > 222, compared with only 40% of patients with hGIQ < 222.
Conclusion: PI hGIQ is a useful tool for the management of HIV patients, providing a target Ctrough for lopinavir and atazanavir required to achieve virologic response. In summary, this method might be highly helpful for individualized therapeutic management of HIV-1-infected patients.

CO 11

Infection 2010; 38 (Suppl. I): 16

Modification of the abbott real-time HIV-1 assay to quantify minimal residual viraemia: standardization and performance evaluation

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Background: Currently available therapeutic regimens control HIV-1 replication ensuring plasma viral load suppression below 50 copies/ml in most patients (85%). However when viraemia is reduced below the limit of detection (LOD) of commercial diagnostic tests, minimal residual viraemia (MVR) can still be detected. Numerous studies investigating the clinical significance of MVR are ongoing. The assessment of viral load below the LOD of current diagnostic platforms is proving increasingly useful in monitoring viral suppression, to determe the relative effectiveness of different regimens.
Objectives: As the Abbott Real-time HIV-1 diagnostic system shows high accuracy and precision. This real-time PCR- based assay is linear from 40 to 107 copies/mL, and the official LOD is 40 cp/mL. Recently, for samples with <40 cp/ml, we showed that this method is able to detect viral concentrations down to 29 cp/mL (95% CI: 22.2-52.2 cp/mL) with a probability of 95% or greater and a coefficient of variation of less than 20%. In the present study we modified the sample processing protocol and the extent of the calibration curve to obtain a ultrasensitive version of the method.
Methods: The following changes were introduced into standard procedure: A) a different calibration curve with lower levels in order to achieve better accuracy at low-end concentration and B) increased input volume and a sample enrichment via ultracentrifugation.
A) Calibrators with lower concentrations were prepared starting from kit calibrator A, diluted to 1000, 300, 100, and 30 cp/ml (3 replicates for each dilution). Calibrators, samples and controls were prepared according to the manufacturer's instructions. Quantification of viral load was obtained with the m2000rt Abbott instrument using an open mode protocol. For the assay validation, the following parameters were considered: internal control cycle threshold, slope and R2 of the linear regression equation.
B) Plasma samples were concentrated 4 times by ultracentrifugation at 20,000 g for 70 minutes at 4°C and analysed after supernatant removal.
A probit analysis of a serially diluted HIV-1 RNA Working Reagent for NAT assays (NIBSC code:99/63) was performed. In total 27 replicates with concentration ranging from 128 down to 1 cp/mL were analysed.
Results: The probit analysis showed that the in house ultrasensitive version of Abbott Real-Time HIV-1 test is able to detect HIV RNA concentrations down to 3.2 cp/mL with 95% probability (95% CI: 1.29-8.13 cp/mL).
Conclusions: Although this study is still ongoing, preliminary results suggest that a few changes in the standard procedure, easily attainable by routine diagnostic laboratories, could increase analytical sensitivity from 40 to 3.2 cp/mL. Further verification studies are needed to fully define the characteristics performances of this HIV-1 RNA ultra sensitive protocol and to prove that quantitative results below 40 copies /mL can be reliably used in clinical practice.

CO 12

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Underestimation of viremia of HIV-1 variants by commercial Real Time PCR assays

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Background: Nucleic acid technology (NAT) based laboratory methods for the detection and quantification of HIV-1 viral sequences are currently used to identify potentially infectious blood donations in parallel to serological tests, and for the diagnosis and the monitoring of therapy in HIV patients. The diffusion of non-B subtypes infections and recombinant strain infections is rapidly increasing in Europe and North America, and may have important implications for diagnosis.
We previously identified an unusual case of a blood donor seroconverting to anti HIV testing with initially negative NAT results using the AmpliScreen Roche assay (Blood, full manuscript submitted). The donor was infected by a BF recombinant form harboring mutations affecting the performance of amplification of Roche tests.
Aim. We prospectively investigated if this new HIV variant is related to significant underestimation of the viral load among HIV positive patients attending our center.
Methods: We prospectively tested the 553 patients on follow up at our center using both the Roche quantitative COBAS Ampliprep/Taqman and our in house quantitative assay targeting two regions of the HIV genome. Sequencing analysis of HIV gag and env genes was performed and multiple sequence alignment was evaluated with GenBank reference sequences. Phylogenetic programs were used to construct consensus trees.
Results: In 19 patients viral load values were higher (between 1 and 5 log10) than those estimated by the Roche quantitative assay. Eleven patients (58%) were infected by the same HIV-1 BF recombinant strain infecting the donor, which included all the critical mismatches within the probe and primer regions previously described in the index case. In the 8 subjects not infected by the BF strain, 2 were infected by non-B HIV-1 subtypes, related to a A/G and B/G subtypes, since their gag sequences were close to CRF02 and CRF14, respectively. In 5 subjects, we did not identified sequence variations potentially affecting the results of viral load determination. In one patient sequence analysis did not give conclusive results.
The new generation NAT and qRT-PCR assays revealed a more efficient HIV detection.
Conclusions: The BF variant recently identified in a blood donor of our area is a cause of substantial underquantification of the viral load among HIV patients on active follow up at our center. The extraordinary genetic diversity of HIV raises concern about the ability of the commercial assays to detect all known HIV-1 variants, and serological screening remains an indispensable tool for ensuring viral safety of blood components. Surveillance programs aimed at detecting genetically divergent HIV strains should be implemented and maintained worldwide.

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CO 13

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A Linear Trimannoside Mimic Inhibits DC-SIGN Mediated HIV Infection by Polyvalent Presentation

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Background: Development of topical microbicides is a promising approach to prevent sexually transmitted HIV infection. DC-SIGN, expressed by dendritic cells at mucosal tissues, captures HIV by binding envelope glycoprotein gp120. Then DCs migrate to lymph nodes where mediate trans infection of CD4 T lymphocytes, promoting HIV dissemination. Therefore inhibition of HIV interaction with DC-SIGN may represent a strategy to prevent early stages of HIV infection. The main DC-SIGN ligand on HIV gp120, is the high mannose glycan Man9. Structural analogues of high mannose terminal di or trisaccharides, able to compete with binding of DC-SIGN to HIV gp120, were synthesized. These compounds were prepared in multivalent systems to improve the affinity to DC-SIGN.
Methods: Synthesized DC-SIGN inhibitors were tested in a trans infection in vitro assay. The B-THP1/ DC-SIGN cells (a B cell line transfected to express high DC-SIGN levels and supporting efficient DC-SIGN-mediated HIV transmission) were pre-treated with different concentration of compounds, prior to exposure to HIV-1 R5 and X4 tropic strains, in the continued presence of compounds. Then B-THP1/DC-SIGN cells were co-coltured with CD4 T cells purified from healthy donors. After three days viral infection was evaluated by measuring p24 levels in co-culture supernatants. In a different protocol inhibitors were washed after pre-treatment, to evaluate duration of antiviral activity. Cytotoxicity of the compounds was evaluated by staining with 7AAD and cytofluorimetric analysis.
Results: One of compounds tested, a tetravalent dendron containing four copies of a linear trimannoside mimic, was able to inhibit HIV trans infection of CD4 T lymphocytes at low micromolar range, with an IC50 of 5microM. At 100 microM the compound almost completely abrogated the transmission to CD4 T cells of HIV-1 laboratory strains or primary isolates, both R5 and X4 tropic.
Notably the antiviral effect persisted up to 12 hours when the compound was removed after a 30 minutes pre-treatment. Moreover toxicity of the compound was neglectable at the highest concentration tested in infection assay.
Conclusion: The tetravalent dendron presenting trimannoside mimic, in consequence of its anti-infective activity independent of viral tropism, absence of toxicity and long-lasting effect is potentially suitable for development as a vaginal microbicide.

CO 14

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High frequency of man having sex with man with unknown duration of infection in epidemiological networks involving primary resistance in HIV-1 naïve individuals

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Background: HIV epidemics in South Europe underwent to profound changes in the last twenty years. Sexual transmission had substantially replaced intravenous drug use and, according to COA data, heterosexual and homosexual modality of infection represent 40% and 30% of the total infections in Italy, respectively. We studied transmitted drug resistance (TDR) and sexual epidemiological networks in naïve HIV-1 infected individuals to infer epidemic dynamics among risk groups and subjects according to time of diagnosis, using recently developed phylogenetic techniques.
Methods: We analyzed protease and RT sequences of 412 naïve patients carrying HIV-1 B subtype, of whom 23.5% (n=97) were seroconverters (SCs), collected between 2002 and 2008 at 'L. Sacco' Hospital of Milan. The starting tree was performed with MrBayes using a GTR+I+G model. The MCMC search was run for 10x106 generations sampled every 100th generation. TDR mutations were identified according to the 2009 Surveillance Drug Resistance Mutation list for naïve patients.
Results: Modality of infection was as follows: 59.5% (n=245) MSMs, 36.2% (n=149) HEs and 4.3% (n=18) other or unknown risk. Subjects with a chronic infection were 76.5% (n=315). As a whole, 86.9% (n=358) were males and overall TDR was 14.3%.
We identified 34 clades involving 145 sequences (35.2%).
A significantly higher proportion of MSMs (68%, n=98) compared to HEs (30%, n=44) was detected in clusters (p=.003). Ten of 34 clusters involved MSMs only (29.4%), while 2 clades included HEs only (5.9%). In homogeneous clusters the proportion of MSMs was slightly higher than that of HEs (36.7 %, n=36 vs 20.5%, n=9; p=.07). Nine clusters (26.5%) involved resistant strains. Patients with TDR in clusters were 11.7% (17/145), of whom 15 (88.2%) were MSMs. The comparison of proportions of risk groups among patients with TDR indicated a trend for a probability for MSMs to be involved in epidemiological clusters (15.3 %,n=15 vs 4.5%, n=2; p=.08).
Twelve clades included only subjects with unknown duration of infection (35.3%, 12/34), while 1 cluster encompassed SCs only (2.9%, 1/34). Therefore, a highly significant association was found between subjects with unknown duration of infection and homogeneous clusters (p<.001). No difference could be seen in the distribution of SCs or patients with unknown duration of infection and clusters of sequences carrying resistant mutations (7.3%, n=3 vs 14.4%, n=15).
Conclusions: A high prevalence of epidemiological clusters was found in the metropolitan area of Milan, indicating high likelihood of transmission events involving HIV-1 naïve individuals. MSMs have a higher probability to be detected in epidemiological networks and in cluster of patients carrying mutations associated to antiretrovirals. The cluster analysis of the epidemiological networks suggested that the source of new infections was mainly represented by males and MSMs who have a long lasting HIV-1 infection.

CO 15

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Clinical significance of JCV DNA replication in plasma and urine of PML patients

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Background and Objectives: JCV DNA detection in CSF is the only diagnostic biomarker of Progressive Multifocal Leukoencephalopathy (PML), however this disease may be associated with JC virus (JCV) replication in peripheral blood. The availability of less invasive markers in plasma, such JCV DNA, would be an additional tool for diagnosing, predicting and monitoring the disease. The objective of our study was to assess whether JCV DNA detection in plasma can be useful for diagnosis of PML and provide information to better understand its natural history.
Methods: JCV DNA levels were measured by real-time polymerase chain reaction in plasma nearest to the time of PML symptoms from 61 patients with HIV-related PML, 43 HIV infected patients without PML and 74 HIV-negative healthy controls. Levels in plasma were compared to anti-JCV-VP1 Ig G titres, and CSF and urine JCV DNA levels in both PML patients and controls. In a subgroup of cases, JCV NCCR was sequenced from plasma, CSF and urine-derived JCV, to distinguish between "archetype" virus (usually found in urine, non associated with PML) and "rearranged" virus (usually found in brain and associated with PML).
Results: JCV-DNA was found in plasma from 20/60 (33%) HIV infected patients with PML, 3/43 (7%) HIV-infected patients without PML and no HIV-negative control, giving a sensitivity of 33% and specificity of 93% of this test for diagnosis of PML in HIV-infected subjects. JCV DNA load was significantly higher in patients with PML (median 2.00 log c/mL, range 2.00-6.00) than in HIV infected controls (median 2.00 log c/mL, range 2.00-4.30)($p<0.0001$). In CSF, JCV DNA was found in 49/58 patients with PML (84%; median 3.35 log c/mL, range 2.00-7.62) but in none of 10 HIV+ controls, and in urine of 13/23 patients with PML (56%; median 3.17 log c/mL, range 2.00-8.72) and of 10/51 controls (20%; median 2.00 log c/mL, range 2.00-7.88). In PML patients, plasma JCV DNA levels correlated to CSF JCV DNA load ($r=0.4864$, $P<0.0001$), but not to urine JCV DNA load or IgG titre. In the control group JCV DNA load in urine correlated to IgG titre ($r=0.4477$, $P=0.001$). In PML patients, the JCV NCCR was rearranged in 6 of 7 plasma and 10 of 11 CSF examined and was identical within 4 of 5 plasma/CSF pairs; in contrast all urine-derived NCCR sequences from both PML patients and controls were archetype.
Discussion: Although low sensitive for the diagnosis of HIV-related PML, the finding of JCV DNA in plasma might support a clinical suspicion of PML in HIV infected patients. The correlation between CSF and plasma JCV DNA levels, the identity of NCCR sequences in plasma and CSF, and the higher prevalence of JCV in CSF compared to plasma suggest circulation of the virus between the two compartments, more likely from CSF to blood. Finally, JCV-specific B-cell immunity seems to be enhanced in the presence of high replication activity in the urinary tract in healthy controls, although this seems not be the case in PML.

CO 16

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JCV specific CTL responses against a novel HLA-A*02 restricted VP1 epitope

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Background and Objectives: Progressive multifocal leukoencephalopathy (PML) is a severe demyelinating disease of the central nervous system (CNS), caused by the polyomavirus JC (JCV) that affects patients with HIV infection or other immune disorders. Previous work in patients with HIV-related PML has shown that disease remission following initiation of combination antiretroviral treatment (cART) is partially associated with restoration of JCV-specific CD4 and CD8 T-cell responses. Aim of our study was to develop an Elispot assay for the assessment of JCV-specific CTL responses by selecting immunogenic VP1 JCV-specific epitopes, in order to both investigate their biologic role in the immune response against JCV and their potential for use in clinical management.
Methods: We synthesized a library of seventy 10-mer peptides, overlapping by 5 amino acids, spanning the entire coding sequence of JCV viral capside protein1 (VP1, 699 aa). Peptides were pooled by a matrix method, where each peptide was contained in two pools only, and tested by IFN-gamma Elispot assay. The assay was applied to fresh peripheral blood mononuclear cells (PBMC) from 14 healthy donors and 9 cART-treated PML "survivors", i.e., PML patients undergoing PML remission. The subjects were also typed for the MHC class I allele A using Sequence Specific Primer (SSP) and tested by IFN-gamma Elispot using the previously described A*02-restricted JCV peptides VP1-p36 and p100.
Results: 5/7 (71%) healthy subjects and 8/9 (89%) PML survivors showed selectively high CTL responses against 2 pools, leading to the identification of a new immunodominant peptide, named VP1-p53. Using the SYFPEITHI Epitope Prediction, a high binding score was observed for VP1-p53 with HLA-A*02 and A*11. Indeed, all the 9 individuals that were either A*02 or A*11 positive showed a response against this peptide. These responses were confirmed by testing VP1-p53 individually in a larger study population, which consisted of 14 healthy subjects (12 seropositive and 2 seronegative for anti-JCV-VP1 antibodies), 9 cART-treated PML survivors and 4 PML progressors. A response against VP1-p53 was observed in all the 15 HLA-A*02 or A*11 JCV seropositive healthy subjects or PML patients (including 5 PML survivors and 2 progressors) and 6 non HLA-A*02 subjects; no response was observed in the two JCV seronegative subjects. In contrast, only 6/15 subjects responded to either VP1-p36, VP1-p100 or both.
Discussion: We have identified a new immunodominant A*02-restricted VP1 epitope, which provides a new tool (VP1-p53 based Elispot assay) for real-time monitoring of JCV CD8+ T-cell specific responses in PML patients. However, PML progression in cART-treated patients showing adequate responses against VP1-p53 suggests that other mechanisms beyond CTL responses may direct PML outcome.

CO 17

Infection 2010; 38 (Suppl. I): 19

Analysis of HIV-1 quasispecies by ultra-deep pyrosequencing in gut biopsies and plasma samples from acutely infected patients

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Background and objectives: Early events taking place during primary HIV infection are fundamental in subsequent disease progression. During the acute phase, massive viral replication occurs in gut-associated lymphoid tissue, leading to viral dissemination in the body and progressive filling of reservoirs. Aim of the study was to compare HIV-1 quasispecies in gut and peripheral blood in acutely and chronically infected patients.
Methods: Five HIV-acutely infected and 4 chronic patients were enrolled, while being free of therapy. To study viral quasispecies, ultra-deep pyrosequencing (UDPS) of env V3 loop region was performed on both duodenal biopsy and plasma HIV. Genotypic prediction of co-receptor usage was assessed by Position Specific Score Matrix analysis.
Results: Both acute and chronic patients displayed predominant R5 genomes both in the circulation and in the gut. Frequency of X4 variants and extent of genetic diversity were highly correlated ($r=0.84$, $p<0.0001$). Neither X4 frequency nor genetic diversity in gut tissue were correlated with the corresponding parameters in plasma, in both acute and chronic patients. Genetic diversity tended to be lower in circulating virus from acute as compared to chronic patients, with one exception represented by one acute patient with low CD4 counts, high viral diversity, and high frequency of X4 variants in plasma. On the contrary, gut virus diversity was similar in acute and chronic patients.
Discussion: UDPS represents a breakthrough in the study of HIV pathogenesis, providing quantitative evaluation of frequency of variants in viral quasispecies. By this approach, we showed a strong correlation between X4 frequency and viral diversity in HIV quasispecies, consistent with the enrichment of X4 variants along virus evolution within each individual. The lack of correlation between X4 frequency and genetic diversity in gut and plasma during both acute and chronic infections suggests that viral compartmentalization is an early event during natural history of HIV infection.

CO 18

Infection 2010; 38 (Suppl. I): 19

Formal breaking of B tolerance to induce HIV blocking CCR5 Specific antibodies as new vaccinal strategies

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Background and objectives: The aim of the project is to investigate the induction and the biological properties of systemic and mucosal anti-HIV protective antibodies in animal models, such as mice, by a bacterial antigen presenting system.
Methods: We engineered a bacterial vector system, based on the capsid precursor protein of the insect Flock House Virus (FHV). It has a number of sites (L1, L2, L3, I2, I3) suitable for epitope display without substantial changes in the whole structure. In this way, the inserts are placed on the exterior surface of the protein. We designed inserts to express murine CCR5 epitopes (ECL1, ECL2, N Terminus-1 and N Terminus-2) in frame. We induced recombinant proteins expression in E. Coli BL21 cells by standard methods. After each mice immunization with this carrier vector, we assessed if there were present antibodies against these epitopes by ELISA assay. We verified whether these antibodies could induce internalization of CCR5 through flow citometry assay. We also tested these antibodies in HIV blocking assay to verify if they were able to interfere with HIV entry.
Results: FHV system led to both IgG and IgA responses to the different domains of murine CCR5 receptor, without any autoimmune perturbation evaluated by necroscopy.
We immunized mice with autologous CCR5 sequences and results obtained were found similar to those achieved with human sequences, although we observed a delayed peak of the immune response. According to the results found with ELISA assay, the higher titer of IgA was obtained with ECL-1 and of IgG with NT-1. We also analyzed the capability of each specific antiserum to down-regulate CCR5 in vitro. Our results suggest that the best downregulating epitope is ECL-1. Moreover, Blood samples from immunized mice were tested in flow citometry to assess if our immunization protocol induces internalization of CCR5 in vivo. A good level of CCR5 downregulation is present in the majority of immunized mice. Of note is that sera samples were able to block HIV infection with a mean of IC50 >1:160 dilution and this activity is present at dilution of 1:600.
Discussion: Our data suggest that this antigen presenting system could effectively break the B tolerance in mice, thus inducing HIV blocking CCR5 down-regulatory specific antibodies. These findings could have important implications in the design of an HIV vaccine able to induce an high antibody generation and a long lasting protective response.

CO 19

Infection 2010; 38 (Suppl. I): 19

Adiponectin and Osteoprotegerin in HIV-infected patients: an unexpected association between protective and dangerous factors for cardiovascular diseases

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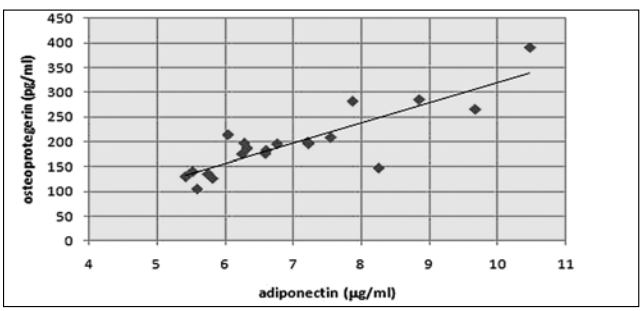
Background: Dysregulation of adiponectin is implicated in the etiology of metabolic syndrome, but it is also related to increased cardiovascular risk. In fact low circulating levels of adiponectin are strictly related with progressive atherosclerosis and increased risk of coronary disease. Also high osteoprotegerin (OPG) concentrations have been associated with the severity of coronary artery disease and predict future cardiovascular events. We investigated the relationship between plasma adiponectin and osteoprotegerin levels in HIV positive subjects with low cardiovascular risk and absence of coronary diseases.
Methods: We studied 20 HIV-positive patients on a first line stable and effective antiretroviral therapy. 10 age-matched healthy HIV-negative patients were included as controls. Anthropometric, metabolic and immunovirologic parameters were measured in all patients. All patients presented low cardiovascular risk (<10%) according to



the Framingham Scoring, and did not meet criteria for diagnosing metabolic syndrome. The levels of OPG and adiponectin were measured using commercially available ELISA. Coronary CT-scan was performed in all patients.
Results: The mean age of patients was 41 years. CD4+ cell count was 443.7±153.7 cells/mmc (mean±SD) and HIV-RNA<50 copies/ml. The mean of metabolic and anthropometric parameters were normal in all HIV population. Plasma adiponectin (7.004±1.407mg/ml) and OPG (196.8±67.2pg/ml) levels in the group of HIV positive patients were lower than in the group of HIV-negative controls (P=0.2). On the other hand we observed a direct association between OPG and adiponectin in HIV+ patients (r=0.777, P=0,001) (Fig 1). Coronary CT-scan did not evidence critical stenosis (>50%) in coronary vessels of all patients and medium coronary artery calcium (CAC) score was low.
Conclusions: Our data show that the adiponectin and OPG levels are unexpected impaired in HIV positive patients without metabolic syndrome. Coronary risk of HIV positive patients is low according to the Framingham Scoring, but dysregulation of adiponectin observed predict an unexpected great increase of cardiovascular risk. Anyway all patients were without significant coronary stenosis and present low CAC score. It is possible that low circulating levels of OPG observed in this population could indicate a protective factor for coronary disease. Moreover the association between OPG and adiponectin in HIV+ patients could represent a possible "mechanism of homeostasis" for the control of cardiovascular diseases.
These data, although obtained in a small population, confirm that coronary risk is poorly understood at the moment in HIV+ patients and more studies are required.

CO 20

Infection 2010; 38 (Suppl. I): 20

Anaemia in HIV pregnant women and their neonates exposed to non-ZDV-based HAART

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Background: In countries with adequate resources, an increasing number of HIV positive women become pregnant while taking non ZDV-based HAART regimens, and meet the criteria to maintain such regimens during pregnancy. Although some studies have reported some data on the tolerability and side effects of TDF, FTC, and ABC, there are limited data on the effects of these NRTIs on maternal and neonatal haemoglobin (Hb) levels.
Aim: to compare the rates of maternal and neonatal anaemia in HIV pregnant women and their neonates exposed to HAART regimens including or not including ZDV.
Methods: HAART treated pregnant women with immunovirological evaluation and a complete haematological profile within 12 weeks of pregnancy and at week 36 were enrolled.
Three groups were compared: women that started a ZDV-3TC based HAART after the first trimester of pregnancy (ZDVs, n=18); women assuming ZDV-3TC-based HAART from the conception to end of pregnancy (ZDVc, n=61), and women with ZDV-free HAART from conception to delivery (ZDVf, n=40). Data regarding birth outcome and neonatal Hb were registered, and the T–Student and chi-square tests were used for statistical analysis.
Results: Overall,119 HIV pregnant women were enrolled. Protease inhibitor was present as third drug in 82.0% independently from groups. NRTI backbones in the ZDVf group were: TDF-3TC (35.0%), TDF-FTC (32.5%), 3TC-d4T (20%) and 3TC-ABC (12.5%). At the beginning of pregnancy, Hb levels did not show differences among groups, ranging from 12.5 in ZDVs to 13.1 g/dl in the other two groups. The percentage of women that started pregnancy with anaemia (Hb <11.0 g/dl) was 10.0 in ZDVs, 0% in ZDVc and 3.2% in ZDVf.
At 36 weeks of pregnancy, ZDVf women had a significantly greater decrease in Hb compared ZDVs women (-1.91 g/dl vs -1.27 g/dl, p=0.049), but not statistically different from ZDVc group: (-1.49, ZDVc, p=0.345). This finding was accompanied by a similar trend in the occurrence of anaemia at 36 weeks (ZDVf: 52.5%, ZDVs: 43.3%, ZDVc: 35.3%; p=0.445).
Maternal anaemia in the ZDVf group was not accompanied by neonatal alterations in Hb levels: ZDVf neonates had Hb levels within the normal range (16.1+1.4 g/dl), while ZDV-exposed newborns presented a significantly lower Hb levels compared to the ZDVf group (ZDVs : 14.3+2.0 g/dl, ZDVc: 14.6+2.4 g/dl, p:0.044 and 0.003, respectively).
Conclusions: Almost 60% of ZDVf mothers had low Hb levels in late pregnancy. However, the occurrence of anaemia in ZDVf mothers did not influence neonatal Hb levels, that resulted within the normal parameters. On the contrary, incidence of anaemia in late pregnancy was relatively limited in ZDV-exposed mothers, but appeared to strongly affect their neonates, independently from the timing of ZDV exposure.
In conclusion, ZDV free regimens did not affect neonatal Hb levels, but further studies are required to explore the relationship between to the impairment of foetal Hb-synthesis and the occurrence of maternal anaem.

CO 21

Infection 2010; 38 (Suppl. I): 20

People with intermediate level of adherence taking PI or NNRTI have different viro-immunological outcomes

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Objective: To evaluate differences in virological and immunological efficacy between PI- and NNRTI- based regimens according to the adherence level
Methods: Prospective, cohort (Ad-UCSC), monocenter study. A short questionnaire on adherence to antiretrovirals was longitudinally administered to any outpatient taking cART at Catholic University, Rome, Italy. Self-reported adherence was estimated on a 0-100 scale. Patients were stratified according to the self-reported adherence level (A<75, B between 75 and 90 and C >90). Virologic failure was defined if, at the moment of the survey, HIV RNA was >50 c/ml. CD4 cell count and other epidemiological and clinical characteristics were also collected.
Results: At December 2009, 903 patients filled the questionnaire. 32.5% females, mean age 47 yrs (SD 8.5), IDU 20%, HCV+ 25%, median log HIV RNA 1.7 c/ml (IQR 1.7-1.7), 13.3% had HIV RNA>50 c/ml, median CD4 563/mm3 (IQR 405-745), 4% had CD4 <200/mm3. 26% were grouped in group A, 39% in group B and 33% in group C. 504 (57%) were taking PI and 269 (29.7%) NNRTI. Mean SelfAdher was 80 (SD 18). 15.6% of people reported an adherence <60 and 23.2% of people reported having discontinued drugs at least once in the previous 2 month for more than 24 hours.
While for people in group A and C, no statistically significant differences were found in virological failure between people taking PI or NNRTI (group A: 21.3% for PI and 20.5% for NNRTI; p=0.91; group C: 15.3% for PI and 9% for NNRTI; p=0.13), in group B 18% people taking PI had a virological failure compared to 6.6% for people taking NNRTI (p=0.007). Similarly, mean of CD4 cell count was not different in people of group A and C (group A: 500 [SD 254] for PI and 573 [SD 192] for NNRTI; p=0.09; group C: 596 [SD 246] for PI and 636 [SD

232] for NNRTI; p=0.19) but was different in group B (595 [SD 289] for PI and 714 [SD 363] for NNRTI; p=0.002).
In group B people taking NNRTI had higher Physical Health score (74.2+15.5 versus 69.2+16.7; p=0.05) and lower symptom score (11.4+10.2 versus 15.8+9.7; p=0.004) when compared to people taking PI. Lower symptom score in people taking NNRTI compared to those taking PI was also found for people stratified in group C (8.4+7.3 versus 10.6+7.4; p=0.02).
Conclusions: Differences in virological and immunological outcomes as well in Physical Health and Symptom score were found for people taking PI or NNRTI only within the intermediate strata of adherence (between 75 and 90).

CO 22

Infection 2010; 38 (Suppl. I): 21

The ritonavir pro-atherogenetic activity prevention by PPARα agonist in ApoE-/- mice is mediated by CD36

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Background: Protease inhibitors (PIs) inhibit HIV replication , thereby delaying or preventing the onset of AIDS. Despite its efficacy in controlling the disease progression, PIs therapy is associated with an increased risk of development of premature atherosclerosis, so that, in HIV-infected persons receiving highly active anti-retroviral therapy, lipid-lowering interventions based on Peroxisome proliferator-activated receptor (PPAR)α agonists, such as fibrates, are recommended to prevent atherosclerosis development.
Aim: In this study, in a rodent model of atherosclerosis, the mechanisms of vascular injury induced by the widely used PI ritonavir have been investigated.
Methods: Ten weeks old ApoE null (ApoE-/-) mice were randomized into three groups: group 1, no treatment; group 2 intraperitoneally administration of ritonavir (5 mg/Kg) alone and groups 3, ritonavir (5 mg/Kg) in combination with Gemfibrozil (100 mg/kg by gavage). All drugs were administered five days a week for twelve-weeks. In vitro experiments were performed using a murine macrophage cell line (RAW264.7).
Results: Administration of ritonavir for 12 weeks increased the atherosclerotic plaque score in ApoE -/- mice ($P < 0.05$). Co-treating ApoE-/- mice with gemfibrozil reduced the formation of aortic plaque score by 90% ($P < 0.01$). Gemfibrozil administration to ApoE-/- mice treated with ritonavir reduced ($P < 0.05$) aortic expression of IL-1β, IL-6, TNFα, CD11b and CD36 mRNA while ritonavir upregulated ($P < 0.05$) these inflammatory mediators, including CD36 mRNA ($P<0.05$ versus naïve ApoE-/- mice). Twelve-weeks administration of ritonavir did not worsened dyslipidemia and gemfibrozil administration had no effect on triacylglycerol and cholesterol plasma levels in ritonavir-treated ApoE-/- mice. However, treatment with gemfibrozil attenuates CD36 expression on circulating monocytes obtained from ApoE-/- mice treated with ritonavir ($P < 0.05$). Exposure of RAW264.7 cells to 10 μM ritonavir for 16h increased CD36 mRNA and cell surface expression, while pre-treatment with gemfibrozil reduced this effect ($P<0.05$). Modulation of ritonavir-induced CD36 expression in vitro correlated with attenuation of the uptake of acetylated-LDL ($P<0.05$). Gemfibrozil increased cholesterol efflux from macrophage by upregulating ABCA1 expression.
Conclusions and Implications: We found that ritonavir administration to ApoE-/-mice worsens the trend toward the development of atherosclerotic plaques. This effect is linked to induction of CD36 expression on macrophages. I in this model n this model Gemfibrozil is effective in reducing atherosclerotic plaques formation by a mechanism that involves modulation of CD36 expression/activity.

CO 23

Infection 2010; 38 (Suppl. I): 21

Virological rebound after more than 6 months of follow-up in HIV-infected patients with residual viremia vs. <1 HIV RNA copy/mL

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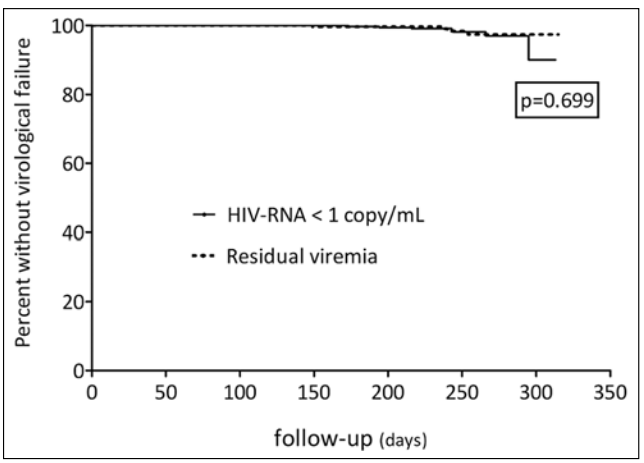
Background: We previously found that, among patients responding to antiretroviral (ARV) therapy, attaining <1 HIV RNA copy/mL was independently associated with female gender, the detectability ratio (DR) measured since the start of ARV up to the first kPCR testing, and being on a NNRTI- vs. a PI/r-based regimen.
With the present prospective study, we aimed at investigating whether attaining <1 HIV RNA copy/mL vs. residual viremia (1-49 copies/mL) prevents from virological rebound (VR).
Methods: Patients on ARV followed at our center, with both HIV RNA <50 copies/mL at the last 2 viral loads (VLs) tested by Versant bDNA before testing by Versant kPCR and HIV RNA <50 copies/mL at the 2 subsequent VLs tested by Versant kPCR (limit of quantification 1 copy/mL), were eligible in this study. Two groups of patients identified: group A (HIV RNA values of <1 copy/mL confirmed in 2 consecutive samples) and group B (patients with residual viremia, i.e. with HIV RNA values of <1 copy/mL in one sample and not in the other or 2 HIV RNA values between 1 and 49 copies/mL).
Time to VR (HIV RNA >50 copies/mL during follow-up) was assessed by Kaplan-Meier analysis in the 2 groups. In this analysis, patients who changed any drug of the regimen during follow-up for reasons other than VR (e.g toxicity or simplification) were censored at the time of switch.
"New-drugs"-based regimens were those containing enfuvirtide, darunavir/r, raltegravir, maraviroc or etravirine. The DR was calculated as the number of HIV RNA values of >50 copies/mL divided by the number of HIV RNA values measured since the start of ARV up to the first kPCR testing.
Results: Since March 2009, all patients at our center had VL tested by Versant kPCR.
739 patients (77% males) fulfilled inclusion criteria. At first kPCR testing, they had a median (Q1, Q3) age of 46.6 (42.2, 51.5) years, were on ARV since 11.1 (5.3, 13.9) years, on their last ARV regimen since 1.4 (0.6-2.9) years, had 545 (390, 736) CD4+/μL, a CD4+ nadir of 213 (107-297) cells/μL, and a DR of 0.42 (0.2, 0.65); 135 (18.3%) were in C3 CDC stage, 275 (37.2%) were receiving a PI/r-based regimen, 139 (18.8%) an unboosted-PI-based, 204 (27.6%) a NNRTI-based, 46 (6.2%) a NRTI-based, and 75 (10.2%) a "new-drugs"-based regimen.



446/739 (60.3%) were in group A.
After a median follow-up of 239 (200, 259) days, 155 (21%) patients changed ≥1 drug of the original regimen while HIV RNA was <50 copies/mL; of the remaining 581 patients, 11 (1.9%) had VR (7 in group A and 4 in group B). Time to VR in the 2 groups was not statistically different (Log-Rank test: p=0.699; figure 1).
Conclusions: HIV-infected patients attaining <1 HIV RNA copy/mL by kPCR do not have a lower probability of VR than those with residual viremia, after a median follow-up of more than 6 months.

CO 24

Infection 2010; 38 (Suppl. I): 22

Durability of a novel salvage therapy in R5 HIV-infected patients: maraviroc, raltegravir, etravirine

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Background: Efficacy and safety data of darunavir, etravirine, raltegravir, maraviroc for salvage therapy are now available.In TRIO trial (etravirine, darunavir/r and raltegravir) at week 48 86% of patients had HIVRNA<50 copies/ml, CD4 gain was 103 cells/mmc; in etravirine early access program at week 48 62.3% of patients achieved HIVRNA<75 copies/ml, CD4 gain was 100/mmc.We recently published data on 48 weeks outcome of a novel PI and NRTIs sparing regimen for salvage therapy in a small sample size of 28 R5 HIV-infected patients, including maraviroc, raltegravir, etravirine:92% had HIVRNA<50 copies/ml, increase in CD4 counts was 267 cells/mmc.
Objective: To present 96 weeks efficacy and safety data.
Methods: We prospectively evaluated triple-class failing subjects harbouring R5-virus treated with maraviroc, raltegravir and etravirine. Trends of laboratory parameters was tested by ANOVA for repeated measures and Greenhouse-Geisser probabilities were calculated. Changes between week 48 and 96 were evaluated by Wilcoxon sign test.Results as median (Q1-Q3) values.
Results: 25/28 enrolled patients completed 96 weeks of treatment.24/25 (96%) attained HIV-RNA<50 copies/mL at week 96, the other had a decrease from 111,380 to 71 copies/mL; increase in CD4+ counts, CD4+ percentage and CD4+/CD8+ ratio was statistically significant (P<0.0001 for each variable).CD4+ counts increased until week 48, afterward the level reached a plateau; variation in immunological recovery between week 48 and 96 was not significant.Significant weight gain and increased waist circumference were recorded. Haemoglobin, white blood cell, uricemia increased, and creatinine levels decreased significantly.Lipid profile (total cholesterol, LDL cholesterol, tryglicerides) and glicyde profile (fasting glucose, fasting insulin) didn't change significantly except for HDL cholesterol that increased significantly.No significant changes in AST ALT and CPK value were observed.Main findings are summarized in Table 1.

Table 1. Main findings in 25 failing HIV-infected failing patients, resistant to all the standard therapies, receiving raltegravir, maraviroc and etravirine. Results as median (Q1-Q3) values.

	Baseline	Week 24	Week 48	Week 72	Week 96	p-value
CD4 cells/mm³	247 (68-355)	481 (350-612)	517 (410-616)	481 (360-549)	472 (398-562)	<.0001
CD4%	12.6 (8.1-19.5)	20 (13.6-25.3)	21.1 (14.5-25.3)	18.9 (14.5-22.9)	19.7 (14.2-26.2)	<.0001
CD4/CD8 ratio	0.21 (0.13-0.35)	0.42 (0.23-0.52)	0.45 (0.29-0.57)	0.38 (0.26-0.53)	0.44 (0.28-0.62)	<.0001
HIV-RNA log10 copies/mL	4.34 (3.87-5.11)	1.69 (1.69-1.69)	1.69 (1.69-1.69)	1.69 (1.69–1.69)	1.69 (1.69–1.69)	<.0001
Hemoglobin (g/dl)	13.6 (12.3-14.8)	14.6 (14.2-15.4)	15.1 (14.6-15.9)	15.3 (14.7-15.6)	15.3 (14.6-15.9)	<.0001
Platelet count (109/mm³)	181 (151-204)	206 (182-219)	200 (184-241)	193 (183-248)	185 (164-217)	0.028
White blood cells (109/mm³)	5.0 (3.9-5.6)	6.6 (5.4-8)	6.6 (5.7-8.3)	6.9 (5.6-8.3)	6.2 (5.3-7.8)	0.0002
PMN (109/mm³)	2.4 (2-3.7)	3.2 (2.3-5.2)	3.6 (2.6-4.4)	3.3 (2.8-4.3)	3.2 (2.7-4.3)	0.068
Lynphocytes (109/mm³)	1700 (1200-2000)	2300 (2100-3000)	2200 (2000-2700)	2600 (2000-3100)	2300 (1900-3000)	0.125
BMI	23.0 (20.5-25.5)	24.2 (21.9-26.3)	24.4 (21.5-26.3)	23.8 (22.2-27.1)	24.2 (22.5-26.6)	0.0002
Cholesterol (mg/dl)	180 (146-213)	186 (173-211)	186 (154-218)	182 (151-211)	199 (166-214)	0.337
Col HDL (mg/dl)	39 (35.5-45.5)	46 (39-52)	41.5 (38-46.5)	43 (39-52)	43 (39-55)	0.029
Col LDL (mg/dl)	114 (82-129)	109 (84-129)	108 (80-124)	110 (88-127)	104 (88-128)	0.847
Tryglicerides (mg/dl)	139 (99-190)	104 (77-159)	106 (73-168)	94 (74-132)	100 (76-186)	0.223
Glucose (mg/dl)	86 (75-90)	83 (79-93)	86 (79-96)	89 (78-93)	85 (78-90)	0.582
Insulin (U/L)	10 (7-15)	11 (8-19)	12.2 (6.9-19.1)	13.8 (8.7-18.5)	13.2 (8-18.5)	0.322
CPK (U/L)	114 (69-160)	129 (82-188)	129 (82-188)	143 (89-229)	142 (98-237)	0.142
AST (U/L)	30 (25-49)	32 (26-49)	29 (20-34)	25 (19-34)	26 (19-38)	0.310
ALT (U/L)	26 (21-59)	40 (28-64)	40 (26.5-59)	38 (20-49)	44 (28-75)	0.300
GGT (U/L)	33 (20-97)	30.5 (22-52)	26.5 (20.5-49)	36 (27-67)	35 (28-49)	0.480
Creatinine (mg/dl)	1.01 (0.87-1.25)	0.96 (0.85-1.06)	0.88 (0.84-1.06)	0.89 (0.82-1.01)	0.88 (0.83-1.03)	<.0001
Uricemia (mg/dL)	5.44 (3.8-6.14)	5.61 (4.66-7.3)	6.1 (4.6-6.9)	6.1 (4.3-7.2)	6 (4.5-6.9)	0.008

3/28 patients didn't complete treatment:two stopped therapy at week 72 (one for AST and ALT increase due to alcohol abuse, one for chemotherapy for Hodgkin's lymphoma);one patient dead at week 72.
Four serious adverse events were reported in all 28 patients:one recurrence of mycobacterial spondylodiscitis and three malignancies (one anal cancer and two Hodgkin's lymphomas with one death) were newly diagnosed during follow up.Two events (anal cancer and spondylodiscitis) led to transitory discontinuation of therapy due to drug-drug interaction.
Conclusions: In this small sample size, despite the high pill burden and the possible weakness of its genetic barrier, at 96 weeks this regimen was associated with high rates of virological success and maintenance of marked increase in CD4 cells.The positive impact on bone marrow function, creatinine and lipid profile observed at week 48 was confirmed at week 96.Safety surveillance including careful monitoring of cancer occurrence will con continue.

CO 25

Infection 2010; 38 (Suppl. I): 23

Phase II study of intrathecal long acting liposomal cytarabine (Depocyte®) in the prophylaxis of lymphomatous meningitis in HIV-related non-hodgkin's lymphoma

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Background: Around 5% of patients with aggressive non-Hodgkin's lymphoma (NHL) develop central nervous system (CNS) progression or relapse during the course of their disease. Patients with human immunodeficiency (HIV)-related NHL often develop CNS progression despite the use of adequate prophylaxis. Liposomal cytarabine has show a significant activity in lymphomatous meningitis but there are limited data in the prophylactic setting.
Methods: Since May 2006, we are running a prospective phase II study of intrathecal liposomal cytarabine (Depocyte®) at the dose of 50 mg in 40 patients with HIV-NHL with the aim to evaluate the feasibility and activity of this drug in the prevention of lymphomatous meningitis.
Results: Thirty-five patients were males and the median age was 44 years (range 18-69 yrs). As far as the histological subtype of NHL, 47% of patients had a diffuse large B-cell (DLBC) NHL and 40% Burkitt NHL. Stage III-IV was diagnosed in 80% of patients and 68% of DLBC were age-adjusted IPI 2 or more. An extranodal involvement was diagnosed in 70% of patients (gastrointestinal 30%, bone 27%, spleen 10%, liver 22%, bone marrow 17%). Liposomal cytarabine was well tolerated with headache grade I to III being the most frequent side effect in only 37% of patients. Less common toxicity (all grade I) included cortical changes (5%), fever (3%), vomiting (3%), hypertension (3%), chills (3%). With a median follow up of 12.4 months only one patient (3%) with Burkitt lymphoma developed a combined systemic and meningeal relapse. Moreover, in our experience previously the present study, we used methotrexate as practical use in 426 HIV-NHL with a meningeal progression or relapse of 14% (p=0.09). The use of a liposomal formulation allowed to significantly reduce the number of lumbar injections in comparison to the standard schedules (approximately of 50%) with an improvement of quality of life of patients and with a reduction of professional exposure risk for health care staff.
Discussion: In this first prospective study on prophylaxis of lymphomatous meningitis in HIV-NHL reported in the literature, liposomal cytarabine seems safe and active and it reduces of approximately 50% the number of lumbar punctures and exposure risk for health staff as well.

CO 26

Infection 2010; 38 (Suppl. I): 23

Long-term follow-up of rituximab and infusional cyclophosphamide, doxorubicin, and etoposide (CDE) in combination with HAART in HIV-related non-Hodgkin's lymphomas (NHL)

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Background: The combination of Rituximab plus chemotherapy (CT) is more effective than CT alone in the treatment of high grade NHL. Objective: To report the long-term follow-up of CDE plus Rituximab in HIV-NHL.
Methods: In June 1998, we started a phase II study using infusional CDE (Cyclophosphamide 187.5 mg/m2/day, Doxorubicin 12.5 mg/m2/day and Etoposide 60 mg/m2/day) administered by continuous intravenous infusion for 4 days every 4 weeks and Rituximab 375 mg/m2 i.v. on day 1. HAART was given concomitantly with CT.
Results: Seventy-four patients (pts) have been enrolled. The median CD4+ cell count was 161 (range 3-691) and the median Performance Status was 1 (range 0-3). Diffuse large B-cell NHL was diagnosed in 72% of pts and Burkitt in 28%. Seventy per cent of pts had advanced stage (III-IV) disease and 57% of pts had an age-adjusted international prognostic index >2. Fifty-two out of 74 pts (70%) achieved a complete remission (CR), 4/74 (5%) had a partial remission and 18 pts progressed. With a median follow-up of 61 months, only 17% of CRs have relapsed and 41/74 pts are alive. The overall survival, disease free survival and time to treatment failure (TTF) at 5 years were 56%, 81% and 52%, respectively. Four cases of secondary tumors have been observed. No case of late pulmonary or cardiac toxicity has been reported.
Conclusions: The combination of Rituximab and CDE in HIV-NHL treated concomitantly with HAART is very active. CR rate (70%) and TTF at 5 years (52%) are comparable to those observed in high grade NHL of the general population. Our data confirm that in HAART era a high proportion of HIV-NHL can be cured.

CO 27

Infection 2010; 38 (Suppl. I): 23

High prevalence of anal human papillomavirus infection among HIV-infected patients in the absence of anal intercourse

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Introduction: Anogenital infections with human papillomaviruses (HPV) is one of the most common sexually transmitted infection. In

Table 1

CD4 limphocytes nadir (cell/mmc)	172,4 + 13,83
HIV-RNA viral load copies/ml	50 + 0.0
Cytologic abnormalities suitable with HPV infection in DA HIV+ patients	41 patients (61%) of 62 Low-grade Squamous Intraepithelial Lesion (LSIL): 22 pz High-grade Squamous Intraepithelial Lesion (HSIL): 14 pz Anal Intraepithelial Neoplasia 1 (AIN1): 5 pz
Cytologic abnormalities suitable with HPV infection in MSM HIV+ patients	26 patients (54%) of 48 Low-grade Squamous Intraepithelial Lesion (LSIL): 14 pz High-grade Squamous Intraepithelial Lesion (HSIL): 6 pz AIN1: 4 pz Anal Intraepithelial Neoplasia 2 (AIN2): 1 pz Anal Intraepithelial Neoplasia 3 (AIN3): 1

our study we compared HPV prevalence, type distribution, and HPV-associated cytological abnormalities in anal specimens from 2 HIV-infected cohorts: ex and active injection drug abuser (DA) patients and men who have sex with men (MSM). In addition we evaluated immunity status by CD4+ T-cells and Natural Killer (NK) cells. This is a cross sectional study that includes a total of 110 HIV patients, with an average age of 40.64 years. The sample examined in this study was made of 62 DA and in particular: 8 actual and 54 ex drug abusers patients and 48 MSM. All patients were on HAART and had VL <50 copies/ml. CD4 at the enrolment was 426,7+ 38,5 cell/mmc (mean + SEM).CD4 T-cells nadir are reported in the table1.
Methods: cytology examination was performed on anal brushing and the criteria of Bethesda for the cytology classification were used. Molecular HPV identification was performed by PCR. CD4+ and NK cell count were measured by FACS.
Results: Molecular evaluation PCR test was found positive in 52% of DA and in the 61% of MSM patients (p>0.05).
Cytologic evaluation: cytology results are reported in table 1. Cytology exam was comparable to PCR in 94% of MSM subjects and in 75% of DA (p<0.008).
Evaluation of genotypes with carcinogenic risk: 33% DA showed genotype at high risk of progression to cancer vs 27% of MSM subjects (p=0.67).
Immunologic evaluation: 62,5% of DA vs 5% of MSM patients showed CD4 nadir <200 cell/mmc vs (p<0.05). NK cells were higher in the group of DA vs MSM (p<0.05).
Conclusions: our data show that the incidence of anal HPV infection is higher in the group of MSM HIV+ patients vs drug using patients. However anal HPV infection and anal squamous intraepithelial lesions may be acquired also in the absence of anal intercourse in HIV-positive men. The prevalence of high-grade squamous intraepithelial lesion (HSIL) is high among HIV-positive injection drug users. All HIV-positive men regardless of history of anal intercourse, should be considered for anal cytologic screening.

CO 28

Infection 2010; 38 (Suppl. I): 24

Monitoring the toxicity related to HAART from 2001 to 2009 in Burkina Faso: clinical adverse events vs. laboratory adverse events: prevalence, grading and outcome

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Objectives: The aim of this study is to assess prevalence and grading of adverse events (AE) related to HAART according to international WHO guidelines and national Burkina Faso guidelines. We performed an analysis on clinical adverse events (CAE) vs. laboratory adverse events (LAE), on clinical and therapeutical outcome.
Methods: We analyzed clinical and laboratory AE occurred under HAART from 2001 to 2009 in 1245 patients from 2 urban medical centers, placed in tha capital Ouagadougou, and 1 in the rural Health District of Nanoro (893, 71.7% were female; 1040, 83.5% came from urban area). Statistical analysis was performed with Epi-Info 3.5
Results: Showed AE 254/1245 patients; over 1724 tratment admistrated we had 386 events. Patients who showed AE were treated with: 2NRTI+NNRTI (83.2%); 2NRTI+PI/r (15%); 2NRTI+PI (1.3%); the rest with another protocol type.

Table 1

AE			Severity			
			I	II	III	IV
LAE	**Anemia**	**34** (8,8%)	0	4 (11,8%)	14 (41,2%)	16 (47,1%)
LAE	**Hepatotoxicity**	**15** (3,9%)	3 (20%)	8 (53,3%)	3 (20%)	1 (6,7%)
CAE	**GI intollerance**	**61** (15,8%)	25 (41%)	24 (39,3%)	12(19,7%)	0
CAE	**Periph. Neur.**	**162** (42%)	42 (25,9%)	100 (61,7%)	15 (9,3%)	5 (3,1%)
CAE	**Skin Rash**	**33** (8,5%)	10 (30,3%)	12 (36,4%)	9 (27,3%)	2 (6,1%)
CAE	**CNS toxicity**	**69** (17,8%)	43 (62.3%)	23 (33.3%)	3 (4.3%)	0
LAE+CAE	**Others**	**12** (3,2%)	2 (16,7 %)	4 (33,3%)	3 (25%)	3 (25%)

EA prevalence and severity according to WHO guidelines is shown in table 1.
Therapeutical impact of CAE (331/386; 85.7%) vs. LAE (55/386; 14.3%) was: HAART continuation in 57% overall (CAE=91.4% - LAE=8.6%); switching in 31.6% (CAE=80.3% - LAE=19.7%); dose modification in 2.6% (CAE=100% - LAE=0); in 8.8% (CAE=64.7% - LAE=35.3%) HAART was interrupted.
AE clinical outcome was: clinical resolution in 85%; AE not resolved in 15%. CAE were resolved in 83.4% (276/331) of the events. LAE were resolved in 94.5% (52/55) of the events.
We observed the impact of treatment modifications due to AE compared to all treatment modifications during the study time: 479 treatment modification among 1724 administrated treatments, 25.5% due to AE (122/479) and 74.5% (357/479) due to another cause (failure, pregnancy, simplification, drugs availability, patient's lack of money).
Conclusions: Despite AE prevalence, the impact of these events on treatment modifications was small, and most treatments were continued. Almost all AE were clinical, however a strictly clinical and laboratory monitoring was useful to diagnose at low grade probably avoiding unfavourable evolutions of these events, by changing treatment only when necessary.

CO 29

Infection 2010; 38 (Suppl. I): 25

Early markers of mitochondrial tubular injury in patients treated with tenofovir vs abacavir-including backbones

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Background: The role of tenofovir (TDF) in inducing tubular renal injury is not well understood. A selective mitochondrial toxicity has been hypothesized, but no definitive data are presently available. The dosage of urinary Cytochrome C (Cyc) has been recently proposed as a marker of proximal tubular mitochondrial injury. The aim of our study was to evaluate changes in urinary values of Cyc together with other classic markers of subclinical renal impairment, in patients treated with TDF vs abacavir (ABV)-including regimens.
Methods: We evaluated 99 patients shifted from timidinic backbones to TDF or ABV-including backbones (respectively 72 and 27). The third drug (PIs or NNRTIs) was well balanced between the two groups. Patients with diabetes or renal failure were excluded. Patients underwent 24-hour urine collection before the shift (T0), after 1 (T1), 3 (T2), 6 (T3), and 12 (T4) months. Samples were analyzed for Cyc and alpha-glutathione S-transferase (α-GST) as markers of mitochondrial and cytoplasmic proximal tubular toxicity. Data were corrected for urinary creatinine (UCr) (pg/mg). Serum creatinine (SCr), serum phosphate (SPhos), and urinary albumin (UA) and phosphate (UPhos) were also evaluated. Statistical analysis was performed by ANOVA or Kruskal-Wallis where appropriate, or linear regression (Spearman).
Results: Patients under ABV regimen showed non-significant fluctuations of urinary excretion of αGST and Cyc. In the group of TDF-treated, α-GST did not vary significantly. While Cyc excretion increased significantly at 3 months from the shift and returned to near basal levels at 12 months. Cyc levels of TDF group were significantly higher than the levels of ABV group at T1 (p=0.02); while α-GST of TDF increased significantly over ABV at T2 (p=0.043). SCr and UA did not vary at all time points in both groups. SPhos levels and percentage of hypophosphatemic patients were comparable in both groups at all time points; instead, UPhos increased from basal, up to 6 months after the shift to TDF-regimen. At T1 and T2 there was a correlation between Cyc excretion and UPhos levels.
Conclusions: In the TDF group, and not in the ABV group, we observed a significant increase in Cyc at T1, and T2; while after 12 months the value decreases to basal levels and probably reflected a transient mithocondrial toxicity. α-GST excretion was higher in TDF after 6 months of therapy. The other parameters did not show significant changes. Interestingly, UPhos increased just after 1 month of TDF therapy and correlated early with Cyc. UPhos was elevated till the end of the observational period. This finding confirms an involvement of the tubular mitochondria, at least in the first months of therapy with TDF. We hypothesize that although Cyc excretion decreased after three months, a subclinical tubular injury persists during TDF therapy and, in some cases, in concomitance with other factors, may evolve to overt renal tubular damage.

CO 30

Infection 2010; 38 (Suppl. I): 25

APRI and FIB-4 for the evaluation of liver fibrosis: concordance analysis, evolution and predictors in a cohort of HIV patients without HCV or HBV infection: results from the EPOKA-a MASTER Cohort

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Background/Aims: Liver fibrosis (LF) progression is fated to become one of the major long-term toxicity of HAART in the future. The aim of this study is to assess LF progression in HIV patients without HCV or HBV infection and associated risk factors. The main hypothesis is that early antiretroviral therapy may slow down LF progression.
Methods: Observational retrospective study. All HIV naive patients in 2 large referral clinics, who started HAART from 1996 to 2006 were included. Kappa test was used to assess concordance between APRI and FIB-4 ranked into three classes. Rates of progression from class 1 of APRI or FIB-4 (<0.5 and <1.45, respectively) to higher classes was estimated through Kaplan-Meyer analysis. This transition to low grade liver fibrosis was chosen to increase sensitivity for any progression of liver disease. Cox regression models were applied to assess possible predictors at baseline (amongst gender, age, risk factors for HIV acquisition, HIV-RNA, and CD4+ T-cell count).
Results: 1,112 naïve patients were selected (69% men, sexual risk factor for HIV 90%, mean age 38 years, HIV-RNA 215,105 copies/mL, CD4+ cell count 219 cells/cmm). At baseline, 785 (70.6%) patients were in class 1 for APRI and 832 (74.8%) for FIB-4. Cohen's Kappa test for concordance was 0.573 (95%CI 0.524 to 0.623), showing moderate concordance. 318 (40.5%) patients had LF progression to >/= class 1 APRI accounting for an incidence of 0.096 (95%CI 0.087-0.108) per PYFU. In contrast, as for FIB-4, 243 (29.2%) patients had LF progression to >/= class 1 with an incidence of 0.062 (95%CI 0.054-0.070) per PYFU. Cox regression models showed different independent baseline predictors for APRI with respect to FIB-4 transition. Only male gender was independently associated with APRI transition to grade >/=1 (HR: 1.472, 95%CI 1.137-1.906; P: 0.0033); as for FIB-4 transition, age >/= 40 years was associated with increased risk of progression (HR: 2.048, 95%CI 1.573-2.667; P<0.0001), while sexual risk factor for HIV acquisition resulted to be protective (HR: 0.581, 95%CI 0.358-0.944; P: 0.0282). CD4+ T-cell count (<350 vs. >/=350 cells/cmm) was not associated with either APRI or FIB-4 transition.
Conclusions: In this cohort, HAART initiation at CD4+ >/= 350/cmm did not seem to slow down progression of LF. It has to be seen whether higher CD4+ cut-offs for HAART initiation or better immune-reconstitution during follow-up have an impact. Although the rate of LF progression was substantial, discordant results were found between the two scores (overall 40% APRI vs. 29% FIB-4). Discordance between the two test was also found both in terms of staging of LF at

baseline and in terms of predictors of LF progression. This indicates that standardization and validation of these surrogate methods are necessary. In the meantime, males, older patients, and (ex)-intravenous drug users were suggested to be the most vulnerable populations.

