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8th International Workshop on HIV & Hepatitis Co-infection

30 May – 1 June 2012,
Madrid, Spain

Abstracts
Oral Presentations
Abstract: O_01

Liver toxicity

Genetic determinants of non-cirrhotic portal hypertension in HIV-infected patients treated with didanosine

E. Vispo1, J. Morello1, M. Cevik2, M. Nelson2, J.K. Rockstroh3, A. Scourfield4, E. Alvarez5, C. Boesecke5, I. Maida1, J.C. Wasmuth3, V. Soriano1

1Hospital Carlos III, Infectious Diseases Department, Madrid, Spain; 2Chelsea & Westminster Hospital, HIV Clinic, London, United Kingdom; 3University of Bonn, Department of Medicine I, Bonn, Germany

Background: Non-cirrhotic portal hypertension (NCPH) is a rare but potentially life-threatening complication in HIV-infected patients. Prior exposure to didanosine (ddI) is an important predisposing factor. However, it is unclear why NCPH only develops in a small subset of patients exposed to ddI.

Methods: A prospective, multicenter, case-control study was conducted by NEAT, a European Commission funded network, to investigate the role of pharmacogenomics in the development of NCPH in HIV-infected patients. Demographics, laboratory data and PBMC were recorded from all individuals who fit the diagnosis