CO 31

Infection 2010; 38 (Suppl. I): 26

HIV incidence estimate in Lazio Region combining HIV/AIDS surveillance with data about testing history and biomarker HIV test results to identify recent infections

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Background: Surveillance of new HIV diagnoses has been improved in the last years using serological methods that identify persons with recent infection. One of these methods, the avidity index (AI), is largely used in Italy. According to this method, recent infections are those with an AI<0.8, with a mean window period of 142 days since seroconversion.
We applied the incidence estimator proposed by Karon et al. (Stat-Med 2008), that accounts for the effect of testing practices on the number of persons detected as recently infected.
Methods: We combined data from HIV diagnoses surveillance of Lazio with that of SENDIH study that, in the same region, collects information about HIV history testing and performs AI for about 50% of new HIV diagnoses.
The incidence was estimated as the number of persons detected as recently infected divided by the estimated probability of being detected as recently infected during the window period. This probability was assumed to depend on the following factors: individuals choosing whether and how frequently to seek HIV testing, variation of testing frequency, the reporting of test results only for infected persons, and infected persons who never had an HIV-negative test. Some of these probabilities were estimated directly from the data and other parameters were derived from specific studies.
Results: During the period 2004-2008, 3541 new HIV diagnoses were reported; the AI test was available for 23.3% of cases while testing history was available for 46.9%. Among those with an AI test, 14.3% were identified as recent infections (78 were heterosexuals (HET), 133 men-who-have-sex-with men, (MSM) and 24 were drug users, (DU)). This percentage was 28.3% and 7.5% among those with and without a testing history, respectively. We estimated that in 2004-2008, there were 5612 infections (95%CI: 3127-10070). Incidence per year was 824 (2004), 993 (2005), 1480 (2006), 1285 (2007), and 789 (2008). The higher estimated absolute numbers of infection, was among HET (2201), followed by MSM (1741) and by DU (617).
Sensitivity analyses showed that results are strongly dependent on some parameters such as the mean window period, the percentage of those with unknown testing history and the percentage of those without AI result.
Discussion: This is the first study in Italy that provides estimates of HIV incidence for the most recent years. The incidence in Lazio was high with more than 1,000 cases per year. It is interesting to note that the higher number of new infections was estimated among heterosexuals while the number and of recent infections was higher among MSM. This is likely due to the different testing behaviors of these two groups. The estimates had very large confidence intervals. This uncertainty could be reduced with a revision of HIV surveillance collecting information about HIV history testing for all new diagnoses and extending AI to all new HIV diagnoses in patients with CD4>200 cells/ mm^3.

CO 32

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Potential impact of routine testing of patients with HIV ID in preventing late HIV diagnosis

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Background: Late diagnosis is associated with an increased risk for HIV-associated morbidity and mortality and with an increased potential for transmission from individuals unaware of their HIV status. Routine testing of individuals with HIV indicator diseases (ID) has been suggested as an intervention to prevent late HIV diagnosis. We aimed to estimate association of having had "at least 1 HIV ID occurred before HIV diagnosis" with late HIV diagnosis and to evaluate the proportion of individuals with late HIV diagnosis who could have been diagnosed earlier if tested at the time of an ID.
Methods: We studied individuals with a HIV infection newly diagnosed from 1/10/2004 to 30/04/2009, in 10 public counselling and testing sites in Latium Region, Italy, who had a CD4 count determination available within 3 months from HIV diagnosis. We considered the following IDs: viral hepatitis infection (HBV/HCV), STD, seborrhoeic dermatitis, tuberculosis. Logistic regression analysis was performed to estimate association of having had "at least 1 HIV ID" with late HIV diagnosis. "Late diagnosis" was defined when the CD4 count was < 200 cells/ mmc at HIV diagnosis and/or AIDS, excluding those with a negative HIV test performed 6 months before diagnosis. For each individual we estimated the time since HIV infection by assuming an average baseline CD4 count and an average rate of change per year derived from the CASCADE collaboration on HIV seroconverters.
Results: Among the 1776 patients included in our analysis the prevalence of late HIV diagnosis was was 34.2% (608/1776). 511/1776 (28.8%) patients reported at least one ID before HIV diagnosis (122 patients more than one). Distribution of IDs was: 213 viral hepatitis (128 HBV); 388 STDs (199 syphilis, 68 gonorrhoea, 33 genital herpes, 86 genital condylomatosis, 2 infectious virginities), 38 seborrhoeic dermatitis and 11 tuberculosis; 122 patients reported more than one diagnosis. In multivariable analysis having had at least 1 ID was associated with a lower probability of late diagnosis (OR=0.64; p=0.001).
However, 146 patients were not tested for HIV shortly after an ID. Based on our assumption, 32 patients (5.3%) among 608 late presenters were already infected at the time ID and ID was diagnosed a median time of 42 months before HIV diagnosis.
Discussion: In this population the probability to have a late HIV diagnosis was significantly lower for patient who have had at least 1 indicator disease before HIV diagnosis. For 5.3 % of late HIV patients, diagnosis could be have been anticipated if they would have been tested at the time of a HIV indicator disease. Further interventions for active offer of HIV testing are needed in order to favor timely diagnosis of HIV infection.

CO 33

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Main features of newly diagnosed HIV patients

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Objective: To point-out the main epidemiological, behavioural and laboratory features of newly diagnosed HIV+ patients observed at the Infectious Diseases Department of the A.O. Spedali Civili of Brescia (Italy).
Methods: We reviewed the data collected in an out-patients surgery, open in our Department for counselling and first clinical evaluation of the newly diagnosed HIV+ pts.
Results: Since 1st April 2006 to 30th September 2009 we evaluated 362 newly diagnosed HIV+ patients (M 279, 77.1%; F 83, 22.9%; mean age 38 yrs, range 17-75 yrs.); 195 out of 362 (53.9%) acquired HIV infection by heterosexual intercourses, 134 (37.0%) by homo/bisexual contacts, 12 (3.3%) by I.V. drug use and 21 (5.8%) referred another way or a not known way for infection. For 132 pts. (36.5%) the current or previous drug use was reported (cocaine in most cases: 79 out 132, 59.8%).
A previous negative HIV test was reported for 166 pts. (45.9%) and in the multivariate analysis this fact was related to homo/bisexual intercourses (OR = 2.25, CI95% 1.42-3.58, P < 0.001), age ≤ 40 years at HIV diagnosis (OR = 2.05, CI95% 1.27-3.31, P = 0.003) and generic drug use (OR = 1.61, CI95% 1.00-2.58, P = 0.048) but not cocaine (OR = 1.36, CI95% 0.79-2.35, P = 0.271).
Before the first visit, 40 out of 358 pts. (11.2%) had not yet informed anybody about their own serostatus and only 174 out of 358 (48.6%) had already informed their partners; in the multivariate analysis the latter characteristic was related to the test motivation, i.e. after an at risk sexual intercourse (OR = 2.25, CI95% 1.18-4.30, P = 0.014) or for clinical symptoms (OR = 2.28, CI95% 1.33-3.94, P = 0.003), compared to a generic screening without asserted specific at risk sexual intercourses.
The mean CD4+ lymphocyte count at HIV diagnosis was 350 cells/cmm (range 2-1668 cells/cmm) and a count < 350 cells/cmm was related in the multivariate analysis to clinical symptoms (OR = 3.04, CI95% 1.78-5.17, P < 0.001) and age > 40 yrs (OR = 1.94, CI95% 1.22-3.10, P = 0.0035).
Conclusions: In our newly diagnosed HIV+ population, pts. with age < 40 yrs., with homo/bisexual intercourses and with current or previous drug use (but not cocaine) are more used to the HIV screening. At the first contact with the hospital, less then 50% of pts. has already informed the partners. Pts. older than 40 and with clinical symptoms show a greater degree of immunodeficiency.

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Infection 2010; 38 (Suppl. I): 27

Characteristics trends of AIDS and tuberculosis cases in Italy: 1993–2009

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Background: According to the most recent ECDC surveillance report, the HIV/AIDS and Tuberculosis (TB) co-infection remains a severe health problem in the European Region. We estimated the extent of this phenomenon in Italy and described and analyzed the characteristics of persons with AIDS and TB reported to the National AIDS Registry.
Methods: The characteristics of all cases of TB reported to the National AIDS Registry in Italy since 1993 (the year in which TB was introduced as an AIDS-defining disease) were analyzed.
Results: From 1993 to 2009, 44,324 cases of AIDS were reported. Among these 3,953 (8.9%) were infected with TB (any site). Since 1993, a progressive increase in the proportion of persons with TB can be seen, from 6.8% in 1993 to 10.6%in 2009. Males accounted for 76.4%; the median age at diagnosis was 35 years (IQR 30-40 years), and 31.6% were non-nationals. The proportion of non-nationals increased from 10.8% in 1993 to 76.9% in 2009. About 50% of these persons originated from Africa, and this proportion remains stable over time, whereas the proportion of persons from Eastern Europe has increased from 8.6% in 1993 to 14.3% in 2009. The proportion of persons from South America has decreased (1993: 40%, 2009: 14,3%). Among non-nationals the most common HIV exposure category was heterosexual contact (59.2%), among Italians was injecting drug use (61.0%).
The proportion of individuals with a HIV/AIDS and TB co-infection who are unaware of being infected with HIV at the moment that they are diagnosed with AIDS has increased from 17.7% in 1993 to 57.0% in 2009. Among Italians this proportion was 33%, among non-nationals 64.6%.
Conclusion: These data suggest that the occurrence of TB among persons with AIDS is increasing in Italy, especially within the non-national population. This emphasizes the need for HIV screening among all persons diagnosed with TB.

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Temporal trend of HIV incidence among patients with sexually transmitted infections in Italy, 1991–2007

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Background/objectives: The best way for monitoring the dynamics of HIV infection in the population, in terms of changes over time, is to calculate incidence rates. Patients with sexually transmitted infections (STI) represent an early alert population for HIV prevention. Aim of this study was to estimate the HIV incidence among STI patients and evaluate the trend of HIV infection in Italy.
Methods: Patients with a confirmed STI diagnosis were included by 10 public STI clinics through Italy from 1991 to 2007; only individuals tested for HIV concurrently with the STI diagnosis and reporting at least one previous documented HIV-negative test were included. Individuals who tested HIV-positive at the time of STI diagnosis were defined as "seroconverters". Seroconversion date was estimated as the midpoint between the dates of the last HIV-negative and the first HIV-positive test. HIV incidence over calendar time and incidence rate ratio (IRR) were calculated by Poisson model.
Results: Out of 3,151 patients, 62 were HIV-seroconverters, with an incidence of 1.2 per 100 person-years (%PY) [95% confidence interval (CI), 0.9-1.6].
The HIV incidence was higher among men having sex with men (MSM) compared to heterosexual patients (IRR 10.3, 95% CI 4.1-26.0), among patients having had more than two partners in the previous six months compared to those with less than three partners (IRR 5.3, 95% CI 1.2-23.0), and patients diagnosed with a bacterial STI compared to those with a viral STI (IRR 2.3, 95% CI 1.2-4.5).
IRR of HIV over calendar time tended to increase: specifically, compared to the IR observed in the period 1991-2001(IRR=1), the IRR increased to 3.1 (95% CI: 1.6-5.8) in the period 2002-2004, and to 4.3 (95% CI: 1.6-11.4) in the period 2005-2007.

Discussion: Compared to data from the national HIV surveillance system, which show a stable trend in HIV incidence during the last decade, the results of the present study show an increase in HIV incidence among STI patients in the same period, especially among MSM. These findings suggest the potential for a new increase in HIV incidence in the medium term, and stress the relevance of monitoring HIV infection among STI patients.

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Alternative and not-invasive screening to implement hiv prevention program: easy test performed in street-lab

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Background/objectives: HIV infection is underestimated by 30% or more; due to unawareness, ignorance, social stigma and other factors.
The objective of the study is to sensitize people while making the test and, above all, to make people more conscious about the risks. In order to reach a larger number of population, the test has been offered with different and easier modality.
Methods: A skilled biologist tested volunteers with the new rapid (20') and easy test OraQuick ADVANCE, a qualitative immunoassay detecting antibody to HIV-1 and HIV-2 in saliva. Testing took place over a 14 day period in Milan with a mobile unit. Volunteers were counselled by an infectivologist and a psychologist and signed an informed consent form.
If the test was positive, a rapid test on blood was performed immediately. If confirmed positive, the blood sample was sent to the virology laboratory of San Raffaele Hospital for a standard ELISA and Western Blot testing procedures and the results achieved into one day.
Results: A total of 886 tests on saliva were performed, 7 (0,8%) of which turned positive. All the positive saliva tests where confirmed by rapid blood test and by the ELISA and Western Blot. The HIV positive patients were immediately addressed to our clinical department for all medical needs related to HIV infection.
The 50% of volunteers were blood donors, and were negative in the saliva test or standard HIV serology, thus confirming that saliva test does not give false negative results.
The majority of volunteers were men (65,7%), coming from Italy, between 31-40 years of age. The participation of young people (teenagers) has been very low. In 57% of cases this opportunity represented the first approach to HIV testing.
Discussion: The trial received positive feedback from the population intercepted during our experience. Based on this positive results we believe that it could be possible to reach a further 30% of population offering, with appropriate counselling, an alternative and easier access (lab-street or general practitioner).

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Molecular epidemiology and prevalence of Human Immunodeficiency Virus infection in adult cases of Acute Hepatitis A in the Rome metropolitan area, 2002–2008

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Background: Several outbreaks of hepatitis A affecting homosexual men have been reported in Europe. In 2008-2009 a fourfold increase, compared with the previous 10 months, of hepatitis A was observed at our institution. The high male-to-female ratio (M:F=6.1) indicated the possibility of an ongoing outbreak among MSM. In order to compare HAV strains circulating among men having sex with men (MSM) with those circulating among other risk groups during the same period, a phylogenetic analysis was performed. Moreover, the prevalence of HIV infection in all cases of acute hepatitis A throughout a seven years-period (2002-2008) was established.
Methods: All adult cases of acute hepatitis A, reported by the National Institute of Infectious Disease "L. Spallanzani", Rome-Italy, in 2002-2008 , were retrospectively analyzed. Data on HIV infection were obtained by chart review and cross-linkage with laboratory records. Information on risk factors were collected from the standard questionnaire of the Local Health Unit. Primary outcome was the prevalence of HIV testing confirmed result (negative, positive or unknown) during hepatitis A. Phylogenetic analysis was performed using Neighbor-Joining method, based upon the VP1-2A junction of HAV genome.
Results: We analyzed a total of 473 cases of hepatitis A, 368 (77.2%) males, accounting for the 75% of all reported cases in Rome aged 25-64 years (same gender distribution). M:F was always above 2.4, except in 2006. Among male patients HIV serology was available for 203/368 (55.2%) and the overall HIV prevalence was 15.2% (56/368) significantly associated with same gender sex. HIV prevalence was 5.6% for those not reporting same gender sex. Among HIV+ patients, 13/56 discovered their infection concurrently with hepatitis A (2 primary HIV infections). Phylogenetic analysis, performed on samples from 35 patients (30 males) showed one large monophyletic cluster (genotype 1A), including 2 females and 26 males. Among males, 73% (19/26) reported to be MSM. Eleven/28 (39.3%) patients, all MSM, were HIV-positive, one with concomitant HIV and HAV acute infection. The HAV sequences from other 7 patients (4 males) appeared not phylogenetically correlated with the cluster. The phylogenetic analysis of 84 stored samples of patients diagnosed from 2002 to 2010 is currently under way.
Discussion: Our results show a large and long-lasting (≥8 months) monophyletic outbreak of hepatitis A occurred in Rome since July 2008, that probably is still ongoing, involving a high proportion of HIV-infected MSM. Moreover our data suggest that in the period 2002-2007, a high percentage (115/368) occurred in MSM with high HIV prevalence. Data from the ongoing phylogenetic analysis may clarify if homologous HAV strains are circulating exclusively among MSM since 2002, resulting in an strain-specific endemic situation.

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The migration project in Veneto Region: evaluation of epidemiological impact of Tubercolosis, HIV, HBV, HCV infections and syphilis

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Objectives: The immigration wave occurred in Italy in the last decade is dramatically acting on the epidemiology of infectious diseases.
This study aimed at:
- conducting an epidemiological survey on the prevalence of HIV, HBV, HCV infections, Syphilis and Tuberculosis (TB) in the immigrant population;
- evaluating the economical impact of appropriate prophylaxis and therapeutic strategies on the immigrant population in an area of northern Italy (Veneto Region).

Methods: This survey is a multicentric-observational prospective study which involved 9 Health Centres in Veneto Region.
In order to guarantee a rappresentative sample of the immigrants living in Veneto Region, each centre was asked to recruit a specific number of patients stratified according to their country of origin and their legal status (with or without a regular visa) in Italy.
All patients aged >18 years and having access to care in the ER unit of each Centre for whatever health problems were invited to partecipate in the study.
The patients enrolled were screened for HIV, HBV, HCV, Syphilis and Tuberculosis by blood tests.
Moreover, all patients enrolled filled in a questionnaire in order to asses:
- demographic and social profile,
- sexual behaviour,

of the immigrants tested.
The patients were enrolled followed written informed consent.

Results: From March 2009 to February 2010 a total of 109 immigrant patients has been enrolled in the study, 60 (55%) were male and 49 (44.9 %) female. The 25-34 year age group was the more rappresentative (39.4%).
Of the 109 patients enrolled, most (45.8 %) came from South America and Southeast Asia, 29.3% from East Europa, 22.9 % from sub-saharan Africa,only 2 patients were from West Europe.
18.3 % of these were irregular immigrants.
Of the 109 patients enrolled only 2(1.8%) resulted HIV infected positive, 6(5.5 %) were HBsAg positive, 4(3.6%) had a positive result for Hepatitis C antibody test while 5(4.5%) for VDRL test.
31.1%(34) of the patients enrolled had a positive result for Quantiferon-TB test. Their socio-demographic characteristics are reported in the Table 1.
A positive result of this test suggests that M.Tuberculosis infection is likely. In these subjects Active TB has to be excluded and treatment for Latent TB has to be considered.

Conclusions: These preliminary results, confirming the international data, show that immigrant population is made up almost of young people.
The prevalence of sexual transmitted diseases among immigrant patients is relatively low, less than 2% for the HIV infection, less than 4% for HCV infection and about 5% for HBV infection and syphilis, while we found an high prevalence of people with positive Quantiferon-TB test. That suggests the importance to implement, as public health measure, the TB screening in the immigrant population, especially in people coming from low-income countries where TB prevalence is high, in order to prevent the TB transmission and the rebound of TB in the developed countries.

Table 1: Characteristics of patients with positive Quantiferon-TB test result.

	ABSOLUTE FREQUENCY	PERCENTAGE
Area of origin		
Sub Saharan – Africa	9	26.5%
East Europe	11	32.3%
West Europe	0	0
South America and Southeast Asia	14	41.2%
Sex		
Female	20	58.8%
Male	14	41.2%
Legal status in Italy		
Regular	26	76.5%
Irregular	8	23.5%
Age		
18-24 years	4	11.8%
25-34 years	12	35.3%
35-44 years	9	26.5%
45-55 years	7	20.6%
54-65 years	1	2.9%
+ 65 years	1	2.9%
Concomitant Infections		
HIV	0	
HBV	0	
HCV	0	
Syphilis	1	

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The necessary surveillance of screening of HIV infection in pregnant women: not a matter taken for granted

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Background/Objectives: The rate of vertical transmission of HIV dramatically declined after the introduction of antiretroviral (ARV) treatment before and at delivery, elective caesarean section and elimination of breastfeeding. However, such measures can only be applied if the woman is aware of being infected. Unfortunately it is not uncommon to have a first assessment for HIV infection once pregnancy is already established: national data about pregnancies of HIV-infected women reported a rate of 26.6% first diagnosis during pregnancy. The objectives of our study were to assess the rate of women arriving at the time of delivery with unknown HIV status and to register the tim-

ing of the availability of laboratory results in order to detect the risk of an unrecognized diagnosis before delivery.
Methods: Data were collected during 4 sample-months between 2008-2009, by computer-based consultation of the clinical documentation of pregnant women delivering at the S. Orsola Hospital, where more than 3500 deliveries take place every year. By reviewing prenatal care records, which woman submit at admission, we recorded the notation in the patients' charts of HIV testing performed during pregnancy and we evaluated the time elapsed between the availability of laboratory results (enzyme immunoassay, EIA) and the delivery, where it was performed at admission in women with no documented HIV testing records.
Results: HIV status was present in 1136 (99.5%) charts of 1142 women: in 1002 cases (87.7%) HIV testing was performed during pregnancy and it was absent in 134 (11.7%) women, so EIA was performed at admission. Laboratory results were available prior to delivery in 74 cases (55.2% of women tested at admission), in time to carry out all known preventative strategies. In 28 cases (20.8%) EIA result was received after delivery, but still in time for the possible start of ARV prophylaxis on the newborn. In 32 cases (23.9%) the test results were received more than 12 hours after delivery, late to implement the necessary prevention strategies.
Discussion: We found an important percentage of pregnant women arrive at their due date without having had HIV screening during pregnancy, this underlines the necessity of close surveillance that midwives and obstetricians must keep by active suggestion of the screening in the early stages of pregnancy. The attention of maternity hospital personnel given to registering prenatal records is also of crucial importance for a complete preventive intervention. Our study emphasizes the importance of a rapid HIV test that can be performed during labour, for those patients who have not already undergone the test, making it possible to carry out the eventually preventative strategies. We want to underline the necessity of simplified screening, adopting an opt-out approach and the abolition of a specific written informed consent, to permit a major efficiency of pre-natal care and a better management of high risk pregnancies.

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Causes of death in persons infected with the Human Immunodeficiency Virus

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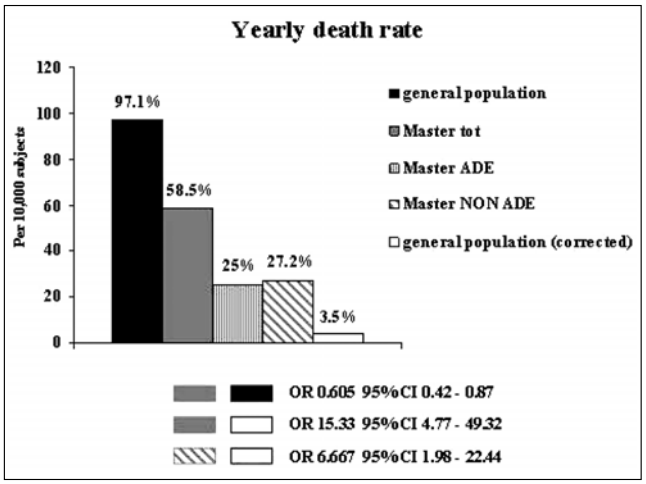
Background: The widespread use of HAART has substantially improved the prognosis of HIV-1-infected patients, however doubts remain about the real death risk in this population. We aimed to examine the clinical outcome in HIV-1 infected patients in a large clinical cohort.
Methods: Data on 7798 naive patients, counting for 35.383 patient-years of follow-up, that started a HAART regimen from 1998 to 2009 extracted from the Italian MASTER cohort were examined. Death rates either general or caused by specific pathologies in the selected population were calculated and compared with the death rate for the same causes in the general population. The most recent ISTAT data referring to the Italian territory were used for comparison.



Results: There were 548 deaths. Overall, the leading causes of death were malignancies (28.7%), end-stage liver diseases (23.6%), infections (23.3.%), cardiovascular diseases (11.9%), traumas (8.2%) and other causes (4.3%). Overall, 42.7% were AIDS-related and 46.5% were non-AIDS-related. The Kaplan-Meier median survival estimate was 395 days (95% CI 298-483) for AIDS-related deaths and 1037 days (95% CI 839-1234) for non-AIDS-related (P <0.0001). Statistically significant predictors of an increased risk of death included male gender, trasfusion as risk factor for infection, older age, early calendar year, non boosted protease inhibitor as third drug in first line regimen, lower CD4 cell count. When analysed according to the year of first HAART there was a sharp decrement of death incidence that lowered from 12.2% (1998-1999) to 2.5% (2008-2009) (P <0.0001). However, the calendar year analysis confirmed a decrease in AIDS-related yearly death rate from 8 cases/1000 patients (1998) to 2.9 cases/1000 patients (2009), but showed that non-AIDS-related deaths did not decrease: 1.3-4.6 cases/1000 patients in 1998-1999 to 4.3 in 2009. Consequently, cumulative yearly death rate was unaffected. Yearly death rates were similar in HIV-infected patients and in the crude general population (OR 0.605; 95 % CI 0.42-0.87) but when adjusted for age and gender, HIV infected patients showed a much greater risk of death (OR 15.33; 95% CI 4.77-49.32) (Figure).
Conclusions: HAART did reduce AIDS-related deaths but did not influence death rates due to other causes and, cconsequently, the overall yearly death rate. Despite HAART, HIV-infected patients remain at significantly greater risk of death compared to a matched uninfected population.

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Infection 2010; 38 (Suppl. I): 30

Antiretroviral Prophylaxis following Sexual HIV Exposure in Italy

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Objective: To describe use of HIV postexposure prophylaxis (PEP) following sexual exposure (SE), protocol compliance and follow-up (FU) outcome. Methods: We reviewed SE PEP courses provided in 41 centres participating in the Italian Registry of Antiretroviral PEP (2002-2009). Demographics, type of exposure, source serostatus, regimen and duration, adverse effects (AE), reasons for discontinuation

(DISC, i.e., at 3 and 6 months) and FU data were analysed, and their association with PEP and FU DISC assessed through multivariate logistic regression odds-ratio (OR).

Results: After excluding 17 cases with HIV-neg source for which PEP was stopped, and 8 (6 of whom MSM) found to be HIV+ at baseline, a total 750 cases were analysed (39% women; median age 32 years, range: 13-68). Serodiscordant stable couples (SC) accounted for 324 (43%) cases, casual partners (CP) for 368 (49%), rape for 58 (8%). 51 persons performed multiple PEP (CP 4% and SC 11%, p<0.001). 93% received 2 NRTI+PI, mostly AZT+3TC plus IDV (13%), NFV (17.5%) and LPV (49%). 440 were exposed to a HIV+ source (171 with detectable and 161 undetectable viraemia). PEP was completed in 553 (74%) cases, 53% despite AE; of the remaining 197, 58 and 38 discontinued due to AE or risk re-evaluation, and 101 dropped-out. A negative FU HIV test was available in 51% of cases at 3, and in 34% at 6 months. AE were less frequent with AZT+3TC and NFV (46%) than IDV (53%), or LPV (60%), but no difference were found among different IP with respect to DISC. Among subjects treated with PI, use of AZT+3TC vs two other NRTI was associated with higher rate of AE (56% vs. 45%, p=0.03) and PPE DISC (28% vs. 20%). Four HIV seroconversions in MSM were observed, 2 following CP SE (with 1 simultaneous HCV acquisition) and 2 SC SE; three of these (1 CP+2 SC) were due to unprotected SE following or preceding PEP. A significantly higher rate of PEP DISC was observed among heterosexual male (OR=1.8) and female (OR=2.1) vs MSM, youngers (OR=0.7 for each 10 years increase of age), and HIV unknown source (OR=1.7). FU DISC (both at < 3 as well <6 months) was significantly associated with PEP DISC and absence of AE. Known un-detectable viraemia in the source did not account for an higher PEP or FU discontinuation.

Discussion: The study confirmed previous evidences showing that PEP suffers of an high rate of drop-outs and lost to follow up, the potential source of exposure is rarely available for testing, MSM appear to be at higher risk of being positive at baseline as well of seroconverting, multiple PEP are frequent. All these findings suggest the need for testing different modality of counselling and PEP provision, and for identifying the reasons for the low adherence in order to enhance the effectiveness of PEP. Previous or subsequent at risk exposures should be carefully investigated. Although the high rate of adverse effects does not seem to influence adherence to treatment, available safer regimens should be provided.

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Acceptability of the Contact Tracing (CT) & Partner Notification (PN) procedures

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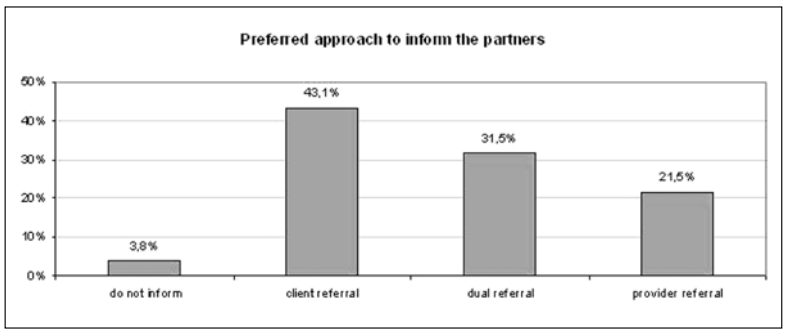
Background and objectives: The CT&PN procedures aim to find as soon as possible people (contacts) who have had unprotected sexual intercourses with HIV positive partners (index cases) in order to inform them about the possibility of infection. The purpose of our survey was to establish the acceptability of the voluntary submission to the CT&PN procedures by our clients. The main approaches of the methodology are: the "client referral" (where the HIV positive client directly informs their partner); the "dual referral" (where the healthcare provider assists the client to inform the partner); the "provider referral" (carried out by the healthcare provider alone while the index case remains anonymous). Therefore we analysed the opinion of the tested subjects regarding the following issues: i) the effectiveness of the CT&PN procedures to stop HIV infection; ii) the reliability of the proposed method in mantaining the privacy both of the subject index and their partners ; iii) the appropriateness of the method to inform the previous partner about HIV risk exposure; iv) the usefulness of disclosing the partner's identity in case of sexual risky behaviours; 5) the preferred choice to inform the partner.



Methods: The questionnaire was presented to the patients visiting our Center in a twenty days period (from Feb 15th to Mar 8th 2010).

Results: A total of 135 individuals (80% HIV positive) filled in the questionnaire (60% male, 40% female). On average the age was 41.5 (s.d. 9.5).

123 individuals (91.1%) agreed that subjects being diagnosed with HIV should inform previous and current partners. 111 subjects (82.2%) believed that this initiative could effectively prevent the HIV diffusion. 107 individuals (79.3%) thought that the CT&PN do not impair the subject's confidentiality and it is appropriate that previous partner are informed about HIV risks. 101 subjects (74.8%) confirmed that the CT&PN protects also the confidentiality of the partners. Less agreement was obtained on the item concerning the appropriateness of the disclosure of partners' identity, in case of risky behaviours: only 51.1% of individuals (69) agreed, while 20% (27) were in disagreement and 28.9% (39) did not have a clear opinion. Regarding the approach used to inform the occasional partners only 5 subjects tested (3.8%) would not inform them; 56 subjects (43.1%) would prefer informing them personally; 41 subjects (31.5%) would prefer being assisted by an healthcare provider and the remaining 28 individuals (21,5%) would prefer not being involved in the communication and would like to be unidentified (provider referral).

Discussion: Overall the survey showed that the CT&PN procedures might be applied regularly. The provider referral approach should be studied carefully and led in the full respect of the confidentiality of people involved. Properly qualified staff is also needed, due to the complexity of the procedures to apply and the confidentiality of the situations to manage.

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Detection of IgG against JC Viral Protein-1 (VP1) for management of patients with Progressive Multifocal Leukoencephalopathy (PML)

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Background: Progressive multifocal encephalopathy (PML) is a demyelinating disease of the central nervous system (CNS) caused by JC virus (JCV), presenting in the context of immune deficit. JCV DNA detection in cerebrospinal fluid (CSF) is the only diagnostic biomarker of PML. The availability of less invasive and repeatable markers such as detection of antibodies against JCV would be additional tools for management of PML.

Objective: To assess the significance and dynamics of anti-JCV VP1 IgG titer detection in plasma of patients with PML.

Patients and methods: Plasma samples nearest to the onset of PML symptoms (median days 32, IQR 18-60) were retrospectively investigated from 80 HIV-infected patients with PML observed between 1992-2010. 37/80 patients (46%) were receiving HAART for a median of 45 days (IQR 45-282), whereas 15 additional patients started HAART following sampling (52/80 patients, 61%). 56 patients were classified as PML progressors (PML-P; 27 HAART-untreated and 29 treated patients) and 24 as PML survivors (PML-S; one HAART-untreated and 23 treated patients). Sequential samples were available from 40 patients (22 PML-P and 18 PML-S). 97 HIV-positive patients without PML and 45 healthy donors were studied as controls. Anti-JCV VP1 IgG titer was determined in plasma using a viral-like particle (VLP)-based ELISA . The Mann-Whitney or Kruskall-Wallis test were used to compare IgG titer in the different patient groups and the slopes of IgG titer over time (b coefficients) in serial samples.

Results: Antibodies for JCV VP1 were detected in 77/80 patients with PML (96%; median OD 1.37, IQR 0.85-2.03; 53/56 PML-P and 23/23 PML-S), 69/97 HIV-positive controls (71%; median OD 0.57, IQR 0.26-1.49) and 35/45 healthy donors (78%; median OD 0.75, IQR 0.35-1.43). IgG titer was significantly higher in PML patients than HIV-infected controls and healthy donors ($p<0.0001$), but there was no IgG titer difference between PML-P and PML-S or between HAART-treated and untreated patients. An inverse correlation was found between IgG titer and plasma HIV RNA load at the time of sampling ($r=-0.311$; $p=0.028$), but not between IgG titer and CD4+ cells, plasma or CSF JCV DNA load. The analysis of longitudinal samples showed that the coefficient trend of IgG titer over time was significantly higher in HAART-treated compared to untreated patients (median b coefficient 0.39 vs -0.09; $p=0.031$), but no different trend were observed between PML-P and PML-S.

Conclusions: High JCV-VP1 IgG titer in patients with PML suggests that humoral immune response may play a role in JCV infection control. The inverse correlation between IgG titer and HIV RNA load and the better trend of IgG titer in HAART-treated patients over the course of PML suggests that HAART-induced control of HIV replication could improve JCV-specific immune responses. This however does not seem to turn into better control of JCV replication and PML outcome.

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Neurosyphilis incidence and screening practices among HIV infected patients

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Objectives: Neurological complications of syphilis infection seem to occur more frequently and progress more rapidly in HIV infected people. Optimal practices for the screening of neurosyphilis in HIV patients are still controversial. The aim of our study was to investigate adherence to the institutional guidelines for criteria to perform lumbar puncture (LP) among patients with syphilis and HIV co-infection. The secondary endpoint was to assess the prevalence of neurosyphilis in this population.

Methods: All HIV infected patients attending the Department of Infectious Diseases, Spedali Civili, Brescia, with a first diagnosis of syphilis (any stage) through a positive serum TPHA and all cases of syphilis reinfection (fourfold increase in serum RPR titer), during the period 2005-2009, were included in the analysis. Criteria to perform LP were defined as: clinical manifestations of neurosyphilis, OR serological or clinical treatment failure, OR late latent syphilis or syphilis of unknown duration regardless of the CD4 count or RPR titer, OR primary/secondary or early latent syphilis if the CD4 cell count was ≤350 cells/ml and/or RPR titer ≥1:32. Neurosyphilis was defined as: CSF-RPR positive, OR CSF-TPHA positive with pleocitosis (>10 cells/µl).

Results: During the study period 378 episodes of syphilis were diagnosed among 325 patients: 53 patients (14%) had more than one episode (43 had two and 10 had three new episodes). Most episodes were diagnosed in men (89%), Italians (74%) and men who have sex with men (MSM; 53%). Three patients were excluded from the analysis as data were not complete. On the basis of departmental guidelines, LP should had been performed in 299/375 (80%) syphilis episodes: 112 (37.5%) were actually performed; LP was performed in 9 additional cases for a total of 121 LP performed. Patients who did not undergone LP (187/299;62.5%) were more likely to be male (OR=2.87; CI 95%: 1.21-6.77; p=0.02), intravenous drug users (OR=3.57; CI 95%: 1.39-9.09; p=0.008), to have a negative serum RPR result (OR=7.70; CI 95%: 4.29-13.9; p=0.005). Neurosyphilis was diagnosed in 16% of the cases who performed LP (19/121). CD4+ T cell count was ≤ 350 cells/mm3 in 6/18 (33%), in 8/19 (42%) cases serum RPR titer was ≥ 1:32. No case of neurosyphilis was detected among 9 patients who had undergone LP without indication. All patients diagnosed with neurosyphilis had a serum RPR positive result.

Conclusions: Current departmental guidelines for the screening of neurosyphilis lead to an indication for LP in the vast majority of HIV infected patients. Adherence to the guidelines is low. The prevalence of neurosyphilis is high.Though the clinical consequence of neurosyphilis in HIV infected patients are not clearly documented these data warrants for an evaluation of current guidelines on performance of LP and targeted effort to improve their implementation.

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Cervico-vaginal HIV shedding is not related to cervical HPV infection

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Objectives: To evaluate the association between Human Papillomavirus (HPV) cervical infection and Human Immunodeficiency Virus (HIV) shedding in cervico-vaginal lavage fluid (CVL) of HIV-infected women.
Methods: Cross-sectional investigation of HIV-infected women recruited at the Department of Infectious Diseases of Brescia (Italy) between July 2003 and August 2007. HPV was searched by PCR real time in endocervical brushing; HIV-RNA (branched-DNA) was measured in paired peripheral blood and CVL samples.
CD4 cell count, plasma HIV viremia, use of antiretroviral therapy (ARV), time from HIV diagnosis, HIV exposure category, presence of genital dysplasia and genital infections were the confounders considered in univariate and multivariate analyses.
Results: Fifty-three percent of women (47/89) were on ARV and 57% had a detectable plasma viral load; the median CD4 cell count was 492 cells/µl. Globally, genital infections had a prevalence of 40%.
Valid HPV and HIV data were available for 89 women. Seventy women (78.6%) were positive for HPV infection, but only 29% of them had a type 16 and/or 18 infection. Cell-free HIV-RNA was detected in 30% of CVL samples. HIV shedding in CVL was found in a similar proportion of women with and without cervical HPV infection (OR:0.93; 95% CI 0.28-3.19; p=0.88). No correlation was found between quantitative cervical HPV-DNA and HIV-RNA in CVL (r=0.09).
HIV viral shedding was associated with sexual acquisition of HIV in the logistic regression analysis (OR 2.96; IC95% 1.11-8.6; p=0.04); the HIV-RNA load in CVL was also associated to sexual acquisition of HIV in the linear regression analysis (p=0.04).
Among the 27 women with detectable HIV in CVL, we found a statistically significant correlation between HIV vaginal and plasmatic viral load (r=0.4; p=0.04). Of the 38 women with undetectable plasma HIV load 13 (34%) had cervico-vaginal HIV shedding; 90% of these women were on ARV versus 20% of those with HIV-RNA detectable both in CVL and plasma.
Discussion: HPV infection is very common among HIV infected women, but it is not associated with increased cervico-vaginal HIV shedding. 34% of women with undetectable plasma HIV-RNA had a positive HIV in CVL, thus representing a risk of HIV sexual transmission: almost all of these women were on ARV.

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Longitudinal assessment of pre-transplant mortality risk among HIV-infected and uninfected patients with end-stage liver disease: the role of delta-meld score

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Background/methods: The need for liver transplantation (LTx) has recently increased due to higher rates of end-stage liver disease (ESLD) associated with hepatitis C virus co-infection. Hence, LTx is now considered a definitive therapeutic option for selected HIV-positive patients. The model for ESLD (MELD) scoring system is the prevailing criterion for organ allocation, but its reliability has not been fully established in HIV-infected patients. Moreover, the change in MELD score over time (Delta-MELD) may be a more accurate predictor of adverse outcomes in this population. The primary objective was to assess the role of Delta-MELD score as indipendent predictor of pre-transplant mortality in HIV-infected LTx candidates. The secondary objective was to determine factors associated with predictors of pre-transplant mortality in this population.
Methods: Single-centre, prospective, case-control study of pre-transplant mortality among consecutive adult HIV-infected and uninfected individuals placed on LTx waiting list at our Institution between August 1, 2002 and December 31, 2009. Patients were required to meet standard criteria for placement on the LTx waiting list as well as HIV-specific study criteria (for cases only) and to have serial MELD score measurements for at least two times.
Results: Forty-five HIV-infected LTx candidates (32 men, 13 females) were enrolled and matched by gender, ethnicity and initial MELD score with 45 HIV-uninfected LTx candidates (33 men, 12 females). In multivariable Cox regression models for death for the overall cohort and HIV-infected cases the only significant predictor of pre-transplant mortality was MELD score with a hazard ratio (H.R.)= 1.37 (95% confidence intervals (C.I.)= 1.15;1.64), P-value < 0.001, and H.R.= 1.53 (95%C.I.= 1.09;2.15), P-value= 0.014, respectively. Conversely, Delta-MELD score was not associated with greater hazard of death for both the overall cohort (H.R.= 1.11 (95%C.I.= 0.51;2.42), P-value= 0.790), and HIV-positive LTx candidates (H.R.= 0.79 (95%C.I.= 0.23;2.69), P-value= 0.707), respectively. In multivariable GEE regression analysis for the overall population and HIV-infected patients antiretroviral therapy (ART) initiation or reintroduction after a decompensation episode was a significant predictor of MELD score variation with β= -6.61 (95%C.I.= -8.89;-4.33), P-value < 0.001, and β= -6.90 (95%C.I.= -9.44;-4.36), P-value < 0.001, respectively.
Discussion: Our findings clearly support the use of MELD score to predict mortality and to guide the allocation of limited organs among HIV-infected LTx candidates, while do not provide strong evidence that Delta-MELD score is a significantly better predictor of pre-LTx mortality in this population. Furthermore, this was the first study to demonstrate that ART use was a significant predictor of MELD score variation suggesting a protective role in HIV-infected patients. Further properly designed trials are necessary to validate our results.

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Measurement of endothelial function in HIV-infected pregnant women: a case-control study

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Background: Endothelial function play a significant role in cardiovascular adaptation of physiological changes occurring during pregnancy.
Hypertension in a pregnant women may be considered an endothelial dysfunction secondary disease. No studies have explored functional integrity of vasculature by mean of brachial artery diameter (BAD) and flow mediated dilation (FMD) in HIV infected women during pregnancy so far. Our objective was to describe endothelial function changes and predictors in pregnant women with and without HIV infection.
Methods: Prospective case control study including consecutive HIV pregnant women recruited at the Infectious Disease Clinic and age matched HIV negative controls recruited at the Obstetric-Gynaecologic Clinic in Modena University. Biochemical parameters, blood

pressure, BAD and FMD were evaluated at each trimesters of pregnancy in the two groups.
Results: 19 HIV-negative and 14 HIV-positive pregnant women were enrolled. Systolic blood pressure in HIV-infected group was significantly higher, although within the normal range, than in the negative controls. A higher increase of body weight was highlighted in the third trimester in the HIV-negative group, 11 (IQR 4;17) in comparison to 6 (IQR -2;12) in case group. Serum level of total cholesterol, triglycerides, apolipoproteins were significantly increased at third trimester in both groups. No significant change was shown for BAD and FMD in pregnancy trimesters but a non statistically significant reduction in FMD was found in HIV positive pregnant women in the third trimester. BAD was the only independent predictor of FMD at multilevel regression model analysis (β = -1.032; CI -1.672;0.392). Unexpectedly metabolic variables and HIV group were not predictors of FMD.
Discussion: Endothelial function changes were not different in pregnant women with and without HIV infection. Further studies with higher number of participants are needed to prove association between endothelial dysfunction and pregnancy associated cardiovascular diseases including hypertension.

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Infection 2010; 38 (Suppl. I): 34

HBV Evolution and Drug Resistance Emergence in HIV-HBV Co-infected Patients depends upon the Synergistic Interaction between Immunological and Pharmacological Selective Pressure

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Background: Our work aims to study how, in a treated HBV+HIV co-infected population, immunological and pharmacological selective pressure synergistically act in leading viral evolution toward antigenic variation that facilitates escape from immune responses and amino acidic substitutions in polymerase gene that can confer resistance to the antiviral therapy.
Methods: This study includes HBV RT and HBsAg sequences from 69 HBV+HIV co-infected pts receiving 1st line regimen including 3TC (but not tenofovir), and 40 HBV mono-infected 3TC-treated pts (as control). Co-infected pts with a CD4 increase beyond 250c/ul (median CD4 gain=142[IQR:86-290]c/ul) are defined as immunological responders (IR), while pts with a CD4 decrease below 100c/ul (median CD4 drop=53[-217;94]c/ul) are considered as immunological non responder (INR). Phylogenetic analysis was based on MEGA, HyPhy and PAML packages.
Results: HBV mono- and co-infected pts fail 3TC-therapy after a median-time of 2.0(IQR:0.8-4.6) and 2.0(IQR:0.8-4.0) year, with median HBV-DNA of 4.9(IQR:3.3-7.2) and 3.1(IQR:2.4-4.5) logIU/ml, respectively.
The overall HBV RT and HBsAg genetic diversity is not affected by CD4 count variation from baseline to 3TC-failure. Indeed, the mean number of substitutions/site in mono- and co-infected IR pts is comparable with that observed in INR pts (0.068 and 0.066 versus 0.078 for RT, and 0.049 and 0.042 versus 0.054 for HBsAg, P>0.5).
Conversely, the immune reconstitution correlates with higher proportion of codons under specific positive selection (P<0.001) in both RT and HBsAg genes, and with higher rate of drug resistance emergence. Indeed, the prevalence of drug resistance mutations was higher in patients with a CD4 gain, respecting to those who experienced a CD4 cell loss (P=0.01).
Drug-resistance associated positions rtV173, rtL180 and rtM204 and immune escape-associated position sD144 in HBsAg gene were found under a strong positive selective pressure (dN/dS>1) exclusively in IR pts. M204I/V is described as CTL escape RT mutations, and is known to affect HBsAg antigenicity.
Conclusions: Our study highlights that HAART-driven immune reconstitution can act synergistically with pharmacological pressure in driving drug resistance emergence. This can accelerate HBV evolution (and potentially disease progression) also in immunological responder pts.

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Health care expenditure for HIV-patients by Health States

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Background: The adoption of HAART has led to a dramatic decrease in the morbidity and mortality of patients infected with HIV. Also, the cost of treating HIV-patients has increased: there is still the need to evaluate whether the costs introduced by the latest therapies can be compensated by the reduction of the expenditures due to the clinical management of patients exposed to the risk of developing AIDS disease.
Objective: The aim of this study is to evaluate the relationship among the cost components of care and to examine how (over a 2 year period) a change in clinical status affected cost expenditures, from the perspective of the Lombardia Region's health care system.
Methods: A retrospective observational study based on a HIV-patient cohort was carried out. The patients were taken from the 1st and 2nd Departments of Infectious Diseases at Luigi Sacco Hospital, and were identified from 2006 to 2007. Patients were stratified by Health States (HS), as defined by CD4 count and HIV RNA level: HS1 has the lowest CD4 level (CD4 50) while HS8 has the highest (CD4 > 500, HIV

HS	CD4	Viral Load	I Sem 2006 Mean Cost (€)	II Sem 2006 Mean Cost (€)	I Sem 2007 Mean Cost (€)	II Sem 2007 Mean Cost (€)
1	<200	>50	7,262.74	7,718.10	6,433.94	5,743.94
2	<200	<50	9,481.91	4,704.97	6,379.67	6,458.21
3	200-349	>50	4,137.66	5,477.98	4,066.45	2,627.55
4	200-349	<50	4,950.62	4,914.85	5,281.93	5,375.02
5	350-500	>50	3,680.67	2,785.51	3,900.63	2,721.19
6	350-500	<50	4,993.78	4,603.09	5,467.31	3,950.08
7	>500	>50	3,718.49	3,376.86	4,109.53	2,670.65
8	>500	<50	4,543.42	3,656.48	4,580.41	4,456.41

RNA > 50): an HS increase in the patient frequently reflects a clinical improvement and the ART success. We examined four different categories of public health costs: Hospitalizations, HIV-drugs, Non-antiretroviral drugs and Out-patient care. In this preliminary analysis, a sample of 200 patients, in continuative treatment for at least two years, was selected. Cost data were collected from Lombardia Region Database and were revised by CREMS.
Results: Public health six-monthly mean costs per patient per HS are reported in the table below. Antiretroviral therapy costs are the major driver of the overall costs. Hospitalisation costs tend to decrease by improving HS (data not shown).
Conclusions: Our findings demonstrate an important relationship between six-month per patient expenditures and Health States, with patients in the lowest CD4+ categories (HS 1 and 2) costing more than patients in the highest CD4+ cell count categories (HS 7 and 8). Antiretroviral therapy represented 45% to 86% of the overall costs; however, the improvement in clinical status associated with successful antiretroviral therapy, as demonstrated by improvement in Health States, led to a reduction in health care expenditures in other areas.

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Analysis of HAART combinations and costs in first line treatment in HIV-positive naïve patients at the Hospital-University Center "L. Sacco" in Milan

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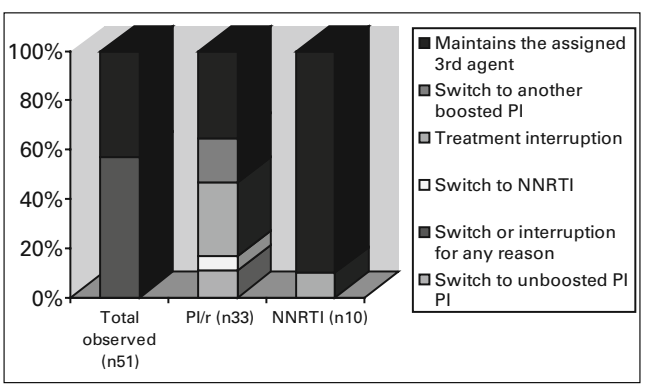
Background: The analysis of the drug utilization and the monitoring of the use of the antiretroviral drugs in comparison with European Guidelines are a good tool to control the appropriateness of the therapeutic choice and costs. We describe the prescription patterns in the first line of treatment for HIV in the 1st Division of Infectious Diseases at the "L. Sacco" Hospital.
Methods: HIV-positive adults who started the treatment from 1/1/2008 to 30/6/2008 were included in the analysis. Prescription information obtained from the drugs distribution cards were recorded for 12 months. Prescription data were elaborated by the software ENCO, including the cost analysis.
Demographic characteristics and reasons for switch were collected from the patients clinical charts.
Results: Fifty-one patients have been included in the analysis (W/M: 16/35; median age: 40 yrs (range: 25-72).



The therapeutic combinations mostly used were 2NRTI+PI/r (group A n=33, 64,7%) and 2NRTI+1 NNRTI (group B n=10, 19,6%). Two patients received an unboosted PI and 8 patients had different combinations.
In the group A, only 12/33 patients (36%) maintained the same treatment pattern for 12 months: 30% interrupted the treatment, 10% switched to an unboosted PI regimen, 6% switched to a NNRTI including regimen and 17% switched to a different boosted PI.
Conversely, in B group, all patients but one maintained the prescribed 3rd agent for the duration of the study.
94% percent of prescriptions were adherent to the European Guidelines. Of these 8% included a drug combination which was indicated as preferred in the Guidelines but was off label according to the Italian information sheet. The monthly cost for the first treatment ranged from 498,00€ to 998,57€ /month, (mean 773,85€/month). The monthly therapy cost in the group A ranged from 689,32€ to 998,57€/month, (mean 819,52€/month). In this group the incident rate about the change of therapy through the 12 months is 33%, and the switch resulted in a 20% increase in cost. In the group B (2N/NrTI+1NNRTI) the cost ranged from 664,61€ to 627,07 €/month .
Discussion: The drug prescriptions for the first line treatment of HIV patients analyzed in our study were overall adherent to the guidelines indications. The low number of patients included in the B group doesn't allow to draw conclusions, although in this group that the choice of a NRTI plus a NNRTI as first regimen resulted in a lower rate of changes and interruptions in the first 12 months and a lower monthly cost.
Some important factors regarding the patients' clinical situation (HIV-1 RNA, CD4 cells count, presence of concomitant conditions) might have had an impact on therapeutic changes.
Proper health technology assessment analyses are critical to evaluate these findings in a broader setting.
TAB1. Rate and reason for changes and interruptions in 1st line treatments

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Drug-specific risk of adverse events onset related to HAART in a resource-limited setting from 2001 to 2009: the experience of 3 Medical Centers in Burkina Faso

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Background/Objectives: To assess prevalence and grading of adverse events (AE) related to HAART according to international WHO guidelines and national Burkina Faso guidelines. To analyze the risk of adverse events after single or class of antiretroviral drugs exposure.
Methods: We analyzed clinical and laboratory AE occurred under HAART from 2001 to 2009 in 1245 patients from 2 urban medical centres located in the capital Oauagadougou, and rural 1 located in the Health District of Nanoro (893, 71.7% were female; 1040, 83.5% came from urban area). Statistical analysis was performed with Epi-Info 3.5
Results: Showed AE 254/1245 patients; over 1724 tratment admistrated we had 386 events. Patients who showed AE were treated with: 2NRTI+NNRTI (83.2%); 2NRTI+PI/r (15%); 2NRTI+PI (1.3%); the rest with another protocol type.
Observed prevalence of the AE was: 42% (162/386) peripheral neuropathy, 17.8% (69) CNS toxicity, 15.8% (61) gastro-intestinal intoler-

Table 1

Drug	Adverse Event	Relative Ratio	Odds Ratio	p-value
NVP	Skin rash	2.49	2.53	<0.05
D4T	Peripheral neuropathy	9.7	11.28	<0.01
AZT	Anemia	57.9	60.79	<0.01
LPV/r	gastro-intestinal intolerance	2.6	2.74	<0.05
EFV	CNS toxicity	24.89	28.63	<0.01

ance, 8.8% (34) anemia, 8.5% (33) skin rash, 3.9% (33) hepatotoxicity, 3.2% (12) others AE.
Relative ratio (RR) of AE resulted statistically significant for female sex: RR 0.81, Odds Ratio (OR) 0.77 (p<0.05,); was not significant for place of origin (urban or rural area), HIV serotype, baseline CD4+ cell count, WHO clinical stage.
Exposure to EFV, d4T and 3TC is related to a increasing risk of AE: for EFV RR observed was 1.23, OR 1.31 (p<0.05); for d4T the RR was 1.26, OR 1.35 (p<0.01); for 3TC the RR was 1.82, OR 2.06 (p<0.01).
Comparing the exposure with the NOT exposure to a drug overall protocols administrated (1724), we analyzed the RR onset of a specific AE and resulted statistically significant the correlations as shown in table 1.
Discussion: Risk analysis and related factors to EA's onset in a resource limited setting, as well as diagnosis in early grade is essential to avoid switching and interruption treatment when therapeutical choice is still limited. Exposure to some drugs increases very much the risk of AE onset. Our data suggest that we need availability of more effective and less toxic antiretroviral drugs.

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Arterial stiffness assessment in Tanzania by Pulse Wave Velocity: a case-control study of a HIV-infected cohort

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Background: The expansion of HIV epidemic and scaling up of antiretroviral therapy (ART) in developing countries raise a concern for the development of cardiovascular disease (CVD) in HIV-infected patients living in those areas.
Aortic pulse wave velocity (PWV) is a non-invasive and objective measure of arterial wall elasticity. Arterial stiffness measures vascular damage secondary to ageing, hypertension and inflammation of the vascular wall. An elevated PWV has been established as an indicator of CVD.
Methods: Cross-sectional case-control study of 89 HIV ART-naïve, 75 HIV ART-exposed patients undergoing first line treatment with Triamune®, and 93 healthy controls referring to a Care and Treatment Clinic (CTC) in Usokami, Mufindy District, Tanzania. This CTC is run by Physician Assistants in a rural area.
Exclusion criteria were smoking, hypertension, diabetes mellitus and known CVD. HIV negative controls were recruited among the CTC employees. PWV was measured with Complior® (Alam Medical, Vincennes, France).
Univariate analyses were performed using Fisher's exact test, ANOVA and Kruskal-Wallis tests. Multivariable regression analyses were performed to determine factors associated with PWV.

Table 1. Patient's characteristics of entire population (257 pts)

	HIV-	HIV+ no ART	HIV+ on ART	p-value
DEMOGRAPHIC[5]				
N (% of the cohort)	93 (36.19)	89 (34.63)	75 (29.18)	-
Women n (%)	92 (98.92)	56 (62.92)	46 (61.33)	< 0.001
Age mean (± SD)	21.6 (5.0)	35.9 (9.0)	38.4 (7.7)	< 0.001
ANTHROPOMETRICS				
BMI mean, Kg/m² (± SD)	23.4 (3.8)	20.4 (2.5)	21.0 (2.2)	< 0.001
Waist girth, cm (± SD)	75.3 (8.4)	77.9 (7.5)	79.5 (8.4)	0.002
Hip, cm (± SD)	92 (12.7)	89.6 (7.5)	91.5 (7.6)	0.227
HIV history				
WHO stage				0.037
1 n (%)	–	5 (5.62)	0	
2 n (%)		19 (21.35)	13 (17.33)	
3 n (%)		58 (65.17)	48 (64.00)	
4 n (%)		7 (7.87)	14 (18.67)	
CD4+ Current median (range)	–	272 (12; 924)	300 (5; 953)	0.147
Months of ART exposure median (range)	–	0 (0; 0)	16 (6; 62)	< 0.001
CARDIOVASCULAR				
Diastolic blood pressure, mmHg (± SD)	77.8 (10.2)	73.9 (10.1)	76.9 (10.1)	0.027
Sistolic blood pressure, mmHg (± SD)	119.6 (15.3)	112.0 (14.9)	121.2 (17.8)	< 0.001
Mean BP (dbp+(sbp-dbp)*0.4), (± SD)	47.8 (6.1)	44.8 (5.9)	48.5 (7.1)	< 0.001
Femoral PWV, m/s (± SD)	8.3 (2.7)	10.6 (3.4)	10.1 (3.3)	< 0.001

Table 2. Multivariable analyses of entire population.

	β	95% C.I.	p-value
Gender			
Women	- (Ref.)	-	-
Men	0.22	-0.80; 1.25	0.66[3]
Age (per 1 yr increment)	0.06	0.01; 0.11	0.028
Group			
HIV negative	- (Ref.)	-	-
HIV+ ART-naive	1.26	0.01; 2.52	0.049
HIV+ ART-expirenced	0.53	-0.81; 1.86	0.436
BMI	-0.08	-0.22; 0.05	0.224
Heart rate	0.002	-0.02; 0.03	0.862
Mean BP	0.05	-0.01; 0.11	0.092

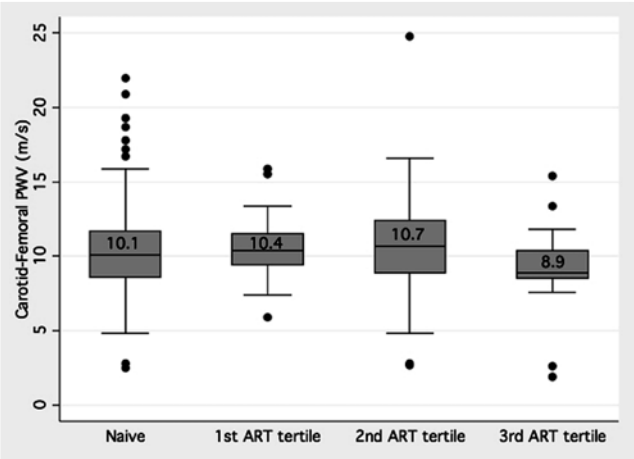

Figure 1: Box-plot of carotid-femoral PWV in HIV-infected subgroups according to ART status.

Results: Patients' characteristics are shown in Table 1. In univariate analyses, controls had lower mean PWV than HIV patients (8.3 vs. 10.4, p<0.01). Table 2 shows multivariable analyses of PWV predictors in the entire population: after adjustment for age and sex, PWV was higher in ART naïve patients (β=1.26, 95% C.I.: 0.01; 2.51, p=0.049). To better appreciate PWV differences between HIV subgroups, ART exposed patients were grouped in tertiles of cumulative ART exposure. Figure 1 depicts differences in PWV according to ART exposure and Table 3 shows the results of multivariable regression analyses of PWV predictors. Longer exposure to ART (> 21 months) was associated with reduced PWV (β=-1.50, 95% C.I.: -2.99; -0.01, p=0.047).
Discussion: This study is proof of the feasibility of measurement of arterial stiffness as organ damage in HIV infected patients living in developing countries.
We confirm HIV as an independent predictor of arterial damage. In a young non-hypertensive population we hypothesize increased PWV may be associated with HIV induced arterial inflammation.
Given the cross sectional nature of our study, we cannot confirm (nor exclude) that longer exposure to Triamune® is a protective factor for arterial stiffness rather than representing a survivor's selection bias.

Table 3. Multivariable analyses of HIV-infected subgroups.

	β	95% C.I.	p-value
Gender			
Women	- (Ref.)	-	-
Men	0.12	-1.03; 1.28	0.831
Age (per 1 yr increment)	0.02	-0.04; 0.09	0.416
ART Group			
ART-naive & 1st ART tertile	- (Ref.)	-	-
2nd ART tertile	0.06	-1.46; 1.59	0.931
3rd ART tertile	-1.50	-2.98; -0.02	0.047
BMI	-0.20	-0.44; 0.03	0.092
Heart rate	0.001	-0.04; 0.04	0.946
Mean BP	0.06	-0.02; 0.14	0.153

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Infection 2010; 38 (Suppl. I): 37

Learning from the past: the possible impact of migration, late HAART initiation and prescription of non-HAART regimens on the risk of positive HIV-RNA at delivery

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Background: Revised guidelines of antiretroviral therapy during pregnancy recommended to avoid regimens based on one or two drugs and start HAART as soon as possible. The aim of our study was to describe management of pregnant HIV-positive women presenting to our Clinic and to show variables associated with detectable HIV-RNA at delivery.
Methods: Observational retrospective study in pregnant women attending a large outpatient HIV Clinic in Brescia (northern Italy) from September 2002 to May 2008.
Univariate and multivariable logistic regressions were performed using STATA software.
Results: 154 women were included (158 pregnancies, 128 deliveries). 46.8% came from Italy, 42.4% from Africa, 6.3% from Eastern Europe, and 4.5% from other Countries. Mean age was 33.4 years in Italians vs. 29.9 years in women from other Countries (p=0.016). Risk factor for HIV acquisition was heterosexual contact in 54% among Italians and in 84.5% among migrants (p<0.001). HIV diagnosis was made during pregnancy in 8.7% Italian women vs. 38% women from other Countries (p<0.001). At the beginning of pregnancy, mean CD4+ T-cell count was 495 cells/mm3 in Italian patients vs. 435 cells/mm3 in migrants (p=0.150), with 74.3% Italians already on HAART before pregnancy vs. 46.4% migrants (p=0.005). HIV-RNA was undetectable in all children. 18.9% Italian women vs. 31.5% migrants presented detectable HIV-RNA at delivery (p=0.182). Multivariable logistic regression showed that risk of detectable HIV-RNA at delivery was inversely associated with increasing number of antiretroviral drugs during pregnancy (OR=0.30; p=0.048) and higher CD4+ T-cell counts at the beginning of pregnancy as a continuous measure (OR=0.99; p=0.015). At the same model, a delay in the beginning of antiretroviral therapy during pregnancy was associated with increasing risk of detectable HIV-RNA at delivery (per trimester, OR=1.5; p=0.087). By contrast, patient age and calendar year did not appear to be associated with HIV-RNA at delivery, as well as nationality "per se".
Conclusions: Although the combination of antiretroviral therapy and obstetric interventions were always effective to prevent vertical transmission of HIV, pregnant migrants appeared to have later HIV diagnosis and started antiretroviral therapy later than Italian women. These factors resulted significantly associated with detectable HIV-RNA at delivery. Thus, they may explain why migrant women had higher prevalence of detectable HIV-RNA at delivery than the Italian ones, although this difference did not reach statistical significance. Our results reinforce the recommendation to avoid prescription of suboptimal regimens and start HAART timely. This is only achievable by testing for HIV as soon as possible and must be urgently implemented, especially in migrant patients who are unaware of their HIV status at the time of pregnancy more frequently than Italians.

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The ISS-HIV-symptom scale: the routine evaluation of health related quality of life

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Background: To design the self-completed "ISS-HIV-symptom scale", a specific tool for HIV people in the era of potent combination therapies (cART), to routinely monitor the health related quality of life (HRQoL) in clinical settings.
Methods: The symptom scale was developed by an Italian network (coordinated by the Italian National Institute of Health), including researchers, physicians, people living with HIV. The basic steps in the list construction were: 1) review of existing HRQoL literature; 2) selection of relevant symptoms measuring HRQoL in HIV-infected people from the physician's point of view; 3) drafting of the final list of symptoms through the conduction of two focus group analyses in independent groups of HIV-positive people (n=10); 4) validation analysis of the Italian version of ISS-HIV-symptom scale (sample: 200 pts); 5) translation into several languages for 12 different European countries. The project is funded by the NEAT project of the European Commission (FP6 contract 037570).
Results: The self-completed ISS-HIV-symptom scale consists of 38 HIV-related symptoms that include: fatigue, gastroenteric disorders, mental disturbances, sexual dysfunction, body image changes, anxiety, pain, and sleep disturbances. The validation results of the Italian HIV symptom scale will be presented. The English version is now available, while the others translations are being implemented in each country.
Conclusions: Periodic monitoring of patient-centred symptoms improves communication between patient and physician, increases the adherence to therapy and, helps identify the most appropriate long-term treatment for individual patients with consequent benefits in terms of overall effectiveness of treatment and better quality of life.

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Infection 2010; 38 (Suppl. I): 38

Carotid artery intima-media thickness and arterial stiffness in HIV infected patients

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Background: HIV-infected patients have an high risk of atherosclerosis and cardiovascular disease (CVD). Endothelial function, a central mechanism in atherosclerosis, is impaired among patients treated with combination antiretroviral therapy (cART). Carotid ultrasound measurements of carotid intima-media thickness (IMT) and atherosclerotic plaques, as surrogate markers of vascular risk, and of flow-mediated dilation (FMD) of the brachial artery, as expression of endothelial function, allow non-invasive predictions of vascular risk. Increased arterial stiffness as assessed by pulse wave velocity (PWV) has been associated with adverse cardiovascular outcome in general population. The aim of this study was to evaluate the intimal damage and arterial stiffness in HIV infected patients.
Methods: A total of 74 HIV positive patients were enrolled into the study: 64 subjects were treated with cART for >or=12 months and 10 were naïve. A control group of 34 healthy non infected patients was included. Viro-immunological parameters, triglycerides (TGs), total cholesterol (TCh), HDL (HDL-C) and LDL (LDL-C) cholesterol, fasting glucose, HOMA-IR, VES, CRP, microalbuminuria, and systolic (SBP) and diastolic blood pressure (DBP) values were measured. Carotid intima-media thickness (IMT), flow-mediated dilation (FMD) of the brachial artery and pulse wave velocity (PWV) including the heart rate corrected augmentation index (AI), were used to evaluate measures of arterial stiffness and endothelial function in all enrolled subjects. Brachial artery flow-mediated dilation (FMD) was determined by B-mode ultrasound. Arterial stiffness was assessed non-invasively by PWV.
Results: Group of HIV infected subjects showed statistically higher TGs and CRP levels and lower HDL-C, microalbuminuria, and SBP (116.2±11.3 vs 132±6.1, p=0.0001) values than control group. IMT and FMT did not show significant differences between these two groups, while PWV was statistically higher (7.7±2.7 vs 6.5±1.5, p<0.02) and AI was lower (10.4±12.5 vs 24.1±11.7, p<0.0001) in HIV positive patients respect to non-infected. In HIV positive group, naïve patients showed statistically higher levels of VES and CRP and reduced SBP, DBP and IMT (0.055±0.01 vs 0.069±0.02, p=0.007) values in comparison to cART-treated patients. Finally, a significant linear correlation was observed between CD4+ cell count and IMT values (p=0.001) in HIV positive group.
Discussion: Patients with HIV infection showed metabolic alterations and altered PWV and AI respect to healthy subjects. Furthermore, cART treated patients showed higher BP and IMT values than naïve patients. So the cART-treated patients seems to have an impaired stiffness that may be due to an higher vascular risk in this group.

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Naturally C-Terminally truncated STAT5 (STAT5Δ): a novel negative controller of HIV-1 transcription and expression

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Background: Signal transducers and activator of transcription (STAT) proteins, namely STAT1 and STAT5, are often constitutively activated in the PBMC of most of HIV-1+ individuals; furthermore, most patients are characterized by the dominant expression of a C-terminally truncated isoform of STAT5 (STAT5Δ). STAT5Δ is also the prevalent isoform of STAT5 found in the chronically HIV-1 infected promonocytic cell line U1, characterized by a constitutive state of viral latency and inducibility of virus expression by PMA or several cytokines.
Results: GM-CSF-mediated STAT5Δ activation induced a delayed expression of integrated HIV-1 in U1 cells. Selective inhibition of STAT5Δ expression or activation enhanced viral expression in GM-CSF stimulated U1 cells. Moreover, activated STAT5Δ can directly in vivo bind to STAT consensus sequences in the HIV-LTR promoter with an impaired recruitment of RNAPol II in U1 cells stimulated with GM-CSF.
Conclusions: STAT5Δ can act as a negative regulator of HIV-1 expression in GM-CSF stimulated U1 cells. We are currently investigating whether the reduced recruitment of RNA Pol II and the consequent decreased viral transcription and delayed kinetics of HIV expression that follow GM-CSF stimulation could be entirely attributed to the negative role of STAT5Δ alone or whether other proteins participate to the negative control of HIV transcription in U1 cells.

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HIV-1 infection of cervico-vaginal tissue ex vivo

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Background: The mucosal immune system of the lower female genital tract plays a key role in HIV-1 transmission and pathogenesis. While in other tissues HIV-1 infection of CD4 T cells is known to depend on cellular activation, differentiation and expression of HIV-1 co-receptors for cervico-vaginal tissue (CVT) these key characteristics of CD4 T cells remain unknown. To address this problem we developed an ex vivo system of cervical explants that efficiently support HIV replication.
Materials & Methods: We investigated by FACS analysis the differentiation and activation state of CD4 T cells extracted from CVT blocks obtained from HIV-1 negative (HIV-1neg) volunteers. CVT blocks were infected with either CCR5-dependent (R5-HIV-1BaL) or CXCR4-dependent (X4-HIV-1LAI) HIV-1 strains; productive infection of HIV-1 was documented by ELISA for p24Gag, and by RNA quantification by real-time PCR. Also, we identified p24gag expressing cells by FACS analysis. In order to distinguish between absorption and viral replication inhibitors of HIV reverse transcriptase (RTi), such as 3TC or of viral entry (PSC-RANTES) were used.
Results: CD4 T cells isolated from CVT showed predominantly an effector memory phenotype (TEM, TEMRA) with a peculiar pattern of expression of activation markers including high levels of CCR5 expression (51±3%). CVT inoculated with R5-HIV-1BaL efficiently supported virus replication, whereas X4-HIV-1LAI replicated only in the few tissues enriched in CD27 + CD28 + CD4 TEM cells. Ex novo HIV replication rather than virus absorption was demonstrated to occur and was abolished by either RTi or PSC-RANTES. For R5-HIV-1BaL, p24Gagpos cells were mostly activated (CD38+) CD4 T cells although a similar state of activation of p24Gagneg (bystander) CD4 T cells was also observed.
Conclusion: CD4 T cells present in CVT of HIV-1neg individuals are in a predominantly activated state and express CCR5. These features are likely responsible for the susceptibility of CVT to support productive infection of R5-HIV-1. In contrast, X4-HIV-1 replication was negligible except in a few tissues (enriched in CD27 + CD28 + CD4 TEM cells) implying that co-expression of CD4 and CXCR4 in lymphocytes of CVT is not sufficient to support productive infection of X4 HIV-1.

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Effect of envelope cholesterol withdrawal on HIV ability to induce type I interferon production and pDC activation

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Background: Chronic activation of plasmacytoid dendritic cells (pDC) may play a key role in HIV immunopathogenesis. The binding of gp120 to CD4 triggers virion endocytosis by pDC, an essential step for pDC activation. An envelope-associated lipid raft, characterized by tightly packed cholesterol, is the site of virus-cell interaction. Partial cholesterol withdrawal from the envelope, by treatment with 2-hydroxy-propyl β-ciclodrexin (βCD), destabilizes the envelope organization but leaves the virion intact. Extreme cholesterol removal results in HIV permeabilization, loss of viral RNA and part of the capsid proteins. We tested whether alterations of the HIV envelope may prevent the induction of pDC-mediated immunopathogenesis.
Methods: PBMCs from healthy donors were cultured in presence aldrithiol-2 (AT-2)-inactivated HIV or AT-2 HIV treated with different concentrations of βCD (20, 80, 120mM). Treatment with 120mM CD resulted in HIV permeabilization. Using flow cytometry we analyzed the expression of: CD80, CD86, CD83 and PDL1 on pDC; CD38 and CD69 on T cells; MHC class I and CD86 on mDC. In culture supernatants we tested the activity of the immunosuppressive enzyme indoleamine 2,3-dioxygenase (IDO) by HPLC measurement of tryptophan and kynurenine. IFNα and IFNβ concentrations were determined by ELISA..
Results: Our data showed that: 1) Partial cholesterol withdrawal (βCD20-80) reduced the ability of HIV to induce type I IFN and IDO activity; 2) permeabilization abolished the ability of HIV to induce type I IFN and IDO, probably due to viral RNA loss; 3) partial pDC activation may be achieved even with permeabilized HIV in spite of the lack of type I IFN and IDO activity; 4) βCD120 HIV, but not βCD20-80 HIV, showed reduced ability to upregulate PDL1 expression; 5) βCD20-80 HIV but not permeabilized HIV induced CD38 and CD69 on T cell, markers associated with HIV disease progressions; and 6) βCD120 HIV was still capable of up-regulating MHC-I and CD86 on mDC, albeit less potently than βCD20-80 HIV.
Conclusions: We found that partial cholesterol withdrawal reduced the ability of HIV to stimulate type I IFN production and IDO activity. However, this was still sufficient to sustain the expression of immune activation markers by pDC and T cells. Conversely, permeabilized βCD120 HIV particles completely lost their ability to activate pDC-mediated immunosoppresive mechanism, but conserved most of viral antigens and retainined the capacity to partially activate mDC and pDC. Our data suggest that permeabilization by cholesterol withdrawal may abolish the immunopathogenic potential of HIV without completely crippling its ability to stimulate antigen presentation by DC.

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The mucosae-associated epithelial chemokine (CCL28) modulates mucosal immunity in balb/c mice immunized with HIV-1 virus like particles

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Background: CCL28 (MEC) binds to CCR3 and CCR10 and recruits IgA-secreting plasma cells in the mucosal lamina propria; mucosal HIV-specific IgA are detected in HIV-exposed uninfected individuals. HIV-1 virus like particles (VLP) are a novel vaccine approach based on the assembly of HIV-1 Pr55gag precursor protein as non-infectious VLP with effective induction of both arms of the immune response. CCL28 suitability as an adjuvant for induction of specific humoral immunity at mucosal sites was verified in a mouse model receiving HIV-1 VLP.
Materials and methods: Balb/c mice were immunized intramuscularly with a prime-boost regimen based on VLP expressing gp120 from HIV-1 III B in the presence/absence of CCL28. HIV-specific Th1 and Th2 cytokine production and flow citometry evaluation of CCR3 and CCR10 expression were performed on purified splenocytes. Env-specific IgA antibodies were evaluated in plasma samples and in vaginal

secretions by an enzyme-linked immunosorbent assay (ELISA). Immune sera and vaginal secretions were tested for ex vivo neutralization activity against different clade B HIV-1 strains.
Results: The following immune parameters were significantly augmented in VLP-CCL28 compared to VLP or CCL28-alone mice: 1) env peptides- stimulated IFN and IL-5 production (IL-5 p= 0.026); 2) the percentage and the surface density (MFI) of CCR3 and CCR10 on CD19+ splenocytes ($p<0.05$ in all cases). Total IgA titers were significantly augmented, compared to baseline values, in vaginal secretions of VLP-CCL28 mice compared to controls ($p<0.01$); HIV-specific IgA levels were similarly significantly increased in plasma samples and vaginal washes of VLP-CCL28 alone ($p<0.05$ vs. controls). Preliminary data show the presence of neutralizing activity against autologous HIV-1 clade B strains of IgA from sera and vaginal washes of VLP-CCL28-receiving mice.
Conclusions: CCL28 mediates mucosal immunity; the effect is reproducible using this chemokine as an adjuvant in murine models of HIV infection. CCL28-containing adjuvants should be considered in the development of HIV vaccines to prevent infection of mucosal sites via modulation of mucosal IgA.

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Emergence of exhausted B and T cells in asymptomatic HIV-1-infected patients naïve for HAART is related to reduced immune surveillance

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Background: HIV-1 infection induces a general status of perturbation on the majority of immune system cells making patients susceptible to opportunistic infections and tumours. Immune cells of HIV-1-infected patients are characterized by several functional defects that are mainly due to the chronic HIV-mediated cell hyperactivation followed by cell exhaustion. Most of the immune cell impairments have been observed on chronically infected patients in advanced stage of HIV-1 disease with pronounced CD4+ T cell lymphopenia and ongoing HIV-1 replication. The aim of the present study is to investigate if signs of B and T cells exhaustion and impaired surveillance on endogenous virus replication are present in asymptomatic HIV-1-infected patients with preserved CD4+ T cell counts and naïve for Highly Active Antiretroviral Therapy (HAART).
Methods: A cohort of 43 asymptomatic HAART-untreated HIV-1-infected patients with CD4+ T cell counts > 350 cells/μl was evaluated for immunological parameters defining immune exhaustion of B and T cells. Patients were also studied for HIV-1 and Torque Teno Virus (TTV) viral loads. Twenty aviremic HAART-treated patients and 34 healthy individuals were used as control groups. Peripheral blood samples were analyzed by flow cytometry for the identification of B cell subpopulations defined by the expression of CD19, CD10, CD21 and CD27 markers. T cells were also examined for the expression of interleukin-7 (IL-7) receptor (CD127), and for IL-7 serum levels quantified by ELISA. TTV viral load was determined by real- time PCR. Mann-Whitney U-test and Spearman rank correlation coefficient test were used for statistical analysis.
Results: Asymptomatic patients showed dramatic expansion of an exhausted tissue-like B cell subset, which correlated with HIV-1 and TTV viral loads. They also displayed increased serum levels of IL-7 and decreased CD127 expression on T cells. Normal B cell subsets and TTV viral load were observed in HAART-treated patients negative for HIV-1 viremia.
Conclusion: Asymptomatic HAART-untreated HIV-1-infected patients showed the emergence of exhausted B and T cell elements that was mirrored by an impaired control of TTV replication. Successfully HAART-treated patients showed normal B cell subpopulations frequency and TTV viral load. These findings suggest that the early application of HAART may prevent the loss of immune functions.

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Predictors of complete early virological response (cEVR) and sustained virological response (SVR) in HIV-HCV co-infected subjects treated with Pegilated interferon/ribavirin (PEG/RBV)

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Background: PEG/RBV combination is currently the standard treatment for chronic hepatitis C virus infection in HIV-infected patients. Emerging data, mainly derived from small studies, suggest that higher RBV exposure is associated with EVR, SVR and haematologic toxicity in HCV and HIV/HCV coinfected subjects.
Aim of the study: to investigate the association between RBV trough plasma concentration (Ct) and EVR, SVR and haematologic toxicity in the cohort of HIV/HCV coinfected patients treated with PEG/RBV in our Institute.
Materials and Methods: cEVR and SVR were defined as negative HCV-RNA respectively after 12 weeks of therapy or 24 weeks after the end of treatment; HCV RNA was measured by qualitative PCR assay (COBAS 3.0) after week 4 and every three months of treatment thereafter. Haematologic toxicity was defined as a loss of at least 2 or 4 g of haemoglobin (Hb) or as a drop in Hb level to values below 10 or 8.5 g/dL during the treatment.
RBV Ct was assessed by HPLC method at week 4 of treatment.
Quantitative variables are expressed as median and interquartile (IQR) range; predictive factors of EVR and SVR were analyzed by univariate and logistic regression analisys.
Results: 59 HIV/HCV coinfected patients were analyzed (84,7% males, age 42 (40-44), 42,4% genotype 1-4, 30,5% with cirrhosis, 73% never treated with interferon; at baseline 93,2% of them had undetectable HIV-RNA and median CD4 cell count was 398/mL (325-520); median RBV pro kg/die was 14,5 (13,4-16) mg: 15,6 (13,7-16.4) in genotype 1-4 and14,1 (13,3-15,1) in genotype 2-3 (p=0.03). EVR and SVR were reached by 40 pts (71,4%) and 26 pts (48,1%).
RBV Ct in pts with EVR was significantly higher than in pts without EVR (1421 (1020-1966) versus 894 (625-1569) ng/mL (p=0,01).
82% of pts with RBV Ct above 1200 ng/mL reached EVR whereas only 54% of pts with RBV Ct below this value reached EVR.
In the multivariate analysis the independent predictors of EVR were: genotype 1-4 (OR 0,03 (IC 95% 0.003-0.45) p=0,009), RBV Ct > 1200 ng/mL (OR=17, (IC 95% 1,42-205) p=0,02) and HOMA score 100 (OR=5,3 (IC95% 1,3-21,7) p=0,01).
Moreover a RBV Ct 1m> 1500 ng/mL was associated with a drop of Hb values below 10 g/dL (OR 5.5; IC 95% :1,03-29,4; p=0,02) while a RBV Ct > 1800 ng/mL was associated with a 4 g drop of Hb at week 12 of treatment (OR 6; IC 95%: 1,4-24,9; p=0.009).
Conclusions: to our knowledge this is the first time that RBV CT has been identified as an independent predictor of EVR in a model comprising classical factors (i.e. genotype) and metabolic factors.
A sort of therapeutic range for RBV Ct has been identified and the fact that our cut off is different from those identified in other studies underlines the importance of defining this range in every laboratory performing this analysis until a standardization program will be carried out.

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Association between hepatitis C viremia and serum triglyceride in Italian national cohort observational study (OPERA)

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Background: metabolic parameters are involved in the virological response to peginterferon alfa 2a and ribavirin (PegIFN/RBV). Lower level of cholesterol is reported in HCV infected persons with or without HIV co-infection. No data are available about the association of HCV virological status with serum triglycerides and cholesterol levels in HIV/HCV co-infected patients.
Material & Methods: The OPERA study (Optimization of Pegylated interferons Efficacy and anti-Retroviral Approach) is an Italian national cohort observational study including all consecutive patients with HIV/HCV coinfection who were prescribed anti HCV treatment from 17 January 2005 in 102 Italian centres for the care of HIV. We reviewed the epidemiological, clinical data and the virologic and metabolic baseline parameters of all patients enrolled in order to analyse the correlation between HCV-RNA level and metabolic parameters.
Results: 1640 HIV/HCV subjects were enrolled , 76,9% males, mean age 42,1 (+6,0) years, 64 patients (3,5%) were active drug abusers. An AIDS defining event was identified in 520 subjects (33,3%). Five hundred and twelve (33,3%) had a mild, 576 (37,4%) a moderate and 55 (10,1%) a severe hepatitis. Cirrhosis was in 107 (7%) persons. Genotype (G) was available in 1539 subjects: G1 in 631(41%), G4 in 170(11,0%), G2 in 70(4,5%) and G3 in 604(39,2%).
HCV-RNA was >800.000 UI/ml in 763(51%) and < 800.000 IU/l in 733(49%) subjects.
Subjects with G1-4 had higher HCV-RNA level than patients with G 2-3 (56,6% vs 43,4% p <0,0001)
Mean cholesterol level was 161 mg/dl(+41), higher in G1-4 (168 mg/dl+37) than in G2-3 (153 mg/dl +43) p<0,0001. There non difference of cholesterol serum level and HCV-RNA at baseline.
Mean triglycerides level at baseline was 150 mg/dl(+112), higher in G1-4 (163 mg/dl+126) than in G2-3 (133 mg/dl +85) (p<0,0001) and higher in subjects with HCV-RNA >800.000UI/ml (157mg/dl +127 mg/dl) than in subjects with HCV-RNA <800.000 UI/ml (142 mg/dl +83)(p0,01).
Conclusion: Based on the results of this large cohort study, HCV viremia appears to be associated with genotype and triglyceride level which implies that HCV itself might play a significant role on serum lipid profile in patients with HIV/HCV co-infection and could in part explain the role of metabolic parameters on virological outcome of PegIFN/RBV even in HIV/HCV co-infected persons.

CO 63

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Raltegravir and enfuvirtide as a "bridge" antiretroviral therapy in kidney-transplanted patients with HIV infection receiving everolimus and low-dose cyclosporine: a case-control study

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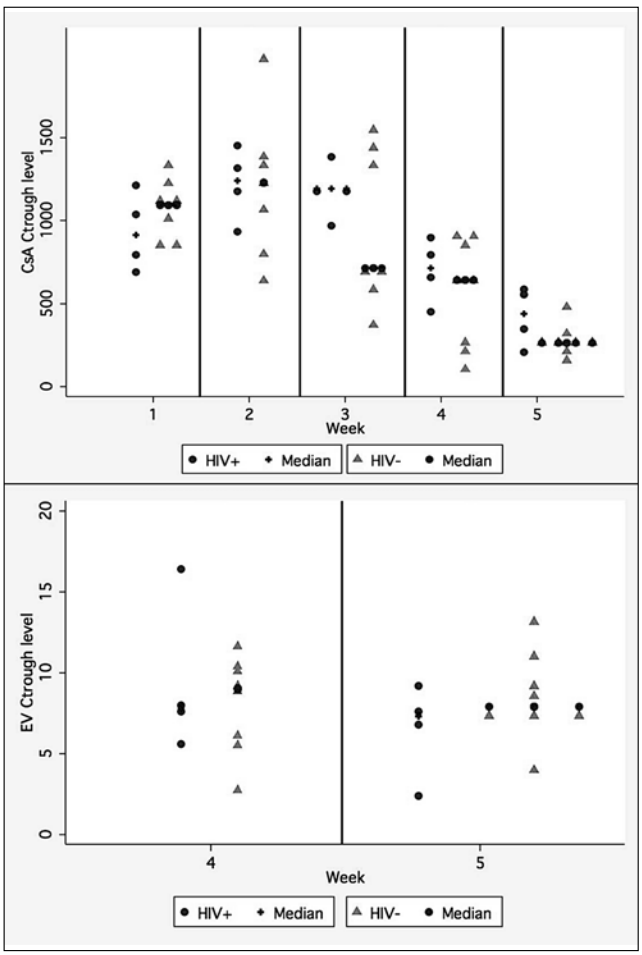
Background: Pharmacokinetic interactions between antiretrovirals and immunosuppressants are critical elements in the management of HIV-infected patients who undergo kidney transplantation (KTx) thus most transplant centres discontinue antiretrovirals until IS steady state is reached. The objective of the study was to assess the impact of an antiretroviral regimen based on enfuvirtide + raltegravir + NRTI on everolimus and cyclosporin pharmacokinetics in the early post-KTx period.
Methods: Pilot prospective case-control study in HIV-infected and uninfected patients undergoing KTx followed-up for 5 weeks (early post-operative period). All subjects were treated with basiliximab at induction. Cyclosporin 2h post-dose (C2) and everolimus Ctrough (EV0) levels were assessed at each week. Cyclosporin was introduced at 2-2.5 mg/kg every 12h when creatinine reached <2.5 mg/mL (C2: 1000 ng/mL), then it was halved and combined with everolimus from 21st post-operative day, with a rapid steroid tapering (C2: 400-500 and



EV0: 6-8 ng/mL). Micofenolic acid was used in HIV-negative patients only before everolimus introduction. Both groups were offered the same dosage of immunosuppressants up to reaching IS steady levels. Enfuvirtide + raltegravir + NRTI were introduced on 1st post-operative day.
Results: From March 2006 to March 2009, 4 HIV-infected subjects (2 men) and 8 HIV-negative controls (5 men) underwent KTx. Mann-Whitney test did not reveal differences in median plasma values of immunosuppressants between groups at each week. Once achieved IS steady state, the "bridge" antiretroviral therapy was modified: enfuvirtide was replaced with unboosted atazanavir (lamivudine + raltegravir + atazanavir), unboosted fosamprenavir (lamivudine + raltegravir + fosamprenavir) or raltegravir (lamivudine + abacavir + raltegravir). At week 5, immunosuppressants plasma levels were stable within their therapeutic ranges with a median creatinine of 1.3 mg/dL for cases and 1.2 for controls. Figures 1a and 1b describe, respectively, C2 and EV0 plasma levels between the two groups during the initial post-operative period.
Conclusions: This is the first report of association between antiretrovirals and everolimus. In our series raltegravir and enfuvirtide did not alter appreciably immunosuppressants plasma levels compared to controls, confirming the low potential for pharmacokinetic interactions and everolimus was safe and effective. In both groups there were no episodes of rejection or HIV virological failure.

CO 64

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High prevalence of HPV infection in genital and oral sites in HIV-infected patients: predictors of oncogenic genotypes and abnormal genital cytology

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Objectives: We aimed to assess the prevalence of HPV infection at different mucosal sites (oral, cervical/anal) and the prevalence and predictors of High Risk (HR)-HPV and Squamous Intraepitelial Lesions (SIL) in a cohort of HIV infected subjects.
Methods: We enrolled 139 HIV pos patients of both sexes. All patients underwent oral and anorectal (male) or cervical (female) swabs. Each specimen was analyzed for cytologic abnormalities (Bethesda System 2001: Low and High Grade SIL, LSIL-HSIL) and for HPV detection and genotyping by PCR. Demographic, clinical, immunovirological and therapeutic characteristics were recorded. CD8+CD38+ T cells were analyzed by flow cytometry. Logistic regression was used to explore possible risk factors for dysplasia and for HR oncogenic HPV genotypes.
Results: The median age of the enrolled subjects was 43 years (IQR: 38-48); 96 (69%) were males, 74 (77%) were MSM. 115 (82%) were on ART, 116 (83.5%) had HIV-RNA <40 cp/ml. Median CD4+ T cell counts were 510 cells/μL (IQR 364-667), median CD4+ at nadir were 260 cells/μL (IQR 150-360).
92 (66.5%) were HPV pos at only one mucosal site, 27 (19.5%) were HPV pos at both genital and oral sites. The prevalence of HPV infection at any site was higher in men (p=.002), in MSM (p=.001) and in patients with a positive history for MTS (p=.018). 51 patients (42.5%) displayed infection with >1 HPV genotype. In addition, HPV pos patients displayed higher CD8+CD38+ compared to HPV neg subjects (median cells/mmc 42.9 vs 20.6, p=.001).
HR-HPV were present in 91/119 (76.5%) and LR-HPV in 28/119 (23.5%). The most frequent HR genotypes were HPV-16, HPV-18, HPV-33 and HPV-58. The presence of HR-HPV was independently associated to multiple genotypes (AOR 8.4, 95%CI 2.20-31.74, p=.002) and to higher CD8+CD38+ cells/μL, compared to LR-HPV (AOR 1.04 for each cell more, 95%CI 1.001-1.05, p=.043).
The prevalence of SIL was 29.5% (41/139 genital pap smears): 32 LSIL, 9 HSIL. Independent factor associated to dysplasia (LSIL and HSIL) was the spread of HPV in both oral and genital sites (AOR 15.6 compared to HPV neg, 95% CI 1.6-147.9, p=.017), while ongoing ART was a protective factor (AOR 0.31, 95% CI 0.11-0.94, p=.039).
The prevalence of oral HPV infection in our cohort was 21.5% (30/139). 11 patients (8%) showed HR-HPV with HPV-16 being the most frequent. No oral dysplastic lesions were observed.
Conclusion: 86% of subjects displayed HIV-HPV coinfection. Interestingly, almost 20% of patients were positive at both oral and genital sites. HR-HPV genotypes were more frequent than LR-HPV ones and appear to be associated with an immunological pro-activated pattern and multiple HPV genotypes. While no dysplasia was found at oral site, almost 30% of patients showed abnormal genital cytology, being ART protective of SIL. These data support the need to screen and follow up all HIV pos subjects for HPV infection at different mucosal sites.

CO 65

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HIV-1 and HPV: high risk of cervical cancer

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Background: HIV infected people have elevated HPV-cancer risk including oro-faringeal, vulvar-vaginal and penile cancers. Particularly, HIV infected women have more likely abnormal cervical cytology and oncogenic HPV infection. Moreover, with increasing access to HAART, HIV infected women may now live long enough for a persistence and a progression to cervical cancer of high risk HPV infections. This prospective analysis collects data from our cohort of HIV+ women to assess the HPV oncogenic expression and cervical cytology according to CD4+ count and HIV-1 viral load. The our aim was to determine the effect of HIV infection on the incidence of oncogenic HPV (mainly 16, 18, 31, 33 and 45) in HIV+ women.
Methods: Between January 2006 and December 2009 we have analyzed 153 cervical samples form 153 HIV-1 positive women. CD4+, HIV-1 viral load, ethnicity, sex, antiretroviral therapy, MRSA and hepatitis viruses co-infection was also recorded. To all of them a cytological diagnosis was performed. HPV-DNA status was assessed using the Hybrid Capture II to value oncogenic subtypes. Median age was 36 (range 22-55). The HIV-1 infected women recruited in this study were 50% Africans, 40% Italians, 7% East Europeans and 3% sud-Americans. Results: Of 153 vaginal specimens from HIV-1 positive women tested for HPV-DNA, 90 (60%) (p=0,003) were positive. 73/90 resulted positive for high risk oncogenic HPV subtypes and only 17/90 were screened for low risk oncogenic subtypes (p<0,001). Among women with high risk oncogenic, 48/73 women (65,7%) (p<0.001) presented CD4+ <200 x 10.6/L. The most of these 48 women were African sex-workers. Among 73 women with high risk oncogenic, 27/73 had a high HIV-1 RNA (>90.000 cp/mL), 46/73 had a viral load < 90.000 cp/mL (28/73 had an undetectable viral load) (p<0,01). 2 patients had HBV-coinfection, 2 syphilis and 13 HCV hepatitis. Cytological abnormalities were present in 87/153 (13 H-Sil, 72 L-Sil, 2 CIN 1); these were significantly linked to the presence of HPV (p<0.05).
Conclusions: Oncogenic HPV infection was prevalent in our cohort. There was a significant association with CD4+ count <200 x 106/L and

presence of HPV highly oncogenic subtypes, but there was no significant correlation with HIV-1 RNA levels. HPV infection was associated with cytological abnormalities. These data suggest that immunodeficiency, in HIV positive women, independently increases HPV oncogenic risk. Detection of precancerous lesions and early stage of cancer lead to effective treatment that can reduce morbidity and mortality from cervical cancer.

CO 66

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Haemostatic markers and cardiovascular risk in HIV naïve patients

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Background: Large studies suggest that cardiovascular disease among HIV-infected patients is associated with traditional risk factors such as smoking, hypertension, dyslipidemia as well as specific metabolic abnormalities linked to antiretroviral therapy, including diabetes. The objective of this pilot study was to evaluate the haemostatic parameters of cardiovascular risk in naïve HIV patients.
Methods: 18 HIV+ subjects naïve for antiretroviral drugs were enrolled in this study. Markers of endothelial damage and hypercoagulability were evaluated. These included prothrombin activation fragment F1+2 (F1+2), plasma levels of thrombin-antithrombin complex (TAT), D-Dimer (DD), plasminogen activator inhibitor (PAI), tissue-type plasminogen activator (t-PA), homocyssteine, and von Willebrand factor (vWF).
Results: The mean age of the study population was 41.5 years, 94% were male, 25% were smokers, 18% had hypertension, 12% had reduced carbohydrate tolerance. Mean CD4 cell count was 485/mmc and mean plasma HIV-RNA load was 125.506 copies/ml. The average time of known HIV status was 3 years. The Framingham cardiac risk score was not applicable in three patients because of age less than 30 years. In the other 15 patients mean CHD risk was 6%. None presented personal or family history of CHD. As regarding markers of endothelial damage and hypercoagulability, vWF resulted to be elevated in 44.4%, PAI in 33.3%, t-PA in 11.1% and TAT in 22.2% of the patients.
Conclusions: Our data underline the presence of a hypercoagulability state in a high percentage of naïve HIV+ patients which may represent an adjunctive risk for cardiovascular diseases. In patients at high risk, cardiovascular prophylaxis could be indicated.

CLINICAL SCIENCES: EFFICACY AND LONG TERM TOXICITY

PO 01

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Relationship between carotid arteria intima-media thickness, plasma osteoprotegerin/RANKL levels in HIV infected patients exposed to cART

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Backgroud: HIV-infected patients using c-ART have an increased risk of cardiovascular diseases. These subjects have an higher rates of atherosclerosis and its progression is faster than in HIV-negative individuals. Atherogenesis is characterized by an intense inflammatory process involving immune and vascular cells. Ours hypothesis is that in the progression of atherosclerosis several risk factors play an important role, such as vascular calcification, condition strongly associated with plaque rupture. There is a strong evidence for an implication of RANK-RANKL-OPG system in vascular calcification.
The aim of our study was to evaluate the relationship between the carotid arteria intima-media thickness (C-IMT) and plasma RANKL/OPG levels.
Materials and methods: Study population included 15 HIV+ patients treated to c-ART, exposed to PIs since at least 12 months, and 15 healthy donors, matched to age, gender and other CV risk factors. C-IMT was measured ultrasonically. OPG and RANKL plasma levels were measured by an enzyme-linked-immunosorbent assay.
Results: The overage values of C-IMT was (mean±SE) 0.73±0.02 HIV+ vs 0.6±0.04; p<0.05. The overage values of OPG plasma level was (mean±SE) 7.45±2.37 pmol/l HIV+ vs 4.4±0.9pmol/l. The overage values of RANKL plasma level was (mean±SE): 0.31±0.29 pmol/HIV+ vs 0.26±0.1pmol/l. Regarding OPG, patients with higher c-IMT had lower levels of OPG (p<0.01) There was no significant correlation in RANKL plasma levels and c-IMT. Comparing to controls HIV+ patients had an higher triglicerides levels no significant difference in HDL and LDL cholesterol, thyroid function and PTH etc.
Conclusions: The progression of atherosclerosis is influenzed by metabolic, inflammatory and immunological factors. This study showed that OPG levels are significantly correlated with c-IMT: the mechanism linking RANK/RANKL/OPG axis and vascular diseasesrequire further study to support their role as a biomarker for HIV infected patients at risk of CV.

PO 02

Association between osteopenia/osteoporosis and RANK/RANKL/OPG system in HIV-infected patients

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Background: Reduced bone mineral density (BMD) has been observed during HIV infection. Both HIV itself and cART contribute to determine osteopenia/osteoporosis: bone remodelling is regulated by many factors, especially osteoprotegerin (OPG)/ receptor activator of NF-κb-ligand (RANKL)/ RANK system. The aim of our study is to determine the role of OPG/RANKL/RANK system in naive and cART-treated patients and to evaluate immune/virological and clinical factors associated with reduced BMD.
Patients and methods: We investigated 73 HIV-1 infected patients: 41 protease inhibitor (PI)-treated patients (lopinavir/r, LPV and atazanavir/r, ATZ >48 weeks) and 32 naïve patients. BMD was measured by bone densitometry. Blood samples were collected to determine CD4+ (nadir and at the time of investigation), HIV-RNA (zenith and at the time of investigation), calcium, phosphate, vitamin D, bone alkaline phosphatase, cholesterol (LDL, HDL), triglycerides, etc. RANKL and OPG plasma concentrations of all patients was determined by ELISA kit. Atazanavir and lopinavir concentrations (Ctrough) were measured by HPLC.
Results: We found an increase of OPG in all 73 HIV+ patients, although OPG plasma concentration in naive patients was lower than in treated patients. In particular, there was a negative correlation between OPG and nadir CD4 (p<0.05), whereas positive correlation with HIV-RNA plasma level (p<0.05) was found. RANKL plasma concentration was found to be higher in naïve HIV+ than in cART-treated patients. Concerning patients on cART, a negative correlation was found between OPG, Ctrough of ATZ and LPV, and reduced BMD.
Conclusion: Bone remodelling is regulated by RANK/RANKL/OPG system. OPG plasma concentration were increased in treated and naive HIV + patients. The alteration of RANK/RANKL/OPG system is implicated in osteopenia/osteoporosis and could be used as a predictive parameter for bone disease.

PO 03

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Cardiovascular risk determinants in HIV-1 infected patients eligible for antiretroviral treatment simplification studies: preliminary results

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Objectives: We aimed to show the baseline characteristics of cardiovascular parameters (Intima Media Thickness-IMT, Flow Mediated Dilatation-FMD, serum lipid concentrations) in HIV-1 infected patients with undetectable viral load enrolled in two treatment simplification trials and to analyse the potential predictors of pre-defined alterations of the vascular parameters.
Methods: We enrolled patients eligible for treatment simplification in our Clinic with HIV RNA<50 cp/ml at least from 3 months, CD4>200 cells/mm3 and with no resistance mutations to any drug of the new regimen. Biochemical and immunovirological parameters were evaluated at the time of therapeutic switch (baseline) as well as the IMT and FMD via an ecodoppler of the carotid and brachial artery. Data regarding clinical history, exposure to antiretroviral drugs and concomitant medications were also collected from clinical records.
Results: 86 patients were evaluated; 67.5% were male, 40.7% heterosexual. At baseline, 21.8% were stage C CDC, median age was 45.8 years, median (IQR) CD4 cell count was median (IQR) 611 (456-780) c/μL, HIVRNA was <50 c/mL per protocol; median (IQR) baseline glucose values were 87.5 (79.8-97.3) mg/dL, baseline lipid values were respectively 194 (171-220) mg/dL for TC, 44 (38-55) mg/dL for HDLc, 113 (97-137) mg/dL for LDLc, 130 (101-219) mg/dL for TG.
At baseline, 5/84 (6%) of patients had a previous diagnosis of diabetes, 18/84 (21.4%) of hypertension, 5/84 of an ischemic heart disease, 3/84 (3.6%) of a cerebrovascular disease, 7/84 (8.3%) of either a cardio- or a cerebrovascular disease (CVD), 10/84 (11.9%) were treated with a statin, 9/84 (10.7%) with other lipid lowering agents and 7/84 (3.8%) with ASA.
Median (IQR) IMT was 0.7 (0.6-0.8) mm; 10/65 (15.4)% had IMT>0.9 mm but none had IMT>1.2 mm; median brachial artery's diameter was 4.3 (3.9-4.8) mm, median post-dilatation diameter at the same level 4.8 (4.3-5.4) mm for a median FMD of 10 (7-16.7)%.

At univariate linear regression analysis, an increased risk of presenting a lower FMD was observed for an older age (per higher quartile B -3.76, 95% CI -6.87, -0.64, P=0.019) and for a longer exposure to HAART (per year longer B -0.07; 95% CI -0.13, -0.02, P=0.006). Neither the prior or current exposure to abacavir, the nadir CD4, time from HIV diagnosis, nor any other traditional risk factor was related to FMD. At multivariable analysis, after adjusting for age, gender and time from HIV diagnosis, duration of HAART exposure (B-0.07, 95% CI -0.13, -0.01, P=0.015) was independently associated with lower FMD. No parameter was associated with IMT>0.9 mm.
Conclusions: In this preliminary analysis of a selected group of patients with controlled viral replication, IMT was consistent with preatherosclerotic lesions in 15%of cases. The FMD was inversely associated with longer exposure to HAART, independently from traditional and HIV-related risk factors.

PO 04

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HIV+ pregnant women reported similar adherence level but better virological parameters and mental health measures compared to non pregnant women

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Objective: To evaluate adherence level, self-reported symptoms and virological and immunological outcomes in HIV+ pregnant women.
Methods: Prospective, cohort (Ad-UCSC), monocenter study. A short questionnaire on adherence (0 to 100 scale, SelfAdher), satisfaction with therapy, belief in antiretrovirals efficacy, Physical and Mental Health, and self-reported symptoms was administered to any outpatient taking cART at the Infectious Diseases Department, Catholic University, Rome, Italy. Patients are required to fill the questionnaire at any clinic visit. Self-reported adherence was estimated on a 0-100 scale. A Symptom Score was built summing self-reported scores (from 0 –at all -to 4 – very much-) for each of 19 listed symptoms. Possible scores ranged from 0 to 76. Regimen was defined according to drug classes and number of daily doses. Virologic failure was defined if, at the moment of the survey, HIV RNA was >50 c/ml. CD4 cell count and other epidemiological and clinical characteristics were also collected. Data of HIV+ pregnant women were compared to data of HIV+ women with less than 47 years.
Results: At December 2009, 903 patients filled the questionnaire. Of these 187 females were included in the study, mean age 42 yrs (SD 7.2), IDU 14.4%, HCV+ 22.6%, median log HIV RNA 1.7 c/ml (IQR 1.7-1.7), 15.4% had HIV RNA>50 c/ml, median CD4 598/mm3 (IQR 446-761), 2.2% had CD4 <200/mm3. 62% were taking PI and 26.4% NNRTI. Mean SelfAdher was 75.9 (SD 21.1). 21.7% of HIV+ women reported an adherence <60 and 31.3% reported having discontinued drugs at least once in the previous 2 month for more than 24 hours. Mean of Physical Health was 72.3 (SD 17.7) and of Mental Health was 72.7 (SD 21.3) The questionnaire was filled by 15 HIV+ pregnant women. 11 patients were in the third trimester of pregnancy and 4 in the first trimester. When compared to HIV+ non-pregnant women, pregnant women were younger (35.3+6.6 versus 42.8+7.0 in non-pregnant women; p<0.001), less frequently HCV+ (p=0.02), and reported better Mental Health (82.3+15.4 versus 71.8+21.5 in non-pregnant women; p=0.02). Mean of CD4 cell count did not differ between pregnant and non pregnant women. No pregnant women had detectable HIV RNA. Similar self-reported adherence, rate of self-discontinuations, rate of errors in timing of therapy, rate of women reporting finishing the drugs before the next visit, satisfaction with therapy, belief in therapy, Physical Health score and symptom score were reported between HIV+ pregnant and non-pregnant women.
Looking at symptoms, pregnant women reporting statistically significant lower grade of headache, abdominal bloating, anxiety, depression, lipoaccumule and lipoatrophy.
Conclusions: Pregnant women reported adherence level that did not differ with those of non-pregnant women. However, pregnant women had better virological outcomes and better Mental Health score.

PO 05

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Bone density and renal function and their predictors in a cohort of HIV infected patients eligible for a simplification regimen

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Objectives: To show baseline characteristics of bone density and renal function in a cohort of patients eligible for a simplification regimen and to analyze if renal function is involved in predicting osteopenia.
Methods: We enrolled patients eligible for treatment simplification in our Clinic with HIV RNA<50 cp/ml at least from 3 months and CD4>200 cells/mm3. The baseline evaluation was done for: biochemical and immunovirological parameters, bone density by DEXA and renal function with 24 hours urinalysis. Data regarding major clinical events and antiretroviral drug exposure were also collected from clinical records.
Results: 86 patients were enrolled; 67.5% were male, 40.7% heterosexual. At baseline, 21.8% were stage C CDC, median age was 45.8 years, median (IQR) CD4 cell count was 611 (456-780) c/μL, HIVRNA was <50 c/mL per protocol; mean months of NRTI experienced (+SD) was 77.4 (+54.75), in particular TDF was 31.5 (+26.6), NNRTI was 21.83 (+32.17), PI was 18.29 (+27.22). 12/37 (32.4%) had proteinuria>0.15 g/L, 4/78 (5.1%) had creatinine>1.3 mg/dl, 1/38 (2.6%) had calciuria>300mg/L, 9/38 (23.7%) had phosphaturia> 870 mg/L. MDRD was >89 ml/min in 9.2%, between 89 and 60 ml/min in 73.8%, between 30 and 59 ml/min in 16.9% of patients. At DEXA, 29/76 (38.2%) had lumbar T score <-1 >-2.5 (osteopenia) and 17/76 (22.4%) <-2.5 (osteoporosis), 19/76 (25.2%) had lumbar Z score <-1 >-2 (osteopenia) and 15/76 (19.7%) < 2 (osteoporosis), 25/76 (32.9%) had femoral T score indicating osteopenia and 2/76 (2.6%) osteoporosis and 13/76 (17.1%) femoral Z score as for osteopenia and 4/76 (5.3%) for osteoporosis. At linear regression univariate analysis, a femoral T score as for osteopenia or osteoporosis was predicted by baseline calcitonin>10 pg/ml (P=0.018), proteinuria> 0.15 g/L (, P=0.004). At multivariate analysis, proteinuria> 0.15 g/L (P=0.002) and CDC stage C (P=0.007) were independently predictive. Similar results were obtained for femoral Z-score defined osteopenia/osteoporosis. Univariate analysis for predictors to lower MDRD showed male sex (p=0.07), age per year higher (p<0.001), calciuria (p=0.019), phosphaturia (p=0.010), osteopenia (lumbar Z-score) (p=0.06), osteopenia (femoral T-score) (p=0.045) and prior cerebrovascular events (p=0.039). At multivariable analysis age and osteopenia (lumbar Z score) predicted lower MDRD and calciuria showed a trend towards significance (p=0.06). Exposure to boosted PIs significantly predicted proteinuria> 0.15 g/L at univariate (1.04, 1.004-1.07, P=0.025) but not at multivariate analysis.
Conclusions: In our cohort, lower bone density was predicted by proteinuria and a lower MDRD was predicted by age and osteopenia. These findings underline the importance of bone and renal assessment in HIV infected patients, particularly in the elderly ones.

PO 06

Infection 2010; 38 (Suppl. I): 46

Cardiovascular risk assessment in HIV patients on HAART: the role of Framingham risk score and ultrasound analysis

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Background: HIV patients on HAART represent a particular category exposed to cardiovascular risk because of the complex pathogenesis based on inflammation, metabolic abnormalities and traditional risk factors. Early identification of individuals at high cardiovascular risk is an important issue in clinical management: ultrasound examination is a simple and reproducible method to evaluate early carotid atherosclerosis even if bias selection due to inter-reader variability may occur. Framingham risk score (FRS) has not been validated in HIV patients; furthermore literature has not an unanimous opinion on its utility due to a possible underestimation of cardiovascular risk.
Objectives: the objective of this study was to evaluate the prevalence of pathological intima-media thickness (IMT) and to identify factors associated to this finding in a cohort of experienced patients attending our outpatient clinic for metabolic toxicities.
Methods: data about cardiovascular risk factors (smoking, familiarity for cardiovascular disease, diabetes, antihypertensive drugs), physical examination (body weight, height, waist circumference, systolic and diastolic blood pressure) and biochemical analysis (lipid profile, apoA, apoB, 25 OH vit.D, PCR, creatinine) were collected. For every patients we calculate the estimated risk for coronary heart disease (CHD) according to Framingham's algorithm. Metabolic Syndrome (MS) was defined according to ATPIII criteria and creatinine clearance was calculated with the EPI-formula. Patients underwent color Doppler ultrasonography: the presence of plaques and/or an intima-media thickness ≥ 1 mm were considered pathological.
Results: 180 patients were included, 58.9% were male, mean age was 47.8 years. 77 patients were on PI-based therapy while 27 had abacavir on their regimen. 15 patients were at high risk for CHD, 36 were at medium risk and 86 were at low risk. 38 patients (21%) had pathological IMT: males were 71%, median FRS was 13.2 % (range 7.1-23.0). MS was detected in 43.3% of these patients. Pathological IMT and Framingham risk categories were significantly associated (Mantel-Haenszel p=0.0001). FRS was significantly correlated with waist circumference (r= 0.36), BMI (r=0.25) and Waist Hip Ratio (r=0.46). FRS and age were identified as associated factors with pathological IMT in the multivariate analysis while nor the presence of MS, BMI or high PCR values reached statistical significance. HAART regimens containing ABC or any PI were not significantly associated with a pathological IMT.
Discussion: the main finding of our study is the close relationship between FRS estimation model and pathological IMT. FRS is a better predictor of subclinical atheromatous lesions than MS or biochemical markers. Several data reported on literature stressed the importance of classical risk factors in HIV patients and maybe this is why this algorithm is still useful to stratify risk in our patients.

PO 07

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Reasons to switch highly active antiretroviral therapy

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Objectives: The aim of the study was to determine in an Italian cohort the incidence of treatment switches and their causes to modify the highly active antiretroviral therapy (HAART).
Methods: We included in the study the outpatient population on antiretroviral therapy of the 1° Division of Infectious Diseases in a two years (2008-2009) follow up period.
The endpoints were substitution or discontinuation of at least one HAART component of the regimen for any reason, poor adherence, simplification, intolerance/toxicity and immunovirological failure. When a patient discontinues a drug in the antiretroviral regimen, regardless of whether or not he switches to another regimen, clinicians were asked to report the reason for interruption. The clinician was asked to choose only one of these reasons for each stopped drug. Descriptive analysis was performed.
Results: A total of 897 patients were included in the study: 28.5% were female, 44% were HCV coinfected; their median age was 44 years. The main causes of switching (see Table) were the simplification to improve adherence (140 out of 897 patients; 16%) and toxicity (101 out of 897 patients; 11%); the virological failure occurred in only 6 patients.
In 211 patients (23.5%) the NRTI-backbone was changed, in general, within-class substitutions use a newer agent and coformulated drugs or to prevent/interrupt toxicity.
Switches with PIs or NNRTI (65; 7%) were done only in patients without resistant virus and to reduce dosing frequency, pill count, drug-drug interactions, or metabolic and gastrointestinal/hepatic complications.

Table 1:

PREVENTION Variables and N°/year	**2008 N° 60**	**2009 N° 119**	**Total N° 179 (100%)**
simplification/adherence	52	88	140 (78%)
risk for cardiovascular disease	4	18	22 (12%)
risk for toxicity	3	11	14 (8%)
pregnancy	1	2	3 (2%)
COMPLICATION	N° 47	N° 54	N°101 (100%)
metabolic	15	20	35 (34%)
haematologic	6	14	20 (20%)
renal	6	12	18 (18%)
gastrointestinal	12	2	14 (14%)
hepatic	1	6	7 (7%)
hypersensitivity	7	0	7 (7%)
VIROLOGICAL FAILURE	N°4	N°2	N° 6

Conclusions: It seems important to evaluate reason-specific trends in the incidence of discontinuation in order to better understand the determinants of changes over time. The incidence of discontinuation for intolerance/toxicity is not declined over time while simplification strategies have become more frequent in recent years.

PO 08

Infection 2010; 38 (Suppl. I): 47

Adherence level and NNRTI regimens are independentely correlated with immunological response

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Objective: To evaluate variables correlated to CD4 cell count in a cohort of HIV-infected people taking cART
Methods: Prospective, cohort (Ad-UCSC), monocenter study. A short questionnaire on adherence to antiretrovirals was longitudinally administered to any outpatient taking cART at Catholic University, Rome, Italy. Self-reported adherence, was estimated on a 0-100 scale. A Symptom Score was built summing self-reported scores (from 0 –at all -to 4 – very much-) for each of 19 listed symptoms. Possible scores ranged from 0 to 76. Regimen was defined according to drug classes. CD4 cell count was the outcome of the study. Epidemiological and clinical characteristics were also collected.
Results: At December 2009, 903 patients filled the questionnaire. 32.5% females, mean age 47 yrs (SD 8.5), IDU 20%, HCV+ 25%, median log HIV RNA 1.7 c/ml (IQR 1.7-1.7), 13.3% had HIV RNA>50 c/ml, median CD4 563/mm3 (IQR 405-745), 4% had CD4 <200/mm3. 504 (57%) were taking PI and 269 (29.7%) NNRTI. Mean SelfAdher was 80 (SD 18). 15.6% of people reported an adherence <60 and 23.2% of people reported having discontinued drugs at least once in the previous 2 month for more than 24 hours.
At univariate analysis, gender, age, HCV+, log HIV RNA, regimen class, self-reported adherence, self-discontinuation of drugs, and symptom score were correlated to CD4 cell count. At multivariate analysis using a linear regression model, age (B -3.7; 95% CI -6.2; -1.3; p=0.03), log HIV RNA (B -49.2; 95% CI -93.8; -4.7; p=0.03), taking NNRTI compared to PI (B 79.6; 95% CI 34.9; 124.4; p=0.001), self-reported adherence (B 1.9; 95% CI 0.71; 3.1; p=0.002), and symptom score (B 3.20; 95% CI 1.0; 5.4; p=0.004) were independently correlated to symptom score.
Conclusions: Self-reported adherence level and taking NNRTI were correlated to CD4 cell count. Even though the results should be confirmed in longitudinal analyses, adherence to antiretrovirals was confirmed as a crucial factor for the efficacy of regimens.

PO 09

Infection 2010; 38 (Suppl. I): 47

Accelerated coronary aterosclerosis in patient with HIV/HCV co-infection

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Introduction: HIV-infected patients are at a significantly higher risk from coronary heart diseases compared to non-infected individuals. Several studies have assessed HIV/HAART-associated ischemic cardiovascular disease risks. Anyway rapidity of progression of atherosclerosis is linked principally to inflammation and immune activation in HIV-infected patients.
Case report: We describe the case of a 45-year-old woman with HIV/HCV co-infection and accelerated progression of coronary atherosclerosis after execution of percutaneous coronary intervention (PCI). The patient was an ex drug abuser and was affected by irritable bowel syndrome. From 2005 her HAART regimen consisted of Abacavir+Lamivudine+Lopinavir/r with a persistent undetectable HIV-RNA and a good recover of CD4+ (647 cells/mmc). The risk of presenting a fatal cardiovascular event according to the "score system" was 0.2%, almost similar to the expected risk for the general population. Blood tests reviled only hypertriglyceridemia (190 g/dl) HCV-RNA 1200000 cp/ml and high C-reactive protein (hs-CPR). In November 2008, due to intense fatigue and atypical chest pain, the patient underwent blood tests and clinical examination: A coronary CT Scan reviled severe stenosis (73%) of the medium third of the circumflex artery due to a concentric atheromatous plaque of mixed density but no significant alterations were found on other tract of other coronary vassals. This clinical situation was confirmed by a coronarographic exam that gave indications for the execution of PCI with coronary by-pass positioning. In February 2009 the patient was admitted in hospital to undergo PCI, which was partially successful but didn't yield cause any complications. Following cardiologic evaluation, the patient was started on antiagregants (ASA), beta-blockers and nitrates. At 6 months follow-up, no significant abnormalities were found on ECG and during myocardiospecific enzyme monitoring and triglyceride values remained at borderline. In August 2009, the patient complained of symptoms which were suggestive of exertion angina; coronary CT Scan reviled an unexpected presence of new lesions that were not present 9 months before. There were a right dominant coronary artery with a long concentric atheromatous plaque of soft density that determined a lumen stenosis of 75%. The first branch of the obtuse margin had a mixed density plaque that determined a lumen stenosis of 50%.
Conclusion: Based on the above findings, it is possible to suppose that inflammation and immune-activation can depend by a concourse of factors (i.e. chronic C-hepatitis, irritable bowel syndrome, PCI execution) not directly associated with HIV infection. A faster progression of coronary atherosclerosis is possible also in patients with suppressed HIV-RNA, high CD4+ cell count and under an effective antiretroviral therapy. A strictly monitoring of coronary atherosclerosis is required in management of HIV/HCV co-infected patients.

PO 10

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HIV infection in the elderly: a multicentre study

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Introduction: HIV infected population in industrialized countries is ageing as a result of both prolonged survival in patients treated with HAART and late diagnosis in patients > 50 years of age. Aging individuals experience HIV infection as a complex chronic disease , often with multiple co-morbidities and with an accelerated course of several age-related conditions. Older patients have better virological response than younger, but the natural decline of immune-function with age could blunt their CD4 reconstitution . Medication toxicity further complicates HIV management in older adults.
We sought to determine the characteristics of HIV infection in older individuals, including co-morbidities, virological response, immunologic restoration and tolerability to HAART.
Patients And Methods: A retrospective multicentre study (1 Jan 2000-31 Dec 2008) was performed including patients from Infectious Disease Clinics of Perugia, Brescia, Rome, and Foggia. All medical records of newly diagnosed HIV infected outpatients >50 years, were reviewed. Demographic data, route of infection, CDC stage, CD4 cell count, HIV-RNA copies/mm3 , laboratory abnormalities at the time of HIV infection diagnosis, co-morbid conditions, HAART regimen class and tolerability of therapy, were recorded. When available, data on CD4 cell count and HIV-1 viral load from 3 months to 84 months

after beginning of treatment, side effects, and treatment modifications were collected as well.
Results: We identified 300 patients (83.1% males, 93.8% born in Italy); heterosexual intercourse was the more frequent risk factor (54,7%), but 25% of patients did not declare any risk factor.
Median CD4 cell count was 214/mm3. At diagnosis 77.4 % of subjects were symptomatic.
These patients suffered significant co-morbidities (hypertension 56%, diabetes 18%), and blood count abnormalities were found in 54,3% of patients at baseline.
After a median interval of 8 months from diagnosis, 81.7% of patients started HAART.
After 12 months of HAART, 80% of patients had a virological response (< 50 cp/mL) and 57,3% of patients had a CD4 cell count increase of 100 cell/mmc. After 5 years of therapy only 34% of patients had a CD4 cell count > 500 cell/mmc. The immunological restoration was worse in patients with advanced disease (CD4 < 200 cell/mmc) at baseline.
Old patients had a high number of side effects (20% during the first year of therapy) and changed treatment because of toxicity (24% during the first year of therapy) .
Conclusion: Our study demonstrates good virological response, a slow but continuous immunological recovery even in the long term period in HIV infected patients older than 50 years.
The main problem was treatment tolerability, which caused frequent side effects and early switch of antiretroviral therapy .
Clinical trials involving old patients are needed to increase our understanding on the correlation between HIV infection and aging and to develop specifically targeted tr.

PO 11

Infection 2010; 38 (Suppl. I): 48

High prevalence of coronary stenosis detected by Coronary CT angiography in asymptomatic HIV-infected subjects with low cardiovascular risk

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Background: Coronary heart disease (CHD) is a leading cause of mortality and morbidity in HIV+ infected individuals. Both traditional and non traditional risk factors, including HIV exposure, immune activation and antiretroviral therapy appear to contribute to the high rate of major cardiovascular events Elevated levels of surrogate markers of CHD, such as coronary calcium score, have been found in asymptomatic HIV+ individuals, to further explore the extent of CHD in this population, we utilized 64-slice multidetector-row computed tomography (MDCT) to assess the prevalence of coronary stenosis in 55 HIV+ asymptomatic subjects selected for a low cardiovascular risk
Methods: Study population consisted of 55 asymptomatic HIV+ subjects with low cardiovascular risk, defined as: Framingham risk score<10, absence of metabolic syndrome, Body Mass Index < 25, negative resting and exercise electrocardiogram.
The presence and degree of coronary stenosis were assessed in all patients by a 64-slice computed tomography scanner. Stenosis .was graded I to IV (I=30-49%; II=50-69%; III=70-99%; IV=complete occlusion). Selective Coronary Angiography (SCA) was performed in all patients that showed significant (i.e: grade II-IV) coronary stenosis.
High sensitive C-reactive protein (hs-CRP) was measured in all patients before MDCT.
Student's T test , Fisher exact test and Pearson's correlation test were used for statistical analysis
Results: Fifty-five subjects were studied. 82% of them had been on HAART for 8.6+5 years. 73.1% had HIV-RNA<50 copies/ml; mean CD4 cell count was 500+242 cells/µl. Mean values of hs-CRP were 1.38ug/ml (range, 0.001-2,44 ug/ml).
A total of 54,5% of HIV positive patients showed luminal stenoses: 25,4% grade I; 14,5% grade II; 12,7% grade III; 1,81% grade IV. The mean CAC score was 21,2±63,5 and baseline Agatston was>100 in only 10,9% of patients. In presence of significant calcium load 100% of patients had significant CAD. Agatstont's score progressively and significantly increased with patient's age (r=0.538; P=0.001). The number and the extension of the lesions were increasing to the severity of stenosis. When the two groups, with or without significant MDCT abnormalities, were compared, a longer exposure to Protease Inhibitors or Abacavir was observed in the former. However, no direct correlation between the degree of stenosis and time to exposure to antiretroviral drugs was found. SCA revealed 11 significant stenoses in 54 vessels (20.4%) of 8/16 patients. A total of 17 stent was implanted.
Conclusions: In an asymptomatic population of HIV+ subjects carefully selected for a low cardiovascular risk, MDCT revealed an unexpectedly high rate and severity of coronary stenosis, that was not clearly associated to any of the explored variables. Based on these findings, of intensified screening programs for CHD should probably be considered for all HIV+ subjects.

PO 12

Infection 2010; 38 (Suppl. I): 48

Evolution of estimated creatinine clearance by gender and type of HAART in previously naïve patients over 96 week follow-up

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Objective: We aimed at evaluating changes in creatinine clearance in patients prescribed abacavir (ABC) or tenofovir (TDF) with protease inihibitors boosted by ritonavir (PI/r) or non nucleoside reverse transcriptase inhibitors (NNRTI) stratifying by gender.
Methods: Creatinine clearance was estimated by Cockroft-Gault (CrCl_CG) equation. All HIV-patients who initiated TDF or ABC as first line between January 2002 and December 2008 were included. Non Caucasian patients were excluded. Intent-to-treat (ITT) population comprised all patients prescribed TDF or ABC, while, at on-treatment (OT) analysis, patients' data were censored at the time of any drugs discontinuation. Population was stratified by gender and type of HAART. T-test was used to assess CrCl_CG evolution. Covariance analysis assessed predictors (including age, CD4+ and HIV-RNA at baseline, gender and type of HAART).
Results: The overall ITT population comprised 346 males (264 prescribed tenofovir, 76.3%) and 97 females (76 prescribed tenofovir, 78.4%). In this population, significant decreases of CrCl_CG associated with TDF+PI/r were found in both males and females from week 24 with respect to baseline. By contrast, in patients prescribed TDF+NNRTI regimens, only females showed significant decrease at week 96. No significant declines from baseline, in terms of eGFR, were observed in the proportion of subjects treated with abacavir. (Table 1)
An increased renal toxicity for regimens containing TDF+PI/r was confirmed in OT population, constituted by 275 males (210 treated with tenofovir, 76.4%) and 67 females (55 treated with tenofovir, 82%). In particular, variance analysis showed significant decrease of CrCl_CG in patients prescribed TDF+PI/r compared to baseline values, both in males (mean decrease by –15.0 ml/min, p<0.001 at week

Table 1. Evolution of CrCl_CG in patients prescribed TDF (+PI/r or NNRTI) over 96 week follow-up (ITT analysis)

Type of regimen	Gender		Baseline	24 weeks	48 weeks	96 weeks
TDF+PI/r	M	Mean	129.2	114.9	120.9	118.8
		SD	41.2	30.3	29.5	26.2
		N	124	122	91	65
		P		<0.001	<0.001	0.003
	F	Mean	102.5	93.9	89.15	95.29
		SD	33.3	26.3	22	27.3
		N	30	30	24	15
		P		0.015	0.013	<0.001
TDF+NNRTI	M	Mean	120.1	119.7	122.9	120.7
		SD	39	32.3	34.6	33.3
		N	105	105	83	45
		P		0.84	0.049	0.66
	F	Mean	106.4	103.7	102.4	96.3
		SD	24.1	26.8	27.1	22.8
		N	46	45	42	33
		P		0.54	0.09	<0.001

NOTE: Mean and standard deviation (SD) are expressed as ml/min. N: number of patients, P: P-value at T-test for paired data.

24; -15.4 ml/min, p=0.001 at week 48; -18.8 ml/min, p=0.014 at week 96) and females (mean decrease by –9.24 ml/min, p=0.023 at week 24; -13.4 ml/min, p=0.012 at week 48; -13.5 ml/min, p=0.165 at week 96). However this association was not independent from other variables.
To verify the actual impact of TDF during the period of assumption a covariance analysis was applied to OT population. TDF was associated with CrCl_CG decreases compared to baseline (mean decrease by –8.05 ml/min, p=0.028 at week 24; -12.3 ml/min, p=0.005 at week 48; -15.8 ml/min, p=0.016 at week 96), especially if associated to PI/r (-15 ml/min, p<0.001 at week 24; -18 ml/min, p<0.001 at week 48; -19.5 ml/min, p=0.001 at week 96). At the same models, no associations were found for gender, HIV-RNA at baseline and age, while lower CD4+ counts were independently associated with statistically significant CrCl_CG decreases. When the cut-off of 90 ml/min was used to define more clinically significant decrements of CrCl_CG, no statistically significant differences were found within the four arms, both in ITT and OT population.
However more women than men on TDF had CrCl_CG <90 ml/min than those prescribed ABC at weeks 24 and 48 (at week 24: 16.35% men and 46.3% women on TDF vs 12.9% men and 25% women on ABC; at week 48: 15% men and 41.9% women on TDF vs 14.6% men and 22.2% women on ABC).
Conclusions: TDF-based regimens, especially with PI/r, appeared to be associated with statistically significant CrCl_CG decreases in comparison to ABC-regimens. However differences were small and their clinical significance needs to be assessed in larger cohorts of patients and over extended follow-up with a focus on gender. Lower CD4+ counts predicted CrCl_CG decrement, suggesting the need of a more intensive monitoring in patients whose immune status is more severely impaired.
Consistent results of ITT and OT analysis suggest incomplete reversibility of TDF related renal toxicity.

BASIC SCIENCES: VIROLOGY

PO 13

Infection 2010; 38 (Suppl. I): 49

Vebep regimen and highly active antiretroviral therapy (HAART) in patients (PTS) with HD and HIV infection (HD-HIV): final results of the italian cooperative group on aids and tumors (GICAT) study

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Background: The outcome of pts with HD-HIV is still poor, because the duration of complete remission (CR) is short. To improve the prognosis of HD-HIV, a feasibility study with the VEBEP regimen and HAART was started in previously untreated H! D-HIV pts.
Methods: CT included epirubicin 30 mg/m^2/day (days 1-3), cyclophosphamide 1000 mg/m^2 (day 1), vinorelbine 25 mg/m^2 (day 1), bleomycin 10 mg/m^2 (day 3) and prednisone 100 mg/m^2/day (days 1-3).
Results: Since September 2001, 71 pts have been enrolled. The median age was 41 yrs. The median CD4+ cell count was 248/mm^3 and 51% of pts had a detectable HIV viral load. Stage III-IV was present in 50/71 (70%) pts. Histologic subtypes were: MC 70%, NS 20%, LD 4%, LP 2%, unknown 4%. Four toxic deaths were observed (septic shock, PCP, hepatic failure and pneumonia during neutropenia). An absolute neutrophil count <500 was noted in 60% of pts. Grade 3-4 anemia was observed in 38% of pts and severe thrombocytopenia in 22% of pts. Twenty-two per cent of pts had febrile neutropenia with 19 documented infections in 16 pts (4 varicella, 4 bacterial pneumonia, 3 bacterial sepsis, 2 PCP, 1 cerebral toxoplasmosis, 1 esophageal candidiasis, 1 HBV reactivation, 1 HCV reactivation, 1 prostatitis, 1 salmonellosis). CR was obtained in 47/71 pts (66%) and PR in 9/71 pts (13%). With a median follow up of 22 months, only 4 pts have relapsed. OS and TTF at 24 months are 69% and 59%, respec! tively.
Conclusions: Our preliminary data demonstrate that VEBEP regimen in combination with HAART is feasible and active in pts with HD-HIV. This study was supported by ISS grants.

PO 14

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GP41 protective Epitopes in the αlpha-helix of "Neisseria Meningitidis Adhesin (NADA)" as new vaccine against HIV infection

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Background and objectives: the aim of project focuses on the use a novel carrier vectors (NadA) and suitable adjuvant formulations, which have already been shown able to maintain native conformation of inserted epitopes and consequently, to elicit a proper neutralizing immune response.
The most promising scenarios in HIV vaccinology deal with the generation of novel immunogen systems capable of preserving native alpha-helical conformation and/or trimeric nature of immunodominant neutralizable epitopes, likely to circumvent immune tolerance and to elicit broad, polyspecific responses to the virus.
Methods: we used a plasmidic vector based on the bacterial protein NadA from N. meningitides. Due to its trimeric, alpha-helical conformation, recombinant NadA is able to host and present epitopes in native conformation. We cloned into NadA vector three different

HIV-1-gp41 epitopes: QARILAV epitope within the α-helix region HR1, found in a ESN cohort; 2F5 and 4E10 within MPER. These chimeric proteins were generated in the pET system and expressed on the surface of E. coli BL21 (DE3) strain as trimers. These studies were supported by a molecular dynamics analysis.
Results and Discussion: because QARILAV, 2F5 and 4E10 epitopes are naturally exposed in the α-helix region HR1 and HR2 of HIV-1-gp41, we inserted corresponding peptides into the NadA α-helix region.
We evaluated the maintenance of α-helix structure of such epitopes by molecular dynamics studies which supported our results.
We hypothize that alpha-helical conformation could prove helpful in enhancing QARILAV, 2F5 and 4E10 immunogenicity. The whole gp41-HR1 domain was also tested, in order to assess whether its long aminoacidic string is more likely to assume the alpha-helical conformation.
preliminary data showed that studies of molecular dynamics are relevant to present the epitopes of gp41 in the best possible way to immune system.
These findings suggest the importance of alpha-helical conformation in increasing immunogenicity. To further address this issue, we will test different immunization schedule and formulations in mice.

PO 15

Infection 2010; 38 (Suppl. I): 50

Ultra-deep pyrosequencing to assess HIV-1 co-receptor usage of circulating and proviral quasispecies in patients candidates to CCR5 antagonists treatment

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Background and objectives: Ultra-deep pyrosequencing (UDPS) combined with genotypic algorithms for predicting HIV-1 co-receptor usage offers the opportunity to analyze the tropism of each variant present in the viral quasispecies together with its relative abundance. Aim of the study was assess co-receptor usage by UDPS combined to Position Specific Score Matrix (PSSM) analysis of circulating and proviral HIV-1 in patients eligible to CCR5 antagonists treatment.
Methods: Seventeen patients were enrolled. A sub-group of 5 patients started Maraviroc treatment with optimized background therapy; virological response was monitored during a follow-up of 20.75 ± 1.89 wks. UDPS performed in all patients on both plasma virus RNA and PBMC proviral DNA, amplifying env V3 loop region. Genotypic prediction of co-receptor usage was assessed by PSSM analysis. Concordance between phenotypic and genotypic assays was assessed by considering a threshold of 5% and 0.3% for X4 detection according to sensitivity of the two versions of Trofile used (standard or enhanced).
Results: A total of 130,999 V3 sequences were considered (mean coverage/site: 5,955). Concordance between phenotypic and UDPS results was 0.60±0.24 (Cohen K index ± SE). Quasispecies archived in PBMC was significantly more heterogeneous than in circulating virus (median diversity : 589.0 x 10-4 vs 234.5 x 10-4 substitutions/site, p=0.023, respectively). All but one patient harboured X4 variants at variable frequency in proviral DNA. In the sub-group of patients who underwent Maraviroc treatment, X4 variants were detected in the circulation at frequencies below Trofile sensitivity, whereas in PBMC the frequency of X4 variants ranged from 1.0 to 52.7%. Of these, 4 showed durable response during follow-up, and one (with <0.1 % X4 variants in RNA and 1.06% in DNA) showed viral rebound after initial response.
Discussion: UDPS allows a detailed characterization of HIV V3 quasispecies in both circulating and archived sequences. Almost concordant results were obtained by UDPS and reference phenotypic tests. The importance of circulating and archived X4 variants in clinical response to CCR5 antagonists remains to be better evaluated, particularly when optimized background therapy may be a major determinant of virological suppression.

PO 16

Infection 2010; 38 (Suppl. I): 50

Combination of mucosal and systemic immunization routes elicit the highest hiv protective humoral immune responses to CCR5

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Background and objectives: The objective of this study is to find the best immunization protocol to induce systemic and mucosal anti-HIV protective antibodies in animal models, such as mice, by a bacterial antigen presenting system.
Methods: Mice were immunized with engineered CCR5-FHV chimeric proteins by four different routes such as intraperitoneal (IP), intramuscular (IM), intranasal (IN) and intrarectal (IR) using Freund's Adjuvant only for systemic administrations. Immunizations were also carried out using a combination of systemic and mucosal routes, in details 3IP+3IN and 3IN+3IP were used. We assessed if such immunization protocol could elicit antibodies against the external domain of CCR5 (N-Terminus, ECL1 and ECL2) in sera and in cervical-vaginal lavages by ELISA assay. We also tested antisera in HIV blocking assay to verify if they were able to interfere with HIV entry.
Results: FHV system led to both IgG and IgA responses to the different domains of murine CCR5 receptor. We immunized mice with autologous CCR5 sequences and results obtained were found similar to those achieved with human sequences, although we observed a delayed peak of the immune response. According to the results found with ELISA assay, the higher titers of IgG in mice sera has been obtained with the only intraperitoneal immunization while the higher titers of IgA has been obtained with the combination of intraperitoneal and intranasal route. Low titers of immunoglobulins have been obtained in cervical-vaginal lavages with all protocols. According to preliminary data in HIV blocking assay, mice antisera immunizated with the combination of intraperitoneal and intranasal route show good level of neutralization, thus suggesting a protective role of systemic IgA.
Discussion: Our data suggest that this antigen presenting system could effectively break the B tolerance in mice, thus inducing HIV blocking CCR5 specific antibodies. These findings could have important implications in the design of an HIV vaccine able to induce an high antibody generation and a long lasting protective response.

PO 17

Infection 2010; 38 (Suppl. I): 50

Insertion of different epitopes of murine CCR5 in a new antigen presenting system to break b tolerance in mice

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Background and objectives: The aim of this study is to create constructs containing three different epitopes of murine CCR5 which are the candidate immunogens to induce anti-CCR5 autoantibodies HIV blocking in animal models like mice.

CCR5 is the main HIV coreceptor involved in virus entry and cell-to-cell spread. In order to break the B tolerance and than to induce CCR5 blocking antibodies is need to develop new antigen presenting systems that mantains the native conformational structure of coreceptor. As there is a high level of homology among human and mouse CCR5, comparable immune responses were expected in mouse model.
Methods: The FHV epitope presenting system based on a modified capsid precursor protein of the insect flock house virus. This system is composed of a set of five modified capsid gene sequences, cloned in the expression vector pET-3, in each of which the nucleotide sequence corresponding to a peptide loop was replaced by a single Bsu361 restriction site to allow the oriented insertion of a synthetic polynucleotide coding for a foreing epitope in five distinct sites L1,L2,L3;I2 and I3. Each of the corresponding DNA sequences has been deleted and replaced with a Bsu361 site, which allows the directional isertion of an epitope-coding oligonucletide.
Results and Discussion: We engineered three different immunogens contains murine CCR5 epitopes: ECL1(the first extracellular loop), involved in natural protection as previously found in some exposed seronegative ESN individuals and in some HIV-positive long-term non progressors; ECL2 and N-terminus, both involved in the CCR5 binding of HIV envelope (gp120). These epitopes was cloned in position I2 (FHV) proved to be the best site in terms of CCR5 Elisa-reactive antibodies. This clone was previously supported by studies of molecular dynamics that allowed to insert epitopes of the murine CCR5 receptor in the its native conformational structure.
These studies demonstrated that these constructs should be a good antigen presenting system that may confer HIV protection in vivo and be significant for design of an HIV vaccine.

CLINICAL SCIENCES: ANTIRETROVIRAL THERAPY

PO 18

Infection 2010; 38 (Suppl. I): 51

Rosuvastatin, pravastatin, and atorvastatin for the treatment of hypercholesterolaemia in hiv-infected patients receiving protease inhibitors. a 24-month follow-up

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Background: Highly active antiretroviral therapy (HAART) including protease inhibitors (PIs) has been independently associated with an abnormal lipid profile, and recent studies have shown an increased risk of cardiovascular complications in patients with prolonged exposure to HAART. Even though a hypolipidaemic diet and physical exercise may certainly improve dyslipidaemia, pharmacological treatment becomes indispensable in patients with high risk of cardiovascular diseases and when serum lipid levels excessively increase or persist for a long time, since suspension or change of an effective antiretroviral therapy are controversial still today.
Methods: Aim of our open-label, randomized, prospective study is to evaluate the role of different statins in the management of PI-associated hypercholesterolaemia. Ninety-two adult patients on a stable PI-based antiretroviral therapy since at least 12 months, and presenting hypercholesterolaemia (total cholesterol level >250 mg/dL) of at least 3-month duration and unresponsive to a hypolipidaemic diet and physical exercise, were randomized to a hypolipidaemic treatment with rosuvastatin (10 mg once daily), pravastatin (20 mg once daily) or atorvastatin (10 mg once daily), and were followed-up for 24 months.
Results: Among the 79 subjects who completed the study, rosuvastatin was employed in 25 cases, pravastatin in 29, and atorvastatin in 25. At the close of 24-month follow-up, statins led to a mean reduction of 19.6% and 20.4% versus baseline total cholesterol and LDL cholesterol levels, respectively (p=0.006). Mean decrease in total cholesterol concentration was significantly greater with rosuvastatin (23.2%) than with pravastatin (16.5%; p=0.02) and atorvastatin (17.9%; p=0.01). Similarly, reduction in mean LDL cholesterol levels was significantly higher with rosuvastatin (23.6%) than with pravastatin (17.7%; p=0.04) and atorvastatin (19.9%; p=0.02). During these 24 months, all administered statins showed a favourable tolerability profile, and patients' plasma HIV viral load did not present any variation.
Conclusions: All used statins showed a significant efficacy and a good tolerability in the treatment of diet-resistant hyperlipidaemia, but rosuvastatin was found to be more effective in reducing total and LDL cholesterol levels.

PO 19

Infection 2010; 38 (Suppl. I): 51

A case report of progressive multifocal leukoencephalopathy in HIV+ patient with high CD4 cell count and undetectable viral load :can it be IRIS?

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Progressive multifocal leukoencephalopathy (PML) is a demyelinating disease due to JC virus replication in oligodendrocytes of immunocompromised patients with acquired immunodeficiency syndrome and low CD4 cell count (<100 cells/µl). PML can be observed in HIV-infected patients with high CD4 cell count as an immune reconstitution inflammatory syndrome (IRIS). We report a case of PML in a woman with undetectable viral load and high CD4 cell count.
In September 2009 a 45-year-old woman with HIV-1 infection was admitted with an history of the onset of a neurological syndrome rapidly evolving, characterized by progressive generalized weakness, ataxia, dysarthria, dysphagia and diplopia. HIV-1 infection was diagnosed 18 years before, when patient was hospitalized for CMV-coryoretinitis. Patient experienced several antiretroviral regimens because of and virological failure. One year before the hospital admittion CD4 cell count was 280/mm^3 and viral load <50 copies/mL, therefore she began a regimen of HAART with TDF/FTC, DVR/r and RAL. On admission CD4 cell count was 661/mm^3 and viral load undetectable. Neurological examination relevaed an alert, not compliant woman; she was tetraparetic with hypertone and hyperreflexia of lower limb. EEG showed diffuse increase in slow activity. CFS studies revealed no pleocytosis, normal protein and glucose; JC virus PCR was positive (17.560cp/ml), HIV-RNA 106 cp/ml. Brain MRI showed multiple enhancing lesions involving white matter and cerebellum. Treatment with cidofovir was started. Symptoms worsened progressively and she died in 3 months.
Our report is the first case of PML in a HIV patient with a well controlled HIV infection for more than 24 mounths.Probably, a pre-existing tissue damage caused by previous infection or drug neurotoxicity or the use of drugs with low CPE score was a predisposing condition for the reactivation of JC virus.Another hypothesis explaining this case is a delayed IRIS after two years from the recovery of immune system.This case report highlights the diagnostic difficulties concerning white matter pathology in a patient with HIV on HAART.

PO 20

Infection 2010; 38 (Suppl. I): 52

Mobile phone intervention based on short message system (SMS) improve adherence behavior in HIV-infected non-adherent to antiretroviral therapy. The HI-Vision Study

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Background: Although a large body of research has improved an understanding of factors related to adherence behavior, there is currently little evidence supporting specific approaches for improving adherence to antiretroviral regimens. This study is aimed to determine whether an intervention based on the delivery of short message system (SMS) on mobile phone improves adherence to antiretroviral therapy (ART)
Methods: A multi-site single-arm prospective study was conducted. Inclusion criteria were: treatment with cART, availability of a mobile phone, and reported non-adherence. Adherence was assessed through a self-reported questionnaire. Different non-adherence behaviors were investigated: % of therapy taken in the last month; <100% doses taken over the last week; timing deviation; drug holidays over the last month. The SMS were anonymously send as reminder every time the patient had to take the medication and consist of short text whit slogan or smile. The perceived intrusiveness or helpfulness of receiving SMS was also investigated. Participants are evaluated at baseline, and then every 3 months until 1 year of observation. Only subjects with at least one follow-up (FU) were entered into this analysis. Differences in adherence behavior were evaluated by the mean of paired t-test for continuous and x-square McNermam test for categorical variables.
Results: A total of 71 participants had at least one FU , 41 had 6-month FU and 14 were evaluated at 9-month FU (75% were male; 34% MSM, 32% heterosexual, 18% ex-IDU, 10% active-IDU).
Mean percentage of doses taken over the last month raised from 79.59% at baseline to 94.27% at 3M (P<0.0001), 93.9% at 6M (P<0.0001), and 93.2 (P=0.003). Prevalence of patients reporting <100% doses taken over the last week decreased from 63.4% to 25.4% at 3M (P<0.0001), 36.6% at 6M (P=0.01), and 28.6% at 3M (P=0.03). Prevalence of reported drug holidays also significantly decreased from 42.3% to 15.5% at 3M (p<0.0001), 14.6% at 6M (p<0.0001), and 7.1 (P=0.03). Timing deviations did not seem improve with the intervention (P=n.s. for all assessment).
Discussion: These preliminary results support the hypothesis that a structured mobile phone intervention based on SMS can help people to correctly take their medications.

PO 21

Withdrawn

PO 22

Infection 2010; 38 (Suppl. I): 53

Thrombocytopenia among HIV-infected persons treated with combined antiretroviral therapy (cART): analysis of incidence, temporal trends, and predictors within the ICONA Cohort

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Background: Thrombocytopenia (TP) is a relatively common disorder in HIV-infected persons, and may be a challenging illness to treat, mainly because of its multifactorial aetiology. However, the epidemiology and predictors of TP in the era of potent HIV antiretroviral therapy has not been well defined.
Methods: The study was carried out using the data of the Icona Foundation Study Cohort. All previously ART-naïve starting cART with normal value of platelet count were included. TP has been defined as PC <100 x 109/L persisting in at least 2 consecutive determinations for at least 3 consecutive months. For each patient person-years of follow-up (PYFU) while receiving cART were calculated, and used to estimate the incidence rate of TP. A multivariable Poisson model was performed to elucidate the contribution of HIV viremia, CD4 cell count, HCV infection (based on HCV antibody and HCV-RNA testing), cirrhosis (as based on provider documentation), ARV drug-class, and other potential risk factors for TP. Current HIV-RNA and CD4 count entered into the model as time-dependent covariates.
Results: A total of 2771 patients were included: 69.4% male, median age of 36 (IQR: 32-41), 38.5% co-infected with HCV. At initiation of HAART, mean viroimmunological paramenter were CD4: 295 cells/mmc, and HIV-RNA: 4.75 log10 cp/ml. Median value of baseline platelet count was 189 x 109/L (IQR 149-231). A total of 431(15.5%) patients had a diagnosis of cirrhosis at baseline. Overall patients contributed to 13.787 pyrs. During follow-up, 105 patients developed a TP accounting for an incidence rate of 7.6/1000 pyrs (95CI% 6.3-9.2). A trend for a reduction in the TP incidence rates over the more recent time periods was found (1997-1999: 9.8/1000 pyrs; 2000-2004: 4.6/1000 pyrs; 2005-2009: 4.5/1000 pyrs; P at Chi-square for temporal trend<0.001). At multivariable model, a higher risk of TP was associated with male gender (HR 1.71; 95%CI 1.02-2.86; P=0.040), with HCV co-infection (HR 2.96; 95%CI 1.82-4.82; P<0.001), and with cirrhosis (HR 1.82; 95%CI 1.16-2.86; P=0.009). Moreover, both lower level of current CD4 (HR 3.77 for 0-200 cell/mmc stratum vs >350 cells; 95%CI 2.31-6.14; P<0.001), uncontrolled HIV replication (HR 1.33 for each log10 cp/ml higher; 95%CI 1.12-1.57; P=0.001) were significantly associated with TP onset.
Discussion: Thrombocytopenia remains a relatively common disorder in the late HAART era, even if a trend for a reduced incidence over the most recent years was observed. In a large unselected cohort of antiretroviral naïve starting treatment, HCV co-infection, cirrhosis, uncontrolled HIV replication and lower current CD4 count were all independent predictors of TP.

PO 23

Infection 2010; 38 (Suppl. I): 53

Switching to darunavir/ritonavir (DRV/r) from lopinavir/ritonavir (LPV/r) improves metabolic assessment in HIV positive patients in combination anti-retroviral therapy (cART)

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Background: Metabolic abnormalities associated with cumulative exposure to cART, including dyslipidaemia and insulin resistance, have been linked to an increased risk of myocardial infarction in HIV positive individuals. Boosted darunavir is generally well tolerated in patients with HIV-1 infection and has been associated with a lower incidence of lipid abnormalities than other protease inhibitors.
The aim of this study was to evaluate if the switch to DRV/r from LPV/r in HIV positive patients with HIV-RNA < 50 copies/ml and metabolic abnormalities improves their lipid and glucidic profile.
Methods: Seven Caucasian HIV positive patients in cART included LPV/r for > or =12 months (mean age 49 years, 6 males), with high plasmatic levels of total cholesterol and triglycerides and HIV-RNA < 50 copies/ml for at least six months, were switched to receive 600/100 mg DRV/r twice daily, without a change in their backbone (4 patients taking fixed-dose TDF/FTC and 3 ABC/3TC). Viro-immunological parameters, triglycerides (TGs), total cholesterol (TCh), HDL (HDL-C) and LDL (LDL-C) cholesterol, fasting glucose, HOMA-IR, CRP, indexes of hepatic and renal functionality, microalbuminuria and cystatin C were measured at baseline (T0) and after 3 months (T3).
Results: Three months after switching, TCh, LDL-C and TGs levels decreased with statistical significance (TCh 228 ± 47.1 vs 194 ± 29.1 mg/dl, p<0.01; LDL-C 127 ± 44.2 vs 108 ± 34.5 mg/dl, p<0.03; TGs 432 ± 280.2 vs 211 ± 51.1 mg/dl, p<0.02), whereas HOMA-IR showed a trend to decrease. Cystatin C serum levels statistically decreased (0.87 ± 0.12 vs 0.81 ± 0.1, p<0.02), while microalbuminuria showed a trend to decrease. Indexes of hepatic and renal functionality did not change. Finally, CD4 cell count increased with statistical significance (404 ± 268.1 vs 533 ± 282.2, p<0.007) while HIV-RNA did not change throughout the study, being always below 50 copies/ml in all patients.
Discussion: The compliance of patients to the study was complete, and adverse events were not observed. Treatment with 600/100 mg DRV/r twice daily was well tolerated and showed a more favorable lipid profile than LPV/r. The switch from LPV/r to DRV/r indeed showed an improvement of metabolic abnormalities with a 15% reduction of TCh and LDL-C, and a 51% decrease in TGs levels, as well as a possible beneficial effect on some factors of cardiovascular risk (CVR). This may also be confirmed by the significant decrease of 6.5% in cystatin C, which is considered an important predictor of CVR in the general population. Furthermore, DRV also induced a good immunological response as documented by the increase of 32% of CD4 cell count value, and it was effective in maintaining suppressed viremia. Thus, the switch to DRV/r should be considered and preferred in HIV positive cART treated patients showing abnormalities in lipid profile.

PO 24

Infection 2010; 38 (Suppl. I): 54

Specific non-b subtypes spread and response to haart compared to B subtype with baseline wild-type genotype

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Background: Despite of the growing proportion of non-B subtypes in Europe, few data exist on the virological efficacy of cART in these patients. We evaluated non-B subtypes prevalence, temporal trends and associated epidemiological factors. Moreover, the response to therapy in patients carrying the most prevalent non-B clades was studied.
Methods: For the epidemiological study we analysed 3,670 pol sequences derived from a single reference laboratory (University of Siena) and stored in the ARCA (Antiretroviral Resistance Cohort Analysis) database. For the treatment response analysis 558 subjects beginning PI or NNRTI-based cART, with available wild type baseline pol sequence and a virological follow up at week 12 (range 8-16) were selected. Response to treatment was defined as viral load <50 copies/ml. Differences between proportions were analysed using Fisher test; multivariate analysis were also performed.
Results: Overall, 417 (11.4%) patients carried non-B subtypes. Non-B strains increased from 2.6% to 18.9% before and after 1993 (p<.0001) in a subset of 2,479 subjects with a known year of diagnosis. Multivariate analysis indicated African ethnicity, heterosexual infection route, and time of diagnosis as independent predictors of higher odds of non-B infection. The most represented non-B variants were CRF02_AG (n=107, 25.7%), F (n=99, 23.7%), A (n=53, 12.7%) and C (n=47, 11.3%). When we evaluated patients with available baseline genotype and virological follow up (405 on PIs and 153 on NNRTIs), the proportions of subjects achieving virological suppression was comparable in patients with non-B compared to those with B variants (50%, n=43 vs 42.2%, n=199). No difference in response to treatment was detected in subjects carrying wild type non-B or B subtypes treated with PI (44.4%, n=28 vs 38.6%, n=132), or NNRTI-based cART regimens (65.2%, n=15 vs 51.5%, n=67). However, a better response in patients on PIs carrying CRF02_AG rather than B clades (73.3%, n=11 vs 38.6%, n=132 p=.007) was found. In the multivariate analysis HIV-1 viral load at baseline was associated with a worse response (p<.001), whereas the time between cART initiation and virological follow up was predictive of a better response (p=.007). In contrast, no significant difference was observed in the proportions of patients achieving viral load below 50 copies/ml when comparing F1 and C subtypes to B variants (33.3%, n=5 and 55.6%, n=5 vs 38.6%, n=132, respectively).
Discussion: In the context of a considerable spread of non-B clades in Italy, we observed a comparable response in patients carrying non-B on a PI or NNRTI-containing cART. Noteworthy, this was confirmed in a subset of patients carrying F1 variants, not previously investigated. PI-treated patients with a CRF02_AG wild-type variants seem to show a better virological response, a finding that may be explained by factors other than subtype (ie. adherence, limited size of the sample) and warrants further investigations.

PO 25

Infection 2010; 38 (Suppl. I): 54

Darunavir (DRV)/r plus raltegravir (RAL) dual regimen in multi-experienced population: long term efficacy and tolerability

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Background: In multi-experienced patients, the administration of an antiretroviral (ARV) regimen containing at least three active drugs is often very difficult, due to the accumulation of resistance associated mutations. Some studies explored the utility of including non active drugs from the nucleoside reverse transcriptase inhibitors (NRTI) class as backbone, showing no clinical utility. This study describes a 70 weeks' experience of a NRTI-sparing dual regimen including DRV/r plus RAL in patients failing their current ARV regimen with no other treatment option.
Methods: To be included in the study, patients had to be RAL-naïve, have a detectable HIV RNA and a genotypic resistance profile at failure, and not having the possibility based on the resistance and treatment history profile to receive a ARV combination including 3 active drugs. For each patient the 3rd agent was selected based on the genotypic score. Data on HIV RNA, CD4 cells count, AST ALT, lipid profile were collected at baseline, w4 and every 3 weeks thereafter. Adherence was assessed through the pills count at every visit. Descriptive analysis of these parameters overtime was performed. Here we present the results of the subset of patients who received RAL+DRV/r.
Results: Nineteen patients have been included in the analysis. A summary of the baseline characteristics is detailed in Table1. At week 70 after the initiation of DRV/r +RAL including ARV 100% of the patient had a HIV1-RNA<50copies/ml; 84% of these had an undetectable viral load at week12. Two patients had a transient increase in HIV-RNA within the first 24 weeks but they re-obtained a complete viral load suppression with the same regimen at the next control. The CD4 cells count raised from a median value at baseline of 209 cells/mmc (range: 24-716) to a median of 412 cells/mmc (range 219-887cells/mmc) at week 70 (p<0.001).
The median ALT and AST values remained stable throughout the study period, as well as the median total cholesterol and triglycerides; three patients developed a G3 increase in total cholesterol and statins have been added successfully.

Table1: Baseline characteristics

N=19		
Sex F/M	4/15	
CDC stage B3/C3	7/12	
HCV positive	8	
	Median	**Range**
Age (years)	46	32-60
HIV RNA (log)	3.25	3.10-5.66
CD4 cells count (cells/mmc)	209	24-716
Number of previous ARV regimens	8	4-12
PI RAMs at baseline	7	2-12
GSS score RAL-DRV regimen	1,56	1,5-2

Comments: The results of the analysis of this subset of patients remarks the observation already made in several studies that the number of active drugs, and the GSS score in particular, is key to obtain a durable control of HIV RNA even in extensively treated patients, allowing also a progressive increase in the CD4 cells count. Despite the fact that 50% of the patients had partial resistance to darunavir, all reached optimal HIV RNA suppression (< 50 copies/ml) and maintained it at week 70. The accurate selection of the single patient and the single drug, the close monitoring of adherence and the fact that the patients remained in the previous failing regimen for less than 6 months had a favourable impact on our results. In patients where three effective drugs can't be administered, this option can be considered if the genotype allows it.

PO 26

Infection 2010; 38 (Suppl. I): 55

Does comorbidity affect adherence to ART? Data from a cohort of HIV positive outpatients

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Objectives: The ageing and the rising survival of HIV infected persons suggest they will experience increasing comorbidity. Aim of our study is to verify the effective presence of comorbid diseases in HIV population and if they can affect adherence (AD) to antiretroviral therapy (ART) or depression (D)
Methods: 300 HIV positive outpatients (71% males), mean age of 45,9, were consecutively enrolled; all of them were on ART. 285 (95 %) were caucasian. The risk factors for HIV were : 77 IVDU, 223 sexual intercourse. The mean time on HIV infection was 10,1 years; regarding clinical CDC state, 163 were A, 77 B and 60 C; mean CD4 count was 539 cells/mcL, HIV-RNA was undetectable (< 50 copies/ml) in 261 patients (87.1 %). Charlson score (modified for age) was utilized for assessing comorbidity; an AGTG modified questionnaire (yet used in the INTESA study, XVII IAC, poster CDB0498) and the Beck Depression Index (BDI) were used for exploring AD to ART and D respectively.
Results: 23 pts (7,7%) had an AD rate < 85%, 13 (4,3%) between 85 and 95 %, 264 (88%) > 95%. 238 (79,3%) out of 300 had BDI < 14, in 42 (14%) patients BDI was > 14 (20, 6,7%, no data). Comorbidity index was 0 for 78 patients (25,9%), 1-2 for 62 patients (20,7%) and 3+ for 160 patients (53,4%). Comorbidity significantly influenced adherence (P = 0.024) ; no correlation was found with BDI.
Discussion: Our observational and crossectional study is one of the first exploring the relationship between comorbidity and AD. Comorbidity is very frequent in HIV population (> 70% overall). The negative impact of comorbidity on AD seems to be not depression related. If confirmed also in longitudinal studies, comorbidity may have important implications for the care of HIV infected people, particularly in the not easy issue of promoting and sustaining AD.

PO 27

Infection 2010; 38 (Suppl. I): 55

Raltegravir (RAL) based antiretroviral regimen: clinical experience of a single centre

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Background: Raltegravir(RAL) is a the first compound of a novel class: integrase inhibitors . Aim of our study was to evaluate efficacy and safety of RAL based regimen.
Materials and Methods: We proceeded to retrospective analysis from patients(pts) referring to our service. We searched our databases for epidemiological, clinical, immunological and virological issues. Moreover we recorded HCV and HBV status. We focused our attention on the reason of ARV switching , immunological gain, virological suppression and tolerability of the prescribed regimen. We followed side effects in order to define safety of prescribed regimen.
Results: We enrolled 46 pts.(male 34: female 12), according to CDC 1993 they were classified as A(12); B(16);C(18). Median age was 48 years, 27 pts.were HCVpositive and only 2 presented an active HBV coinfection. Risk factors for HIV infection resulted: injective drug abuse(22), homosexual(13) and heterosexual(11)exposition. They were switched to RAL therapy for drug resistance(35); regimen semplification(5) or drug toxicity (6). Most of patients presented multiple drug failures to ARV therapy(almost two different classes resistance). 27 pts. were coming from a PI failure whereas 6 from NNRTI based regimen and one from 3TC monotherapy. The most represented drug associated in new ARV regimen was DRV/rtv (23) followed by maraviroc (8) and etravirine(6).
We collected data of immune and virological response after 3 and 6 months , so at 6 months 26 pts.(65%) presented undetectable(<20) viral load and a medium CD4 gain of 122 cc/ml.No relevant side effects were observed
Conclusions: Pts. treated with RAL based therapy presented a good outcome, most of them achieved(after 6 months) virological suppression and immunological recovery.
In our caselist darunavir/rtv and RAL obtained the best results with no relevant side effects.So more studies are needed to confirm that RAL based ARV could be very efficacious and safe even in long term follow up period.

PO 28

Infection 2010; 38 (Suppl. I): 55

Switch to Raltegravir in patients with suppressed viremia

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Introduction: Raltegravir (RAL) is indicated with other antiretroviral (ARV) agents for treatment of HIV-1 infection in naïve and treatment-experienced adults. The few adverse events and lack of cross resistance to other ARV agents make RAL suitable as a component of effective alternative ARV therapy for those subjects with intolerance to Enfuvirtide, NRTI, NNRTI and RTV-boosted PI containing regimens.
Objective: We sought to evaluate efficacy and safety of this switch-strategy in patients with full virological suppression.
Methods: Due to toxicity or intolerance to previous therapy, we made one drug substitution to RAL in 46 patients: switch from NRTI 57%, switch from PI 24%, switch from NNRTI 2%, switch from T20 17%. Data included demographics, history of HIV infection, ARV history and laboratory parameters that were extracted from medical records. Changes in CD4 cell counts were expressed by the median of their rate of change from baseline.

Results: The HIV risk behaviour patterns were: homosexuals 39%, IDU 22%, heterosexuals 39%. HCV-coinfected patients were 11% and HBV-coinfected patients were 7%. The percentage of patients with subtype B was 90%. The percentage of patients with CDC class C was 20%. Median age was 49 years (IQR 45-54) and 77% of enrollers were male. Median HIV-infection duration was 14 years (IQR 12-17) and median CD4 nadir was 137 cell/ml (IQR 88-208). Median number of ARV agents stood at 9 (IQR 7-11). On historical genotype, median of resistance mutations to NRTI was 4 (IQR 3-5), to NNRTI was 1 (IQR 1-2), to PI was 2 (IQR 0-4). Median GSS on historical genotype was 12 (IQR 9-14). Median CD4 count was 396 cell/ml (IQR 309-659) at switch. Median follow-up was 14 months (IQR 11-15). RAL was associated with NNRTI in 22% of patients and with PI in 72% of patients, among PI, atazanavir was mostly used (39%). Median CD4 increase from baseline was 54 cell/ml (IQR 11-145). CD4 median monthly increase was 4 cell/ml (IQR 1-13). No virological rebound was observed. The lipid profile with respect to the baseline did not have statistically significant changes. Also other laboratory parameters maintained stable after switch. Two patients discontinued RAL one due to fatigue and the other one due to hypertransaminasemia.
Conclusion: The switch to RAL lead to increase in CD4 counts. No virological breakthrough and no changes in laboratory parameters were observed. Larger sample size and longer follow-up are required to ensure the durability of the observed benefits.

PO 29

Infection 2010; 38 (Suppl. I): 56

Antiretroviral treatment and expression of the mRNA levels for PGP, MRP1, MRP4 and MRP5 in HIV antiretroviral naïve patients: follow-up at 48 weeks

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Background: The ATP-binding cassette genes represent the largest family of transmembrane proteins [including multidrug resistant proteins (MRPs) and P-glycoprotein (Pgp)] able to drive the transport of various molecules across cell membranes. Several studies have demonstrated that most of the above transporters are also able to transport antiretrovirals.
The aim of this study was to evaluate whether the antiretroviral treatment might affect the mRNA expression of Pgp and of some MRPs.
Methods: Blood samples were collected from 13 HIV-positive treatment naïve patients. After the beginning of the treatment, samples were collected at 12, 24, 36 and 48 weeks. Eight patients were treated with Kaletra and Truvada (group I) and five patients with Efavirenz and NRTIs (Truvada or Combivir) (group II). Expression of mRNA of the Pgp, MRP1, MRP4, and MRP5 was evaluated by real-time-PCR using the TaqMan technology (ABI Prism 7000; Applied Biosystems).
Results: At all time analyzed, the mRNA levels of these transporters did not significantly differed from the mRNA levels detected before the beginning of treatment. Only for MRP1 a weak increase, of mRNA expression was detected after 48 weeks of therapy. A high inter-individual variability was observed before and after the beginning of treatment. Looking at the individual trend of the mRNA expression of the above transporters in each patient it can be seen that the expression levels of these transporters seems to change during follow up, but it is independent of the type and time of treatment. MDR1 and MRP4 expression was not affected by treatment with PI and NRTI. In fact, at all time analyzed the mRNA levels of these transporters did not significantly differed from the mRNA levels detected before the beginning of treatment. As far as MRP1 and MRP5 are concerned, a modest, but not significant, reduction in the mRNA expression levels was observed after beginning of treatment .
Discussion: Antiretroviral treatment does not significantly affect the expression levels of mRNA of the membrane transporters analyzed. However an interindividual variability in the expression of these mRNA has been documented during the follow up and further studies are needed to evaluate whether the over-expression of these mRNA may affect the success of therapy.

PO 30

Infection 2010; 38 (Suppl. I): 56

Study of the mutations associated to integrase inhibitor resistance in subtype B and non-B human immunodeficiency virus type 1

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Background: The emergence of mutations that confer resistance to the integrase (IN) inhibitors has been observed and characterized, but viral polymorphisms at the integrase gene caused by immune selection and/or associated with non-subtype B is not completely understood. Here we plan to study the genotypic resistance pattern associated to IN inhibitor resistance in plasma-HIV RNA derived from B and non B HIV-1 infected individuals.
Methods: Fifty-one IN inhibitors naïve HIV-1 infected patients were studied: thirty-six non-B HIV-1 samples were collected from patients from Cameroon and 15 subtype-B HIV-1 samples derived from Italian patients. RNA was extracted from 140 µL of plasma using a QIAmp Viral RNA kit (Qiagen, Milan, Italy) following the manufacturer's instructions. Sequencing was undertaken using CLIP, a DNA sequencing technique for direct sequencing of small quantities of amplified template (Open Kit-TruGene HIV-1, Siemens Healthcare Diagnostics).
Results: Among the 36 non B strains, the distribution of subtypes was as follows: 22 subtypes CRF02_AG, 4 subtypes CRF02_AE, 5 subtypes D, 1 subtype CRF11_cpx, 1 subtype F2 and 3 subtypes G. No major mutations associated with resistance to IN inhibitor were detected in HIV-1 subtype B samples. On the contrary, mutations at amino acid positions involved in IN resistance were found in non-B subtype samples. Specifically, 14 % of samples showed Y143 H/R/C mutation (2 CRF02_AG, 2 CRF02_AE and 1 D subtype) and at the same position the Y143S polymorphism was detected in 11 % of samples (2 CRF02_AG, 1 CRF02_AE and 1 CRF11_cpx subtype). Interestingly in 1 sample belong to subtype G the Q148H pathway (Q148H+E138A+G140S) was found. Other mutations detected at the resistance sites were E92D and E157G/K. E92D was found in 7% of subtype B samples and in 3 % of non-B strains (1 CRF11_cpx). E157G/K was detected in one HIV-1 subtype CRF01_AE.
Discussion: These findings indicate that IN inhibitor resistance mutations can be detected in non-B subtype patients in the absence of drug exposure. This underlies the need for studies to further evaluate the role of IN inhibitors mutations in the management of HAART in HIV patients.

PO 31

Infection 2010; 38 (Suppl. I): 57

Shallow decline in CD4 before start of cART as determinant of long-term poorer immunological response in CASCADE study

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Background: In many cohort studies individuals started cART even if they reported a shallow pre-HAART CD4 decline, both in naïve and in ART-experienced, or among those with initial CD4 above or less than 350 cells. The long-term restoration of CD4 (i.e., at least two CD4 > 500) was then, compared in patients with shallow vs. those with steepest pre-cART decline.
Methods: Patients were selected from a prospective European collaboration cohorts study with seroconversion dates (CASCADE). Patients when still AIDS-free were included if at least two CD4 counts before and two after cART were available. To estimate the pre-cART decline, the differences of 2 years pre-cART CD4 cell count with CD4 at cART were considered for each patient. Cox models were applied to study the effect of CD4 decline on the probability of observing two consecutive CD4 >500 after cART. Confounders were evaluated at start of cART: CD4 and viral load, age, gender, transmission category, presence or absence of HCV and class of antiretrovirals.
Results: 1,728 patients fulfilled inclusion criteria. The median pre-cART CD4 decline in the last 2 years before cART was of 68 cells/mmc (IR: -140; -10). Individuals with a decline less than 50 cells were considered as with a shallow pre-cART (n1=436) and those with a median decline > 50 cells were considered as steepest decline (n2 =1,008). Applying a stratified (by initial CD4 less or greater than 350 cells) Cox model the estimated RH of two consecutive CD4 >500 from 0.5 to 5 years after cART in group n1 vs. group n2 was 0.80 (95% CI: 0.67-0.96). When adjusting for possible confounders the RH tended to decrease yet (RH = 0.70; 95% CI: 0.55-0.90).
Conclusions: Patients with a shallow CD4 decline before cART showed a poorer long-term immunologic response, also when controlling for initial CD4 greater or less than 350 cells/mmc.

PO 32

Infection 2010; 38 (Suppl. I): 57

Prevalence of HLA-B*5701 and access to genetic test in Sicily. A multicenter study

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Obiective: Prevalence of HLA-B*5701 is not homogeneous and little is known about Sicily. We speculated that publication of DHHS guidelines (3 Nov 2008), which designated abacavir as an "alternative" drug because of potential cardiovascular risk, might have modified modality of access to the test. The present study proposes to evaluate, among subjects born in Sicily, the percentage of HIV+ patients carrying HLA-B*5701, the clinical indication for the performance and procedures for execution of genetic test in relation to clinical need and treatment.
Methods: A multicenter retrospective observational study was assessed into 12 clinical infectious diseases unit in Sicily to explore prevalence, indications, modality of execution of genetic test for HLA-B*5701. Data were obtained by online questionnaire.
Samples have been obtained through salivary swab or entire blood; typization of HLA-B*5701 was performed by sequence specific primers or sequence specific oligonucleotide polymerase chain reaction (PCR-SSP or PCR-SSO) and cytofluorimetry-Luminex.
Results: 332 HIV+ patients (average age 42.1 years) were included in the analysis: 73.8% male; 38.8% heterosexuals, 33.9% homo-bisexuals, 24% injection drug users; 89.5% receiving HAART. Among 280 patients born in Sicily, 17 (6.1%) resulted positive for HLA-B*5701. Regarding indication to execution of genetic test: 55.7% were required as screening (19.6% naïve), 44.3% in view of therapeutic switch (16.3% intolerance to other NRTIs, 16.3% simplification strategy, 5.1% dismetabolism, 4.8% proactive switch, 1.8% resistance to other NRTI). 14.8% of the samples were obtained by salivary swabs, 85.2% by whole blood. 49 tests (14.8%) were executed through PCR on salivar swabs, 129 tests (38.9%) through PCR-SSP, 7 tests (2.1%) through PCR-SSP-SSO, 21 (6.3%) through cytofluorimetry and 126 tests (38%) through PCR-SSO. Before November 2008, 104 tests (47%) were required as screening and 117 (53%) for switch whereas after this date, 81 (73%) as screening and 30 (27%) for switch.
Conclusion: Immunologically-mediated hypersensitivity reaction, the most important adverse event related to abacavir, is strongly associated with HLA-B*5701. In this analysis the prevalence of HLA-B*5701 measured in Sicilian patients (6.1%) is similar to that observed in large studies performed on the Caucasian population (4.04%-6.5%). Although some of the more interesting features of abacavir have been once-daily intake, few drug interactions and a favourable long-term toxicity profile, since the year 2008, different studies associated surprisingly use of abacavir with cardiovascular risk. The significant reduction of tests performed in view of therapeutic switch (27% vs 53%) ($p<0.0001$) could be related to Nov 2008 DHHS guidelines publication. A different perception of cardiovascular risk from physician could have consequently changed indication to request genetic test.

PO 33

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Effect of chemotherapy on immunereconstitution in patients with HIV infection and lymphoma

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Lymphomas are diagnosed more frequently among HIV-positive patients than among similarly aged HIV-negative persons. The effect of chemotherapy on immunereconstitution in patients who survived a lymphoma diagnosis is still unknown.
A case-control study was conducted in the Modena cohort in order to evaluate immunereconstitution ofter chemotherapy. Patients with HIV and a diagnosis of lymphoma who survived for at least 6 months were included in the analyses and were compared to patients presenting for HIV diagnosis with an AIDS event other than lymphoma (AIDS presenters [AP]) who survived at least 6 months after diagnosis. Changes in CD4 count and the percent of patients with an undetectable viral load were described at 6-monthly intervals after diagnosis.
13 patients with lymphoma and 108 APs were included in analyses. At diagnosis patients with lymphoma had significantly higher median

		Months after diagnosis								
Patient group		0	6	12	18	24	30	36	42	48
AP	Number of patients	108	108	101	91	85	82	76	66	54
	Median	61	175	228	262	345	353	380	389	445
Lymphoma	Number of patients	13	13	13	12	11	8	7	7	6
	Median	219	120	125	218	351	364	422	461	411
P-value		<0.0001	0.28	0.11	0.34	0.74	0.92	0.68	0.71	0.68
Percentage of patients with an undetectable viral load										
AP				75.2	75.8	65.9	76.8	74.5	69.7	72.2
Lymphoma				76.9	75.0	90.9	87.5	100.0	85.7	83.3
P-value				0.90	0.95	0.09	0.49	0.13	0.37	0.56

CD4 count 220 vs 61 cells/uL (p<0.0001.) All patients started antiretroviral therapy and continued it throughout follow-up. Over the first 18 months after diagnosis, patients with lymphoma experienced a drop in CD4 count during their chemotherapy, but CD4 counts subsequently increased and by month 24 no statistical difference was seen between the two groups of patients.
Chemotherapy does not seem to impair the long-term capability of the immune system to reconstitute after initiation of antiretroviral therapy. When starting HAART, the majority of patients are able to attain an undetectable viral load.

PO 34

Infection 2010; 38 (Suppl. I): 58

Sentinel Mutations in Standard Population Sequencing Can Predict the Hidden Presence of RT Major Mutations Detected only by Ultra deep pyrosequencing

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Background/objectives: This proof-of-concept study aims at identifying in drug-naïve patients whether few selected mutations, T69S, L210M and K103R, found at 3 reverse transcriptase (RT) resistance positions and easily detected by standard population sequencing (GRT), can act as sentinel mutations by predicting hidden minor species with primary drug resistance mutations (DRMs).
Methods: Ultra deep pyrosequencing (UDPS) of RT was performed with GS FLX Roche, for 9 coupled plasma/cellular (PBMCs) samples and 31 additional plasma samples from 40 HIV-1 B subtype infected drug-naïve patients, without primary transmitted resistance at standard GRT (years 2004-2008) (Bennett et al., 2009), and with VL>4.0 log cps/ml.
Thirty RNA samples with T69S, L210M and K103R mutations at GRT were selected (10/10/10, respectively). The other 10 RNA samples were considered as control viruses. DRMs in RT detected by UDPS at level >0.1% and <20% of viral species in both forward and reverse direction were considered minor variants. For each sample, only positions covered by at least 300 reads (reads-number/position range analyzed: 303-3371) were analyzed.
The association between GRT mutations and drug resistance minor variants was assessed by Fisher exact test.
Results: According to the Stanford/IAS 2009 mutations lists, UDPS revealed the presence of at least one RT DRM in 25/40 (62.5%) RNA plasma samples and 5/9 (55.6%) DNA samples, respectively. In particular, the presence of NRTI and NNRTI resistant minority species was found in 20 (50.0%) and 13 (32.5%) RNA samples, and in 5 (55.6%) and 3 (33.3%), DNA samples, respectively. Eight RNA samples (20.0%) and 3 DNA samples (33.3%), respectively, showed minor variants resistant both to NRTI and NNRTI.
HIV-1 drug-naïve patients with L210M and T69S mutations detected by standard GRT showed more NRTI and NNRTI minor variants than control patients. Of note, L210M and T69S were positively associated with minor variants resistant to Thymidine Analogues (TAMs) if compared to control virus plus K103R virus (30.0% and 40.0% vs 0.0%, P=0.03 and P=0.001, respectively). Such minor variants were at levels of 0.5-0.8%, corresponding to copy number of mutants ranging from 294 to 2197 cps/ml. Interestingly, the Q15IM complex minor variants (A62, V75I, F77L) were frequently found in patients with L210M (50.0%) and T69S (40.0%).
Discussion: This proof-of-concept study suggests the existence of genetic markers that can act as sentinel mutations of hidden DRMs. A detailed map of association between sentinel mutations, detected by GRT, and minor drug resistance variants, only detectable with high resolution methods, may help to select patients at high risk of carrying resistance in reservoirs, hence providing a surrogate marker of hidden DRMs easily detectable by routine testings.

PO 35

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Frequency, predictors and outcome of viral rebounds in HIV-infected patients on suppressive antiretroviral therapy

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Background: Intermittent episodes of low-level viral rebound preceded and followed by undetectable viraemia (viral blips), and persistent low-level rebounds (two or more consecutive values > VL threshold) in patients on successful HAART are frequently observed in clinical practice. The aim of this study was to retrospectively examine rate and predictors of this phenomenon in a cohort of HIV-infected patients with full virological response to HAART, and to determine its long-term clinical, immunological and virological outcomes.
Methods: All medical records of HIV infected subjects, on at least triple drug therapy on regular follow-up from June 1997 to December 2009 at the Infectious Diseases Department of Perugia, were reviewed. Patients that achieved a confirmed undetectable viraemia were enrolled. The end-points were the following events: virological failure (plasma HIV-RNA > 500 copies/mL), discontinuation or change of the entire regimen, end of follow-up. Demographic, clinical and genotypical data, data on CD4 cell count and virological status at baseline and after achieving virological suppression were collected. The rate and the magnitude of intermittent or persistent low level viral rebounds (plasma HIV-RNA < 500 copies/mL) were measured and

subsequent clinical, immunological and virological outcomes were investigated.
Results: Out of 404 distinct HIV-infected individuals enrolled (total follow-up 1847 patient-years), 128 (32%) maintained undetectability whereas 276 (68%) developed at least one viral rebound during the study period: 194 (48%) had only blips, 82 (20%) had at least one episode of persistent low level viremia. 3 distinct patterns of virological control were so identified but none of them was associated at univariate analysis with demographic, clinical, viro-immunological and treatment characteristics. The median time from HAART start to first rebound was 29 months. Rebounds were frequently preceded by new not-ARV drugs (15%), immunizations (10%), intercurrent illnesses (8%). The immunological restoration was not worse among the patients with virological rebounds and the clinical outcome did not differ significantly comparing different virological patterns. 73 virological failures occurred in the study period, for a failure rate of 2.76, 2.87 and 9.03 per 100 person-years among patients with consistent undetectability, single viral blips and persistent rebounds respectively. Amplitude of viral rebound seems to predict risk of failure, with a significant threshold of 400 copies in patients with single blips and 200 in those with persistent rebounds.
Conclusions: Transient increases in viral load are common in patients on effective HAART, the isolated ones being the most frequent but lacking clinical and virological negative outcomes. Patients showing a persisting viral rebound are instead at higher risk of treatment failure. Plasma HIV-RNA level at rebound must also be accounted for when considering a treatment change.

Overall	BL	M 1	p	M3	p	M6	p	M9	p	M12	p
ALT (UI/L)	45(27-93)	51 (32-96)	0.8	46 (32-67)	0,6	37 (237-83)	0.4	35 (24-84)	0.6	38 (25-51)	0.1
AST (UI/L)	35 (23-66)	41 (25-61)	0.9	33 (23-55)	0,6	27 (17-54)	0.2	27 (18-52)	0,7	26 (20-43)	0.1
No CH versus CH	BL	M 1	p	M3	p	M6	p	M9	p	M12	p
ALT (UI/L) (NO CH)	30 (23-44)	38 (24-50)	0.3	40 (24-43)	0.8	27(22-35)	0.3	26(22-33)	0.2	26(18-36)	0.3
ALT (UI/L) (CH)	91 (47-167)	95 (49-109)	0.9	66 (57-109)	0.3	78(34-101)	0.3	81(36-108)	0.1	43(38-101)	0.1
AST (UI/L) (NO CH)	24 (17-29)	23(18-45)	0.4	20(16-24)	0.4	20(15-23)	0.1	18(16-23)	0.2	20(18-27)	0.5
AST(UI/L) (CH)	65(46-86)	57(35-71)	0.8	52(36-76)	0.5	52(26-58)	0.2	51(30-78)	0.7	35(25-74)	0.1
FIB4 >3.25 versus <3.25	BL	M 1	p	M3	p	M6	p	M9	p	M12	p
ALT (UI/L) (>3.25)	82 (56-173)	107(96-111)	0.8	63(43-94)	0.3	68(55-100)	0.5	94(38-130)	0.9	40(38-86)	0.3
ALT (UI/L) (<3.25)	33(27-80)	49(27-64))	0.6	43(27-67)	0.9	31(24-83)	0.5	29(22-41)	0.1	36(18-51)	0.3
AST (UI/L) (>3.25)	65(50-150)	61(54-107)	0.8	52(29-68)	0.1	56(51-58)	0.3	76(40-144)	0.9	35(35-85)	0.2
AST (UI/L) (<3.25)	29(21-62)	29(19-49)	0.8	29(19-41)	0.9	25(16-41)	0.9	23(17-34)	0.1	25(20-43)	0.5

Values are expressed as median and interquartile range (IQR)
All p values are calculated versus baseline
CH=chronic hepatitis
BL= baseline

PO 36

Infection 2010; 38 (Suppl. I): 59

Hepatic toxicity of etravirine (ETV) in HIV-monoinfected and HIV-HCV coinfected patients enrolled in the expanded access program (EAP) in the outpatient HIV-clinic of the Institute of Infectious and Tropical Dieseases of Brescia (Italy)

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Background: ETV is a second generation non-nucleoside reverse transcriptase inhibitor (NNRTI) with a relatively high genetic barrier; in the registration trials DUET 1 and 2 ETV showed an hepatic tolerability profile similar to that of placebo even in coinfected patients.
So far no informations are available concerning hepatic tolerability of ETV in patients with advanced liver fibrosis.
Aim of the study: to evaluate hepatic tolerability of ETV in HIV patients enrolled in the EAP in our outpatient HIV-clinic. Patients and methods: all the patients enrolled in the EAP between September 2007 and March 2009 were considered for the analysis. Viro-immunological and biochemical parameters were recorded in our database at baseline, after 1 month and every three months thereafter. Hepatic toxicity was studied through the analisys of the course of AST and ALT at each time point; patients were stratified according to the presence of markers of chronic hepatitis B (HBsAg positivity) or C (HCV Ab positivity) (chronic hepatitis, CH).
Advanced fibrosis was defined as having a FIB-4 score > 3,25.
Results: 37 patients were enrolled in the EAP, 83,8% males, median age 46 (interquartile range , IQR 44-51), 43,2% IDUs, 29,7% heterosexual and 19% MSM.
At baseline (BL) 16/37 pts (47%) had HIV-RNA undetectable; median CD4 cell count was 277/mL (IQR 186-561); AST /ALT levels were 35 (23-66) / 45 (27-93)UI/L.
Median number of previous antiretroviral regimens was 14 (11-18); ETV was prescribed together with a boosted PI (mainly darunavir/ritonavir) in 21 pts (56,7%); raltegravir in 25 pts (69,4%), TDF/FTC in 17 pts (46%). Overall 18 patients (48,6%) had chronic hepatitis B (3) or C (15); 6 out of 35 evaluable patients had a FIB4 score > 3.25; patients with a follow up of at least 1 month (1M)were 35; 21 pts have a follow up of at least 12 M.
At month 12 19/21 pts (90%) had HIV RNA < 50 copies/mL; CD4 cell count was 362 (118-491) (p=0.9 versus BL). BL AST/ALT levels and variation at each time point are summarized in table 1 where patients are stratified according to CH status or advanced fibrosis.
Conclusions: in our analysis ETV seems to show a good hepatic tolerability in HIV monoinfected and HIV/HCV or HBV coinfected subjects with or without advanced fibrosis.

PO 37

Infection 2010; 38 (Suppl. I): 59

Raltegravir plus a boosted protease inhibitor: experience in patients with resistance and/or NRTI-related adverse events

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Objectives: to evaluate the efficacy and safety of a dual therapy of raltegravir (RAL) and ritonavir-boosted protease inhibitor (PIr) in patients with resistance and/or NRTI-related adverse events.
Methods Cohort of HIV infected adults starting a dual therapy with RAL plus PIr from Jan 2008 to Sep 2009 in 3 Italian HIV reference centres. Patients changing ARV for resistance and/or NRTI-related adverse events were included. Demografic, epidemiological, laboratory and immunological-virological data were collected using medical report database.

Results: 24 triple class-experienced patients were included: male 79%, median age 49 years, median baseline CD4 346/mmc, 83% of the patients had HIV RNA below 40 copies/ml. HIV genotipic resistance test were available in 18/24 patients: all of them showed a complete resistance to NRTI drugs. At baseline 19 patients were receiving 2 NRTI+ PI/r, 4 2NRTI+NNRTI. Reasons for change of the previous regimen were virologic failure (n=4), liver toxicity (n=3), renal failure (n=3), cardiovascular events (n=2), simplification (n=12). Patients started therapy with RAL + DRV/r (n=18), TPV/r (n=2), LPV/r (n=2), ATV/r (n=2).
After a median follow-up of 48 weeks, treatment interruption occurred in 1 patient lost to follow-up. At the latest visit, median CD4 was 421/mmc and HIV RNA was below 40 copies/ml in all patients. No adverse events were observed, hepatic and renal function has been improved in patients with previous observed failure.
Conclusion: In this antiretroviral-experienced population a dual therapy of RAL + PI/r seems an attractive regimen in patients with resistance and/or NRTI-related adverse events. Limitation of this study is the low number of patients included. Further randomized clinical trials are needed in order to confirm the efficacy and safety of this strategy.

PO 38

Infection 2010; 38 (Suppl. I): 60

Excellent immune recovery over the long term in patients with sustained undetectable HIV-RNA: concomitant evaluation of CD4+ and CD8+ is more predictive than CD4+ count alone

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Background: As virological potency of current HAART regimens appears to reach a plateau, we now aim at obtaining excellent immunological recovery (EIR) in our patients. Not only restoration of absolute CD4+ count but also normalization of CD4/CD8 ratio is important. Recent studies have demonstrated an inverse association between the CD4/CD8 ratio and AIDS defining and non-AIDS defining illnesses.
Patients and methods: EIR was defined as CD4+ >/=500/cmm plus %CD4>/=29% plus CD4/CD8 ratio >/=1. Patients had to meet the following criteria: (i) c-ART (including at least one PI+/-ritonavir (r), or one NNRTI, or abacavir) started between 2000 and 2005; (ii) undetectable HIV RNA (<50 copies/ml) by 12 months; (iii) sustained undetectable HIV RNA over at least 2 further years; (iv) >/=2 HIV RNA controls per year. Kaplan-Meier and Cox regression models were performed to assess incidence and predictors of EIR among baseline or time-updated variables. A sensitive analysis was performed in patients presenting with severe impairment (i.e., CD4</=200/cmm plus %CD4+</=14% plus CD4/CD8 ratio</=0.3). Baseline and time-updated factors have been investigated as possible predictors.
Results: N=352 patients. Among them, 181 (51%) had CD4+<200/cmm, 36 (10%) had AIDS at presentation. HCV co-infection was present in 80 (23%). 249 (71%) patients received 2NRTI+1NNRTI, 59 (17%) 2NRTI+1PI/r, 22 (7%) 2NRTI+1PI, and 22 (7%) different regimes. Mean (SD) baseline values were: CD4+ count=197 cells/cmm (144), %CD4+=12.8% (7.8), CD4/CD8 ratio=0.24 (0.19). 197 (56%) patients achieved EIR with an incidence of 0.15 (95%CI 0.13-0.17) per PYFU and an estimated median time of 1999 (95%CI 1658-2302) days. Increasing absolute CD4+ and decreasing CD8+, or increasing %CD4, or increasing CD4/CD8 ratios at baseline were all independent predictors of EIR. At the model with CD4/CD8 ratio as independent variable, older age (HR=0.73 per 10 years, 95%CI=0.61-0.88; P=0.001) and increasing CD4/CD8 ratio (HR=2.42 per 0.3 points higher, 95%CI=1.99-2.95; P<0.001) were the only 2 factors associated with EIR. Moreover, increasing number of impaired indicators (absolute CD4, %CD4 and/or CD4/CD8 ratio) inversely correlated with EIR (HR=0.48, 95%CI=0.28-0.85; P=0.01 for 1; HR=0.3, 95%CI= 0.16-0.54; P<0.001 for 2; HR=0.09 95%CI=0.05-0.15 P<0.001 for 3 impaired indicators at baseline). The sensitivity analysis in severe immune-impaired patients confirmed these results. Interestingly, types of HAART regimens (either baseline or time-updated) were not significantly associated with EIR.
Conclusions: Our results indicate that, in determining the time to start HAART, concomitant evaluation of CD4+ and CD8+ counts (or CD4/CD8 ratio) may be more informative than absolute CD4+ count. Letting more indicators of immune status decrease to below cut-offs could be deleterious for EIR. Our results support and may guide the indication of early HAART.

PO 39

Infection 2010; 38 (Suppl. I): 60

Efficacy and safety of Maraviroc in treatment-experienced patients. Personal report

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Background: Maraviroc (MVC) is a small molecule that belongs to a new class of antiretrovirals known as CCR5 antagonists; they can block the virus entry in those cells that express on their surface the chemochinic co-receptor R5.
Methods: from July 2008 to December 2009 40 multiexperienced patients that could have benefit from MVC therapy underwent the TROFILE test to identify the CCR5 tropism; 21 (55%) were positive for R5 receptor, 13 (34%) were "dual/mixed" (mixed phenotype R5/R4), 4 were not referable because of the paucity of viremia or errors in the centrifugation-conservation of the blood sample, and none resulted R4. Two patients died before starting the new therapy, and three subjects were excluded from the Study because they were not adherent to the therapy.
We collected data about the demographic characteristics of the subjects, the history of their HIV infection, and laboratoristic and viroimmunological parameters every three months. The sample was composed as follows: 16 subjects (14 M, 87.5%; 2F 12.5%), mean age 45 years (range 28-56), mean length of HIV infection 15 years (5-25), mean number of therapeutic lines 9 (2-22). At baseline mean HIV RNA was 91962 cp/ml, mean CD4+ lymphocytes count was 282 cell/mmc; the stages of the disease were so divided: A 5 patients (31%), B 6 (38%), C 5 (31%). Maraviroc therapy was associated to NRTI in 7 subjects (43%), to PI in 3 (19%), to NRTI+PI in 6 (38%); raltegravir as integrase inhibitor was used in 11/16 (68.75%).
Results: In 12/16 subjects (75%), HIV RNA became undetectable in 48 weeks of MVC treatment; particularly in 7 was lower than 20 copies/mmc at the 24th week of follow-up. About the remaining 4 patients, 3 had shorter follow-up, even though viremia decreased of at least 1 log since the first observation; and the last one became negative at 21st month of therapy. CD4+ cells count increased on average of 10% in the first three months of observation, reaching 312 cells/mmc, and further of 25% at 24th week. During the following period the immunological recovery was about an ulterior 3%.
Monitoring of transaminases, glucose, total and fractionated cholesterol and triglycerides did not show significant variations than the baseline values. During the Study none adverse event related to the drug was observed, nor treatment failures.
Conclusions: Maraviroc is a safe and effective drug, with an optimal viroimmunological result in multiexperienced HIV patients. The possibility to associate it with different backbones prefigure the hypothesis of extending the R5 tropism test as soon as possible in those subjects.

PO 40

Infection 2010; 38 (Suppl. I): 61

Validation of a sensitive, specific and rapid pharmacogenomic test for the prediction of abacavir hypersensitivity reaction: detection of HLA- B*5701 by Real-Time PCR

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Background/Objectives: International HIV treatment guidelines recommend HLA-B*5701 typing before abacavir (ABC) administration, in order to reduce the incidence of ABC hypersensitivity reaction, the major cause of early therapy discontinuation. Different technologies are available to detect individual HLA types that are routinely used for characterization of tissue compatibility during organ transplantation, such as DNA sequence-based typing (SBT) or sequence specific oligonucleotide probe (SSOP) method with additional DNA sequencing for patients screened as positive with the probes. However, these approaches are time consuming, expensive and not readily available. An alternative method has been developed, validated, and it has been widely diffused for a more rapid screening of HLA-B*5701 positive patients by Mallal's group. This method is based on identification of the HLA-B*5701 allele by sequence specific primers (SSP) and semi-quantitative PCR [Martin AM et al., Tissue Antigens 2005]. Considering that most of the standard semi-quantitative PCR techniques have been replaced by real-time (Q)-PCR, in the present study we have validated an alternative screening test based on the SSP method but using Q-PCR to detect the amplification products.
Methods: Two sets of sequence specific primers were designed, and amplification detected by real time (Q)-PCR. A panel of 28 samples was analyzed in a single-blinded fashion, results were compared with previous typing, and 100% of concordance was found. These data were used to further standardize the method and analyze a panel of 80 samples enriched in HLA-B*5701 positive samples.
Results: A total of 108 samples were single-blind analyzed, and 41 samples were identified as positive. Complete agreement, with Kappa = 1 (SE = 0.0962, $p<0.0001$), was found with a validated methodology, consisting of low-resolution sequence specific oligonucleotide (SSO)-PCR, followed by high resolution SSO-PCR carried out on the HLA-B*57 positive samples.
Discussion: In the present study, we have developed and validated specific test for HLA-B*5701 detection using Q-PCR. Our strategy is therefore rapid, allowing the processing of 30 samples in 24 hours, is sensitive and specific, inexpensive in comparison to already available alternatives, and can be easily implemented into routine clinical practice.

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Infection 2010; 38 (Suppl. I): 61

Efficacy and Safety at 48 weeks of Once-daily (qd) versus Twice-daily (bid) Darunavir/ritonavir (DRV/r) in Treatment-experienced HIV-1-infected Patients with no DRV Resistance-Associated Mutations (RAMs) in the ODIN trial

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Background: ODIN (TMC114-C229) is a Phase IIIb, randomized, open-label study comparing efficacy, safety and tolerability of DRV/r 800/100mg qd vs DRV/r 600/100mg bid at week 48 in treatment-experienced HIV-1-infected adult patients with no DRV RAMs.
Methods: Patients had HIV-1 RNA >1,000 copies/mL, CD4 count >50 cells/mm^3, no DRV RAMs and were receiving a stable HAART regimen for ≥12 weeks at screening. Patients were stratified by HIV-1 RNA (> or ≤50,000 copies/mL) and randomized to either DRV/r 800/100mg qd or DRV/r 600/100mg bid plus optimized NRTI backbone regimen (OBR, ≥2 NRTIs). Primary objective was to demonstrate noninferiority (with noninferiority margin of 12%) of DRV/r 800/100mg qd vs DRV/r 600/100mg bid in confirmed virologic response (HIV-1 RNA <50 copies/mL [intent-to-treat/time-to-loss of virologic response; ITT-TLOVR]) at Week 48. Virologic failures were

Week 48 parameter, n (%)	DRV/r 800/100 mg qd + OBR (n=294)	DRV/r 600/100 mg bid + OBR (n=296)	% difference qd – bid (95% CI)
HIV-1 RNA <50 copies/mL (ITT-TLOVR)	212 (72.1)	210 (70.9)	1.2 (-6.1 to 8.5)
HIV-1 RNA <50 copies/mL (Per protocol-TLOVR)	190 (73.4)	200 (72.5)	0.9 (-6.7 to 8.4)
Virologic failures	65 (22.1)	54 (18.2)	3.9 (-2.6 to 10.3)
Total discontinuations	41 (13.9)	48 (16.2)	
Discontinuations due to AEs	10 (3.4)	14 (4.7)	
Serious AEs	16 (5.4)	27 (9.1)	
Grade 3–4 AEs	23 (7.8)	45 (15.2)	
Grade 2-4 AEs at least possibly related to DRV/r (≥2% incidence in either arm)			
Nausea	11 (3.7)	13 (4.4)	
Diarrhea	11 (3.7)	11 (3.7)	
Vomiting	7 (2.4)	9 (3.0)	
Treatment-emergent Grade 2-4 lipid/liver lab abnormalities (≥2% incidence in either arm)			
Triglycerides	15 (5.2)	31 (11.0)	
Total cholesterol	29 (10.1)	58 (20.6)	
LDL cholesterol	28 (9.8)	47 (16.7)	
ALT / AST	5 (1.7) / 6 (2.1)	10 (3.5) / 10 (3.5)	

determined using a TLOVR non-virologic failure censored-imputation method.
Results: 590 patients (36% female; mean age 40y) received once-daily (n=294) or twice-daily (n=296) DRV/r plus OBR. Baseline characteristics were well balanced across treatment arms. Mean overall baseline HIV-1 RNA was 4.16 log10 copies/mL and median CD4 228 cells/mm^3. Overall, 46% were PI naive and 13% were NNRTI naïve; 86% were susceptible to 8 PIs (excl. RTV); 71.7% were susceptible to 2 NRTIs in their OBR.
At Week 48, 72% qd vs 71% bid DRV/r patients had HIV-1 RNA <50 copies/mL; difference in response = 1.2% (95%CI = -6.1 to 8.5%), establishing noninferiority (p<0.001). Median CD4 increases (LOCF) were 100 and 94 cells/mm3 with DRV qd and bid, respectively. Out of all virologic failures with baseline and endpoint genotype (n=102), only one patient developed primary PI RAMs (qd arm).
Conclusions: Once-daily DRV/r 800/100mg was noninferior to DRV/r 600/100mg bid over 48 weeks. The incidence of lipid elevations with once-daily DRV/r was approximately half that of twice-daily DRV/r. These findings support use of once-daily DRV in treatment-experienced HIV-1-infected adult patients with no DRV RAMs.

PO 42

Infection 2010; 38 (Suppl. I): 62

In vitro analysis of antiretroviral treatment on Natural Killer cells from healthy uninfected donors: an HIV-1 Post Exposure Prophylaxis model of immunomodulation

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Background: NK cells play important role in control of intracellular pathogens. NK cell phenotypic and functional alterations in HIV-1 infected patients are partially restored by anti-retroviral treatment (ART). In vitro effects of anti-retroviral treatment on NK cells derived from healthy uninfected donors are poorly studied. This aspect could be of particular interest in the occupational HIV Post Exposure Prophylaxis (PEP), but at the moment, there no data on short-term effects of ART on the innate immune compartment in exposed uninfected subjects.
Materials and methods: We enrolled 10 healthy uninfected donors from local blood bank. Peripheral Blood Mononuclear Cells (PBMCs) were separated by gradient centrifugation and cryopreserved until processed. NK cells were isolated by immunomagnetic separation and polyclonal activated NK cell populations were obtained. Three and - four colour cytofluorimetric analysis we performed to analysed expression of activatory and inhibitory receptors on polyclonal activated NK cell population cultured in presence or absence of anti-retroviral drugs NRTI (Tenofovir and Lamivudine) and PI (Lopinavir)
Results and Discussion: Natural Cytotoxicity Receptors (NKp46, NKp30 and NKp44; NCR) and inhibitory receptors were studied after supplementation with NRTI or PI drugs at concentrations attained in vivo during standard ART regimens.
In vitro treatment resulted in conserved NKp46 expression, down-regulation of NKp30 and HLA-DR and increased LIR-1/ILT2 induced by PEP-like regimens in terms of proportion of positive cells and Mean Fluorescence Intensity (MFI). Control treatments for comparative analysis were represented by culture medium alone or culture medium supplemented with Metilprednisolone. In vitro supplementation with ART resulted in immumodulatory effects on healthy donor NK cells. These interesting data need further studies to investigate mechanisms involved in immunomodulatory effects and consequences in control of intracellular pathogens infection after HIV-1 PEP and after standard ART in infected patients.

PO 43

Infection 2010; 38 (Suppl. I): 62

Pharmacokinetics (PK) of once-daily etravirine (ETR) without and with once-daily darunavir/ritonavir (DRV/r) in antiretroviral-naïve HIV-1 infected adults

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Background and Objectives: ETR is potent against wild-type HIV (protein-binding adjusted EC50 of 4ng/mL), has a terminal elimination half-life of 30–40 hours, and is a candidate for once-daily (QD) dosing. In healthy volunteers, ETR AUC was similar, Cmax was 44% higher and Cmin was 25% lower for QD vs. twice-daily dosing (Ann Pharmacother 2008; 42:757-65). Once-daily DRV/r was shown to be effective and well-tolerated in antiretroviral (ARV)-naïve patients (AIDS2008;22:1389-97). This multicenter, open-label Phase IIa trial evaluates PK and short-term safety and efficacy of ETR 400mg QD plus TDF/FTC 300/200mg QD without and then with DRV/r 800/100mg QD.
Methods: ARV-naïve adults with HIV-1, no evidence of resistance to study drugs, and without HBV/HCV co-infection were eligible.Subjects received ETR 400mg QD with TDF/FTC 300/200mg QD for 14 days, then added DRV/r 800/100mg QD on days 15–28. ETR was discontinued days 29–42. Intensive PK sampling was performed over 24 hours on day 14 for ETR, and day 28 for ETR, DRV and ritonavir (RTV). All doses were administered following a meal. PK parameters were determined using a non-compartmental model with extravascular input and evaluated by least squares mean (LSM) ratios with 90% confidence intervals (CI).
Summary of results: Twenty-three subjects (20 men) enrolled: nine Black, nine Caucasian and five Hispanic with mean age 35.9 years; mean baseline (BL) viral load (VL) 4.2log10 copies/mL; median BL CD4 402 cells/mm^3. DRV PK was slightly higher and RTV PK slightly lower when compared to historic control (ARTEMIS week 4 PK study). Mean VL decline was 1.7 log10 copies/mL at day 14 (n=21) and 2.0 log10 copies/mL at day 42 (n=20). Median CD4 increase was 56 cells/mm^3 (day 42). Most common treatment emergentAEs were nausea (n = 4), headache (n=3), rash (n=3), and flatulence (n=2). No seri-

Table 1:

Parameter,mean (SD)	Day14 ETR+TDF/FTC n=21		Day28 ETR+TDF/FTC+DRV/r n=20*	
	ETR	ETR	DRV	Ritonavir
C_{max},ng/mL	790(287)	801(327)	7008(1514)	465(231)
C_{min},ng/mL	233(130)	236(168)	1049(616)	27(21)
AUC24 h,ng•h/mL	10410 (4186)	10720 (5459)	76130 (22080)	4128 (1854)

*n=19 for AUC24h

ous or grade 3/4 AEs were reported; no AEs led to discontinuation. The impact on metabolic parameters was small when ETR was given with or without DRV/r. (Table 1).
Discussion: Addition of DRV/r QD to ETR QD had no significant impact on ETR PK and exposure to ETR was adequate with and without DRV/r. PK data and short-term safety and efficacy support further clinical investigation of ETR 400mg QD in HIV-1 infected patients.

PO 44

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TMC278 shows favorable tolerability and non-inferior efficacy compared to efavirenz over 192 weeks in HIV-1-infected treatment-naïve patients

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Background: In the randomized Phase IIb trial, TMC278-C204 (NCT00110305), all three blinded once-daily (qd) doses (25, 75 or 150mg) of the investigational next-generation NNRTI, TMC278, showed non-inferior antiviral efficacy but more favorable tolerability than the open-label control, efavirenz 600mg qd, over 96 weeks in 368 HIV-1-infected treatment-naïve patients. The trial was extended to investigate long-term safety and efficacy. 192-week results are presented.
Methods: No TMC278 dose-response relationships for safety or efficacy parameters were observed after 96 weeks. All TMC278-treated patients were switched to open label 75mg qd at Week 96. At ~Week 144 (range: 131–157 weeks), all TMC278-treated patients were switched to 25mg qd, the selected Phase III dose, since this dose gave the best benefit-risk balance.
Results: TMC278 continued to show non-inferior antiviral and immunological efficacy compared to efavirenz over 192 weeks (Table). The majority of adverse events (AEs) for both NNRTIs were observed in the first 48 weeks of treatment. No new types of AEs were noted between Weeks 48 and 192. At Week 192, the incidences of any grade 2–4 AE and most commonly reported grade 2–4 AEs at least possibly related to TMC278 or efavirenz were lower with TMC278 than with efavirenz (Table). TMC278 was associated with statistically significant smaller lipid increases than efavirenz.

Table

Week 192 virologic and immunologic response	All TMC278[a] (n=279)	EFV 600mg qd (n=89)[b]
Confirmed viral load <50 copies/mL (ITT-TLOVR algorithm), % (95%CI)	59 (53–65)	61(50–71)
Mean(SE) increase from baseline in CD4 cell count, cells/mm^3	210(12)	225(21)
Summary of treatment-emergent AEs at the time of the Week 192 analysis		
AEs (%)		
Any grade 2–4 AE at least possibly related to TMC278 or EFV	24**	44
Any serious Aes	16	17
AEs leading to discontinuation	14	12
Grade 3 or 4 laboratory abnormalities	31	29
Most common grade 2–4 AEs[c] at least possibly related to TMC278 or EFV (%)		
Nausea	4	6
Dizziness	1	3
Headache	1	2
Abnormal dreams/nightmare	1	3
Depression	1	2
Dyspepsia	1	2
Asthenia	1	2
Somnolence	0.4	2
Vertigo	0.4	2
Rash[d]	0.4***	9
Mean(SD) change from baseline in lipids at Week 192		
Total cholesterol,mg/dL	17(35)***	41(31)
LDL-C,mg/dL	10(30)**	22(31)
HDL-C,mg/dL	5(12)***	11(10)
Ratio TC/HDL-C	–0.1(1.3)	0.002(1.1)
Triglycerides,mg/dL	10(107)**	54(101)

EFV = efavirenz; ITT-TLOVR = intent-to-treat time-to-loss of virologic response; [a]From Week96 to ~Week144, all patients received TMC278 75mg qd and were then switched to TMC278 25mg qd; [b]N=88 for CD4; [c]Observed in ≥2% of patients in either the TMC278 group or EFV group and excluding laboratory abnormalities reported as an AE; [d]Grouped term, including the preferred terms allergic dermatitis, drug eruption, erythema, exanthema, rash, erythematous rash, macular rash, maculopapular rash, papular rash, pustular rash, scaly rash, toxic skin eruption, urticaria, papular urticaria; **p≤0.01; ***p≤0.001 for TMC278 vs EFV Fisher Exact test (AEs); non-parametric Wilcoxon rank-sum test (lipids), post-hoc analysis

Conclusion: TMC278 was shown to be non-inferior to efavirenz in terms of efficacy and was associated with lower incidences of grade 2–4 AEs, including rash and nervous system/psychiatric events, and lower lipid increases over 192 weeks.

PO 45

Infection 2010; 38 (Suppl. I): 64

Abacavir use and cardiovascular disease events: a meta-analysis of published and unpublished data

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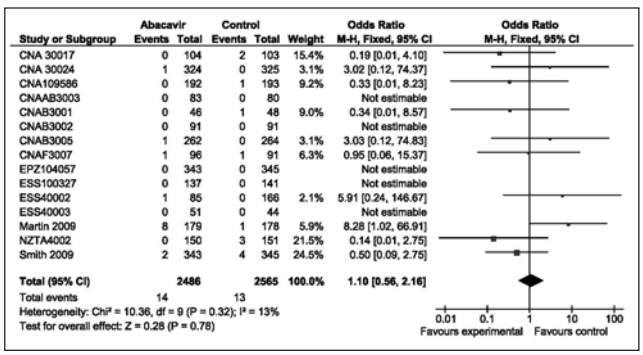
Background: The use of abacavir (ABC) has been associated with an increased risk of cardiovascular disease within the setting of cohort studies and of a randomized trial (RCT). However, no excess risk of myocardial infarction with ABC therapy has been observed in others RCTs and in the aggregated clinical trials database maintained by the manufacturer of ABC. The principal aim of this study is to combine all the evidence from RCTs by means of meta-analysis to estimate the effect of combined antiretroviral therapy (cART) containing ABC on major cardiovascular event.
Methods: A comprehensive search of the available literature was carried out. Information about unpublished trials was attempted by contacting drug manufacturers. Data extracted included: any cardiovascular events and overall mortality. We used a conventional Mantel-Haenszel method, with odds ratio (OR) and 95 % confidence intervals (CI) or, in the presence of heterogeneity, a random-effect model.
Results: We obtained data from 36 RCTs conducted from 1996 to 2009, comparing cART with ABC to other NRTI . Data of 13 RCTs with at least 24 wks of ABC exposure were available from HIV data repository of the manufacturer of ABC. Data on cardiovascular events were available from 16 RCTs (5,051 pts; 1,045 from published trials and 4,006 from data repository), data on mortality from 23 published RCTs (6,372 pts). Compared to the controls, ABC use did not increase the occurrence of major cardiovascular events (OR, 1.10; 95 % CI, 0.56-2.10, see figure), and the overall mortality (OR, 1.84; 95 % CI, 0.71-4.76).



Conclusions: Observational studies are prone to biases and should be interpreted with caution given the potential for confounding. By contrast, randomized trials provide stronger evidence than do observational studies. Our meta-analysis was based on RCTs, and did not show an increase in the occurrence of major cardiovascular events and overall mortality in ABC recipients.

PO 46

Infection 2010; 38 (Suppl. I): 64

Dual Therapy with Raltegravir and boosted or unboosted Protease-Inhibitor as NRTI-sparing regimen: Experience of Infectious Diseases Unit in Pistoia Hospital

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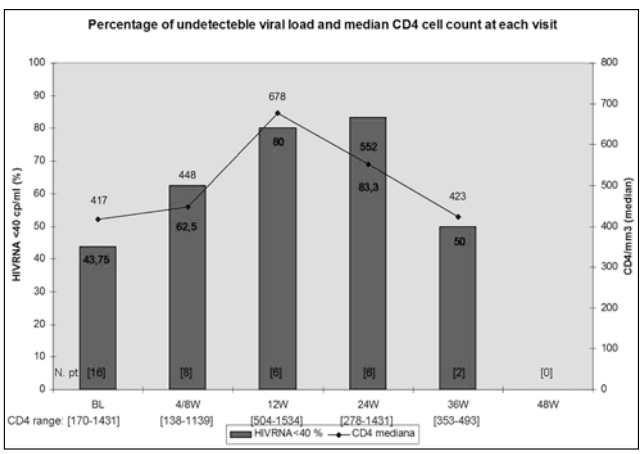
Background: NRTI-sparing regimens are not recommended by guidelines with the exception of documented intolerance to all NRTIs and are an attractive option to provide a full active regimen in patients with extensive NRTI resistance. Raltegravir, Darunavir boosted, Atazanavir boosted and unboosted have a favourable toxicity profile, are effective and well tolerated.
objectives: To evaluate efficacy and safety of a dual therapy in antiretroviral-experienced population and to assess proportion of patients with HIVRNA <40 copies/ml and CD4 cell count variation at week 36.
Methods: Retrospective analysis of a cohort of patients treated with a dual therapy of raltegravir plus boosted or unboosted Protease-Inhibitor, among 318 patients followed in our centre. Adult patients on HAART were switched to dual therapy due to resistance mutations or tolerability/toxicity issues. Reported data have been analysed up to 14 march 2010.
Results: Sixty patients were enrolled. All but two were Caucasians, mean age was 50 (range 43-80) years, 3 (18%) were females and 5 (31%) were HCV coinfected. At switching, median and nadir CD4 counts were 417 (range 170-1431) and 183 (range19-670) cells/µl. Four patients switched from NNRTI-, 3 from PI- and 9 from boosted PI based regimens. Four patients switched due to virologic failure, while 11 for tolerability/toxicity issues and one for simplification. The mean number of NRTI-associated mutations were 1 (range 0-7), while plasma HIV RNA was < 50 copies/µl in 7 (43,75%) patients. After a median follow up of 12 weeks (range 4-36w), plasma HIVRNA was < 50 copies in all except in two patient who viral load was detectable, without INSTI-mutations, due to low compliance. At 24 weeks the median CD4 count increment was 135 cells/µl. No new grade 3 or 4 laboratory value was reported. Therapy was well tolerated and no patient discontinued the regimen. Two patients, with end-stage liver and renal disease, died to HCV-related liver failure.
Conclusions: According to the others experiences (Ripamonti D., Allavena C. and Capetti A.F.), in our cohort (PTH Cohort: PisToia Hospital Cohort), dual therapy with Raltegravir and boosted or unboosted Protease Inhibitor may be a valid alternative option, as NRTI-sparing regimens, to avoid NRTI long-term toxcity. Dual therapy shows good efficacy and a favourable safety profile. Longer follow-up and comparative trials are desirables to confirm and extend these results.



EPIDEMIOLOGY AND SOCIAL SCIENCES: EPIDEMIOLOGY AND PREVENTION

PO 47

Infection 2010; 38 (Suppl. I): 65

The changing spectrum of risk behaviours among Italian drug user and epidemiology of HIV and HCV infections. Observational data on 11.000 subjects followed from 1980 to 2010 in the San Patrignano residential project

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Sexual and drug related risk behaviors were regulary collected from 1980 to 2010 in drug users who entered the San Patrignano drug free residential facility, and analyzed in relation of the risk of acquiring HIV and HCV infection.
Use of syringes. The number of addicts using drugs through non parenteral route has gradually increased from below 5% (subject entered before 1997) to 30% (2007). Also considering heroin addicts, a drug tipically injected, less than 5% of those starting addiction before 1990 were non-injectors, whereas the percentage has increased thereafter: 10% for those starting in 1991, 23% for those starting in 1995, 42% for those starting in 2003, and 67% for those starting in 2007.
Sharing of needles or syringes. During the years a decreasing percentage of intravenous drug users (IDVUs) reported "frequent" sharing (from about 40% in 1986 to 10-15% in the last ten years). Most of IDVUs continues to report "sporadic" sharing, that generally means sharing with the partner or with a trustworthy friend. The percentage of IDVUs referring that "never" shared syringes was below 20% before 1985 (the year of HIV serological test) and is stable (40-50%) in the last 10 years.
Sexual risk. We don't ask our guests about sexual orientation, so we have no data on this topic. "Casual" sexual intercourse is common in drug users (59% of males and 63% of females), independently from prostitution, and the percentage has remained quite stable in the years.
Most of drug using females (85,7%) have their stable relationships with male drug addicts, whereas only 38,8% of drug using males have stable relationships with drug using females.
Not considering prostitution, 12,7% of males and 8,6% of females reported regular prophylactic use, whereas 58,2% of males and 63,8% of females reported "never" using prophylactics. The percentage of regular use of prophylactic has only partially increased in the years (below 10% before 1995 to about 20% in the last years).
Epidemiology of HIV and HCV infections. In Italy, HIV infections diffused among intravenous drug users from 1980 to 1985 (data on about 13,000 subjects), beginning to decline thereafter, when the test become available. The prevalence of HIV infection was 10% in those admitted in1981, peaked to 56% in 1986, and returned to 10% in 1999. Disappointgly the prevalence remained stable to about 10% from 1999 to 2007, confirming the persisting of high risk behaviours in a subgroup of drug users.
Since 1981 to 1999 more than 90% of drug addicts have been exposed to HCV infection, and infection generally occurs very early, in the first years of intravenous drug use. Exposure is clearly associated with syringes use, but not necessarily to syringes exchange; probably some other injected related practice play a role in the diffusion of HCV infection (sharing of spoons and/or filters? Front-loading or after-loading of syringes?).
The recent decrease of prevalence of HCV infection (< 60%), observed in those subjects entered in the Community in the last 3 years is clearly associated with increase numbers of addicts not injecting drugs (also heroin). We suggest that the diffusion of HIV infection occurs in drug users also through unprotected sexual intercourse: the prevalence of HIV infection is higher in females drug users than in males (26,9% vs 18,6%) and this higher prevalence has remained stable over the time. Moreover we have observed cases of HIV infection in non using syringes drug addicts, and the number of these cases are increasing in the last years. More detailed data on epidemiology of HIV and HCV infections, including the role of sexual transmission, will be presented.

PO 48

Infection 2010; 38 (Suppl. I): 65

Different strategies for Tuberculosis Screening in HIV positive Immigrants and Refugees

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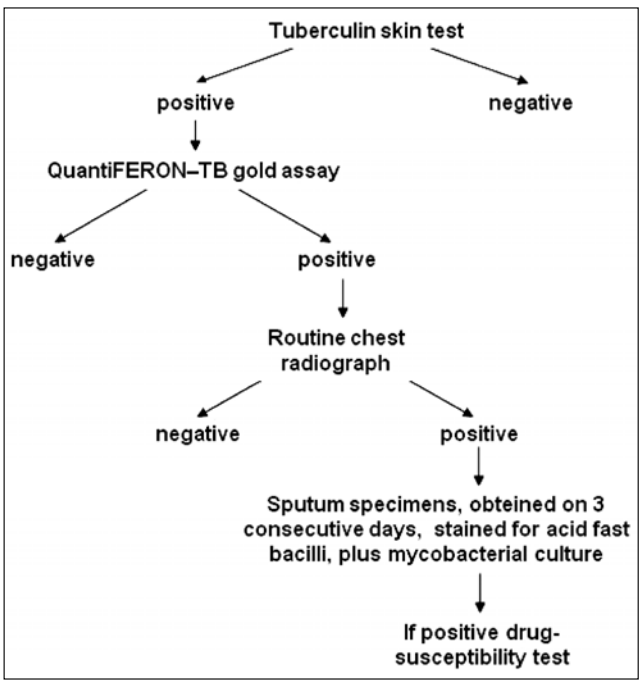
Movement of people between countries has a large influence on the incidence of tuberculosis (TB) in North America and Western-Europe. The concerns around increasing rates of TB among HIV positive immigrants in developed countries and implications for overstretched public-health services, has led to calls for renewed thinking about policies on migrant. Different TB screening strategies among foreign-born HIV positive individuals were published in the last months sparking debate among the scientific community. Screening for TB is primary performed with the aim of detecting the active disease. Anyway TB screening also provides an opportunity to offer preventive therapy for latent tuberculosis infection (LTBI). Because 5 to 10 percent of persons with LTBI are at risk of progressing to active disease, identification and treatment of LTBI are essential for the elimination of TB. Today, in many of developed countries, TB screening policies for immigrants request screening strategy, which uses tuberculin skin test (TST) or chest radiograph as the first step of screening.
Anyway the results of these screening algorithm showed some limitations regarding the target of identifying LTBI. For example Liu et al reported that on follow-up evaluation of patients undergone overseas screening for TB in United States, no TB was diagnosed in 36.6% of those who had received an overseas diagnosis of inactive TB. In addi-



tion it was possible to have overestimated LTBI cases in children, since the screening algorithm used the TST only. For these reasons an alternative algorithm for the TB screening in HIV immigrants is available (Figure 1). It is based on the use of interferon gamma release assays QuantiFERON–TB Gold (QFT-TBG) that offer a second line accurate screening approach for identification of individuals with LTBI in individuals with positive TST results. In fact this test has been shown to have a sensitivity of 90% and a specificity of 93% to detect LTBI. Moreover, although BCG vaccine is extensively used in many developing countries, the interferon gamma production induced by ESAT-6 and CFP-10 is virtually absent in BCG vaccinated unexposed individuals with positive TST results.
Screening for LTBI in populations immigrating to low-incidence countries remains a challenge, anyway the QFT-TBG have an important role in the TB screening limiting the number of HIV immigrants receiving unnecessary preventive therapy for LTBI, reducing the risk of severe adverse effect related to nine months-long treatment for LTBI and resulting in cost saving to the Sanitary System.

PO 49

Infection 2010; 38 (Suppl. I): 66

Sexuality, pregnancy and procreation desire among HIV+ patients in Ouagadougou, Burkina Faso

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Background: The introduction of antiretroviral drugs in resource limited settings has changed the life scenarios of many HIV+ patients. This study aims to assess sexual and reproductive behaviours of a cohort of HIV+ patients in Ouagadougou, Burkina Faso.
Methods: After consensus, a questionnaire was administered to a representative cohort of HIV+ patients in Ouagadougou. Data analysis was done through Epi.Info 3.5 software.
Results: The questionnaire was submitted to 280 patients, 52 (18.6%) men and 228 (81.4%) women. Patients with partners were 66.8% (187/280). Among these 121/187 (64.7%) partners were tested (81 resulted positive and 40 negative). Declared sexual behaviour was as follows: (i) abstinence (14/187; 7.5% of the patients with partners), (ii) systematic use of condoms (107/187; 57.2%), unprotected sexual relations (66/187; 35.3%). Among the latter, 34/81 have sexual relations with HIV+ partner, while 6/40 with negative partner; 26/66 have sexual relations with not tested partner.As many as 47/93 (50.5%) of the subjects without a partner declared the desire of a stable sexual relationship with a negative (3/47), positive (17/47) or irrespective of serostatus (27/47) partner. As many as 57.9% of the sample would like to have children, 62.8% among patients with partners and 49.5% among those without partners ($p< 0.05$).
The children average number among women who wish to have more children is 1.7 (SD±1.5) while it is 3 (SD±1.8) among women who do not wish other children. No relevant differences are observed between the two groups concerning the sex, the follow up site, the education and the followed therapy. Pregnancy occurred in 76/228 (33.3%) women during follow-up.
Conclusions: In the urban context of Burkina Faso, we need to increase family planning services in order to answer to our patients' reproductive needs and decrease the risk of HIV mother to child transmission.

PO 50

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AIDS-defining opportunistic infections in the HAART era: are these again a challenge?

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Background: Introduction of HAART and related immune reconstruction, observed in the majority of treated subjects, dramatically reduced the HIV mortality and the incidence of AIDS-related opportunistic infections (OIs). However, HAART has not modified the prognosis quoad vitam of first AIDS-defining OI. Today, many OIs are less frequent than before the HAART era, others are atypically presenting and can be favoured by the immune reconstruction in course of HAART. Published data are consisting with a correlation between high levels of HIV-VL and absolute CD4+ count (but not CD4+ percentage) and risk of developing an OI.
Methods: We have evaluated the incidence of first OI AIDS-defining in our HIV cohort after introduction of HAART; we have also evaluated the outcome of acute OIs and the immune and virological state at the OI diagnosis.
Results: In the period ranging from January 1997 to March 2010 we consecutively observed 253 cases of AIDS, 39 males and 214 females. Most of these were heterosexuals (182), 38 drug addicts, 21 homosexual men; in 11 patients risk factors for HIV were unclear. In 173 cases (67.2%) an OI was first manifestation of HIV infection. Pneumocistys jiroveci pneumonia (PJP) (71 cases), oesophageal candidiasis (57), tuberculosis (41), toxoplasmosis of the brain (35), MAC infections (13) and CMV retinitis (10) were the most frequent OIs diagnosed. 54/253 patients (21.3%) died due to complications of an OI. PJP was the principal cause of death in our patients. If the study period is divided in two parts, before and after 2004, the percentage of OIs related deaths is increasing in the last period (27.6% vs 16.1%) ($P<0.05$ – X2 test) despite a stable number of observed cases (123 vs 124 respectively). Incidence of PJP and toxoplasmic encephalitis did not decrease during all the study period; conversely a significant decrease was observed for others OIs or AIDS related malignancies such as candidiasis, CMV retinitis, and Kaposi's sarcoma. A decrease was also observed in tuberculosis' incidence despite the high number of Africans observed. One half of the 253 with AIDS-defining first OI had a severe immune suppression (<50 CD4+/mcl); most of these also had high HIV-VL (>900000 couples/ml).
Conclusion: Our observation shows that, in the HAART era, first AIDS-defining OI represents again a challenge in the management of AIDS patients. In fact, the increasing number of late HIV presenters is an important reservoir for developing of OIs; prognosis of some OIs doesn't seem to be influenced by HAART; moreover, OIs related deaths are increasing in the last years probably due to the amount of AIDS presenters subjects. High levels of HIV-VL and low absolute CD4+ count increase the risk of developing OIs. Our data underline the importance of early HIV diagnosis to promptly improve the immunity of patients using efficacy HAART.

PO 51

Infection 2010; 38 (Suppl. I): 67

Attention functioning and memory impairment are correlated to an higher risk of self-chosen discontinuation of cART

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Objective: To estimate determinants of attention functioning and memory impairment in HIV-infected people taking cART as perceived by physicians.
Methods: Thirty physicians were anonimously asked to participate into a survey (POSIT, (Popolazione Sieropositiva Italiana) in December 2009 in cooperation with Nadir Foundation, including items on demographic, social, clinical characteristics of patients. Each physician answered items of about 40 patients in 30 Italian Clinical Centers. Adherence was defined by physicians as optimal (100%) or suboptimal (<99%). Attention functioning and memory impairment, outcomes of the study, were investigated with an appropriate question (Have you perceived any impairment in the attention functioning or memory of your patient?).
Results: 1146 patients were represented in the survey, 31% females, 22% men having sex with men (MSM), 7.5% immigrants, mean age 43.5 years (SD 10.5); 51% smokers, 52% poor educated (as having <8 years of formal schooling). 27% of patients were perceived as suboptimally adherent; 32% had self-chosen discontinuation of cART (scDisc). 13.8% of patients were perceived by the physician to be moderately or seriously depressed. 23% were perceived having an attention functioning impairment and 22% were perceived having a memory impairment. At multivariable analysis, age (HR 1.06; 95% CI 1.04-1.09; p<0.0001), heavy alcohol drinkers (HR 3.78; 95% CI 1.33-10.71; p=0.01), depressed people (HR 3.79; 95%CI 2.17-6.62; p<0.0001), and scDisc (HR 2.22; 95%CI 1.38-3.58; p<0.001) were correlated to having an attention functioning impairment while age (HR 1.05; 95% CI 1.03-1.08; p<0.0001), heavy alcohol drinkers (HR 3.02; 95% CI 1.12-8.17; p=0.03), at most advanced line of HAART (HR 1.16; 95%CI 1.04-1.29; p=0.007), depressed people (HR 2.95; 95%CI 1.70-5.09; p=0.0001), and scDisc (HR 1.66; 95%CI 1.03-2.68; p=0.037) were correlated to having a memory impairment.
Conclusions: Attention functioning and memory impairment are significantly correlated to self-chosen discontinuation of cART.

PO 52

Infection 2010; 38 (Suppl. I): 67

H1N1 vaccination in HIV patients

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Objectives: In the fall 2009, due to the H1N1 influenza-virus pandemic, Lombardy Region asked for the collaboration of the General Hospitals of the Region to vaccinate specific at risk populations. The Authors present the results of the vaccination campaign in the HIV+ population of the Infectious Diseases Department of A.O. Spedali Civili (Brescia, Italy).
Methods: The vaccination period was from 16th of November 2009 to 26th of February 2010. All patients were interviewed about contraindications to the vaccine (allergy, acute diseases, drugs, previous vaccinations) and all patients without contraindications were requested to sign an informed consent. We reviewed the data of the consents.
Results: At our Department on 31st December 2009 3300 HIV+ patients were in follow-up (M 2361, 71.5%). During the vaccination period 2454 of them (74.4%) were evaluated and vaccination was offered to 861 (35.1%) (M 598, 69.5%); 633 out of these (73.5%) were vaccinated (M 439, 69.4%). The compliance to the vaccination was similar in Males and Females (OR = 0.98, IC95% 0.70-1.38), but it decreased during the period (November 280/360, 77.8%; December 290/370, 78.4%; January 46/106, 43.4%, February 5/25, 20.0%; P < 0.0001). There was also a decrease in the proportion between proposed vaccinations and evaluated patients (November 360/564, 63.8%; December 370/744, 49.7%; January 106/703, 15.1%, February 25/443, 5.6%; P < 0.0001).
Conclusions: HIV+ patients showed a good compliance to vaccination comparing to the general population; patients compliance, as well as physicians motivation, decreased with the decreasing of the risk perception after December 2009. However, in a clinical context not confident with the prevention activities, the vaccination was offered to 50-60% of patients until the emergency was perceived.

*H1N1 Vaccination Group: R. Allegri, A. Bergamasco, S. Casari, F. Castelnuovo, I. El-Hamad, M.A. Forleo, F. Gatti, M. Gulletta, A. Matteelli, P. Nasta, G. Paraninfo, K. Prestini, M. Puoti, E. Quiros, S. Rossi, L. Signorini, A. Spinetti, R. Stellini, L.R. Tomasoni, C. Torti, S. Zaltron.

PO 53

Infection 2010; 38 (Suppl. I): 67

Trend in the period 1998–2008 of primary HIV infection in the Modena cohort

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Background: Epidemiological data on new HIV infections are lacking in Italy due to the absence of a National Surveillance System. In Modena it is active since 1985 a surveillance system which provides information on the epidemiological changes in our region. In the present study we considered only patients with a diagnosis of primary (PHI) or recent HIV infection in order to evaluate changes in epidemiology of HIV infection in the period 1998-2008.
Methods: Among 869 patients with a diagnosis of HIV infection in the period 1998-2008 studied in the Modena cohort there were 80 seroconversions (9.2%).
Analyses were restricted to persons with a positive HIV-antibody test and a negative HIV test in the previous 12 months and patients with a diagnosis of PHI as defined by Centers for Disease Control.
Results: Epidemiological trends in the 2 study periods are shown in Table 1.
In particular, in the period 2004-2008 there was an important decrease of new infections among drug users and an increase among men who have sex with men (MSM). There was also an increase among subjects of non-Italian origin indicating an infection acquired in our country.

Table 1. Epidemiological data and trend of subjects with recent HIV infection in the Modena cohort

	1998-2003	2004-2008	Tot	P
Males	323 (66.3%)	258 (67.5%)	581 (66.9%)	0.706
Risk cathegories				
Drug users	104 (21.4%)	28 (7.3%)	132 (15.2%)	
MSM	131 (26.9%)	132 (34.6%)	263 (30.3%)	<0.001
heteroseuals	252 (51.7%)	222 (58.1%)	474 (54.5%)	
Foreign origin	131 (26.9%)	135 (35.3%)	266 (30.6%)	0.007
Age	35 (29-41)	37 (30-44.2)	36 (29-43)	0.004
PHI	28 (5.7%)	52 (13.6%)	80 (9.2%)	<0.001

Considering the rate of PHI, in the period 2004-2008 vs 1998-2003 there was an important increase among MSM: (27.3 vs 7.6) vs heterosexuals (6.3 vs 1.6) and drug users (7.1 vs 13.5) (p<0.001 by each period).
Conclusions: In the Modena cohort there has been an epidemiological change among new HIV infections in the last 10 years. MSM and subjects of foreign origin should be addressed by specific national campaigns, while currently they address heterosexuals, only.

PO 54

Infection 2010; 38 (Suppl. I): 68

Reported HIV-status in TB patients attended in a Infectious Diseases Department in Brescia

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Background: In 1989, CDC recommended that all TB patients be offered HIV testing and, in 2006, called for routine HIV screening of all TB patients after the patient is notified that testing will be performed, unless the patient declines (opt-out screening). In Italy we still perform HIV test on the basis of clinical suspect and of an opt-in strategy.
Objectives: To evaluate prevalence of HIV coinfection and proportion and selected characteristics of subjects not-tested for HIV between tuberculosis patients followed in a Department for Infectious Diseases in Italy.
Methods: Retrospective study including all culture-confirmed cases of TB followed at the Department for Infectious Diseases of Brescia, Italy, from 2004 to 2009.
Results: A total of 526 subjects were included in our study. 67 patients (12.7%) resulted HIV positive, while 114 patients (21.7%) were not tested for HIV.
HIV coinfection was significantly more prevalent in males than in females (15.3% vs 8.6%, p<0.05), in Italians than in immigrants (19,4% vs 11,4%, p<0.05) and in people aged 18-65 years (15,2%) than in subjects aged less than18 years (2%, p<0.01) or more than 65 years (2.5%, p<0,05). At multivariate analysis sex was no more significantly associated with HIV status.
Among the 61 HIVab positive subjects for which the data was available, 34 (55,7%) had been found HIV infected just after the diagnosis of TB or simultaneously, while 7 other patients (11,4%) had started TB treatment in the 2 first month after knowing their HIV status.
Percentage of patients with HIV status not-known was higher among females than among males (30,6% vs 16,8% p=<0,01), among Italians than among immigrants (39,8% vs 17,5% p<0,01); it was lower among subjects aged 18-65 years (12,8%) compared to people aged <18 years (64,7%, p<0,01) or > 65 years (65%, p<0,01). At the logistic regression analysis, HIV test coverage was still significantly associated (p<0,01) with sex and age-group, but no more with nationality. Considering the reasons for missing screening, a refusal to do the test has been reported just for 5 on 114 subjects.
Discussion: HIV coinfection rate is quite high among our population, and many patients discover HIV infection when they present with active TB. Physicians have to remember that increased promotion of routine HIV testing among all TB patients, regardless of sex and age-group, would allow health-care providers to know the HIV status of a greater percentage of TB patients and enable them to provide optimal care.

PO 55

Infection 2010; 38 (Suppl. I): 68

Depression in patients with a newly-diagnosed HIV infection

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Background/objectives: The prevalence of depression among persons with newly-diagnosed HIV infection is high and these have nearly twice the risk of developing major depressive disorders.
The objective of the analysis is to identify characteristics of subjects with newly-diagnosed HIV infection associated with depression.
Methods: SENDIH is a cross sectional, multi-center study which involves 14 public counseling and testing sites in Latium, Italy, which investigates patients newly diagnosed with HIV infection. According to the SENDIH protocol, at diagnosis, routine demographic, epidemiological, clinical and laboratory data are recorded, and patients are asked to complete a questionnaire investigating socio-demographic and psycho-behavioural aspects with The Center for Epidemiological Studies-Depression (CES-D) scale assessed psychological distress.
Data on adult patients seen between 2005 and 2010 who were able to complete an interview in Italian and had received an HIV diagnosis at least 6 months prior to recruitment were analyzed.
The association between Depression (CES-D scale) as dependent variable and socio-demographic factors was analyzed though an independent t-test and a one-way ANOVA, because these factors are reportedly associated with depressive symptoms among HIV-infected adults. The total CES-D score was used in our analyses; a score of 16 or higher indicated possible depression.
Results: 657 subjects with a new diagnosis of HIV infection were interviewed and completed the CES-D scale. Of these individuals, 84% were male and the median age was 36 years (range 20-71 years). 80% were born in Italy and 20% were born abroad. 25% received a contemporary AIDS diagnosis and 76% were employed. 48% declared to be heterosexual and 44% homosexual.
A CD4 cell count at HIV diagnosis was available for 651 individuals, with a median value of 382 cells/mmc; 43% had a CD4 count lower than 350 cell/mmc.
The reliability of the CES-D was high (Cronbach's =0.90). 60% of patients were depressed: women are more depressed than men (t655 = -3.915; p<.001); heterosexual subjects are more depressed than homosexual/bisexual individuals (F2,647 = 5.119; p<.006); housewives are the most depressed with respect to other employment conditions (F5,649 = 6.695; p<.001).
Non parametric analysis (U=46288; p<.039) shows that depressed subjects had lower CD4 counts than non depressed individuals.
Discussion: This analysis found that the prevalence of depressive symptoms is high among newly HIV-infected and is also associated with lower CD4 cell count, female gender, heterosexuals and being a housewife.
Clinical experience and recent researches describe the connections between depressive symptoms and medical outcomes: poor outcomes, more rapid progression of HIV/AIDS and impairment in psychosocial functions are related with depression. Therefore persons that have been diagnosed as severely depressed might benefit from receiving a thorough medical as well as psychological support.

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Frequency of early laboratoristic alterations and their reversibility during post exposure prophylaxis to HIV

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Background: The use of an adequate post exposure prophylaxis (PEP) for 4 weeks (usually 2 NRTI+ 1 boosted PI), correlates to a reduction of the expositive risk, but it is not free from developing collateral effects or adverse events. These alterations are frequent but reversible, as showed from clinical and biochemical follow-up of exposed subjects.
Methods: From January 2001 to December 2009 355 subjects came to our ambulatories because of a verified or supposed exposure at risk; 255/355 subjects (about 72%; 179 M, 76 F; mean age 36 years), resulted eligible for PEP with 2 or 3 antiretroviral drugs. In this Study we evaluated the subjects (153/255, 60% of PEPs) who carried out a 28 days triple therapy (2 NRTI+ 1 boosted PI). The protocol provided laboratoristic controls at T0, T15 and T40, to highlight possible drug-induced changes. In these subjects we checked some clinical parameters (AST, ALT, GGT, ALP, bilirubin, creatinine, glucose, amylase, cholesterol and triglycerides), choosing the cases in which at T15 we observed a rise of 30% than T0.
Data on accidents (collateral effects of drugs, blood tests etc.), have been collected anonymously and sent to the Coordination Centre of Italian Registry of Antiretroviral Post-Exposure Prophylaxis (IRAPEP) at National Institute of Infectious Diseases (INMI) in Rome.
Results: We found laboratoristic alterations at T15 in 49/153 accidents (32%), particularly were highlighted 61 total alterations of blood parameters (in the single accident more than one value could be altered). The most frequently changed parameters were: triglycerides (43 times altered, mean increase of 2,1 folds), cholesterol (10 times altered, mean increase of 1,4 folds), ALT (4 times altered, mean increase of 5,4 folds), AST (2 times altered, mean increase of 7,5 folds), and GGT (2 times altered, mean increase of 3,6 folds). In 8 subjects we found at T15 a rise of both triglycerides and cholesterol. The largest gain of triglycerides (871 mg/ml), and cholesterol (376 mg/dl), have been found in subjects with familial dyslipidemia that however started from frankly pathological values at T0. 49/61 (80%) changes resulted reversible at T40, and in none the alterations conditioned the stopping of therapy.
Conclusions: In our experience the frequency of laboratoristic alterations at T15 during PEP, even if it is not negligible (32% of total), is usually reversible at about 10 days from the end of prophylaxis at T40, and does not condition the interruption of therapy. In some particular cases (familial dyslipidemia), should be evaluated PI sparing treatments.

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Counselling and screening for sexually transmitted diseases in a cohort of prostitutes in the north-east of italy

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Background and objectives: Sirio project is dedicated to immigrant Female Sex Workers (FSWs) living in an illegal status and working in the municipality of Verona. Through the use of an outreach mobile unit, the project is aimed at preventing and reducing risky behaviours among the FSWs population and at leading women to social health services in order to get social, psychological and medical support. The purposes of the study are: i) to assess the prevalence of sexually transmitted diseases (STDs) and Hepatitis C virus (HCV) in this cohort of immigrant Female Sex Workers; ii) to evaluate the principal needs in order to set up specific services.
Methods: A cohort of FSWs working in Verona is the subject of the "Sirio" project. An outreach mobile unit approaches the women and a street operator leads them to the health center. There, counselling and screening test are performed. The screening test includes serology for STDs [including Human Immunodeficiency Virus (HIV), syphilis and Hepatitis B virus (HBV)] and hepatitis C virus (HCV).
Results: In the period 1999-2008 the number of women approached to the test is 395: 83,3% of the women comes from Africa (especially Nigeria) and the remainder from Eastern Europe. The mean age is 24,0 (S.D. 3,9). At the test date 83,5% were still on the street, whilst the remaining withdrew from street activity (of which 13,9% from six months and 2,6% from one year). The number of examined subjects per year is variable: 6 women in 1999, 25 in 2000, 30 in 2001, 14 in 2002, 49 in 2003, 46 in 2004, 80 in 2005, 48 in 2006, 47 in 2007 and 50 in 2008.
Out of 395 street FSWs 18 resulted positive for HIV (4.6%), 12 were positive for HBsAg (3.1%), and 8 were positive for syphilis (2,0%); 3 women were found positive for HCV (0.8%). Nine out of 18 women screened for HIV and found positive are followed at our center and received antiretroviral therapy, the remaining (9) dropped out after on average 1 year. In addition to sexual risk, only 1 woman referred drug abuse. The most significant issue raised from the counselling activity is represented by the illegal condition, in addition to being pregnant (23%) and being abused (3%).
Discussion: The prevalence of HIV and HBsAg was high in the whole analyzed cohort; compared to the general population. The reasons that led almost 50% of the FSW to drop out would require further analyses and evaluation.

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Epidemiologic aspects and clinical outcome in a cluster of subjects with a recombinant BF HIV-1 infection

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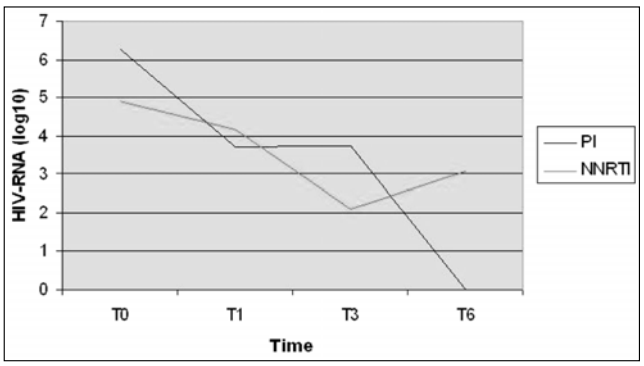
Introduction: Migratory processes determined changes in HIV epidemiology with an increasing role of non-B subtypes; in our area a relevant migratory phenomenon from Africa is occurring, while few migrants come from South America (where F and CRF12-BF are widespread). Recent reports from Northern Italy showed that



CRF12_BF prevalence is < 2%; there are few data about the susceptibility of this CRF to HAART: there aren't in vitro differences in NVP susceptibility for the F subtype, little is known for PIs while no data are available for EFV. The presence of non-B clades was supposed in a cluster of patients with a CD4 count decay and HIV-RNA persistently negative.
Methods: 21 subjects where the routine approach failed to amplify the virus because of polymorphisms in the gag region were identified. The sequencing showed the presence of several non-B subtypes; among these, we found 13 subjects infected with a BF recombinant clade similar to CRF12_BF but with anomalous breakpoints that don't allow to classify it as this CRF. We analyzed their epidemiological aspects and clinical outcome.
Epidemiologic aspects: The prevalence of this recombinant form in our cohort is 2.3%; patients features are summarized in Table 1. This recombinant form has been recently introduced in our area, since it's found in subjects diagnosed after 2006; patient 5-GrU has an older infection but he lived in Milan and moved to Lecco only in 2006. Non-B subtypes are more common among heterosexuals (MSM were 15%, no IVDUs were found). 3 couples are identifiable (subjects 3-4, 6-7 and 8-9); aside from these, no other epidemiological links could be established.
Clinical outcome: The incongruity among immunological and virological status led to a delay in HAART initiation: according to the latest guide lines, there was an average delay of 6.8 months with a mean value of 229 cell/mmc (146-285) at the moment of treatment beginning.
The therapy was seldom started: 4 received FTC/TDF plus NNRTI (EFV or NVP) and 2 FTC/TDF plus ATV/rtv. Genotyping test revealed no mutations on rt, while it found several substitutions on pol: of these, only the M36I is a typical feature of F subtype.
The response was slow: the viral undetectability was obtained at the 6th month with PIs, while the NNRTIs response was even slower and the only failure was subject 9-AlF, who, after less than 6 months of NVP treatment, developed the K103N+Y181C mutations.
Discussion: The diffusion of non-B subtypes is increasing worldwide but their response to HAART is still poor known. Our work suggests that, if good adherence is ensured, PIs have a greater effectiveness rather than NNRTIs for this BF recombinant form: further analyses are needed to recognize more effectively these viral strains and to establish their correct management.

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Characteristics of recent HIV infection among new HIV diagnoses in Turin, Italy

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Background/objectives: The identification of recent HIV infections (RHI) is important for epidemiologic purposes to assess HIV transmission patterns and to evaluate the trend of HIV incidence. The aim of this study was to analyze the characteristics of persons with RHI and to monitor the trend of RHI over time.
Methods: During two study periods (2003-2004 and 2007-2008) serum samples from individuals newly diagnosed with HIV infection were collected in the Infectious Diseases Hospital in Turin. All serum samples were tested for the HIV antibody avidity index (AI); samples with an AI ≤ 0.80 were defined as RHI (≤ 6 months from seroconversion).
Results: In this study, 432 serum samples were collected from newly diagnosed HIV individuals. The number of persons with RHI was 113 (26.2%), and the proportion of RHI significantly increased from 22.1% in 2003-2004 to 30.8% in 2007-2008 (p-value < 0.05).

Table 1. Epidemiological aspects of the BF recombinant clade.

Subject	Age	Sex	Origin	CD4 at diagnosis	Risk factor	Year of diagnosis	CD4 at HAART initiation	CDC state
1-CoA	50	M	Eastern shore Lecco lake	823	Heterosexual	2007	214	B2
2-GaC	40	M	City outskirts	402	Heterosexual	2006	182	A2
3-CeM	28	M	Brianza	669	Heterosexual	2008	146	C3
4-ScS	30	F	Brianza	1059	Heterosexual	2008	266	A1
5-GrU	49	M	Milan	154	Heterosexual	2002	285	C3
6-MoE	54	M	High Como lake	418	Heterosexual	2008	//	A2
7-SaS	55	F	High Como lake	367	Heterosexual	2008	//	B2
8-CaG	45	M	High Como lake	451	Heterosexual	2007	//	A2
9-AlF	31	F	Brazil	565	Heterosexual	2007	283	A1
10-KoT	46	M	Ivory Coast	509	Heterosexual	2008	//	A1
11-NkW	19	F	Kenya	536	Heterosexual	2007	//	A1
12-RoO	47	M	Bergamo	432	Bisexual	2007	//	B2
13-CrG	52	M	Western shore Lecco lake	712	MSM	2009	//	B1

The proportion of RHI was higher among men who have sex with men (MSM) compared to heterosexual individuals (33.0% vs. 21.0%, p-value=0.06). The proportion of RHI among MSM increased from 25.5% in 2003-2004 to 40.7% in 2007-2008, whereas it remained almost stable among heterosexual persons and injecting drug users. The median age of persons with RHI was similar between MSM (35 years) and heterosexual persons (34 years), as well as between 2003-2004 and 2007-2008 (35 years).
A significantly higher proportion of persons who underwent a previous HIV test was observed among RHI (51.3%) compared to those with an established infection (28.5%) (p<0.001). When analyzing the reasons of HIV testing, different proportions of RHI were found: 34.8% among those exposed to unprotected sexual intercourse, 24.5% among injecting drug users, and 11.5% among those screened during pregnancy or blood donation.
Discussion: The proportion of RHI has increased over time in Turin, especially among MSM. However, no changes were observed in the age of HIV acquisition related to sexual orientation and time period. The identification of RHI can be affected by the frequency of HIV testing and this bias should be considered when estimating HIV incidence.

PO 60

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Mortality for bacterial community acquired pneumonia (BCAP) in patients infected with HIV

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Background: recurrent bacterial pneumonia has been considered a cause of AIDS since the expanded European definition was adopted in 1993. The pneumonia is a common cause for hospital admission in HIV infected adults. The use of highly active antiretroviral therapy (HAART) has deeply modified HIV-AIDS related morbidity and mortality, however bacterial community acquired pneumonia (BCAP) still represents one the most frequent infection in HIV infected persons. In east Emilia the influence of combination antiretroviral therapy (CAT) on the outcome of this disease is not well definied.Objective: to study the mortality rate in patients with BCAP infected with HIV hospitalized from 2000 to 2008 and evaluated the presence of risk factors and the influence of CAT receipt on BCAP outcomes.
Methods and results: in a prospective study we have been analyzed 100 BCAP episodes in 86 HIV infected inpatients (76 males and 10 females) of mean age 46,3 years (range 28 – 76) admitted to our Department on Infectious Diseases in three times: from 2000 to 2002 ; from 2003 to 2005 and from 2006 to 2008. 46 patients (53,5%) were in CAT while 40 (46,5%) were not in CAT. The incidence of BCAP was stable with trend to the reduction in last year. Mortality rate was 13,8% from 2000 to 2002, 2,7% from 2003 to 2005 and 7% from 2006 to 2008. Two patients with recurrent BCAP were notified for AIDS. The overall percentage of IVDU was 87,2% and of smokers was 64%. Streptococcus pneumoniae was the most frequently identified pathogen. Time to clinical stability was significantly longer in patients without CAT respect to other. CD4 cell count < 200/mmc was predictors for prolonged illness; while receipt of CAT was protective.Conclusions: in our area the mortality for BCAP in patients infected with HIV is lower as reported in other Italian studies. IVDU and smoking are important risk factors. BCAP mortality seems associated with an advanced immunodeficiency and with severe comorbidities. Strategies for to reduce the mortality should be implemented.

CLINICAL SCIENCES: CO-INFECTIONS AND CO-MORBIDITIES

PO 61

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The diagnostic importance of the bone marrow aspirate in the diagnosis of Visceral Leishmaniasis in patients with HIV infection

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Background: Visceral Leishmaniasis (VL) is an endemic infection in Mediterranean countries, where it has become a frequent complication of acquired immunodeficiency syndrome (AIDS). In HIV+ patients, the coinfection HIV/Leishmaniasis may present with atypical features in addition to the typical form. In this last one, VL has a deceitful course with fever, asthenia, anorexia, weight loss; while pancytopenia and hypergammaglobulinemia are always present. Serological tests, performed for diagnostic purposes, show the presence of anti-Leishmania antibodies. The diagnosis is confirmed by the demonstration of Leishmania amastigotes in tissue samples and bone marrow aspirate is the most often used procedure.
The case that we show, about a patient affected by VL and HIV infection, wants to emphasize the bone marrow aspirate diagnostic importance.
Case report: From 2008 we are taking care, on home care basis, of a 41 year man, ex drug addict, affected by " HIV-1 cat C3 Infection. Cirrhosis HCV-related. Previous tuberculosis of lungs". During one of the visits, the patient referred asthenia, anorexia and weight loss, without fever. Physical examination revealed liver and spleen enlargement. Laboratory examination showed a hemoglobin value of 11.2 g/dL, a leukocyte count of 1,900/ mm3, a platelet count of 90,000/ mm3, a serum gammaglobulin level of 2.4 g/ dL, a CD4+ lymphocyte count of 109 cell/uL (28.54%). The patient, treated many times and with scarce therapeutic options available had started from few weeks a rescue therapy with Retrovir, Tenofovir, Lopinavir/r, Maraviroc and Etravirine. A haemochrome test showed, after two months, a sensitive decrease of haemoglobin value (8.4 g/dL) as well as of white blood cells (leukocytes 1,300/mm3). The Retrovir was suspended since it was thought the worsening in haematological values was due to it. The anti-Leishmania antibodies research was negative in two exams. Because of a further worsening of anaemia, even if the Retrovir administration had been suspended, a bone marrow aspirate was performed and it showed the presence of amastigotes of Leishmania. The patient then started a treatment with liposomal amphotericin B (3 mg/kg), ongoing.
Conclusions: Leishmaniasis is a zoonotic disease due to infection with parasites of the genus Leishmania; it usually affects immunocompetent individuals, predominantly children. Since the mid-1980s, VL has been reported increasingly as a complication of AIDS. In HIV+ patients, this infection may present with atypical features and more than 50% of these patients show no detectable levels of anti-Leishmania antibodies due to functional impairment of cell-mediated immunity. The case we reported confirms what described above and underlines the importance of bone marrow aspirate in the diagnostic phase.

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Lopinavir/ritonavir trough concentrations in HIV-HCV-coinfected patients

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Background: Chronic hepatitis C represents an emerging issue in the management of HIV disease because of the same route of transmission, leading to a very high prevalence of HCV-coinfection in HIV-positive patient population. Lopinavir is extensively metabolized by the hepatic cytochrome P450 3A4, and pharmacokinetics of this protease inhibitor (PI) could be influenced by liver impairment, but data on the impact of HCV-coinfection on lopinavir plasma concentrations are very limited and conflicting still today.
Methods: In this observational, open-label study, adult HIV-infected outpatients on stable antiretroviral treatment including two nucleoside reverse transcriptase inhibitors (NRTIs) plus lopinavir/ritonavir for at least 4 weeks were asked to participate. The trough plasma concentration (Ctrough) of lopinavir and ritonavir was assessed at steady state by a validated high-performance liquid chromatography (HPLC)-tandem mass spectrometry method.
Results: A total of 78 HIV-positive patients were enrolled in the study. These patients were stratified into two groups with regard to HCV-coinfection: 48 were HIV-mono-infected (HIV+/HCV-) and 30 were HIV-HCV-coinfected (HIV+/HCV+). Although there was a clearly higher value of mean trough plasma concentration of lopinavir in co-infected subjects, presence of HCV co-infection was considered to be not significant (p=0.21). Median value (and range) for lopinavir Ctrough was 6,038 (41-12,600) ng/mL in HIV+/HCV- subjects, and 7,502 (388-19,800) in HIV+/HCV+ ones, in absence of a statistically significant difference (p=0.35). Almost all samples were found to be within the therapeutic plasma level range (97% in HIV+/HCV- group and 100% in HIV+/HCV+ group). No correlation was found between lopinavir plasma levels and adverse events or immune-virological parameters of HIV disease.
Discussion: In our study, pharmacokinetics of lopinavir/ritonavir did not show significant changes in HIV-positive patients with HCV-co-infection, and in absence of liver cirrhosis.

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Subclinical carotid atherosclerosis in HIV-infected patients treated with nevirapine or protease inhibitors

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Background: In the post-HAART era, long-term cardiovascular complications have been frequently reported, and an increasing concern is mounting particularly about the increased risk of acute coronary syndromes associated with new potent antiretroviral combinations. There is controversy over whether HIV infection and antiretroviral therapy contribute to early atherosclerosis, or not, and ultrasonographic evaluation of carotid intima-media thickness may be considered to be a reliable surrogate marker of subclinical atherosclerosis.
Methods: A cross-sectional study evaluating subclinical atherosclerosis by carotid ultrasonography in HIV-positive subjects treated with nevirapine (NVP) or protease inhibitors (Pis), was performed.
Results: A total of 64 patients (50 males and 14 females; mean age 45 + 16 years; range 34-63 years) at their first antiretroviral treatment for >24 months were enrolled into the study: 29 subjects were treated with 2 nucleoside reverse transcriptase inhibitors (NRTIs) and NVP (group A) and 35 patients were treated with two NRTIs and one PI (group B). PI treatment included lopinavir/ritonavir in 18 patients, atazanavir/ritonavir in 11, and fosamprenavir/ritonavir in 6. With regard to lipid metabolism alterations, dyslipidaemia was significantly more frequent among PI-treated subjects than among those receiving NVP. The mean intima-media thickness (IMT) + standard deviation (SD) in the common carotid arteries was 0.89 + 0.49 in group A and 1.47 + 0.82 in group B (p=0.006). The mean IMT + SD in the carotid bifurcations was 0.94 + 0.61 in group A and 1.46 + 0.75 in group B (p=0.008). The mean IMT + SD in the internal carotid arteries was 0.85 + 0.58 in group A and 1.41 + 0.88 in group B (p=0.041). Therefore, mean values of carotid IMT in PI-treated patients were significantly higher than in NVP-treated subjects. Prevalence of carotid plaques was significantly higher in group B than in group A (43% versus 21%; p=0.021). Moreover, carotid lesions were structurally comparable to classical atherosclerotique plaques observed in general population, with iso-hyperechonegic aspects and irregular surfaces.
Discussion: prevalence of carotid plaques and mean values of carotid IMT were significantly higher in HIV-infected patients receiving a PI-based therapy than in those treated with a NVP-based one.

PO 64

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APRI and FIB-4 for the evaluation of liver fibrosis: concordance analysis, evolution and predictors in a cohort of HIV patients positive for HCV-Ab: results from the EPOKA-a MASTER Cohort

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Background/Aims: Liver fibrosis(LF) progression is accelerated in HIV-HCV co-infected patients and cirrhosis is a major complication in the HIV population.The aim of this study is to assess LF progression in HIV patients with positive HCV-Ab and associated risk factors.The main hypothesis is that early antiretroviral therapy may slow down LF progression.
Methods: Observational retrospective study.All HIV-naive or early-experienced patients in 2 large referral clinics, who started or changed HAART from 2002 to 2006 were included.Kappa test was used to assess concordance between APRI and FIB-4 ranked into three classes.Rates of progression from class 1 of APRI or FIB-4 (<0.5 and <1.45,respectively) to higher classes was estimated through Kaplan-Meyer analysis.This transition to low grade liver fibrosis was chosen to increase sensitivity for any progression of liver disease.Cox regression models were applied to assess possible predictors at baseline (amongst gender, age, risk factors for HIV acquisition, HIV-RNA, and CD4+ T-cell count).
Results: 248 HCV Ab positive patients were selected (75% men, IVDU risk factor for HIV 69%, mean age 41 years, HIV-RNA 96.646 copies/mL, CD4+ cell count 280 cells/cmm). At baseline, 53 (21.4%) patients were on HAART (62% PI+/-ritonavir, 24.5% NNRTI, 13% other regimens). 98 (39.5%) patients showed class 1 for APRI and 128 (51.6%) for FIB-4.Cohen's Kappa was 0.696 (95%CI 0.624 to 0.767) showing intermediate concordance. 54 (55.1%) patients had LF progression to >/= class 1 at APRI with an incidence of 0.427 (95%CI 0.321-0.557) per PYFU and an estimated median time of 541 days. As

for FIB-4, 53 (41.4%) patients had LF progression to >/= class 1 with an incidence of 0.251 (95%CI 0.188-0.328) per PYFU and an estimated median time of 1145 days. Cox regression models showed different independent baseline predictors for APRI with respect to FIB-4 transition. Male gender was independently associated with APRI transition to grade >/=1 (HR: 2.799, 95%CI 1.386-5.652; P: 0.0041), while age >/=40 years was protective (HR: 0.555, 95%CI 0.318-0.969; P0.0384);for FIB-4,no factors were found to be associated with fibrosis progression.CD4+ T-cell count (<350 vs. >/=350 cells/cmm) was not associated with either APRI or FIB-4 transition.
Conclusions: In this small cohort, HAART initiation at CD4+ >/= 350/cmm did not seem to slow down progression of LF.It has to be seen whether higher CD4+ cut-offs for HAART initiation or better immune-reconstitution during follow-up have an impact. Although the rate of LF progression was substantial, discordant results were found between the two scores (overall 55% APRI vs. 41% FIB-4).Discordance between the two tests was also found both in terms of staging of LF at baseline and in terms of predictors of LF progression.This indicates that standardization and validation of these surrogate methods are necessary.In the meantime, males,and younger patients, were suggested to be the most vulnerable population.

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Frequency of HIV-associated neurocognitive impairment in treated and untreated HIV-infected patients with low nadir CD4 cell counts

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Background: Although cART has caused a dramatic reduction in the incidence of dementia, the prevalence of HIV-associated neurocognitive disorders (HAND) seems to have increased as a result of prolonged patients survival and, possibly, chronic HIV brain infection. Several studies have shown that nadir CD4 cell of <200 c/mL is a consistent correlate of HAND, suggesting that this condition could result from previously established brain damage and thus be poorly affected by antiretroviral treatment (cART). Therefore our objective was to assess whether HAND prevalence is different between cART-treated and untreated HIV-infected patients with low nadir CD4 cell counts.
Methods: Neuropsicological assessment was performed in 44 HIV-infected patients without underlying neurological diseases or illicit drugs addiction, attending our Clinic from January 2008 until March 2010. Two patient groups were examined: untreated patients, including 22 patients who were cART naive or off cART in the previous 6 months with either CD4+cells <200/µL or CD4+ cells<350/µL and viral load >100.000 copies/mL; treated patients, including 22 patients on cART for at least 6 months, with a nadir CD4+ cell <200/µL and undetectable VL. Patients were tested with a QNPZ-5 battery of neuropsychological tests including grooved pegboard (GP), WAIS III digit symbol (DS), trail making test A and B (TMT-A and TMT-B) and timed gait (TG). Each patient received a performance score (Z-score) for each test and a global NPZ-score was calculated as the mean of the Z-scores achieved in each test. The global score was used to define presence of HAND.
Results: The two groups were similar as for demographical data (median age 46 vs. 50; females 3/22 vs. 6/22 in untreated vs. treated), while, as expected, untreated patients had lower current CD4+ cells (median 161 vs. 474). Overall HAND frequency was 19/44 (43%). No significant difference between untreated and treated patients was observed as for both HAND frequency (10/22, 45% vs. 9/22, 41%), global Z-score and Z-scores achieved in each test, except for TG, which performed worse in treated patients (p=0.014). Global NPZ-score did not correlate with current or nadir CD4+ cell count in all patients, with VL in untreated patients and with revised CNS penetration/efficacy (CPE) cART score in treated patients.
Discussion: Frequency of HAND was high in asymptomatic HIV-infected patients with nadir CD4 cells <200 µL, including treated patients with full immunovirological recovery. In addition, HAND frequency was not lower in treated than in untreated patients with low CD4 cell counts, supporting the hypothesis that previously established brain damage might account for most of these forms.

PO 66

Infection 2010; 38 (Suppl. I): 73

Meningitis simultaneously due to Cryptococcus neoformans and HHV-6 infection in a HIV positive patient

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Background: Meningoencephalitis caused by Cryptococcus neoformans is frequent in HIV positive patients with a deep immunodepression. Human herpesvirus 6 (HHV6) has been reported as a rare cause of meningoencephalitis. In literature meningoencephalitis due to both Cryptococcus neoformans and HHV-6 infection is not reported.
Case report: We describe a case of a 36-year-old HIV-infected woman admitted at our Unit for fever, headache. SHe discovered HIV infection in 2004 but she refused to take antiretroviral treatment. At the admission CD4 count was equal to 42 cell/mmc and plasmatic HIVRNA to 920000 copies/ml. The patient underwent magnetic resonance (MR) imaging and MR images showed signal intensity abnormalities, with prominent involvement of the hippocampus, and an involvement of the cortical and subcortical structures. Cerebrospinal fluid examination showed the presence of Crytococcus neofromans and cerebrospinal fluid polymerase chain reaction (PCR) testing for Herpes virus family was positive for HSV-6 DNA. A therapy with acyclovir and steroid was introduce for the treatment of HHV-6 infection and according to international guidelines a combination therapy with ampho B + flucytosine was introduced. Besides the patient started HAART with atazanavir boosted + tenofovir + emtricitabine + enfuvirtide. Progressively as the clinical and neurological status as the immunological parameters improved.
Conclusion: Immunocompromised population should be investigated for the possibility of appareance of rare viral agents causing neurological involvement as HHV6. This case suggests that HHV6 activation in conjunction with Cryptococcus neoformans infection is possible and should be associated in meningoencephalitis.

PO 67

Infection 2010; 38 (Suppl. I): 73

Fib4 is an independent predictor of serious liver disease among HIV-infected patients with or without HBV/HCV co-infection in the Icona foundation study

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Background: Fib4 {AGE [years] x AST [U/L] / (PLT [109/L] x sqrt(ALT [U/L]))} has been validated as a non-invasive and inexpen-

sive marker of fibrosis in HCV+ patients, with and without HIV co-infection. However its prognostic role with respect to severe liver disease (decompensated cirrhosis) or death related to liver disease (SLD) has not been investigated in the HIV+ population, with or without concomitant HBV/HCV infection. The aim of this study is to investigate the prognostic role of fib4 on SLD in the ICONA cohort
Methods: Patients enrolled in the Icona study with at least >=1 clinical visit and a determination of ALT, AST, age and platelets were included. Subsequent Fib4 determinations were evaluated from the date of their first available determination after enrolment in the cohort until the development of a SLD, censoring patients' follow-up at their last clinical visit. Multivariable Cox proportional hazard models with time-updated covariates were used to assess independent predictors of SLD At each Fib4 determination, fitted as a continuous variable, we identified the corresponding HIV-RNA load, CD4/CD8 cell count, previous AIDS events, and treatment status (both anti-HIV and anti-HBV/HCV drugs). Other (time-fixed) covariates were: age, gender, mode of HIV transmission, HBsAg, HCVAb, (HBeAg, HDVAb only in the subset of HBsAg+ patients), and year of enrolment.
Results: 5,751 patients were followed for 31,235 person-year follow-up (PYFU). 70% were males, 37% heterosexual, 36% intravenous drug user (IDU), 7% HBsAg+, 44% HCVAb+, less than 1% HBeAg+ and 1.1% HDVAb+ (3% of the HBaAg+ subset), 68% presenting with a normal Fib4 at their first determinantion.
Incidence of a SLD was 2.53 (95%CI 1.97-3.09) per 1000 PYFU (79 events overall). Kaplan-Meier estimation of the cumulative probability of remaining free from SLD by 2 years was 0.996 (0.995-0.998); by 4 years was 0.981 (0.969-0.993). Variables associated with the risk of developing SLD are shown in the table
Conclusions: In our study population, Fib4 was strongly associated with an increased risk for a SLD, along with being IDU and alcohol abuse.

Table: Relative hazards of a SLD by fitting a time-updated Cox proportional hazard model

Factor	RH	Lower95	Upper95	p-value
Mode of transmission Homo/Bisexual vs Heterosexual	0.40	0.05	3.21	0.38
Mode of transmission IDU vs Heterosexual	4.14	1.36	12.57	0.012
Mode of transmission Other/Unknown vs Heterosexual	1.73	0.36	8.22	0.49
Gender M vs F	0.63	0.37	1.05	0.771
Per current log(Fib4) higher	4.48	3.74	5.37	<0.0001
Per current log10(CD^4) cells/mm3 higher	0.82	0.43	1.59	0.562
Per current log10(CD^8) cells/mm3 higher	0.55	0.19	1.62	0.280
Per current log10($HIV\text{-}RN^A$) cp/ml higher	1.16	0.94	1.42	0.174
HBsAg positive vs negative	1.81	0.94	3.49	0.077
HCVAb positive vs negative	1.34	0.49	3.68	0.573
AIDS event previous or concomitant to current time interval	1.66	0.89	3.10	0.11
On-ART with TDF or 3TC or FTC vs on-ART without TDF or 3TC or FTC	0.95	0.41	2.22	0.908
On-ART-interruption vs on-ART without TDF or 3TC or FTC	1.36	0.57	3.20	0.488
ART-naïve vs on-ART without TDF/3TC/FTC	0.65	0.29	1.49	0.312
enrol year before 1997 vs after 2000	0.67	0.35	1.27	0.221
enrol year between 1997 and 2000 vs after 2000	0.83	0.39	1.75	0.621
Age per 10 years older	1.03	0.65	1.62	0.909
alcohol low_medium vs high	0.45	0.24	0.88	0.018
alcohol no vs high	0.56	0.25	1.26	0.159
alcohol unknown vs high	1.68	0.92	3.06	0.088

PO 68

Infection 2010; 38 (Suppl. I): 74

Immune Reconstitution is Associated with Delayed Occurrence and Longer Survival after Hodgkin Disease in HIV-infected Patients

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Background: Development of lymphomas in HIV-infected population is usually associated with high HIV-RNA levels and low CD4 cell counts. We aimed to investigate whether immuno-virologic response to HAART was associated with different clinical presentation and survival of patients with a diagnosis of lymphoma.
Methods: We designed a retrospective study nested in the Infectious Diseases Database of the San Raffaele Hospital. We considered HIV-infected, HAART-experienced adults with a diagnosis of lymphoma. We defined immune reconstitution (IR) to the ongoing HAART at lymphoma diagnosis (last HAART), according to Shelburne 2005, if patients: started or changed HAART with HIV-RNA >1000 copies/mL, had a decrease in HIV-RNA and an increase in CD4 counts thereafter. Patients charts, pathology, radiology and laboratory records were reviewed. Comparisons were assessed using Chi-square or Mann-Whitney rank-sum test or Kaplan Meier method as appropriate.
Results: We identified 108 lymphoma cases [28 Hodgkin Disease (HD), 80 Non-Hodgkin lymphoma (NHL)]. 80 out of 108 patients (26 HD, 54 NHL) were classified as for IR or not. Overall 39(49%) of patients had a diagnosis of lymphoma during IR [13(50%) HD and 26(52%)].
Both for HD and NHL, IR and non-IR patients did not differ in terms of age [46(45-52) vs 43(40-54) years (ys) for HD and 44(42-50) vs 46(39-51) ys for NHL], year of diagnosis [2005(2004-2008) vs 2002(2001-2006) for HD and 2004(2001-2006) vs 2002(2000-2004) for NHL], years of HIV infection [18(13-21) vs 19(15-19) for HD and and 15(9-21) vs 16(12-19)ys for NHL], duration of previous HAART exposure [11(9-14) vs 11(8-12) for HD and 7(2-10) vs 7(2-4) ys for NHL], CD4 nadir [175(121-210) vs 62(44-132) for HD and 95(53-184) vs 67(32-145) cells/mcl for NHL].
Median time between last HAART initiation and diagnosis of was 561(336-1311) vs 81(44-165) days in IR vs non-IR patients for HD (p=0.008) and 234(140-546) vs 119(29-321) days in IR vs non-IR patients for NHL (p=0.189).
At diagnosis no significant differences were found between IR and non-IR patients in terms of clinical presentation both for HD and NHL: the proportion of patients presenting with a stage III or IV, B-symptoms and bone marrow involvement in IR vs non-IR patients was 46% vs 61%

for HD and 85% vs 84% for NHL; 54% vs 77% for HD and 46% vs 39% for NHL; 33% vs 55% for HD and 21% vs 23% for NHL. After lymphoma diagnosis, 1(7.7%) IR patient with HD died, as compared to 7(53.9%) non-IR patients (p=0.005). 13(50%) IR patients with diagnosis of NHL died, as compared to 17(61%) non-IR patients (p=0.323). One and five-ys survival after lymphoma diagnosis in IR vs non-IR patients was 92% vs 90% and 92% vs 49% for HD (p=0.038) and 51% vs 42% and 45% vs 35% for NHL (p=0.267). (Figure 1)
Discussion: Almost half of lymphomas occurred in patients with IR. Patients with HD diagnosis during IR survived longer than non-IR patients . No such difference was observed for patients with NHL diagnosis.

PO 69

Infection 2010; 38 (Suppl. I): 75

Antiproteinuric effect of telmisartan in an african hiv infected patient with severe proteinuria

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Background: Kidney disease remains a major co-morbidity of HIV infection especially in subjects of African ethnicity. HIV-associated renal disease with overt proteinuria has been associated with poorer outcomes and increased mortality. Telmisartan, an angiotensin II receptor blocker partial agonist of the PPAR-γ approved for the treatment of hypertension, seems to exert a nephro-protective effect independent of blood pressure reduction in the general population. A case is described of an HIV positive African cART treated patient with severe proteinuria treated with telmisartan.
Case Report: A 52 year-old African male HIV infected patient came to our examination because of discovered HIV antibody positivity. He had familiarity for hypertension and his personal history included promiscuous sexual relations, and previous hospitalization in Italy because of high blood pressure (BP) and chronic kidney disease consequent to nephrosclerosis. For these reasons he took 30 mg nifedipine twice a day, 100 mg atenolol daily, 4 mg doxazosin twice a day, furosemide 250 mg/day, and 150 mg allopurinolo daily. On admission he had 738 CD4/mmc; CD4/CD8 ratio 0.99; HIV-RNA 1790 copies/ml; anti HBs and anti HBc antibodies positive; transaminases, glucidic and lipidic parameters within normal limits; BP 130/80 mmHg; glomerular filtration rate (GFR) assessed by the simplified MDRD logarithmic model (MDRD-GFR) 33 ml/min x 173m2, serum creatinine 2.65 mg/dl, proteinuria 150 mg/dl, microalbuminuria 60.30 mg/dl, and cystatin C 2.04 mg/L. After two months, since alterations of BP values and parameters of kidney function persisted, 40 mg telmisartan once daily was started without changes in remaining therapy. After eight months of therapy with telmisartan, proteinuria (30 mg/dl), microalbuminuria (6.75 mg/dl), and cystatin C (2.32 mg/L) decreased while mean BP values, MDRD-GFR remained stable. Even though the patient was not treated with cART, viro-immunological parameters were stable.
Discussion: Telmisartan was well tolerated and effective in decreasing proteinuria and microalbuminuria. Decreased proteinuria, microalbuminuria and cystatin-C observed in this case are indicative of nephroprotective effects of telmisartan also in a HIV infected black race patient.

PO 70

Infection 2010; 38 (Suppl. I): 75

Dual raas blockade in a hypertensive african HIV infected patient with microalbuminuria

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Background: Microalbuminuria, an indicator of glomerular damage, is one of the increasingly prevalent complications of HIV infection, especially in subjects of African ethnicity. Several studies suggest that the use of combination therapy with angiotensin-converting enzyme inhibitors (ACE-I) and angiotensin receptor blockers (ARB) exerts an antiproteinuric effect independent of blood pressure reduction in the general population. A case is described of an HIV+ African combination antiretroviral therapy (cART) treated patient with hypertension and severe proteinuria.
Case Report: A 45 year-old African male HIV infected (CDC A2) patient, treated with TDF+FTC+EFV for one year in another clinical centre, came to our examination. His personal history included injective use of illicit drugs, tobacco smoking, and a chronic HCV infection. On admission he had 603 CD4/mmc; HIV-RNA <40 cp/ml; HCV-RNA >5 x 105 cp/ml; normal transaminases, glucidic and lipidic parameters; high blood pressure(BP) 150/100 mmHg, glomerular filtration rate(GFR) assessed by the MDRD logarithmic model(MDRD-GFR) 114 ml/min x 173m2 and microalbuminuria 150 mg/dl. Treatment with 10 mg lercanidipine daily was started, strictly monitoring possible side effects and interactions with cART. After one month of lercanidipine therapy, BP values were 120/90 mmHg, without adverse effects, while microalbuminuria and MDRD-GFR were 121 mg/dl and 106 ml/min x 173m2, respectively. A change in cART, suspending TDF, was proposed, but the patient refused it. In the following months, microalbuminuria levels progressively worsened (252 mg/dl, while MDRD-GFR was 117 ml/mm x 173m2) in spite of the improved mean BP values (130/85 mmHg). The patient refused renal biopsy and cART changes. Administration of 300 mg irbesartan daily was then started to improve renal dysfunction; after two months, while BP values and MDRD-GFR remained stable, the microalbuminuria decreased only to 150 mg/dl. Therefore, we decided to add 20 mg lisinopril once daily to make a dual blockade of the renin-angiotensin system(RAS). After five months, microalbuminuria was 28.5 mg/dl without a change in BP, MDRD-GRF and viro-immunological parameters.
Discussion: The combination therapy with lisinopril and irbesartan used in this case allowed kidney distress to be improved, with a percent change in microalbuminuria levels of minus 88% from baseline. In our case the race of the patient was a further problem, since antihypertensive regimens inhibiting RAS may be ineffective in black race patients, who are more responsive to diuretics and calcium channel-blockers(CCB). In our patient the main anti-hypertensive effect was achieved with the use of the CCB lercanidipina, in the absence of important interactions with cART. But the use of lercanidipine did not improve the proteinuria. This case shows that a dual blockade of RAS with combined ACE-I plus ARB therapy reduces microalbuminuria even in an HIV-infected African patient.

PO 71

Infection 2010; 38 (Suppl. I): 76

Prevalence of sub-clinical vertebral fractures in a cohort of HIV positive patients and ability of FRAX score to identify patients at increased fracture risk

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Objectives: The high prevalence of osteopenia/osteoporosis in HIV-infected patients has raised concerns on the hightened fracture risk in this population. We evaluated in a cohort of HIV pos patients the prevalence of sub-clinical vertebral fractures and the ability of FRAX score to identify patients at increased fracture risk.
Methods: Sixty-one unselected HIV pos patients naïve or on stable HAART were submitted to DEXA and lateral spine radiograph (Rx). Vertebral deformities were identified by morph-metric analysis of Rx. For each patient the "spine deformity index" (SDI) was calculated by summing grade of vertebral deformities, according to semiquantitative method by Genant. Factors associated with vertebral deformities (SDI) were evaluated by univariate and multivariate logistic regression analysis. The assessment of ten-years major osteoporotic fracture risk was performed by FRAX algorithm, using common risk factors alone and with bone mass density (BMD). The concordance between FRAX score and SDI was evaluated by Spearman Correlation.
Results: Twenty-five patients (41%) had evidence of vertebral deformities: 14 patients with SDI=1; 8 patients with SDI=2; one with SDI=3; two patients with SDI>10. Only the two patients with SDI>10 complained lumbar pain, the remaining 23 patients were asymptomatic.
Patients with vertebral deformities had a median age older than patients without (median age of patients with SDI>=1 = 50 [IQR 46-60.7] vs patients with SDI0 = 42.5 [IQR 39-48]; p=0.001) and were featured by longer exposure to HAART (median time on HAART: patients with SDI>=2 = 114 months [IQR 48-156] vs patients with SDI0-1 = 36 [IQR 1.5-102]; p=0.015). However only older age resulted independently associated with vertebral deformities at multivariate logistic regression (for each 10 years older: AOR=2.08 [IC95% 1.07-4.06]; p=0.031).
Patients with vertebral deformities were featured by a median fracture risk higher than patients without, both considering FRAX risk obtained by common risk factors alone and with BMD (FRAX without BMD: SDI>=1 = 4.6 [IQR 2.9-5.95] vs SDI0 = 2.9 [IQR 2.5-3.9]; p=0.003; FRAX with BMD: SDI>=1 = 5.9 [IQR 3.4-7.7] vs SDI0 = 3.2 [IQR 3.8-5.1]; p=0.005).
The fracture risk was directly correlated with the presence and grade of vertebral deformities (FRAX without BMD-SDI: rho=0.438; p<0.001; FRAX with BMD-SDI: rho=0.543; p<0.001).
Conclusion: In our study on HIV pos subjects we identified a high frequency of sub-clinical vertebral fractures. Older age was the only risk factor independently associated with vertebral fractures, with a doubling in the risk for each ten years older categories. Our data suggest an increased risk after long HAART exposure that should be further investigated in larger cohort. The evaluation of fracture risk by FRAX score seems to be accurate and able to identify HIV pos patients at risk of vertebral fractures.

PO 72

Infection 2010; 38 (Suppl. I): 76

A road map for lipodystrophic syndrome (LS): a clinical program in the north western Italy

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Background: Why a project specifically dedicated to LS in HIV-positive population? LS is the expression of HIV infection chronicity and can negatively affect survival, adherence and quality of life. Currently, about 30% of patients suffer from LS; among them, 30% need a specific treatment for this condition. For these reasons we conceived a multidisciplinary diagnostic and clinical program. The patient is guided step by step, aimed to change some lifestyles, to reverse or control some metabolic alterations and to cope with the distress related to body imagine change. We based our project on the results obtained in a pilot protocol with a small number of patients and on the experience of the Metabolic Clinic in Modena. We report here some preliminary results focused on dietician follow-up.
Methods: The project is carried on in Torino, Amedeo di Savoia Hospital, and in Cuneo, S.Croce e Carle Hospital. The group is formed by specialists in HIV disease, a nutritionist supported by a dietician, a psychologist, a cardiologist, a plastic surgeon and a kinesiologist. The patient is invited to participate to the full "package", which starts with a metabolic assessment and then goes on with a psychological visit and a dietician visit. If needed, the patient can be valued by the other specialists of the group. The more complicated cases and all the problems related to the project are discussed monthly by the group.
Results: At date 71 patients have been enrolled: 27 females, 44 males; mean age 48,5 years; mean age of HIV infection 9,9 years; risk factors for HIV infection: 14 IVUD, 57 sexual intercourse; CDC Classification: 34 A, 19 B, 18 C. At baseline 28 (39%) patients had metabolic syndrome; 27 (38%) had a cardiovascular risk at 10 years ≥10%; 28 (39%) were smokers; 54 (76%) had BMI ≥ 25. All except one were on HAART. At date, 10 (14%) patients dropped out after the metabolic assessment; 2 (3%) after the psychological visit; 8 (11%) after the dietician visit; 11 (15%) underwent a cardiological visit. Actually, 15 patients have a 24 weeks dietician follow-up, among them, 12 (80%) significantly improved their BMI and/or plasma lipids..
Discussion: A program of treatment of LS can only be organized with the involvement of the full range of medical professionals and the patient's complete adherence to the program itself. Such an approach will allow doctors to better identify which patient has the highest motivation for changes in lifestyle, the only possible guarantee of a positive long-term outcome.

PO 73

Infection 2010; 38 (Suppl. I): 76

Lymphoma occurrence does not impair long term CD4 recovery in HIV+ cancer survivors

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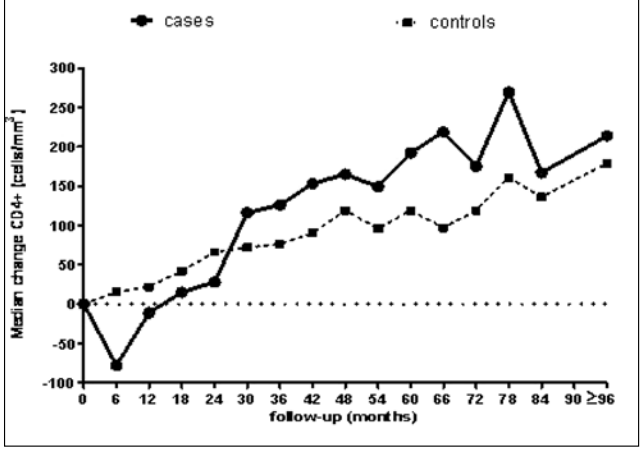
Background: Response and survival rates after chemotherapy (CT) in HIV+ subjects treated with HAART (highly active antiretroviral therapy) approach those in immunocompetent subjects. In order to investigate whether lymphoma occurrence may affect HAART-in-

Panel A

	Cases	Controls	p-value
Males	57 (92%)	191 (91%)	0.999
Age	45.9 (42.3-50.8)	45.7 (42.7-50.1)	0.657
HIV risk factor			
• MSM	16 (26%)	66 (31%)	0.652
• IDU	15 (24%)	58 (28%)	
• HETERO	6 (10%)	16 (8%)	
• Other/unknown	25 (40%)	70 (33%)	
Aids diagnosis before baseline	22 (35.5%)	44 (21%)	**0.028**
Years of HIV infection	14.0 (8.7-20.8)	15.5 (9.6-20.8)	0.583
Years of ARV	11.0 (5.2-14.0)	12.0 (7.3-14.4)	0.300
Years of HAART	9.2 (5.2-11.8)	10.8 (6.4-12.4)	**0.046**
Nadir CD4+	131 (64-210)	142 (50-226)	0.893
Baseline CD4+	278 (122-419)	427 (239-579)	**0.002**
CD4+ at last visit	412 (269-694)	517 (347-667)	0.089
Baseline CD4%	19.3 (7.8-14.6)	19.9 (12.3-25.3)	**0.050**
CD4% at last visit	22.2 (16.2-27.1)	22.1 (17.8-28.8)	0.386
Maximum viral load	137507 (93000-310000)	95500 (28754-267469)	0.565
Baseline viral load	1814 (61-59120)	79 (49-12656)	**0.005**
Viral load at last visit	36 (0.9-49)	0.9 (0.9-36)	0.370

Panel B



duced immune recovery, we compared CD4 count between HIV+ subjects with and without lymphoma.

Methods: Our study is a nested case-control study from Infectious Diseases Database of San Raffaele Hospital. We compared CD4 count in alive and currently followed HIV+ subjects diagnosed with any lymphoma, except for primary central nervous system lymphoma, that have been treated with any CT and HAART, to 1 to 4 lymphoma-free HIV+ subjects. All cases completed CT treatment. Controls were matched to the cases on age (±1 year), sex, nadir CD4 count (± 50 / mmc), year of HIV diagnosis (± 1 year). Baseline was defined as date of cancer diagnosis; end of follow up (FU) was assessed by the time interval between baseline and last available visit. Using multivariate mixed linear model with fixed-effects, we evaluated the mean change of CD4 count, adjusted for baseline CD4 count, CD4% and viral load, HAART exposure and the occurrence of an AIDS event before baseline.

Results: We compared 62 HIV+ subjects with lymphoma to 211 controls (6 cases to 1 control, 6 to 2, 7 to 3, 43 to 4). Number of available visits per subject and median of FU did not differ among cases and controls (respectively 14.5 years [IQR 8-25] vs 15.0 [7-23] and 4.6 [IQR 0.2-8.1) vs 5.1 [IQR 2.2-8.1]). The median baseline CD4 count was significantly different among subjects with and without lymphoma (278 [IQR 122-419], vs 427 [IQR 239-579], p=0.002). Trend of immunological parameters are shown in figure 1 (panel A). Median CD4 changes from baseline to last visit were respectively 174 (-38/347) in cases and 91 (-71/273) in controls (p=0.173), as shown in figure 1 (panel B). Although a significant difference at baseline, median CD4 count at the end of FU was similar in both groups (412/mmc [IQR 269-694] in cases vs 517/cmm3 [IQR 347-667] in controls). In adjusted analysis, CD4 change was significantly associated with baseline CD4 count (p<0.001), it increased over time (respectively p<0.0001) and was Significantly higher in cases than in controls (interaction term: p=0.015).

Discussion: We observed a significant restoration of CD4 count in currently alive HIV+ subjects with lymphoma, furthermore CD4 change was significantly higher over time in cases than in controls, suggesting that lymphoma occurrence did not impair long term CD4 recovery in our population.

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Determinants of erectile dysfunction changes in HIV infected men: a prospective study

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Background: A high prevalence of erectile dysfunction (ED) has been reported in HIV-infected men. However factors associated with ED are poorly understood and the role of antiretroviral therapy, especially PIs, is unclear. The aims of this study were to evaluate prevalence of ED and identify factors associated with improvement in ED during a mean follow-up of 1.5 years (range 0.63; 2.51) among 67 HIV infected men.

Methods: Evaluation tools included: the International Index of Erectile Function (IIF-15) to measure ED, visual analogue scale (VAS) of the face and of the body to measure patient's aesthetic satisfaction, total testosteron to assess hypogonadism. Change in ED (ΔED) was analyzed as a continuous variable.

Univariate and multivariable linear regression analyses were performed to investigate factors associated with ΔED over time. Univariate linear regression analyses included the following variables: age, VAS-face, testosterone plasma levels, current exposure to PIs, and lipodystrophy phenotypes according to HOPS classification. The same variables were included in a backward stepwise linear regression analysis.

Results: Of 67 men evaluated, 43 (64%) reported ED at baseline. 33 patients reported improved ED at the end of follow-up. Multivariable stepwise linear regression analysis confirmed the univariate results and VAS face was the only predictor of ΔED (β 1.81, 95% CI 0.34; 3.27, p-value=0.017; R2 = 0.19) while current PI use (β -6.71, 95% CI -15.86; 2.45, p-value=0.145; R2 = 0.19) was not associated with ΔED. The stepwise analytic method removed testosterone plasma level, age, and lipodystrophy phenotypes from the model.

Change in VAS-face was associated with the number of plastic surgeries received during follow-up (facial infiltration with polylactic acid and polyacrylamide gel) on univariate and multivariable analyses (β 0.32, 95% CI 0.13; 0.50, p-value=0.001; R2 = 0.29; β 0.30, 95% CI 0.10; 0.50, p-value=0.004; R2 = 0.34 respectively), but not current PI exposure (β 1.34, 95% CI -0.66; 3.33, p-value=0.182; R2 = 0.34).

Discussion: ED is a reversible condition in most HIV infected patients.

Aesthetic satisfaction with one's face is the most important determinant of ΔED.

We hypothesize that the association of PIs on ED shown in some HIV studies may be mediated by the impact of these drugs on body image alteration. We found that surgical correction of facial lipoatrophy may improve VAS-face and indirectly psychological determinant of sexual function.

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Sexual dysfunction in HIV+ subjects in eastern Sicily

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Introduction: Sexual dysfunctions (SD) in HIV+ subjects were associated with infection, body image, HAART, use of proteases inhibitors. Few data are published about HIV+ female. Anxiety is very common in HIV+ subjects and should be a cofactor of SDs. Aim of this study is to analyze sexual dysfunction in a group of HIV+ subjects with at least six months of continuous exposure to HAART followed at two different Unit of Infectious Diseases in eastern Sicily. A cross sectional analysis was conducted to evaluate prevalence and factors associated with SD and, secondarily, to correlate it with anxiety.
Methods: Sexual evaluation was performed by self-completion questionnaires: Female Sexual Function Index (FSFI) for females (a full score <23 was considered diagnostic of SD) and International Index of Erectile Function (IIEF) for males (a score of <26 was considered diagnostic of erectile dysfunction). Anxiety was evaluated with Self Rating Anxiety State SAS 054, a self-submitted 20 items questionnaire. A z score ≥ 45 was considered diagnostic of anxiety.
Results: 152 patients were included into the study. Median age 45 (IQR 39-49) years, 24.3% ≥50 years, 71.7% males, 38.8% heterosexuals, 38.8% MSMs, 21.1% IVDUs; 42.8% were single. Median time from HIV diagnosis was 11 years (IQR 5-15). 52.6% CDC A, 23.7% CDC B, 23.7% CDC C. Median CD4 cell count 577 cells/µl (IQR 373-842), 78.9% had HIV RNA <50 copies/ml. Median length of HAART was 8.5 (IQR 4-13) years: 22.4% were naïve, 19.1% on 2nd line, 28.3% 3rd-4rd, 30.3% >4th line of treatment. 61.8% were on PI based treatment, 36.2% on NNRTI. 74 subjects (48.7%) had a z score ≥ 45 diagnostic of anxiety.
11 (7%) females denied any sexual activity (all of them being single or widow) and were excluded from analysis. 82 (58%) out of the remaining 141 subjects showed a sexual dysfunction. SDs were more frequent in male (65% vs 34%, p<0.01), elderly subjects (≥50 yr) (54% vs 28%, p<0.01).
Among males, 71 subjects (65%) showed any erectile dysfunction (ED) EDs were more frequent in elderly subjects (≥50 yr) (78% vs 60%, OR 2.7, 95% CI 1.01-2.26) and in anxiouses (77% vs 54%, OR 3.04, 95% CI 1.3-7.12). No significant association was seen with actual ARV treatment (PI or NNRTI based), clinical stage, HIV RNA >50 copies/ml.
Among females, 11 (35%) had a full score <23 diagnostic for sexual dysfunction (FSD). FSDs were more frequent in elderly subjects (≥50 yr) (100% vs 28%, p<0.05) while were not related to anxiety, actual ARV treatment (PI or NNRTI based), clinical stage, HIV RNA >50 copies/ml.
Conclusion: SDs were highly prevalent in this group of subjects. While EDs appear in explicit way, discretion could make more difficult FSDs evaluation. EDs appear related to elderly age (P<0.05) and anxiety (P<0.01) while FSDs seem associated with elderly age (p<0.05). An accurate evaluation and treatment of anxiety should be undertaken in order to obtain an increase in sexual satisfaction and in quality of life of treated patients.

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Atypical cutaneous lympoproliferative disorders and lack of immune response in a patient with acute HIV infection

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Background: Acute HIV infection (AHI) is a transient phase of HIV infection associated with high levels of HIV replication and expansive immunological response, sustained mainly by HIV specific CD8+ T cells. In 50-80% AHI is characterized by constitutional and mucocutaneous symptoms.
Little is known about the events taken place in the skin during acute HIV infection. We report clinical, laboratory and skin immunohistologic findings in a patient with AHI.
Methods: Three skin biopsy from erythematous plaques were taken, fixed in formalin and processed for histopathologic examination. Analysis with monoclonal and polyclonal antibodies and immunohistochemical examination were performed.
Results: Epidermis presented pronounced acanthosis, spongiosis and diffuse vacuolization. A dense dermal, perivascular and periadnexal infiltrate of CD8+ and granzime B+ was described. Moreover a clonal TCR γ expression was found in a CD8 cell sub-population. Cutaneous lymphoma T (CTCL) was suspected but stadiation diagnosed no pathological findings. After two months skin biopsy showed a different pattern: dermal infiltrate was composed by CD4+ and CD8+ in similar quantities, and no clonal cells for TCR γ gene were found. According to clinical and skin improvement on HAART therapy, the diagnosis turned into an atypical cutaneous lympoproliferative disorder (ACLD) related with primary HIV infection.
Discussion: A 20 years old woman developed a symptomatic AHI with fever, widespread lymphadenomegaly, sore throat and a macupapular skin rash. Skin lesions were characterized by inflammatory, pruritic manifestations evolving in few days from nettle rash to sterile vesicle and finally to scab lesions. Other virological and microbiological test were negative. Because of a rapid slope of CD4, after 3 months, high active antiretoviral therapy (HAART) was started.
In HIV+ patients papular pruric eruption and folliculitis are descript. Thus CTCL and ACLD are rare findings even in late stages of HIV. Patch biopsies are generally characterized by superficial and deep dermal polymorphous infiltrate with atypical, lymphocytes CD4+ and CD8+. In our case we described an ACLD in AHI, characterized mainly by CD8+ cell migration. Moreover in a relatively short time, there was a change in histological features and epidermotropism, turning the diagnosis from a lymphoma to a HIV reactive setting. After 5 months of HAART skin lesions were improved, no new papules were noticed and HIV virologic suppression was achieved. On the contrary there was a lack of CD4 recovery and a progressive decrease of T CD8+ in the peripheral blood.
We show how skin plays an important role in redistribution of HIV specific CD4 and CD8, cells during AHI. Proinflamatory cytokines are probably involved in CD8 skins migration and HAART is not enough to slow this process.
Skin could be an important setting in understanding HIV immunopathogenesis.

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Characteristics and outcome of AIDS and non-AIDS defining malignancies among a cohort of HIV-infected people during the HAART era

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Background: People with AIDS have an elevated risk for cancer, including both ADC (AIDS-defining cancers) and NADC (non-AIDS defining cancers) events.
Methods: We investigated the occurrence of cancers among an HIV-infected adult cohort prospectively followed at two hospital of north-east Italy from January 1996 to January 2010. Information about antiretroviral response, co-morbidities and survival were assessed every 6 months during follow-up.
Results: 827 (84% male, 83% white) patients were followed during the study period. A total number of 108 malignancies were observed: 62 ADC (57%) and 46 NADC (43%) with an overall incidence rate of 13%. The median age at diagnosis was 43 ys (33-63) in ADC vs 40 ys (34-66) in the NADC; the median CD4+ cell count at the diagnosis was 257 cells/µl (23-460) in ADC vs 208 cells/µl (190-462) in NADC; the median HIV-RNA was 53.600(<40-3.000.000) in ADC vs 8890 (<40-58000) in NADC. 63% of NADC developed in patients without a previous diagnosis of AIDS. All but 2 patients with a NADC were treated with effective antiretroviral therapy whereas 43 (55%) patients with an ADC were antiretroviral naïve. Of those whose first cancer was AIDS-defining, Kaposi's sarcoma (KS) was the most frequent (n= 36; 58%). Among NADC, the most common primary cancer was liver cancer, accounting for 15% of cancer cases, followed by colonrectal cancer (13%), anal cancer (11%), lung cancer, melanoma and renal cancer (9% each one); breast cancer, carcinoma of the biliary tract and squamous cell carcinoma of the larynx (6% each one) and gastric cancer (4%). Other cancers accounted for 11%. Four renal cancer were all recorded during the last year out of one center.
Mortality rate was 21% for ADC, a fact that was likely related to the high number of KS in our cohort and 52% for NADC .
Conclusions: Our data show a significant impact of malignancies among HIV/AIDS people despite the introduction of HAART. KS and NHL remain the most common tumors. However NADC are increasing during the last decade, accounting for approximately 43% of all cancer in our population. Some of this increase is associated with longer survival and aging of patients in HAART even thought other co-factors (smoking, coinfections with HCV, HBV, HPV) may play a major role. In our patients the frequency of NADC seems to be associated with a younger age, low CD4 cell count but not with the HIV viremia. Furthermore, the observed heterogeneous pattern of tumors could suggest a largely screening interventions.

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Clinical and virological response to foscarnet in hiv patient with human herpesvirus type 8 disseminated infection

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Background: Infection with human herpesvirus 8 (HHV8) has been consistently associated with development of Kaposi sarcoma (KS) and rare lymphoproliferative disorders as body-cavity lymphomas and Castelman's disease. These conditions have been frequently described in HIV patients and immunosuppression is a relevant cofactor. Is not clear if primary HHV8 infection or reactivation could lead to a non-neoplastic illness. In literature only two cases of co-infection were reported and both of them died by HHV8 sepsis. We describe a 45-yers-old homosexual HIV patient, affected by recurrent episodes of disseminated HHV8 infection.
Methods: We used molecular and serologic methods to study HHV8 infection. In particular lung, spleen, lymph nodal and bone marrow biopsies were investigated for HHV-8 sequences. A nested PCR method was used for amplification of HHV-8 DNA fragments. In addition, we used an in situ hybridization technique and immunohistochemical staining for detection of HHV-8 infected cells.
Results: The patient presented dyspnea, fever, marked interstitial pneumonitis and widespread linfoadenopathy. CT chest scanning delineated a pattern of multi-focal ground-glass opacities. Because of severe hepato-splenomeagaly with thrombocytopenia and anaemia, the patient was submit to splenectomy. Research for other opportunistic infection were negative. HHV8 was the only pathogen detected in serum and in all biological material. The patient started 3 weeks treatment with foscarnet, leading to a dramatic normalization of blood cell counts, concomitantly with the disappearance of HHV-8 viremia. After switching to a maintenance regimen with valgancyclovir, in a few months a viremic HHV8 rebound with fever and pancytopenia was observed. After about several mouths the patient developed cutaneous and mucosal lesions of KS so he was performing treatment with liposomal doxorubicin. Foscarnet concomitant full dose administration was decided, and by now the patient is clinically stationary.
Discussion: Specific therapy for HHV8 is not available. In vitro and observational studies suggest that ganciclovir, foscarnet, cidofovir, based on anti-CMV agents, inhibit HHV8 replication, but no randomized clinical trials have been conducted. In literature cases, HHV8 disseminated infections had fatal outcomes. One patient died for multiorgan failure after a single dose of Paclitaxel. The other received a therapy with daunorubicin and cidofovir, without any result. Only one renal transplanted HIV negative patient with severe pancytopenia HHV8-related, has been successfully treated with foscarnet. In our case we observed a clinical improvement with concomitant administration of liposomal doxorubicin and foscarnet full dose. However the pathogenic role of HHV8 remains unclear and needs further study. Long time specific antiviral therapy could be useful also in treatment of HHV8–related diseases and as potential strategy preventing KS in patient with high HHV8 viremia.

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Erectile dysfunction does not mirror sub-clinical atherosclerosis in HIV infected males

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Background: In the general population erectile dysfunction (ED) and coronary artery disease share the same risk factors and endothelial dysfunction appear to be the common denominator. ED appears to be one of the earliest signs of systemic vascular disease and might be considered as an early marker for subclinical cardiovascular disease. We hypothesised ED as a mirror of subclinical atherosclerosis in HIV infected patients.
Methods: This was an observational retrospective cross-sectional study to evaluate the association between ED and subclinical atherosclerosis by means of functional and structural endothelial dysfunction test, namely Flow Mediated Dilation test (FMD) and Coronary Artery Calcium score (CAC). ED diagnosis was assessed with the International Index of Erectile Function (IIF-15) ,score <25 of erectile domains. The following variables were analysed as potential predic-

tors of ED in univariable and multivariable stepwise logistic regression:
Demografics: age, smoke habit, alcohol intake, BMI, diabetes. HIV: duration of HIV infection, HIV Viral Load (Log10), cumulative exposure of NRTI, PI and NNRTI drugs.
Metabolic: Total cholesterol, HDL, LDL, TG and metabolic syndrome
Patients related outcomes: subjective aesthetic satisfaction of the face and of the body
Subclinical atherosclerosis: FMD, CAC and coronary age. Coronary age was derived from Multi-Ethnic Study of Atherosclerosis (MESA) previously published algorithm based on the extent of CAC of a single subject compared to the median CAC of race, age and sex matched individuals.
Results: 133 consecutive male patients were enrolled: 39 (29.32%) had mild, 14 (10.52%) moderate , and 26 (19.55%) severe ED. CAC >0 was present in 70 (52.63%) pts and FMD<7% was present in 43 (32.33%) pts. The median value of increased coronary age was 10 years (range 1-37).
Pts with and without ED did not show any difference in testosterone (544.28 ± 186.41; 501.43 ± 185.22 respectively; p value 0.19), FMD (7.27 ± 4.00; 7.14 ± 4.89 respectively; p value 0.89) CAC (0 range 0-678; 9 range 0-1515 respectively; p value 0.25), coronary age (53 range 33-85; 56 range 35-85 respectively; p value 0.27) . In a backward stepwise logistic regression analysis, ED was related to VAS face (OR=0.85; 95% CI 0.73; 0.99) and age (OR=1.73, 95% CI 1.02; 2.94) only.
Discussion: In HIV-infected people age and psychological factors, in particular aesthetic satisfaction of face, were independent predictors of ED. Given the young median age of our population atherosclerosis may not represents a significant risk factor for ED moreover HIV may represents a major psychological determinant of sexual function.

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Quantitative ultrasound in HIV-infected patients as a surrogate marker of early bone damage

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Background: Bone demineralization is a common metabolic disorder in HIV-infected patients. The increasing aging of HIV-infected individuals, virus itself, antiretroviral therapy (ARV) and the presence of other concomitants factors could contribute to high prevalence of osteopenia and osteoporosis in this population. There is a need for simple, reliable and low cost methods to identify and monitor early bone alterations both in older and younger HIV+ patients. Recent data showed that bone mineral quality (BMQ), assessed by a quantitative ultrasound (QUS) technique, could be used as a early marker of osteopenia/osteoporosis.
Objective: to study the usefulness of calcaneal quantitative ultrasonography (QUS) for bone health assessment in a cohort of young HIV-infected adults.
Methods: 29 HIV-infected patients and 29 HIV-negative healthy donors were matched for age, sex and classical risk factors for osteoporosis. Bone health was measured using classical dual energy x-ray adsorptiometry (DXA) of spine and hip and calcaneal QUS. Broadband ultrasound attenuation (BUA) and speed of sound (SOS) and quantitative ultrasound index (QUI)/stiffness index (SI) were assessed by QUS. Data were correlated with CD4, VL, immune activation markers (DR+CD38+CD4+ and DR+ CD38+CD8+), 25OH vitamin D (chemiluminescent immunoassay), years of diagnosis. Nonparametric Mann-Whitney test and Spearman coefficient correlation were used.
Results: 14 males and 15 females were enrolled in HIV population (mean nadir CD4, 295/mmc) and controls groups with a median age of was 40+11 years. 3 patients were viremic (ARV-naïve); the remaining subjects were virologically ARV-suppressed. A significant decrease of QUI/SI was found in HIV-infected patients in comparison to control (83.4 ±4.9; 99.7±2.5 p = 0.014) matched for sex and age with a correlation between QUI and DEXA Z-score. No differences were found between patient population and control group for vitamin D levels, even if most subjects showed a moderate or severe 25OH-D deficiency. A significant inverse correlation was found between QUI/SI and age (p=0.02). Bone stiffness positively correlated with CD4 nadir (p=0.004). No correlations were found with immune activation markers and ARV exposure.
Conclusions: In HIV-infected young patients QUS could be a simple and diagnostic tool for bone health assessment in order to identify early signs of bone damage. QUS parameters are closely related to the structural properties and elastic properties of bone and it can provide useful information related to bone quality and bone strength. Because of low cost and versatility the technique should be included in routine clinical practice in a model of risk assessment of HIV-related bone disorders.

PO 81

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Pulmonary arterial hypertension in HIV positive patients: experience of an infectious disease department

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Pulmonary arterial hypertension (PAH) is a rare but severe complication of HIV infection; its prevalence seems to be unchanged in the last years nevertheless the introduction of HAART. New therapies (i.e, prostanoids, endothelin receptor anthagonists and phosphodiesterase inhibitors) seem to be useful in improving the outcome of patients (1,2,3). We describe 13 HIV patients (10 M and 3 F) affected by PAH, observed in our department between 1995 and 2010; HIV infection was transmitted by i.v. drug abuse in 7 cases and by unprotected sexual intercourses in 5. The diagnosis of PAH was based on clinical symptoms (dyspnea was the most common presentation) and strumental data (echocardiography and right hearth catheterization were performed in all cases). Five patients died , two out of them for PAH complications and three for HIV related complications, two patients were lost at follow up and six survive, with good immunological and haemodynamic parameters. The median age at the PAH diagnosis was 37 years, the median length of HIV infection is 15,6 years, the median length of PAH is 11,6 years. All but one patients received HAART; among the six surviving patients four assume TDF, FTC and EFV, one D4T, 3TC and NVP and the last one raltegravir, ATV, TDF,FTC. All of them have undetectable HIV RNA and CD4+ count above 200 cell/mmc. PAH was defined as severe in eight patients, moderate in two and mild in the remaining two ones. Specific PAH therapy was performed in nine patients: Bosentan in five cases, Bosentan associated to epoprost in one case, ambrisentan in one case, diuretic and anticoagulant therapy in two cases. Two out of the dead patients assumed diuretic and anticoagulant therapy with poor adherence and one was treated with bosentan. Our experience suggests the need of early screening for PAH in symptomatic HIV patients and points out the significant role of the PAH specific treatment associated to HAART in improving the survival rate of these patients.
1)Degano, 2010; 2)Talwar 2009; 3)Sitbon 2010.

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Waist circumference and body mass index in HIV infection

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Background: The metabolic syndrome (MS) is considered as an emerging risk factor for diabetes and cardiovascular disease in the HIV-positive population. The recently published guidelines from the European AIDS Clinical Society recommend to measure waist circumference (WC) in clinical practice at the initial and at subsequent visits in HIV patients.
Objective: We aimed to get a specific equation to predict waist circumference (WC) from body mass index (BMI) for HIV-patients.
Methods: In two multicenter Italian studies on metabolic syndrome (MS) in HIV-infected patients, the SIMONE and the HERMES study, we collected WC, weight and height in HIV people. From these two databases, we evaluated the relation between BMI and WC and the BMI values corresponding to a waist circumference of 102 cm in men and 88 cm in women.
Results: The two databases included 1522 patients (mean age 42 ± 9 year, 72% men, 69% on antiretroviral treatment). We performed a regression analysis of WC on BMI, separately in the two genders. As expected, WC was significantly related with BMI in both men (r = 0.73) and women (r = 0.74, both p<0.001). The resulting equations were: for men WC (cm) = 31.2+2.4 × BMI (Kg×m-2); for women WC (cm) = 33.2+2.1× BMI (Kg×m-2).
Thus a waist circumference of 102 cm in men and 88 cm in women was equivalent to a BMI of 29.5 kg/m2 in men and 26.1 kg/m2 in women.
Discussion: Studies on MS should include WC measurement, or at least an estimate thereof derived from HIV-infected people.
We propose that, in the absence of direct measures of WC, the presence of MS should be assessed according to the above equations. This may lead to a better estimate of the prevalence and characteristics of the MS.

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Cardiovascular disease and depression: a cross-section analysis in a cohort of older HIV patients

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Background/objectives: During aging, HIV infection could accelerate the cardiovascular diseases and the emergence of depression. The aim of this study was to investigate the impact of cardiovascular risk in a cohort of older HIV positive patients and correlation with depressive disorder.
Methods: A pilot- study, cross-sectional was performed in a population of HIV-positive patients older than >50 years consecutively seen in out-patients. The Framingham score was used to assess the severity of cardiovascular risk. Current depression was measured on the Zung depression scale, and a Pearson test was applied.
Results: Sixty-one patients were evaluated, 43 male (70,5%). Median age 54 years (r=50-76). Thirty-five patients were smoker (57.3%). Average total cholesterol and HDL cholesterol were 192.5 mg/dl (r=80-315) and 50.9 mg/dl (r=17-121) respectively. Average systolic and diastolic blood pressure were 125 mmHg (SD=17.02) and 82 mmHg (SD=11.92) respectively. Average BMI was 23.72Kg/m^2 (SD=4.29). Average waists circumferences was 88.54 cm (DS=12.8). Twelve patients (19.7%) were AIDS. Thirty-tree patients (54,1%) were intravenous drug abuser, and 30 were positive for HCV-RNA. Antihypertensives were taken by 13 patients. Fourteen patients had a metabolic syndrome (22.9%). HIV-RNA were undetectable in 50 patients (81%). Median CD4+ cell count was 432 (r=31-1272); median CD4+ nadir was 201 cells/mmc (r=3-790). Mean 10—year Framingham coronary risk-factor score was 11%. Framingham coronary risk function estimates more than three times the actual risk of coronary disease observed in equal age population. Zung Score in table 1:

DEPRESSION LEVEL	FREQUENCY	PERCENT
None	14	22.95
Minimal/Mild	24	39.34
Moderate	22	36.07
Moderate/severe	0	0
Severe	1	0.016

There was no significant association between cardiovascular risk and any laboratories parameters, in contrast, there is an association between efavirenz-based therapy and minimal or moderate depression (p=0,0002).
Discussion: In our 61 patients, cardio-vascular risk factors are moderate prevalent but are not associated with depression. Besides efavirenz based-therapy remain a regimen burdened by depression. The respective roles of HIV, antiretroviral therapy, and co-morbidities remain debated.

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Analysis of the effects of specific protease inhibitors on OPG/RANKL regulation in an osteoblast-like cell line

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Background: The loss of bone mass with subsequent osteopenia and osteoporosis development was related to HIV infection and antiretroviral treatment, even though the mechanisms involved has not been yet elucidated. It is noteworthy that the mechanism(s) involved in the bone impairment is (are) not well known: the homeostasis of bone mass in adult individuals is due to a well-tuned balance of osteoblast-related bone synthesis and osteoclast–related bone resorption activities regulated also by several hormones, vitamins and cytokines, into the so-called bone remodeling unit.
Methods: The biological pathway represented by RANKL/RANK/OPG system plays an essential role in bone metabolism control. RANKL is a protein yielded by osteoblasts and T lymphocytes stimulating the differentiation and activity of osteoclasts through the binding with RANK, a receptor detectable on osteoclast cell membrane. Its activity is modulated negatively by the soluble molecule OPG, which inhibits the RANKL/RANK binding. In this study, the early effects of some specific protease inhibitors on OPG/RANKL yielding and cell survival (osteoblast-like HOBIT cell line) were analyzed.
Results: All protease inhibitors, tested at scalar concentrations tested (C1, C2, C3) did not affect the cell survival except for Tipranavir that, at higher concentration (C3), elicited a reliable apoptosis induction. In particular, Atazanavir, Saquinavir and Indinavir did not affect the

OPG/RANKL in the cell surnatant in our experimental conditions. On the contrary, at optimal concentration (C2), Fosamprenavir, induced a significant increase of OPG associated to RANKL decrease, whereas Tipranavir down-regulated both OPG and RANKL (at C2 and C3) and Darunavir increased RANKL only at C3 concentration.
Discussion: Altogether these data (coupled with the analysis of OPG/RANKL ratio) indicated that at early times and at optimal concentrations the protease inhibitors did not impair significantly OPG/RANKL system, with the exception of Fosamprenavir, that really showed a relative positive OPG/RANKL ratio regulation.
On the other hand, cell cultures treated by higher concentration of Tipranavir or Darunavir showed an alteration of cell survival or an increase of RANKL, with a negative effect on OPG/RANKL balance.

PO 85

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Hepatocellular carcinoma in hiv infected patients: check early, treat hard

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Background and aims: Hepatocellular carcinoma (HCC) is an emerging problem for HIV patients (pts), particularly if HCV and/or HBV co-infected. The aim of the study was to evaluate the impact of early diagnosis and effective treatment on survival of HIV infected pts with HCC.
Methods: a retrospective observational multicenter study from 1997 to 2009 identified 87 HIV-infected pts (78 under HAART) with HCC. Controls were 339 consecutive HIV-negative subjects.
Results: At HCC diagnosis, HIV-positive pts were significantly younger than controls (47.6±7.1 vs. 66.6±8.7 years, p=.000). Multiple HCC presentation was more common in HIV infected pts [45/87 (51.9%) vs. 118/339 (34.8%), p=0.004], whereas BCLC C/D stage was more common in HIV negative pts [30/87 (34.4%) vs.163/339 (48%), p=.021]. Globally, a higher proportion of HIV infected pts received some treatment for HCC [80/87 (91.9%) vs. 278/339 (82%), p=.024], but more often underwent non curative or of unproven efficacy treatments [(30/80 (60%) vs. 149/278 (53.5%), p=0.012)]. Time to treatment after HCC diagnosis was significantly lower in HIV negative pts (1.2±0.2 vs. 4.1±3.2 months, p=.000). HCC recurrence was observed with the same prevalence in both groups (about 70%), but HIV negative patients received a second line treatment in 87% of the cases, often with a curative options. Conversely, 61.4 % only of the HIV infected patients received a second line therapy, frequently non curative. In groups who received potentially curative treatments, survival was similar between HIV-infected and HIV-negative patients. Besides an early BCLC stage, absence of vascular invasion and HCC treatment at diagnosis, also time between HCC diagnosis and first line therapy and HCC treatment at recurrence were independent predictors of survival at multivariate analysis.
Conclusions: preventive strategy and effective treatment, even in case of recurrence, are mandatory in this setting of patients.

PO 86

Infection 2010; 38 (Suppl. I): 82

Prescription of anti HCV treatment in persons living with HIV in Italy

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Background: Several recommendations on anti HCV treatment have been published however their impact in clinical practice is unknown. In order to define prescription practices of Italian physician treating hepatitis C in HIV infected persons we have analyzed baseline clinical data of an Italian national cohort study
Methods: The OPERA study (Optimization of Pegylated interferons Efficacy and anti-Retroviral Approach) is an Italian national cohort observational study including all consecutive patients with HIV/HCV coinfection who were prescribed anti HCV treatment since 17 January 2005 in 101 Italian centres for the care of HIV. We reviewed clinical and epidemiological baseline data of 1540 patients enrolled in order to verify the prescription behaviour of Italian physician treating hepatitis C in persons living with HIV.
Results: According to guidelines liver biopsy is optional and could be considered more strongly in patients infected by HCV G1 or 4. Pre treatment liver biopsy, was performed in 41% (627/1539) of the global study population; this proportion was significantly higher in patients infected by HCV G1or 4 (45%) vs G 2 or 3 (35%; p<0.001). Guidelines suggest not to treat patients with CD4 < 200/mmc. Only 1% (18/1535)had CD4 count < 200 cells/mmc. Guidelines does not exclude from treatment patients with normal ALT and on opioid substitution: only 4% and
1.3% (20/1539) respectively were in these conditions.
Ribavirin dose higher than 800 mg/d was used in 77% of patients infected by HCV G1 or 4 (652/851) and in 55% (366/660)of those infected by HCV G 2 or 3. Guidelines advise to avoid usage of zidovudine in concurrent ART however 16% of patients treated with pegylated interferon and ribavirin were assuming zidovudine.
Conclusion: Pre treatment liver biopsy is still performed in a large proportion of patients especially in those infected by HCV G 1 and 4. Even if high ribavirin doses are prescribed in the majority of patients many doctors follow recommendations reported in the summary of product characteristics. Zidovudine is still prescribed in a small group of patients.

PO 87

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Immunereconstitution among HIV patients treated with HAART and receiving anti HCV treatment

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Background: In HCV-HIV co-infected patients immune reconstitution seems to be affected by HCV infection. Aim of the study was to determine if the response to anti HCV treatment could affect long-term immunereconstitution.

Material and methods: Retrospective study of 116 HCV-HIV coinfected patients treated for HCV in the Modena cohort.
Results: 116 HIV infected patients received an anti HCV treatment with PegInterferon and ribavirin, 85 (73,3%) were male, 95 (81,9%) were intravenous drug users. Sustained virologic response (SVR) occurred in 36 patients (31%). 90 patients (77,6%) were on a stable HAART during HCV treatment. CD4 cells count when starting HCV therapy did not differ between SVR and non responder [median and (IQR): 536 (430-654) in SVR and 527 (412-683) in non-SVR, p=0.959]. At 48 months CD4 count increased to 638 (476-733) in SVR and to 532 (442-787) in non-SVR with a CD4 recovery of 47 (-113 – 206) in SVR and 8.8 (-220 -147) in non SVR (p=0.453 and p= 0.793, respectively). No differences were found after stratifying patients for HCV genotype (3 vs non-3). Among patients not receiving HAART at the time of HCV therapy the same proportion start HAART after a median of 21 months (range 10.0-26.0) in non-SVR and after 20 months (range 1.5-41.5) in SVR (p=0.548). At 24 months the percentage of patients with an HIV RNA below the limit of detection (<40 copies/ml) did not differ between the 2 groups (p=0.782).
Conclusions: The response to treatment for HCV does not seem to influence long-term HAART-induced immune-reconstitution.

PO 88

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Lower prevalence of neurocognitive disorders in HIV-infected subjects treated with neuroactive HAART

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Background: Neuropsychological impairment in HIV infection ranges in severity from mild neurocognitive disorder to severe dementing illness. Although HAART is able to produce long-lasting suppression of systemic HIV replication, the prevalence of associated Neurocognitive Disorders (HAND) has remained stable or even increased. In the ALLRT study the most conservative prevalence estimate of cognitive impairment in 1160 patients on stable HAART regimen was 26%. Poor CNS Penetration Effectiveness (CPE) of ARV drugs has been considered among possible explaining factors of viral neurotoxic effect. However, the association between CNS Penetration Effectiveness (CPE) of ARV drugs and cognitive performance is still unclear. The aim of this study is to assess the prevalence of HAND in patients on different HAART regimens, as estimated by CPE rank.
Methods: Trained research psychologists blind to ARV regimens administered the Cotugno Mini Battery (a brief neuropsychological battery including Verbal Memory Span, Auditory Verbal Learning Test, Verbal Fluency, Color Trails 2 and Symbol Digit Modalities Test) to subjects admitted to DH care. Patients included in this analysis were on stable plasma viral suppression and unchanged ARV regimen for at least 6 months before assessment. Exclusion criteria were age > 60, formal educational < 8 yrs., depressive symptomatology (MADRS score >17), other major neurological or psychiatric disorders, current use of illicit drugs. Prevalence of HAND was assessed in subjects with higher CPE rank (CPE+) as compared with those with lower CPE rank (CPE-) (cut-off = 2.0). Impairment on each test was defined as a performance 1.0 or more standard deviations (SDs) worse than the published age-matched norms (NIMH research criteria). Mild Neurocognitive Impairment was defined as an impaired performance on two or more tests with at least mild interference in daily functioning (score >2 on ADL).
Results: 45 subjects were included in the analysis (87% male; median age: 42 years; median years of education: 11). 15 patients were on ARV regimen with a high CPE score (> 2). Prevalence of neuropsychological impairment was significantly higher in subjects with a low CPE rank, on Verbal Memory Span (43.3% vs. 13.3; p<0.05) and Symbol Digit Modalities Test (63.3% vs. 26.7%; p<0.05). The prevalence of HIV-associated Asymptomatic Neurocognitive Impairment (ANI) was 70.0% in CPE- and 33.3% in CPE+ (p< 0.05). Prevalence of Minor Neurocognitive Disorder (MND) was significantly lower in the group of patients on HAART regimens with high CPE score (0% vs. 26.7%; p=0.05).
Conclusions: In this sample of virally suppressed HIV-seropositive individuals in stable HAART treatment and not exposed to other risk factors, the prevalence of ANI and MND was significantly lower in subjects taking neuroactive ARV drugs, suggesting that higher CPE of antiretroviral regimens could lead to a relevant reduction of cognitive decline in HIV patients.

PO 89

Infection 2010; 38 (Suppl. I): 83

Prevalence and risk factors for advanced liver fibrosis in HIV/HCV-coinfected individuals

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Background: Liver disease associated with hepatitis C virus (HCV) has emerged as a significant problem among HIV+ patients, thanks to improved survival in the HAART era. Coinfection with HIV is known to lead to a more rapid progression of HCV liver disease to cirrhosis. Successful HAART slows the progression of liver fibrosis (LF), but antiretroviral-liver toxicity could contribute to hepatic damage in co-infected patients. The advent of transient elastography (TE) has demonstrated to be very helpful for the non-invasive measurement of LF.
The aim of this study was to assess the prevalence of advanced liver fibrosis (ALF) in HIV+, HCV+ and HIV/HCV+ patients using TE and to identify factors associated with more severe LF.
Methods: 71 HIV-monoinfected, 57 HIV/HCV-coinfected and 53 HCV-monoinfected patients on regular follow-up at our Centre were enrolled between September 2008 and October 2009. Alcohol intake, the main parameters of liver function, HIV-RNA, HCV-RNA, duration of HAART and CD4 cell counts were recorded. ALF was defined as liver stiffness (LS) >9.5 KPa, according to De Ledinghen et al. (J Vir Hep 2008).
Results: Table 1 shows that LS values of co-infected patients were increasingly higher than in mono-infected patients (χ2MH = 4; p < 0.04). Indeed, LS ≥ 9.5 was significantly higher in co-infected than in mono-infected patients (χ2= 5; p < 0.03).

Table 1

	HIV (n=71)	HCV (n=53)	HIV/HCV (n= 57)	
<7.1 (F0-F1)	56 (78.8)	23 (43.4)	19 (33.3)	
7.1-9.4 (F2)	11 (15.4)	15 (28.3)	9 (15.8)	
9.5-12.4 (F3)	1 (1.4)	4 (7.5)	9 (15.8)	
≥ 12.5 (F4)	3 (4.2)	11 (20.7)	20 (35.1)	χ2MH = 4; p < 0.04
≥ F3	4 (5.6)	15 (28.3)	29 (50.9)	χ2= 5; p < 0.03

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≥ 12.5 (F4)	3 (4.2)	11 (20.7)	20 (35.1)	χ2MH = 4; p < 0.04
≥ F3	4 (5.6)	15 (28.3)	29 (50.9)	χ2= 5; p < 0.03

In HIV/HCV-coinfected patients extent of LS was significantly associated with alcohol intake > 20 gr (p < 0.04) and lower CD4+cell counts (p < 0.02). In HCV+ patients LS correlated with alcohol intake > 20 gr (p < 0.001) and cholesterol levels (p < 0.03). BMI, diabetes, HCV-, HIV-viremia were not significantly correlated with LS. Moreover 20% of co-infected patients were under virological unsuccessful HAART; in 50% of them compliance was low, CD4 levels were < 400 cells/mm3 and LS was > 9,5 KPa. There was no significant correlation between the extent of LF and HAART exposure, duration of HAART exposure, particularly of specific dideoxynucleoside analogues (didanosine, stavudine, zidovudine). In only 5,6% of HIV-monoinfected patients ALF, evaluated using LS, was found ≥ 9.5.
Discussion: In our population, HIV/HCV-co-infected have more ALF than HCV- and HIV-mono-infected patients. This result was not correlated with long-term exposure to HAART but with lower CD4 cell count, suggesting that immunological successful of HAART may protect the liver damage in HIV/HCV-coinfected patients. Moreover, the detection of unsuspected ALF in HIV-mono-infected patients confirms that FibroScan is very helpful in this population.

PO 90

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Association between hepatitis C viremia and HOMA-IR score in HIV/HCV co-infected patients

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Background: Insulin resistance defined as HOMA-IR score (homeostasis model of assessment-insulin resistance) impairs the virologic response to peginterferon alfa 2/ribavirin(PegIFN/RBV) treatment in HIV/hepatitis C co-infected patients. The association of HCV-RNA with the HOMA-IR score has been assessed in HIV/HCV at baseline in subjects who started a PegIFN/RBV therapy.
Methods: All consecutive patients who were prescribed anti HCV treatment since January 2005 in the Institute of Infectious and Tropical Diseases in Brescia, are including in a prospective observational study. Epidemiological, clinical data, virologic and metabolic parameters were collected at baseline. HCV-RNA by quantitative PCR assay (Versant 3.0) was recorded. At fasting serum total cholesterol, low-density lipoproteins, high- density lipoprotein and insulin resistance, defined with HOMA-IR , calculated as fasting insulin (mIU/l) x fasting glucose (mmol/l)/22.5, were prospectively measured in all patients.
Results: 107 HIV-HCV co-infected patients were enrolled. Mean age was 42,9 (+5,4) years, 90 (84,1%) males, 60 (58,3) with advanced liver fibrosis (F3-4 according to METAVIR classification). Fifty-three (49,5%) had an infection by HCV genotype 1 or 4. One hundred (93,4%) subjects were on HAART.
The mean HCV-RNA level was 5,5 log 10 IU/ml (+0,7). The mean level of HOMA-IR was 3,2(+2,9). HOMA-IR correlates with HCV-RNA log10 (Linear regression correlation coefficient r^2= 0,92; p<0,0001)
HOMA –IR is related with HCV-RNA in patients with genotype 1-4 (Linear regression correlation coefficient r^2= 0,9; p<0,0001) as well in those with genotype 2-3 (Linear regression correlation coefficient r^2 0,6= p<0,0006)
Conclusions: A linear relationship is found between HOMA-IR and hepatitis C viral load in HIV-HCV co-infected regardless genotype. This result could contribute to explain the role of insulin resistance on the anti HCV treatment outcome in HIV/HCV co-infected persons.

PO 91

Infection 2010; 38 (Suppl. I): 84

Insulin resistance is associated with liver stiffness in HIV/HCV co-infected patients who started Peginterferon plus ribavirin (PegIFN/RBV) treatment

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Background: Factors that influence liver fibrosis progression in HIV/HCV co-infected persons are poorly understood. In HCV mono-infected persons insulin resistance increases with liver fibrosis. Few data are available on the association between insulin resistance and liver stiffness.
Methods: All consecutive patients who were prescribed anti HCV treatment since January 2005 in the Institute of Infectious and Tropical Diseases in Brescia, were included in a prospective observational study. Epidemiological, clinical data, virologic and metabolic parameters were collected at baseline. Liver stiffness (LS) measurement was performed with a Fibroscan (EchoSens, Paris, France), a medical device based on one-dimensional transient elastography. At fasting serum total cholesterol, low-density lipoproteins, high- density lipoprotein and insulin resistance, defined with HOMA-IR , calculated as fasting insulin (mIU/l) x fasting glucose (mmol/l)/22.5, were prospectively measured in all patients.
Results: 107 HIV-HCV co-infected patients were enrolled. Mean age was 42,9 (+5,4) years, 90 (84,1%) males, 60 (58,3) with advanced liver fibrosis (F3-4 according to METAVIR classification). Fifty-three (49,5%) had an infection by HCV genotype 1 or 4. One hundred (93,4%) subjects were on HAART.
The median liver stiffness was 9,9 kPa (range 3,3-63,9).
The median level of HOMA-IR was 2,6 (0,1-21,6). HOMA-IR correlates with LS (Linear regression correlation coefficient r^2= 0,95 ; p<0,0001)
The median HOMA-IR in patients with LS <8 kPa was 1,8 (range 0,1-11,3) while it was 3,1 kPa (range 0,1-11,3) in patients with LS> 8 kPa (p 0,01)
After multivariate analysis HOMA-IR <3 [AOR 3,1 (IC95% 1,0-9,8) p 0,041] and older age (AOR 0,8 IC95% 0,7-0,9 p 0,01) are related with the LS < 8kPa
Conclusions: Insulin resistance is associated with liver stiffness in HIV-HCV co-infected patients. This result could contribute to explain the role of insulin resistance on the anti HCV treatment outcome in HIV/HCV co-infected persons.

PO 92

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Liver Stiffness predicts Early Virological Response (EVR) in HIV/HCV co-infected patients treated with Pegylated interferon alpha2a (PegIFN alpha 2a) plus Ribavirin (RBV)

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Background: Liver fibrosis predicts the anti HCV treatment outcome in patients with HCV with or without HIV co-infection. The association of liver stiffness at baseline and early virological response to PegIFN/RBV has been assessed in HIV/HCV subjects who started PegIFN/RBV therapy.
Methods: All consecutive patients who were prescribed anti HCV treatment since January 2005 in the Institute of Infectious and Tropical Diseases in Brescia, were included in a prospective observational study. Epidemiological, clinical data, virologic and metabolic parameters were collected at baseline. HCV-RNA by quantitative PCR assay (Versant 3.0) at baseline and HCV-RNA by qualitative PCR assay (COBAS 2.0) after 4 weeks and every three months of treatment were recorded. Rapid Virological Response (RVR) and Early Virological Response (EVR) were defined as negative HCV-RNA after 4 and 12 weeks of anti-HCV therapy. Sustained Virological Response (SVR) was defined as negative HCV-RNA 6 months after end of treatment. Liver stiffness measurement was performed with a Fibroscan (Echo-Sens, Paris, France), a medical device based on one-dimensional transient elastography. Liver stiffness and EVR were assessed in HCV-HIV co-infected patients who started PegIFN alpha 2a (180 mcg/week) and Ribavirin (1000-1200 mg/die).
Results: 107 HIV-HCV co-infected patients were enrolled. Mean age was 42,9 (+5,4) years, 90 (84,1%) males, 60 (58,3) with advanced liver fibrosis (F3-4 according to METAVIR classification).Fifty-three (49,5%) had an infection by HCV genotype 1 or 4. One hundred (93,4%) subjects were on HAART. The median liver stiffness was 9,9 kPa (range 3,3-63,9). The median level of HOMA-IR was 2,6 (0,1-21,6).
Forty-two patients (39,3%) reached RVR, 69 (67%) reached EVR and 47/100 patients reached SVR (seven patients are ongoing).
The mean liver stiffness in patients with EVR was 11,7 (+8,4) while it was 21,6 (+17,8) in patients without EVR (p0,01)
After adjustment for genotype, liver stiffness <8 kPa remains associated with EVR [AOR 4,8 (IC 95% 1,2-18,6) p0,02]
Conclusion: Liver stiffness contributes to predict EVR response in HIV-HCV co-infected patients eligible to PegIFN/RBV.

PO 93

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Role of Microbial Translocation (MT) and Immune Hyperactivation (IH) in Liver Disease Progression of HIV/HCV+ Patients with well documented HIV seroconversion date and preserved CD4 count

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Background: We investigated the potential role of MT and IH in accelerating liver disease progression in HIV/hepatitis-virus co-infected patients.
Methods: We included patients of Icona with a documented date of HIV neg/pos tests and >=1 plasma stored while ART-naïve and with a CD4 >200/µl. Plasma MT (LPS, sCD14) and IH (IL-6,TNFα) were measured; in a subset of patients , activated CD8+CD38+HLA-DR+ were measured on cell samples. All patients signed consent for DNA use. The association between MT, IH, hepatitis co-infection was evaluated by Kruskal-Wallis test. We also investigated their association with the following endpoints: i) time to single ALT >200 IU/l or liver-related death, ii) time to Fib-4 >1.45 or liver-related death – all analyses using standard survival analysis, iii) change over time in ALT and Fib-4 as continuous variable (multilevel linear model with fixed intercept and slope). Follow-up was censored at time of last clinical follow-up.

	Adjusted* RH (95% CI) p-value	
	ALT >200 IU/l	**Fib4>1.45**
TNF-α, pg/ml <=2.1 (n=59) >2.1 (n=59)	1.00 0.89 (0.24-3.22) P=0.85	1.00 1.06 (0.31-3.55) p=0.93
IL-6, pg/ml <=1 (n=54) >1 (n=61)	1.00 5.36 (1.11-25.83) P=0.04	1.00 1.47 (0.42-5.15) P=0.54
LPS, pg/ml <=75 (n=48) >75 (n=22)	1.00 0.53 (0.06-4.49) P=0.91	1.00 1.76 (0.50-6.25) P=0.38
sCD14, µg/ml <=3 (n=58) >3 (n=56)	1.00 1.06 (0.32-3.56) P=0.92	1.00 2.63 (0.73-9.51) P=0.14

*for age, CD4, VL, hepatitis virus co-infection at time of test, year of test, HIV infection duration, all MT/IH markers besides the one under evaluation

Results: Of 148 patients (contributing 188 tests), 46 (31%) were hepatitis viruses co-infected (41 HCV, 4 HBV, 1 HCV/HBV). Overall median (IQR) CD4, VL, age were 644/µl (519-823), 3.70 log10 copies/mL (3.0-4.3), 33 years (30-37). On average plasma was stored 4 years after the estimated SC (IQR:2-7). Median (IQR) markers in HIV mono-infected vs. co-infected vs. unknown were: LPS, 75 pg/ml (50-76); 75 (61-75); 86 (75-109) (p=0.02), sCD14, 2.81 pg/ml (1.96-3.61); 3.59 (2.22-5.23); 2.82 (1.90-3.81) (p=0.08), IL-6, 1.11 pg/ml (0.59-1.75);1.04 (0.55-1.92);0.71 (0.44-1.49) (p=0.52), CD8+CD38+DR+, 48.4% (41.7-58.4);53.1% (45.5-58.8);51.7% (35.1-75.7) (p=0.78), TNF-a, 2.08 pg/ml (1.53-2.67);2.32 (1.53-3.67);2.20 (1.35-3.66) (p=0.58). At time of first stored sample, median ALT (IQR) were 24 IU/l (17-39); Fib-4-score 0.36 (0.25-0.52). A total of 16 events of ALT and 21 of Fib-4 elevation were observed over 1,004 person-years (no deaths). The adjusted relative hazards comparing patients with values above and below the median are shown in the Table. The multilevel modelling analysis showed no evidence for an association between MT and IH and the slope of ALT and Fib4 over time (data not shown).
Conclusions: HIV/hepatitis virus co-infected ART-naive patients, tended to have higher sCD14 than HIV mono-infected suggesting an exacerbation of microbial-mediated IH induced by the co-infection. Although higher IL-6 was associated with the risk of a clinically-relevant ALT rise, our analysis showed little evidence of an association between MT/IH and the slope of increase in both ALT and Fib-4.

PO 94

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Carotid intima-media-thickness in antiretroviral-naïve HIV-infected subjects and viral hepatitis-infected patients

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Introduction: Several factors may contribute to an increased risk of cardiovascular disease in HIV-infected patients including chronic inflammation due to HIV infection itself in addiction to traditional risk factors. Hepatitis B-C have been investigated for possible atherogenic

effects, although it is not confirmed weather they may be independent risk factors for carotid atherosclerosis. Measurement of carotid artery intima-media-thickness (IMT) with colour-doppler-ultrasonography is a well-accepted, non-invasive method of assessing atherosclerosis.
Patients and Methods: This observational study was carried out between May 2009 and February 2010.Three groups of consecutive subjects were identified and enrolled in the study: HIV-infected naive (group 1, G1), healthy controls among healthcare workers (group 2, G2), and HCV or HBV-mono-infected subjects (group 3, G3). Data on demographic characteristics, triglycerides (normal values, nv, 170 mg/dL), total-cholesterol (nv 200 mg/dL) HDL-cholesterol (nv 60mg/dL), LDL-cholesterol (nv 150mg/dL), serum glucose (nv 110 mg/dL) and cigarette smoking were collected.
In the HIV-infected population only, data on risk factors for HIV, CDC-stage, time of known HIV positivity, current immunovirological status and coinfections were also collected.
Carotid IMT was measured by the same examinator;an IMT of >1 mm was considered to be pathological; plaque was defined as a focal structure protruding the lumen with an IMT >at least 2 mm.
Results: Carotid IMT was evaluated in 243 consecutive subjects, including 76 patients in G1, 67 in G2 and 100 in G3. Demographic characteristics of the three study group were comparable, except for gender (G3 had the higher rate of males, 85%). Median age was similar among three groups. A total of 140 (57.6%) subjects were smokers (39.5% among G1, 52.2% among G2, 75% among G3, no statistical significance with increased IMT). Median cholesterol values was 164 (73-201) with no differences among the three groups; no association with IMT increase was found.
When compared to G2 and G3, in G1 a higher rate of increased IMT was found (p=0.03 and p=0.02, respectively). Moreover, in G1, coinfection with hepatitis viruses was associated with a higher risk of increased IMT (p=0.02). Conversely, in G3 a link between carotid thickness and HCV/HBV infection was not found when compared to G2. Median CD4 count was 317 (16-1050); patients with lower CD4 cell count (<200/mmc) were more likely to increase IMT (p=0.04). Median years since HIV diagnosis was 4 (0-23); a correlation between duration of HIV infection >6 years and presence of IMT>1 was found (p=0.02).
Conclusion: These findings suggest that HIV infection may cause vascular alterations in HIV infected patients. Hepatitis coinfection in HIV subjects could increase the inflammatory damage, favouring the occurrence of atherosclerosis. Therefore, early assessment of the vascular status in HIV-infected patients should be assessed and monitored.

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Anti-inflammatory effect of maraviroc in an HIV-infected patient with concomitant myositis: a case report

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Background: Maraviroc is the first antiretroviral (ARV) acting at a cellular level. Since chemokines promote leukocyte migration, anti-inflammatory effects and a role in the treatment of autoimmunity have been suggested. Recently, the CCR5 32 deletion was described to protect against inflammation-associated mortality in dialysis patients.
Results: We report a multi-experienced elderly HIV-infected patient with disabling inflammatory myopathy and myocardial infarction who had a sought yet unexpected reduction of the myositis after starting maraviroc. AF, a 78-year old heterosexual man, was diagnosed asymptomatic HIV-1 infection in May 1999, having 538 CD4+T-cells/mm3. He started zidovudine, lamivudine and nelfinavir, then switched to trizivir for hyperlipidemia. One year later he developed arterial hypertension, treated with trandolapril, and symptomatic myopathy, with CK levels constantly exceeding 1000 U/L since February, 2003. Since April 2003 his adherence to therapy began to decline and he had multiple drug holidays, also for long periods, without showing relevant reductions of CK levels or pain. This lead to the accumulation of drug resistance to NRTIs and NNRTIs (with RT 67N, 70R, 74V, 100I, 103N, 184V, 215F and 219Q) several ARV regimens have been changed, including boosted PIs and raltegravir. In March 2004, doppler ultrasound showed diffuse atherosclerosis of limb arteries. He underwent electromyography (EMG) followed by muscular biopsy that showed "important inflammatory myopathy with necrotizing areas" and began dexamethasone followed by prednisone, which he continued, with dose adjustments obtaining partial benefit, although his CK blood levels never normalized even with high-dose prednisone (75 mg/day). In December 2008, his muscular function worsened so much that he couldn't rise up from sitting and needed the help of a stick to walk. Admitted in a neurological clinic, diagnosis of chronic polimyositis was confirmed through repeated EMGs. In March 2009 the patient experienced an acute myocardial infarction and underwent angioplasty. In June, the Enhanced Trofile having yielded CCR5-tropic virus, he switched to twice-daily maraviroc 150 mg plus atazanavir 200 mg, and decided to stop steroids. Three months later, CK levels had normalised (50 U/L), clinical symptoms resolved, and with adequate physiotherapy he recovered full ability to stand and walk. After eight months he is still able to conduct a normal life without the need of steroids.
Discussion: Chronic polimyositis belongs to inflammatory myopathies; diagnosis follows major and minor criteria suited for HIV-negative patients. In HIV+ subjects, the prevalence of inflammatory myopathy, apparently CD8- and macrophage-mediated, is around 0.22%.
After six years of myositis this anti-inflammatory effect is likely to be related to the introduction of maraviroc, being this the only new action taken. Further observation may confirm these findings.

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The MONET trial: correlation between Hepatitis C coinfection and HIV RNA responses during darunavir/ritonavir monotherapy, for patients with HIV RNA <50 copies/mL at baseline

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Background: Co-infection with Hepatitis C has been associated with higher rates of treatment failure in cohort studies.
Methods: 256 patients with HIV RNA <50 on current HAART for over 24 weeks (NNRTI based (43%), or PI based (57%), switched to DRV/r 800/100 mg once daily, either as monotherapy (n=127) or with 2NRTI (triple therapy arm, n=129). This sub-analysis investigated the effect of Hepatitis C co-infection on HIV RNA levels during the trial.
Results: At baseline, more patients were HCV antibody positive by serology in the DRV/r arm (17%) than in the control arm (9%). In the primary efficacy analysis at Week 48, 86.2% of patients in the monotherapy arm and 87.8% in the triple therapy arm had HIV RNA <50 copies/mL. Only four of the confirmed elevations in HIV RNA were above 400 copies/mL (two in each arm). In multivariate analysis (Per Protocol), hepatitis C co-infection was a significant predictor of confirmed HIV RNA elevations (p<0.01). For patients infected only with HIV (HCV antibody negative at baseline), the percent HIV RNA <50 was 88.1% in the monotherapy arm versus 87.3% in the triple therapy

arm. For patients HCV antibody positive at baseline, the percent HIV RNA<50 was 61.9% for the monotherapy arm versus 58.3% for the triple therapy arm . Three patients had acute HCV infection during the trial (all in the DRV/r arm): all three had HIV RNA elevations at the time of acute HCV infection.
Conclusions: In this study for patients with HIV RNA <50 copies/mL at screening, switching to DRV/r monotherapy showed non-inferior efficacy versus 2NRTI + DRV/r. Hepatitis C co-infection was more prevalent in the DRV/r monotherapy arm, and was a significant, independent predictor of transient, low-level HIV RNA viraemia. Hepatitis C co-infection might be a marker of poor adherence, or might be directly correlated with HIV RNA viraemia.

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Functionally relevant decreases in activatory receptor expression on NK cells are associated with pulmonary tuberculosis in vivo and persist after successful treatment

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Background: M. tuberculosis is a pathogen that infects up to one-third of world's population. While only 5-10% of infected individuals will develop active disease, latent infection will eventually determine active disease at a rate 0,1-0,5% per year. The mechanisms underlying loss of Mth control in patients developing pulmonary tuberculosis after primary infection are largely unexplored. NK cells have an important role in innate immune response against intracellular pathogens and it has been described that compromised control of microorganism spreading are associated, in some instances, to alterations of NK cell function. There is however no study on NK cell phenotype and function at the onset of disease or around the moment to exit from latency neither in uninfected, nor in HIV-infected patients.
Patients and Methods: In order to analyze if ex-vivo peripheral NK cells from M. tuberculosis infected patients are associated with phenotypical and/or functional perturbations of NK subsets, we studied a cohort of sequential newly diagnosed patients with pulmonary TB in comparison with a control group represented by healthy uninfected donors. Phenotypical analysis of NK cells was performed on PBMC and polyclonal activated NK cells populations in α-IFN presence or absence by four-colour cytofluorometry using monoclonal antibodies specific for activating and inhibitory NK receptors. Functional analysis was studied against FcγR+ P815 cells using redirected activation in the presence of anti-NKp30 and -NKp46 mAbs and α-IFN in culture medium. Intracellular γ–IFN production was evaluated after stimulation with NK-sensitive tumour target cells and/or with anti-Natural Cytotoxicity Receptors (NCR) mAbs.
Results and Discussion: Decreased CD56brightCD16+/-subsets with significantly compromised NKp30 and NKp46 expression and with specifically decreased γ-IFN production upon triggering were evident. These features were not completely restored when purified NK cells were cultured in vitro. Culture supplementation with α-IFN increased only NKp30 expression in TB and healthy donors. Extensive peripheral NK cell triggering was evident in these patients, as shown by the expression of NK cell activation markers and of the lymph node-homing chemokine receptor CCR7 on CD16+CD56dull cells. Significant persistence of decreased NKp30 and NKp46 after successful treatment with a standard four-drug regimen was detected after full recovery. NK cell function is deeply affected in patients at the onset of pulmonary TB. The interactions with HIV co-infection are profound according to comparative analysis of NK cell perturbation during either infection.

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Actualization of a surveillance model for cardiovascular risk

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Data regarding increased cardiovascular risk (CR) in HIV/AIDS patients, linked to the infection itself, to certain drugs or to a higher rate of cardiovascular risk factors (CRF), push infectivologists to rethink surveillance. We proposed a model focusing on monitoring of significant parameters to identify HIV/AIDS patients with potential greater CR. The following CRF were included: Parental cardiovascular disease history; Age >50 yrs in males, >60 yrs in females; Smoking >2 or 3 cigarettes daily; Abdominal Circumference >94 cm in males, >80 cm in females; Systolic Pressure >140 mmHg; Total-Cholest./HDL-Cholest. Ratio >5 in males, >4,5 in females; Triglycerides >200 mg/dl. When dealing with variable markers, we considered results taken 3-6 months apart. Data were gathered between mid 2007 and mid 2008 and reported on a specific form added to the medical folder. We assigned a proximate risk score for each patient (1 point for each reported CRF), thus allowing us to subdivide a cohort of 138 HAART treated patients (94 males and 44 females, average age of 44 yrs, under observation for an average of 8 yrs) in 3 classes of risks: A= 81 patients (CRF from 0 to 1), B= 38 patients (CRF from 2 to 3), C= 19 patients (CRF >/= 4). Patients with CRF >/= 2 (B+C=58 patients) were proposed ulterior exams such as ECG, Echocardiogram or Echo-Doppler carotids scan. In 17 cases (29,3% of patients in B and C classes), cardiovascular alterations resulted. In B and C classes, we offered suggestions, aimed to reduce the specific risk of each patient, relative to the lifestyle (appropriate diet, increased physical activity or smoke reduction) and prescriptions for specific therapies or HAART modifications. From collected data, we found that the following interventions were taken: addition of antihypertensive drugs in 19 cases (32,7%); addition of antidiabetic drugs in 4 cases (6,8%); addition of antilipidic drugs in 28 cases (34,4%). Patients were re-evaluated a year later, between mid 2008 and mid 2009, with the aim to show possible benefits related to the proposed interventions. For this, we selected some simpler markers to evaluate such as Systolic Pressure, Triglycerides, Total-Cholest./HDL-Cholest. Ratio. On this basis we could demonstrate an average reduction of: Total-Cholest./HDL-Cholest. Ratio from 5,6 to 4,8 (from 6,0 to 4,9 in males, from 4,5 to 4,3 in females); Triglycerides from 256 to 169 mg/dl (from 280 to 184 in males, from 121 to 114 in females); Systolic Pressure from 135 to 123 mmHg (from 140 to 126 in males, from 122 to 115 in females). Although we cannot evaluate the reduction of cardiovascular events due to the limited number of patients and time range, we still believe that this approach achieved the goal to better orient the clinical practise toward a more routine evaluation and correction of the CRF and offered a reduction of some significant parameters of CR in our patients.

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A Kaposi's sarcoma outbreak among AIDS-presenter HIV-infected MSM individuals

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Introduction: Kaposi's sarcoma (KS) is the most common AIDS-related tumor; its incidence showed a slight increase from the pre-HAART era (4.9%) to nowadays (5.6%). During 2009, 50 newly infected individuals joined our Site; of these, 36 were males and homo/bisexual intercourse was the main risk factor (22 cases, 44%). AIDS-presenter patients were 15 subjects (30%); a huge amount of them presented KS (skin and/or visceral) as their first AIDS-defining illness.
Results: In 2009, 5 newly diagnosed HIV-infected patients presented KS during their first clinical evaluations; this disease reached a high incidence among AIDS-presenter individuals (33.3%). They were all males, average age 51.8 years and the main risk factor was homo- or bisexual intercourse. They started an ARV regimen based on FTC/TDF plus either an NNRTI (EFV or TMC278) or a boosted PI (LPV or ATV). One patient (1-BoA) developed skin lesions immediately after the initiation of the HAART regimen, therefore supporting the doubt of an immune reconstitution inflammatory syndrome. The mainstay of treatment (pegylated liposomal doxorubicin) was decided for all of them except for 4-CoE because of the isolated involvement of few inguinal lymph nodes.
The antiblastic scheme was prescribed at a dose of 20 mg/m^2 every 28 days for 6 cycles (plus two booster cycles). Cardiotoxicity is a classic feature of all anthracyclines, but it's not reported with this drug; nevertheless, we observed 2 severe heart adverse events in the eldest patients: 3-MiW had a right coronary thrombosis three days after the first pegylated liposomal doxorubicin infusion; 5-MeR showed a diffuse obstruction of the coronary arteries and signs of heart failure so the oncologist decided to stop his treatment waiting for further tests. Of the 3 patients actually evaluable, everybody showed a full response to standard treatment.

Table 1. Demographic data, viro-immunologic status at diagnosis and oncologic condition of the affected patients.

Subject	Age	Gender	Risk factor	HIV-RNA (log10)	CD4+ cells count	ARV treatment	Neoplastic involvement	Prognostic Index
1-BoA	42	M	Bisex	4.82	312	FTC/TDF, TMC278	Skin Nasopharynx Oral cavity Stomach Lung Rectum	7
2-PaM	48	M	MSM	5.43	115	FTC/TDF, EFV	Skin Glans penis Testicle	9
3-MiW	55	M	MSM	5.01	219	FTC/TDF, LPV/rtv	Skin Glans penis Lung Lymph nodes	10
4-CoE	52	M	MSM	5.56	190	FTC/TDF, RAL	Lymph nodes	11
5-MeR	62	M	Bisex	4.98	220	FTC/TDF, ATV/rtv	Skin Stomach Lung	10

Discussion: In our cohort, KS incidence peaked 33.3%, maybe because of the high percentage of homo/bisexual newly diagnosed infections. The start of an antiretroviral treatment is always needful, but there are no evidences of an advantage of a NNRTI- or a PI-based regimen. According to the current guidelines, the decision to treat 4 out of 5 patients with doxorubicin resulted appropriate. However, the same guidelines indicate also to use the Prognostic Index proposed by Stebbing and al.; in compliance with these statements, systemic chemotherapy is reserved for subjects with a score above 12. Our subject with the highest score (4-CoE, who scored 11) is the only one who didn't receive doxorubicin but he outlived with no other complications. Hence, although the new Prognostic Index doesn't appear fully reliable, the traditional indications could lead to an excess of treatment.
Pegylated liposomal doxorubicin is generally well tolerated and tuned out to be effective even if our oncologists prescribed a "softer" schedule (cycles every 28 days). Therefore, doxorubicin should be used cautiously in older people.

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Occult HBV infection in PBMCs of HIV+ individuals

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Backgrund and aim: Detection of HBV-DNA in HBsAg negative patients is defined as occult HBV infection. Previously, we investigated the prevalence and the genomic heterogeneity of occult HBV in the liver of 24 HIV+/HbsAg negative patients: 8 HBsAg- patients were HBV-DNA positive (33%) in the liver. HBV can be detected in PBMCs, so infected PBMCs can act as reservoirs for the cell-to-cell transmission of the virus. We aimed to determine the prevalence of occult HBV infection of peripheral blood mononuclear cells, defined as detection of sequences from ≥2 HBV genes in subjects HIV+ with HBV occult infection in the liver and to detect the viremia of HBV both in the liver than in the PBMCs.
Methods: We focused on 6 HIV+ patients with occult HBV in the liver: HBV DNA levels were quantified using a real-time PCR assay based on Light Cycler technology revealed through SYBR green fluorochrome both in the liver than in PBMCs. Nested-PCR and direct sequencing were performed for S, X and PreC/Core regions. The controls were 14 HIV/HBV coinfected patients: liver+PBMCs+serum of 5 patients and serum+PBMCs of 9 patients.
Results: five individuals positive for anti-HBc but negative for HBsAg had HBV DNA in their PBMCs. These 5 were also positive for HBV genomes in their liver but not in their serum. HBV-DNA, indeed, was detectable in liver, PBMCs and serum of all controls. SYBR green real-time RT-PCR showed a high level of sensitivity as the detection limit of technique was assessed at 20 HBV-DNA copies/15ng liver DNA and 20 HBV-DNA copies/300 ng DNA/10 mln cells.We found a low viremia of HBV in liver of all patients with occult infection . So in the PBMCs: 2 cases were <20 HBV-DNA copies/300 ng DNA/10 mln cells
Conclusions: This study confirm previous data showing that detection of viral genomes in PBMCs may occur in the absence of viremia, antigenemia or specific viral antibodies in serum. Moreover, in the clinical setting, the most difficult parts of

HBV-DNA research include the requirement of liver biopsies, and the lack of sensitive, specific and quantitative methods to detect HBV-DNA from biopsies of HBsAg negative patients.
We found that the real time PCR teqnique can be applied for detection of copies of HBV in the liver and PBMCs of patients with HBV occult infection.

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PEG-INTERFERON-α-2A versus PEG-INTERFERON-α-2B in combination with ribavirin in naives patients with chronic hepatitis C and HIV infection

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Background: Combination of ribavirin plus PEG-interferon-α is the gold standard for the treatment of chronic hepatitis C. Up to date comparative clinical studies don't show definitive evidence of superior efficacy for either of two types of commercially available PEG-interferon in HIV+ patients. We have analysed the efficacy of PEG-2a versus PEG-2b in combination with ribavirin in a prospective randomised study.
Methods: A mono-centre clinical study started on October 2003. Patients were randomized (1:1) to two different treatment regimens : PEG-interferon-α-2a 180 mcg\week or PEG-interferon-α-2b 1.5 mcg\Kg\week, plus ribavirin >10.5 mg\Kg\day. The randomisation lists were separate between patients infected with genotypes 1 or 4 (Group 1: 48 weeks of treatment) and those carrying genotypes 2 or 3 (Group 2: 48 weeks of treatment). By October 2009, 99 patients have been included in the study. Statistical analysis was performed on 74 patients who reached a 6-month post treatment follow-up.
Results: Overall, 40 patients (54.1 %) have concluded the treatment period reaching complete response (ETR). The rate of sustained virological response (SVR) was 40.5 % (30\74). High rates of drop-out (19.0 %) and relapse (25.0 %) were observed. In Group 1 the rate of SVR was 26.3 % (genotype 1: 24.1 %, genotype 4: 33.3%), in Group 2 it was 55.6 % (genotype 2: 100 %, genotype 3: 50.0%) . Comparing the two regimens, SVR was achieved by 37.8 % of patients treated with PEG-IFN-2a, and by 43.2 % of those treated with PEG-IFN-2b (p=ns). While in Group 1 the two treatment arms had identical rates of outcome (23.1 %), in Group 2 the rate of SVR was 61.1 % for PEG-IFN-2b and 50.0 % for PEG-IFN-2a (p=ns).
Discussions: The preliminary analysis on 74 patients included in our study shows similar efficacy for PEG-IFN-2a and PEG-IFN-2b. Similar results were obtained in a parallel study performed in our Centre on 230 HCV infected, HIV negative patients, but the SVR rates were globally higher (66.1 % versus 40.5 %). Even if the small population analysed doesn't allow to find minor statistical significance, PEG-IFN-2a and PEG-IFN-2b seem to be similarly effective.

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Rituximab emergency treatment in an HIV-related lymphoma. A case report

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We report on a case of advanced gastric non- Hodgkin lymphoma presenting as surgical emergency in a foreign male patient, with a long standing HIV infection; he had never received antiretroviral therapy due to alleged satisfactory immune status. He was on vacation in Genoa by the end of January 2003, when he was admitted to our emergency department because of massive gastrointestinal bleeding. An urgent endoscopic examination revealed a gastric ulcer with clear malignant features, involving most of the gastric wall. An exploratory laparotomy was performed and a radical surgical resection was ruled out due to massive spread of disease (gross involvement of stomach, pancreas, ileum, transverse colon, mesocolon). The attending physician reckoned any kind of chemotherapy unfeasible, fearing vessel rupture and/or viscus perforation. In the meanwhile hemoglobin fell to 5.5 g/dL in spite of red blood cell tranfusions, pathology confirmed a diffuse, large B-cell type lymphoma (DLBCL), CD20 positive, with a high index of proliferation, and his immune status was defined (200 CD4+ cells/mmc, with a viral load od 32000 copies/ml). We were called upon as infectious disease consultants to help in the management of the patient. We were confronted with a very challenging case: an immunedepressed patient, with ongoing malignant gastric bleeding and no traditional therapeutic choices available. We chose to administer the monoclonal antiCD20 antibody rituximab, exploiting its very selective mode of action, i.e aiming at neoplastic CD20 cells, while sparing the surrounding tissues.
Upon informed consent a single infusion was administered, with standard dose and premedication. Neither infusion related side effects nor rapid tumor lysis syndrome occurred. Hemoglobin levels rose and remained stable, the patient improved and after a few days asked to be discharged to fly home (in GB) and be admitted to a hospital of his choice. He was never heard of again, but a year later he was met by a nurse on the staff of the surgical ward and was reported to be alive and well, again on vacation in our country.
By 2003 rituximab was not yet accepted as upfront therapy for aggressive lymphomas, and much more so in the HIV infected patients, where concern about further immune depression and the risk of infectious complications were still matter of debate. But then we had no alternative. We don't know how this patient was further treated back home, but we know that our first move was a wise one.

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Dynamic Changes of Hepatitis C Virus Genotype May Influence the Anti-HCV Treatment Response in HIV/HCV Infected Individuals

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Background and Objectives: The anti-HCV treatment response in HIV/HCV coinfection is lower than in HCV monoinfection. This clinical evidence may be related to immune competence and unknown factors. To determine the temporal dynamics of HCV infecting genotype in HIV/HCV coinfected patients under anti-HCV treatment and their role in the treatment response, 18 HIV/HCV coinfected patients enrolled in a pilot clinical trial including individuals under ribavirin and PEG-IFN (LPV monotherapy study Kamon2) were studied.
Methods: The virological response (VR) to anti-HCV treatment was assessed by 2 log decrease or HCV-RNA negativity at 12-weeks treat-

ment and maintenance of HCV-RNA negativity at 48-weeks treatment. 5'UTR HCV sequences analysis was inferred in plasma samples at baseline, week 12, week 24. Ten patients were VR and 8 non responder (NR). Results HCV genotyping at baseline showed that the majority of VR (8/10; 80%) patients was infected with genotype 2 or 3: 2 had genotype 2a/2c, 6 genotype 3a, 2 patients harbored genotype 1b. All NR were infected at baseline with a difficult to treat HCV genotype: genotype 1a was detected in 3 patients, genotype 1b in 2 patients and genotype 4 in 3 patients. Temporal dynamics of HCV strains were analyzed in NR, since all VR were HCV-RNA negative at week 12. A variable pattern of infection was found in NR: 3 (37%) individuals showed the alternance of two different genotypes during therapy: 2 patients infected with genotype 1b at baseline, had genotype 3 at 12-weeks and 24-weeks study, respectively, and 1 patient infected with genotype 4 at baseline, had genotype 3 at 12-weeks study; the remaining 5 patients maintained the same genotype of that detected at baseline.
Discussion: The dynamic pattern of HCV genotype in NR suggests a mixed HCV infection. In this context, the emergence as dominant of a different genotype from that found at baseline is possibly consequent to the pressure exerted by anti-HCV therapy. This peculiar pattern of HCV infection, in addition to HCV genotype "per se" and immune deficiency status, is probably one of the major determinants of the anti-HCV therapy outcome in HIV/HCV coinfected persons.

EPIDEMIOLOGY AND SOCIAL SCIENCES: PHARMACOECONOMICS, ACCESS TO CARE AND QUALITY OF LIFE

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2007–2009: Out-of-hospital accomodation for PLWHA in Lombardy Region

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In 2007 in the out-of-hospital facilities in Lombardy Region there were 159 bedplaces in Highly Integrated Health-Social Care Family Homes (kind C) and 55 bedplaces in Low-Intensity Assistance Family Homes (kind A) (became respectively 149 and 65 in 2008 and 2009) plus 10 places in autonomy projects (in flats), and also 58 places for guests only during the day in some family homes and in 2 Daily Centres. Since August 2007 till August 2009 370 men (76,8%), 107 women (22,2%) and 5 transgender (1%) had been accepted in residential and daily care facilities in Lombardy. In summer 2007 there were 227 persons. In the period September 2007-August 2008 were admitted 119 and between september 2008 and august 2009 136. At the first survey 295 guests were in Homes C, 108 in Homes A, 68 in day care facilities, 11 in protected flats (6 of them also attended daily centres). The age range was between 20 and 79 years. 5.6% had age 19-35, 71.1% 36-50, 20.6% 51-65, while the ultra-65 years represented 2.7%. Women were on average only one year younger than men (45.6 vs. 46.8). 44.9% of persons accommodated in Houses C and 25% of the ones accommodated in Houses A came directly from hospitals. Among the health problems were emerging mental disorders (54.9% Homes C guests, 47.2% Homes A guests, 33.3% other types of accommodations guests) and disability (48.5% Homes C guests, 22.2% Homes A guests, 36.5% daily centres guests). 6.2% of the guests of family homes are bedridden (23/25 in Homes C and 2 in Homes A). Concerning social issues, 19.8% of the guests had criminal problems. 12.7% were active drug users, of which half of them also taking methadone. A further 13.9% had methadone replacement therapy. 13.9% had alcohol dependence, in about half of the cases associated with other addictions. 38 foreign people (7.5% of total) were accepted in Lombard facilities, 25/38 coming from Africa. Between all the guests, 305 routes were concluded with the discharge, some of which related to the same host after riadmission or transfers. 75 guests have died (4 shortly after transfer to hospital or hospice). 51 courses were completed with return to home, 81 with the abandonment, 32 with removal, in 70 cases there were transfers to other facilities. 50% of removals and 71.6% of dropouts occurred within the first 6 months of hosting. 5 people were hospitalized, 8 transferred to hospice, 6 to structures for elder people (RSA), 4 to therapeutic or psychiatric communities, 5 were returned to prison. Of the 43 movements occurred only in the facilities for PLWHA, 19 cases were transferd to lighter structures, 14 to more intensive care units for a worsening of socio-health conditions, in 10 cases the transfer occurred within the same type of accommodations. After 20 years, the out-of-hospital facilities system in Lombardy Region is still proving the forefront in welcoming people with HIV/AIDS in the most fragile clinical and social conditions.

PO 105

Infection 2010; 38 (Suppl. I): 90

Coreceptor tropism results and Maraviroc therapy in HIV-1 patients

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Background: Maraviroc (MVC) belongs to a new class of antiretroviral drugs designed to block entry of HIV-1 into CD4+ T-cells via the CCR5 coreceptor. It is indicated for combination therapy in treatment-experienced adults infected with CCR5-tropic HIV-1 that is resistant to multiple antiretroviral agents. HIV tropism in antiretroviral-experienced populations found CCR5-only virus in 50% to 60% of patients. Tropism determination by the standard phenotypic assay requires HIV-RNA >1000 copies/mL. We aimed at analyzing utility of standard tropism test in clinical practice.
Methods: Coreceptor phenotype was performed with Trofile™ and replaced with ES Trofile™ assay (ESTA) in October 2009. ES Trofile™ was developed by Monogram Biosciences. Descriptive analysis was performed.
Results: 145 patients (see Table) tested with Trofile assay between January 2008-2010: 122 (84%) patients were on stable antiretroviral therapy or no therapy for ≥ 4 weeks and all had triple-class experience or documented resistance to ≥ 1 drug in each of the 3 traditional treatment classes or ≥ 2 PIs and 23 (16%) were naïve patients.
75 patients (52%) had CCR5-tropic virus more frequently founded in naïve patients (70%) than experienced (48%); 35 (24%) had D/M virus and 5 (3%) had X4 virus. Trofile™ assay was not available in 30 (21%) subjects mainly because the viral load was <1000 copies/mL. Median interval time to receive Trofile™ response were 25 days (8-63 days).
After testing for HIV-1 tropism, 2 patients underwent structured treatment interruption and did not resume antiretroviral therapy on the basis of clinical and laboratory indicators; 52 received combinations with Raltegravir, Darunavir/r, Etravirine and Enfuvirtide not including MVC; 20 patients received MVC therapy more frequently associated with Raltegravir (85%). MVC was generally well tolerated: only in 1 case it was discontinued prematurely because of skin rash.
Conclusions: The more frequent cause for not using MVC was the lag-time of viral tropism response together with availability of other new antiretroviral drugs.
Only 20 (34%) of 59 experienced patients with CCR5-tropic virus, 14% of all patients tested by Trofile™, received MVC therapy. Trofile™ assay is expensive and not widely available and cannot be used

BASELINE VARIABLES AT TROPISM TEST	Experienced n° 122 (84%)	Naïve n° 23 (16%)	All n° 145 (100%)
Male n° (%)	87 (83%)	18 (17%)	105 (72%)
Age median years (IQR)	45 (22-74)	41 (26-65)	44
Length of infection median years (IQR)	16 (1-27)	5 (1-22)	14
IVDU n°	66	6	72
Heterosexual n°	38	10	48
MSM n°	15	7	22
Mother to child transmission n°	3	-	3
CD4+ > 500 mmc n°	2	1	3
CD4+ = 200-499 mmc n°	35	20	55
CD4+ <200 mmc n° (%)	85 (70%)	2 (9%)	87 (60%)
HIV RNA (b DNA) median cp/ml	32660	54247	35959
TROPISM TEST RESULTS			
CCR5 n° (%)	59 (48%)	16 (70%)	75 (52%)
CXCR4 n° (%)	5 (4%)	-	5 (3%)
Dual-mixed n° (%)	31 (26%)	4 (17%)	35 (24%)
Unvaluable n° (%)	27 (22%)	3 (13%)	30 (21%)

to evaluate patients with undetectable levels of plasma virus. New genetic determinants of tropism by V3 loop sequencing may provide a cheap and rapid method to improve selection of MVC-candidates in the real clinical setting.

PO 106

Infection 2010; 38 (Suppl. I): 91

Analytical performance of a new point-of-care test for HIV 1-2 Ag/Ab selective and combined detection

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Background: Conventional tests for the diagnosis of HIV are a fast and efficient way to write large numbers of samples simultaneously, but the first results aren't often available within a few hours or days.
All acute healthcare settings should expect to have access to an urgent HIV screening assay result ideally within four hours, and definitely within 24 hours, to provide optimal support for exposure incidents. The immediate response is need to make decisions about antiretroviral prophylaxis for health care workers who have had occupational exposure (needle stick) because this can provide rapid and accurate assessment of the patient source.
For this purpose, we tested a new commercially rapid HIV kit, that offers results in 30 minute or less.
Methods: We have evaluated analytical and diagnostic performances of an immunoassay POC HIV combined test for the distinct qualitative detection of p24 Antigen and/or Antibodies of HIV 1/HIV 2 (Determine HIV1/2 Ag/Ab Combo, Inverness Medical®, USA).
24 selected serum samples (16 negative, 2 positive at first step but not confirmed in Western Blot and 6 positive) previously analyzed and classified by conventional laboratory procedures (HIV Ag/Ab Combo, Abbott® Diagnostics, USA and Western Blot, MATRIX HIV 1/2, ABBOTT®, USA) were investigated by new POC test.
Results: We obtained: 18 negative and 6 positive. We have registered an analytical performance (sensitivity, specificity) and a diagnostic accuracy of 100%. Especially we highlighted that the serum Ag p24 positive by POC it was also confirmed by ELISA assay (ICD-HIV-p24Ag7 Innogenetics®, USA).
Discussion: Diagnosis of HIV infection is basically made by sequential two tests: a screening test by an enzyme immunoassay and a confirmatory test by Western blot. An assay for detection of RNA was also approved as a confirmatory test in early infection.
To reduce barriers to early diagnosis of HIV disease and increase the pointed access to treatment (this is very important in working exposure) it is necessary a short time of laboratory investigations.
The new combined POC test proposed by Inverness® offers an accurate, reliable and low-cost solution for an HIV infection rapid screening; it is an easy and secure diagnostic device and it doesn't require any special laboratory equipment.
The rapid result of POC test can reduce anxiety and adverse effects due to an unnecessary antiretroviral therapy in health care worker and it allows a sharp reduction in social costs.

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BASIC SCIENCES: IMMUNOPATHOGENESIS

PO 107

Infection 2010; 38 (Suppl. I): 92

HIV-1 Tat protein enhances the RANKL/M-CSF-mediated osteoclast differentiation

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Background. The impairment of osteoblast/osteoclast cross-talk and the bone structure homeostasis with osteopenia/osteoporosis occurence are often observed in HIV seropositive patients even though the involved mechanisms are not clearly been elucidated yet. Since Tat shows biological pleiotropic effects acting on several cell lineages through paracrine and autocrine mechanisms regulating signal transduction pathway and cell genes modulation, we investigated Tat activity in the differentiation and function of osteoclasts to elucidate its role in the induction of bone derangement during HIV infection.
Methods. The biological effects of Tat on peripheral monocyte-derived osteoclast differentiation was analyzed. Whole blood samples were collected from health blood donors. The differentiation towards osteoclasts was carried out adding M-CSF and RANKL to the culture medium. Specific real time SYBR green based RT-PCR quantitative analysis was performed to determine mRNA expression of TRAP, cathepsin K, calcitonin receptor, c-fos, beta-actin, chloramphenicol-acetyl transferase and luciferase. Osteoclast formation was determined by quantifying multinucleated TRAPpositive cells stained with the Leukocyte Acid Phosphatase Assay Kit. The c-fos promoter and c-fos promoter deletion mutant were cloned in a chloramphenicol-acetyl transferase report gene plasmid and were employed to dissect the c-fos promoter.
Results. Tat enhances the osteoclast differentiation and activity induced by RANKL plus M-CSF treatment. In fact, Tat significantly increases both the mRNA expression of specific osteoclast differentiation markers such as cathepsin K, and calcitonin receptor and the TRAP expression and activity. This Tat-related biological effect may be related, at least in part, by induction of c-fos expression and AP-1 activity. This c-fos up-regulation is determined by Tat in presence of RANKL/M-CSF treatment and it is characterized by c-fos promoter activation.
Discussion. Our study suggested a complex mechanisms related to HIV infection where HIV-1 infection and gp120 are able to activate M-CSF and RANKL up-regulation that induce the osteoclastogenesis, which in turn is enhanced by Tat. The more rapid and more effective osteoclastogenesis may determine a more consistent osteoclast differentiation and bone resorption associated to the decrease of osteoblastic activity and the HIV induced osteoblast apoptosis may determine an imbalance to osteoblast/osteoclast bone activity with subsequent bone mineral density loss. Altogether, these results showed that Tat may be considered as a viral factor modulating positively the osteoclastogensis and then the bone resorbing activity suggesting a consistent role of this viral protein in the HIV-related osteopenia/osteoporosis pathogenesis.

PO 108

Infection 2010; 38 (Suppl. I): 92

Impact of maraviroc on CCR5 expression, migration and maturation state of dendritic cells: potential role in reducing HIV-induced inflammatory response

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Background: Dendritic cells (DC) play a pivotal role in inducing and modulating both natural and specific immune response in HIV infection. Migration and activation state are important function of DC but it is also implicated in HIV chronic immune activation. Given the central role of CCR5 in governing both trafficking and recruitment of cells into inflamed tissue, the analysis of the effect of CCR5 antagonists on the modulation of DC chemotactic activity could be of interest in reducing HIV-induced inflammatory response.
Objective: to study the in vitro effect of CCR5 antagonist maraviroc (MVC) on immature and mature dendritic cells (DCs) by assessing cell migration using different chemoattractants.
Methods: Immature DCs were generated from adherent monocytes cultured for 6 days in the presence of GM-CSF (50 ng/ml) and IL-4 (40 ng/ml). To induce maturation, cells were cultured with medium containing LPS (0.1 mg/ml) for additional 24 hrs. The chemotactic activity of DC was assessed using FMLP (10-6M), RANTES (100nM) or MIP1-β (100nM) as chemoattractant and measured by both microscopy and cytometry. MVC were used at different concentration, such as 0.1 nM, 1 nM and 10 nM. CCR5, FPR and activation markers (CD80 and 83) were also measured on DCs.
Results: MVC did not affect in vitro DC generation and maturation. Moreover, FMLP receptor (FPR) and CCR5 expression were not modified by in vitro treatment with MVC. As previously demonstrated mature DC express high levels of CCR5 and low levels of FPR. MVC showed an inhibitory effect on RANTES and MIP1-β dependent migration on mature DC (45%+ 8 and 65%+6 of inhibition, respectively). On the other hand immature DC were inhibited (70%+ 9) with higher dose of MVC (10 μM) when tested with FMLP as chemoattractant.
Conclusions: These data indicate that CCR5 antagonist MVC has an effect on DCs by mechanism which could be independent from anti-HIV activity. We demonstrated that in vitro treatment with MVC inhibits chemotactic activity of mature DC These findings suggest that MVC might have a potential role in the downregulation of HIV-associated chronic inflammation by blocking the recirculation and trafficking of DC.

PO 109

Infection 2010; 38 (Suppl. I): 92

Study of intracellular and immunomodulant effects of CCR5 Antagonist Maraviroc

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Background: Several findings suggest that CCR5 antagonist maraviroc (MVC) exhibit immunomodulant properties beyond their capacity to inhibit HIV entry. The study of extravirologic effect of MVC is an area of active investigation.
Objective: to study the in vitro effect of MVC on PBMCs, polymorphonucleate leukocytes (PMNL), U937 (human tumor monocytic cell line), and Jurkat (human T lymphocytic cell line), by assessing apoptosis, cell viability, cell migration, and intracellular oxidative parameters.
Methods: PBMC and PMNL were isolated from healthy donors and HIV naturally infected patients. The cells (U937, Jurkat, PBMC and

PMNL) were incubated for 24 h in presence of medium alone or MVC (200nM and 20 μM) at 37°C under 5% CO2. The pro-apoptotic effect was measured after 24 hrs of incubation with MVC, while the anti-apoptotic effect was measured inducing the apoptosis with both protein synthesis inhibitor puromycin (PMC,10 μg/mL) and topoisomerase II inhibitor etoposide (VP16,100μM). Apoptosis of U937 and Jurkat cells was detected by staining with Hoechst 33342. Apoptosis of PBMC and PMNL was assessed by the activity of caspase 3 in cell lysates. The chemotactic activity of PBMC and PMNL was assessed using RANTES (100ng/ml) as chemoattractant.
Results: MVC did not exert any effects on apoptosis of U937 and Jurkat cells. Regarding the PBMC and PMNL, no significant variations on apoptosis was detectable after 24h incubation with 2 concentrations of MVC (PBMC: CNT=0.21+0.001; MVC 200nM=0.20+0.01; MVC 20μM=0.19+0.01; for PMNL: CNT=0.18+0.09; MVC 200nM=0.13+0.02; MVC 20μM=0.159+0.05). In addition, no significant effect of MVC was seen for PBMC in the modulation of apoptosis exogenously induced with the stressing agents etoposide or puromicin (CNT=0.39+0.01; MVC 200nM=0.37+0.05; MVC= 20μM 0.35+0.01). MVC affects cell migration by reducing the chemotactic activity of PBMC by 15% (200nM) and 80% (20μM), and of PMNL by 65% (200nM) and 70% (20μM). In addition we observed that chemotaxis of PBMC from HIV naturally infected patients was reduced by MVC pre-treatment. Regarding the intracellular oxidative parameters, the ROS, superoxides, and the intracellular concentration of glutathione were not altered in U937 and Jurkat after 24h of MVC incubation. The analysis of basal level of cytosolic Ca2+ in the Jurkat cells treated with MVC showed an increase in the intracellular Ca2+ concentration.
Conclusions: These data indicate that CCR5 antagonist MVC did not affect apoptosis of PBMC, PMNL, U937 and Jurkat and intracellular oxidative parameters, while it has a direct effect on cell migration by mechanism which is independent from anti-HIV activity. The perturbation of intracellular calcium induced in Jurkat cells could be related to the downregulation of cell chemotactic activity induced by the drug. This phenomenon could be involved in the modulation of HIV-associated chronic inflammation by blocking the trafficking of cells into inflamed tissue.

PO 110

Infection 2010; 38 (Suppl. I): 93

Differential restriction patterns of HIV infection and replication in M1 vs. M2 human monocyte-derived macrophages

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Background: The capacity of macrophages to support productive human immunodeficiency virus type 1 (HIV-1) infection is known to be modulated by cytokines and other extra-cellular stimuli. Here, we demonstrate that cytokine-induced polarization of human monocyte-derived macrophage (MDM) into either classical (M1) or alternatively activated (M2a) MDM is associated with a reduced capacity to support productive CCR5-dependent (R5) HIV-1 infection.
Material and Methods: Primary human MDM were polarized into M1 (IFN-γ plus TNF-α) or into M2a (IL-4) and then infected with a R5-tropic HIV-1 strain. Viral replication was monitored by RT assay, receptor/coreceptor presence was monitored by cytofluorimeter.
Results: M1 polarization was associated with a significant downregulation of CD4 receptors, increased secretion of CCR5-binding chemokines (CCL3, CCL4 and CCL5) and a >90% decrease in HIV-1 DNA levels 48 h post-infection. In contrast, M2a polarization had no effect on either HIV-1 DNA or protein expression levels indicating that inhibition occurred at a late/post-integration level in the viral life cycle. Most phenotypic and functional changes were fully reversible 7 days after removal of the polarizing stimulus and a reciprocal downregulation of M1-related chemokines and cytokines was observed in M2a MDM and vice versa.
Conclusions: Since reversion to a non-polarized MDM state was associated with a renewed capacity to support HIV replication to control levels, M1/M2a polarization may represent a mechanism that allows macrophages to cycle between latent and productive HIV-1 infection.

PO 111

Infection 2010; 38 (Suppl. I): 93

Characterization of the translocating microflora in peripheral blood of severely immune depressed HIV+ naive patients: may the microbiota influence the response to HAART?

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Background: Increased passage in the bloodstream of bacterial products has been described in HIV/AIDS, associating with immune activation and CD4 depletion. Given that the enteric microflora can act either as an adjuvant supporting immune function or as an antigenic stimulus exacerbating the inflammatory response, we hypotesized that different translocating microflora might condition response to HAART in HIV+ patients (pts) with severe CD4 lymphopenia. Methods: 44 HIV+ pts with CD4<200 introducing HAART were followed for 12 months (T12). As controls, 13 HIV- subjects were studied. Based on T12 CD4 recovery, pts were classified as Immunological Non Responders –INRs- (CD4 <250) and Full Responders –FRs- (CD4≥250). At T0 and T12 we evaluated: CD38+ and CD45R0+CD38+ CD8 (flow cytometry); plasma lipopolysaccharide-LPS (LAL), sCD14 (ELISA) and bacterial 16S-RNA PCR detection followed by sequencing.
Results: 15 INRs and 29 FRs were studied. At T0, FRs and INRs presented comparable proportion of activated CD38+ and terminally-differentiated CD45R0+CD38+ CD8 (p=.4; p=.24 respectively). At T12, a significant reduction in CD38+CD8 was shown in both FRs and INRs (p=.005; p=.02), with a similar trend in CD45R0+CD38+ reaching significance only in FRs (p=.002; p=.11). At T0, FRs and INRs showed comparable plasma LPS and sCD14 (p=.9), with no major changes at T12 (LPS: FRs p=.06, INRs: p=.5; sCD14 FRs: p=.1, INRs: p=.5). At T0, a significantly higher proportion of INRs yielded a positive 16S rDNA PCR amplification compared to FRs (8/15, 53% vs 6/29, 20%; p=.04), with a similar non-statistical trend at T12 (4/15, 40% vs 3/29, 10%; p=.2) All HIV- controls resulted consistently negative. Sequencing analysis of 10 representative colonies for each PCR+ patient resulted in different bacterial composition between FRs and INRs both at T0 (p=.001) and T12 (p=.008). Interestingly, FRs displayed a higher frequency of Lactobacillus spp (7% vs 0% p=.032) and Pseudomonas spp (15% vs 4% p=.03), whereas INRs displayed a non-significant trend to higher proportion of Enterobacter spp (19% vs 10% p=.2) and Escherichia spp (10% vs 5% p=.3). At T12, FRs presented a trend to reduction in positive colonies for Pseudomonas spp (15% vs 13% p=1); a non-significant reduction in Enterobacter spp was shown in INRs (19% vs 7% p=.1). Interestingly, at T12, INRs featured higher Escherichia spp (17% vs 0% p=.017) and no Lactobacillus spp (0% vs 7% p=.1).
Discussion: Our data show that microbial translocation in severely immune-compromised HIV+ pts involves polymicrobic microflora and associates with different HAART outcomes. Pts with no immunological recovery display outgrowth of Enterobacteriaceae and lack of Lactobacillaceae both prior and after HAART. Given their anti-inflammatory activity, the absence of the probiotic Lactobacillus spp in INRs suggests that a different regulation of resident and/or translocating enteric microflora could have a role in modulating immune reconstitution.

LB 1

Infection 2010; 38 (Suppl. I): 94

New diagnosis of HIV infection (NU.DI.H STUDY): preliminary results

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OBJECTIVE: To describe the socio-demographic, epidemiological, behavioral and clinical-laboratory features of subjects with newly diagnosed HIV infection.
METHODS: Cross-sectional, observational, multicenter study for the evaluation of the epidemiological and socio-behavioral features of subjects with newly diagnosed HIV infection. Seventeen Centers operating in the Lombardy Region participated to the Study. Patients with confirmed positive test for HIV-Ab in the last 90 days, age ≥ 18 years, understanding well the Italian language, without relevant cognitive problems, able to provide informed consent were included. A multi-dimensional questionnaire with 63 items, including psycho-behavioral items and some clinical and laboratory data, was administered.
RESULTS: The study was proposed to 626 patients with HIV diagnosis made from Dec 1st, 2008 to Nov 30th, 2009; amongst these patients, 472 (75.4%) signed the informed consent and were enrolled; males were 368/472 (78%), mean age was 39.8 years (SD ± 11.5) and foreign citizens were 109 (23.1%). The transmission was by heterosexual intercourses in 243 patients (51.5%) and by homo/bisexual contacts in 195 (41.3%). A statistically significant difference between Italian and foreign citizens in the proportion of heterosexual transmission has been observed (47.5% vs. 62.1% respectively; P<0.001). The median CD4+ lymphocyte count at diagnosis was 327 cells/cmm, higher among homo/bisexuals (435 cells/cmm) than heterosexuals (252 cells/cmm) (P<0.001). Lastly, 224 (47.6%) patients reported a previous negative HIV test, more frequently among homo/bisexuals (57.8%) than heterosexuals (27.0%) (P<0.001) and among patients <35 years old (46.4%) than ≥ 35 (36.2%) (P=0.029).
CONCLUSIONS: The study confirms that an high burden of HIV infections is due to sexual risk, including a large proportion of subjects who declared homo/bisexual intercourses. Homo-bisexuals and younger patients presented to clinical Centers at earlier stages of HIV infections, probably because they underwent HIV testing more frequently. The ongoing analysis of the socio-behavioral data could help to understand the reasons for this paradox finding, i.e. the acquisition of HIV infection despite more frequent testing.

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LB 2

Infection 2010; 38 (Suppl. I): 94

Early viral suppression and long-term efficacy outcomes on HAART: analysis of ARTEMIS and TITAN trials

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BACKGROUND: The long-term implications of earlier HIV RNA suppression <50 copies/mL on antiretroviral treatment are unknown. The ARTEMIS trial evaluated TDF/FTC + either DRV/r 800/100 QD or LPV/r in treatment-naïve patients. The TITAN trial evaluated optimised N(N)RTIs plus either DRV/r 600/100 mg BID or LPV/r in experienced patients.
METHODS: In ARTEMIS and TITAN, patients with HIV RNA suppression <50 copies/mL by Week 24 were divided into early suppressors (HIV RNA first <50 before Week 12) and late suppressors (HIV RNA first <50 between Weeks 12-24). Using multiple logistic regression, the probability of subsequent confirmed HIV RNA rebound above 50 copies/mL, by Week 96, was then correlated with baseline HIV RNA, early versus late viral suppression and treatment group.
RESULTS: Overall, 719 patients (67%) showed early HIV RNA suppression, while 354 patients (33%) showed late suppression. In ARTEMIS and TITAN, patients with early suppression had lower mean baseline HIV RNA (4.5 and 4.0 $\log_{10}$ copies/mL respectively), versus patients with late suppression (5.2 and 4.9 $\log_{10}$ copies/mL) (p<0.01). In both trials, patients with higher baseline HIV RNA were more likely to rebound by Week 96 (p<0.001). Of the patients with HIV RNA <50 copies/mL by Week 24, the percentage with subsequent confirmed rebound by Week 96 (adjusted for baseline HIV RNA) were as follows:

Rebound in HIV RNA to Week 96 by early versus late HIV RNA suppression

Trial	DRV/r	LPV/r
ARTEMIS		
Early suppressors (n=352)	3.7%	8.5%
Late suppressors (n=241)	4.5%	10.1%
TITAN		
Early suppressors (n=367)	18.6%	18.1%
Late suppressors (n=113)	7.7%	21.8%

In ARTEMIS, early and late suppressors did not differ in rebound rates within treatment arms. LPV/r treated patients were more likely to rebound than DRV/r treated patients (p=0.01). The same effects were seen in the TITAN trial. In the DRV/r arm, patients with late suppression were slightly less likely to rebound to Week 96.
CONCLUSIONS: In the ARTEMIS and TITAN trials, the time of first HIV RNA suppression <50 copies/mL correlated with baseline HIV RNA. Later HIV RNA suppression was not a significant risk factor for HIV RNA rebound during treatment. The clinical relevance of early HIV RNA suppression was not clear in this analysis of the ARTEMIS and TITAN trials.

LB 3

Infection 2010; 38 (Suppl. I): 95

Plasma darunavir (DRV) and ritonavir (RTV) concentrations versus adherence in the MONET trial

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BACKGROUND: The MONET trial evaluated DRV/r monotherapy versus DRV/r + 2NRTIs in patients with HIV RNA <50 copies/mL at screening. PK analysis was performed to determine whether low DRV plasma levels correlated with a higher risk of HIV RNA viraemia.
METHODS: 256 patients with HIV RNA <50 copies/mL on current HAART for over 24 weeks (NNRTI based (43%), or PI based (57%)), switched to DRV/r 800/100 mg once daily, either as monotherapy (n=127) or with 2NRTI (n=129). Three separate groups of patients were evaluated for DRV and RTV plasma PK levels by validated LS/MS-MS: Group 1 - patients with elevations in HIV RNA >50 copies/mL at two consecutive visits; Group 2 - patients with at least one HIV RNA >50 copies/mL; Group 3 - patients with HIV RNA consistently below 50 copies/mL during the trial. Adherence was evaluated at each visit, using the M-MASRI questionnaire. Multiple linear regression was used to correlate DRV and RTV levels with time since last dose, treatment group, mean adherence and HIV RNA <50 copies/mL at each patient visit.
RESULTS: In the primary efficacy analysis, HIV RNA <50 copies/mL by Week 48 (Per Protocol) was 86.2% versus 87.8% in the DRV/r and control arms, proving non-inferiority for DRV/r monotherapy versus triple therapy. There were 454 PK levels available at patient visits during the trial, from the 257 patients. DRV PK levels were highly correlated with the time since last dose ($p<0.001$) and adherence ($p<0.001$). Mean DRV PK levels were 1528 ng/mL for patients with up to 80% adherence, versus 3199 ng/mL for those with 100% adherence. RTV PK levels were also correlated with time since last dose ($p<0.001$) and adherence ($p<0.001$). Mean RTV PK levels were 66ng/mL for patients with 80% adherence, versus 111ng/mL for those with 100% adherence. Ritonavir levels fell significantly during the trial ($p<0.001$), from a peak of 135ng/mL at Week 12 to mean 65ng/mL at Week 48. RTV levels were slightly higher in the DRV/r monotherapy arm (mean 128ng/mL) versus the DRV/r + 2NRTI arm (mean 107ng/mL). In multivariate analyses, there was no significant correlation between DRV or RTV levels and the risk of HIV RNA levels above 50 copies/mL at each patient visit.
CONCLUSIONS: In the MONET trial, plasma PK levels of DRV and RTV correlated most strongly with time since last dose and mean adherence levels, but not with episodes of HIV RNA viraemia. This result confirms PK/PD analysis from other trials of DRV/r, which also showed no correlation between DRV plasma PK levels and the risk of HIV RNA viraemia.

LB 4

Infection 2010; 38 (Suppl. I): 95

Reversal of severe Vitamin D deficiency after switch from efavirenz to darunavir/ritonavir in the MONET trial

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BACKGROUND: Severe Vitamin D deficiency (<25 nmol/L) is associated with elevated risks of cardiovascular disease, cancer and poor survival in cohort studies of HIV negative people. Use of efavirenz has been associated with severe Vitamin D deficiency in other studies.
METHODS: The MONET trial recruited 256 European patients taking NNRTI or PI-based HAART and HIV RNA <50 copies/mL. Patients were switched to either DRV/r 800/100 mg OD monotherapy or DRV/r 800/100 mg OD + 2NRTIs. 25(OH) Vitamin D was measured at a central laboratory, at baseline and Week 72-96. Multiple regression was used to correlate Vitamin D with gender, season, treatment group and use of antiretrovirals.
RESULTS: Overall, 80.5% of patients were male, and 91% were Caucasian, with a mean age of 44 years. At the pre-baseline visit, 57 patients were using efavirenz based HAART while 140 were using nevirapine or PI based HAART. At baseline, mean Vitamin D levels were lower in the winter season (October to March) ($p=0.02$), for non-Caucasians ($p=0.06$) and for patients taking efavirenz pre-trial ($p=0.0013$). The risk of severe Vitamin D deficiency (<25 nmol/L) at baseline was 3 times higher for patients taking efavirenz pre-trial (17/57 patients, 30%), relative to other antiretrovirals (15/140 patients, 11%) ($p=0.005$). During the MONET trial, 17 patients with severe Vitamin D deficiency on efavirenz switched to darunavir/ritonavir: there was a significant rise in Vitamin D levels for these patients during the trial; only 1 had severe Vitamin D deficiency at their last study visit.
CONCLUSIONS: In this sub-study of the MONET trial, severe Vitamin D deficiency was associated with season, race and use of efavirenz. Routine screening of HIV positive patients for Vitamin D should be encouraged; use of oral Vitamin D supplements, or possibly changes in antiretroviral treatment, may be warranted for those with severe Vitamin D deficiency.

LB 5

Infection 2010; 38 (Suppl. I): 95

Comparison of different antiretroviral neuropenetration scores for the prediction of minor neurocognitive disorders in HIV-positive patients with controlled plasma viremia

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BACKGROUND/OBJECTIVES: The importance of antiretroviral drugs neuropenetration for the prevention of neurocognitive disorders in HIV-infected patients is increasingly recognized. Objective of our study was to investigate the association of two different central nervous system penetration-effectiveness (CPE) scores with the risk of cognitive dysfunction in a cohort of patients on antiretroviral therapy (ART) with plasma HIV-RNA <50 cp/mL.
METHODS: We performed a cross-sectional single cohort study, consecutively enrolling asymptomatic HIV+ subjects during routine outpatient visits. In order to analyse subclinical neurocognitive abnormalities, patients underwent Mini Mental State Examination and an extensive neuropsychological battery of 19 tests exploring memory, attention and executive abilities. Each patient was classified as cognitively impaired using as reference results obtained in age- and education-matched healthy HIV-negative controls. Self-reported adherence was measured on a 0-100 visual analogue scale. According to CHARTER, a CPE-rank was calculated for each ART regimen based on rules proposed in the 2008 original version (orCPE-rank) and the 2010 revised version (revCPE-rank). Neuroeffectiveness categories were analysed based on cut-offs of ≥ 1.5 (orCPE-rank) or ≥ 6 (revCPE-

rank). Association between variables and cognitive dysfunction was analyzed by logistic regression.
RESULTS: A total of 101 patients were enrolled: 65.3% were males, 17.8% injecting drug users, 22.8% with past AIDS-defining events; median age was 47 years (IQR 42-52), median current CD4 620/μL (IQR 454-827), median nadir CD4 171/μL (IQR 62-264); all had HIV-RNA < 50copies/mL. Mean adherence was 81% (SD 16), with 63.6% reporting an adherence ≥ 80%. An orCPE-rank ≥ 1.5 was found in 85.1% (n = 86) of patients, while a revCPE-rank ≥ 6 was observed in 78.2% (n = 79). Neurocognitive impairment of any type was observed in 50 (49.5%) subjects. As compared with patients with a CD4 < 200 cells/□L at nadir, those with a nadir CD4 > 350/μL showed a reduced risk of neurocognitive impairment (OR 0.13, 95% CI 0.02-1.15; p=0.067). In a multivariable model adjusting for nationality, adherence and nadir CD4, orCPE-rank was not associated with impaired cognitive performance (OR 0.77, 95% CI 0.21-2.91, p = 0.704), while revCPE-rank ≥ 6 (OR 0.32, 95% CI 0.11-0.95, p = 0.039), an adherence ≥ 80% (OR 0.39, 95% CI 0.15-0.99, p = 0.047), but not CD4 counts at nadir (p = 0.297), were independently associated with a reduced risk of neurocognitive dysfunction.
CONCLUSIONS: High prevalence of minor neurocognitive disorders was observed in apparently asymptomatic, virologically suppressed HIV+ individuals. The revCPE-rank showed improved association with neurocognitive dysfunction over the orCPE-rank. When a virological suppression is achieved on ART, treatment neuroeffectiveness and medication adherence may overshadow the deleterious effects of lower nadir CD4 counts on neurocognitive performance.

LB 6

Infection 2010; 38 (Suppl. I): 96

Long-term suppression of viral replication in HIV-related lymphoma survivors: a case-control study

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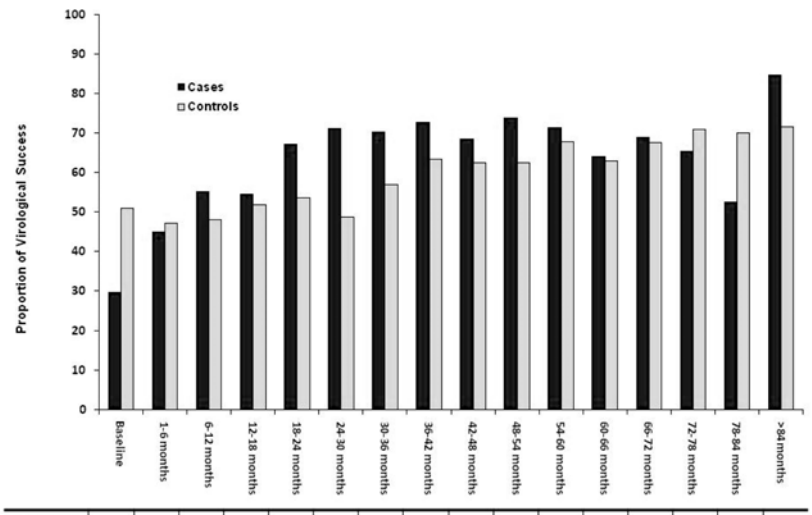
BACKGROUND: Detectable HIV-RNA levels are a risk factor for the development of lymphoma, particularly for Non-Hodgkin lymphoma (NHL). No data are available on viral replication following lymphoma diagnosis and chemotherapy (CT). The aim of this study was to determine if the occurrence of lymphoma may influence the long-term virological success.

METHODS: Case-control study. Cases were patients with a diagnosis of lymphoma who completed CT, alive and currently followed at our clinic. Four alive controls without cancer (when available) were matched for each case on gender, age (± 1 year), year of HIV infection (± 1 year) and nadir CD4+ (± 50 cells). The date of cancer diagnosis of each case was considered as baseline (BL) for cases and for the corresponding controls. Follow-up was calculated as the time interval between the BL and the last available visit. Cochran-Armitage test was applied to assess for linear trend on the proportions of virological success (VS; HIV-RNA<50 copies/mL); the Cochran-Mantel-Haenszel (CMH) test was used to assess trend of VS when controlling for the fact to be a case or a control.
RESULTS: 62 cases [20 Hodgkin Diseases (HD), 42 NHL] and 211 controls were included in the analyses (6 cases with 1 control, 6 cases with 2, 7 cases with 3, 43 cases with 4). The median follow-up was similar between cases: 4.6 (2.2-8.1) years and controls: 5.1 (2.2-8.1) years, p=0.606.
At BL cases presented lower CD4 cell count [278 (122-419) vs 427 (239-579) cells/mm^3; p=0.002] and lower undetectable viremia proportion [30% vs 51%; p=0.005] than controls, while no differences were observed for the proportion of HAART experienced patients.
Trend of the VS in cases and controls is shown in the Figure 1. The proportion of patients with VS significantly increased along time in both groups (p<0.0001).
When considering the classification of lymphoma (HD and NHL), differences were found in virological trend. Among NHL patients, VS proportion significantly increased during follow-up [% at baseline, 6, 12 months and at last visit were: 24%, 39%, 55% and 98%; p for trend: <0.0001] as for the corresponding controls [% at BL, 6, 12 months and at last visit: 65%, 52%, 55% and 84%; p for trend:<0.0001; CMH test: P<0.0001]. Among HD patients the percentage of VS did not significantly increased during follow-up [% at baseline, 6, 12 months and at last visit were: 40%, 60%, 55%, 60%; p for trend:=0.638] in contrast to the corresponding controls [% at baseline, 6, 12 months and at last visit were: 50%, 43%, 46% and 78%; p for trend: <0.0001; CMH test: P<0.002].
DISCUSSION: Lymphoma survivors presented a higher proportion of VS than controls over time; this result was evident for NHL patients and not for HD patients. This finding may reassure clinician about the long-term suppression of viral replication after lymphoma diagnosis and CT.



N°samples Cases	61	69	100	92	79	83	67	55	57	61	42	39	32	26	24	163
N°samples Controls	197	285	298	284	282	263	220	218	192	165	171	140	114	106	83	509

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Infection 2010; 38 (Suppl. I): 97

Immunological response and depression improve with simplification of antiretroviral regimen in HIV-infected adolescents

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BACKGROUND/OBJECTIVES: in HIV infected youths, data on adherence and quality of life (QoL) related to the antiretroviral regimen use are scanty. The objective of this study was to evaluate adherence and quality of life (QoL) in a cohort of HIV-infected youths simplifying their combined antiretroviral therapy (cART) regimen.
METHODS: This is an observational, prospective, cohort study on 30 HIV vertically-infected youths ranging from 14 to 25 years of age and with a median of previous cART regimens of 2 (IQR 2-3). All patients at the enrollment had stable undetectable HIV-viral load and were receiving a cART regimen containing Lamivudine, Tenofovir and Efavirenz from a mean of 64 months (SD 14). Subjects were switched to a single-tablet regimen of Efavirenz, Emtricitabina, and Tenofovir. Each patient filled out an anonymous 36-items questionnaire to assess self-reported adherence, QoL and symptoms. CES-D 10 scale was used to evaluate depression. A questionnaire was administered to each patient 1 month prior to the therapeutic switch (T^{-1}), at the cART switch (T0) and one month after (T^{+1}). Clinical parameters, CD4 count and HIV viral load were collected concomitantly with the questionnaire.
RESULTS*:* 53 % of the patients were orphans of at least one parent, 10% was adopted and 20% lived in foster care. 77 % of the patients completed only the middle school. CDC classifications: N+A 43.3%, B+C 56.7%; current disease stage: N in 86,7% of the patients. 33 % and 76.7% of the patients showed mild to severe signs of atrophy and lipohypertrophy respectively.
From To to T^{+1} all patients retained viral suppression and an increase in CD4% was observed from 35.2 (SD 8.9) to 39.4 (SD 14.1) ($p < 0,05$). As shown in figure 1, a significant reduction in CES-D 10 score was revealed during this time interval, from 8,2 (SD 4.9) to 6.7 (SD 4.4). Furthermore, self-perceived physiological fatigue decreased from 4.3 (SD 3.1) to 3.1 (SD 2.2) ($p < 0,03$) No significant changes were observed regarding adherence level, symptom score and QoL.

DISCUSSION: Simplification to a single-tablet regimen maintains virological suppression, improves immunological response, reduces depression and improves psychological outcomes.

LB 8

Infection 2010; 38 (Suppl. I): 97

Cost-efficacy analysis of the MONET trial using Italian antiretroviral drug prices

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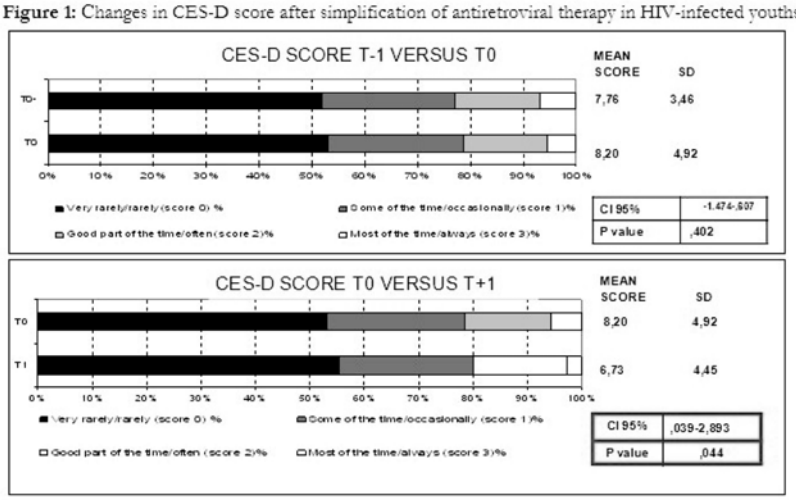
BACKGROUND: In virologically suppressed patients, switching to DRV/r monotherapy maintains HIV RNA suppression, and could also lower treatment costs.
METHODS: In the MONET trial 256 patients with HIV RNA <50 on current HAART for over 24 weeks (NNRTI based (43%), or PI based (57%)), switched to DRV/r 800/100 mg once daily, either as monotherapy (n=127) or with 2NRTI (n=129). The Italian costs per patient with HIV RNA below 50 copies/mL were calculated, using a "switch included" analysis, to account for additional antiretrovirals taken after initial treatment failure.
RESULTS: In the primary efficacy analysis, HIV RNA <50 copies/mL by Week 48 was 86.2% versus 87.8% in the DRV/r monotherapy and control arms; by switch included analysis, efficacy was 93.5% versus 95.1% respectively. Before the trial, the mean annual cost of antiretrovirals was € 7015 for patients on NNRTI based HAART, and € 9048 for patients on PI based HAART. During the MONET trial, the mean annual per-patient cost of antiretrovirals was € 10351 in the triple therapy arm, of which 48% was from NRTIs and 52% from PIs. The mean per-patient cost in the monotherapy arm was € 5999, a saving of 40%. We estimated 50,000 people treated with antiretrovirals in Italy (45% NNRTI based, 55% PI based) and at least 15% of patients (7,500) eligible for PI monotherapy. A switch to DRV/r monotherapy could cut the cost of antiretroviral treatment for these patients in Italy, from € 62 million to € 45 million per year, a saving of € 17 million per year.
CONCLUSIONS: Based on the MONET results, the lower cost of DRV/r monotherapy versus triple therapy in Italy would lead to a saving of up to 17 million Euro per year nationally, if all eligible patients were switched, while maintaining HIV RNA suppression below 50 copies/mL.

Figure 1: Changes in CES-D score after simplification of antiretroviral therapy in HIV-infected youths



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CO = Oral Communication; PO = Poster; LB = "Late Breaker"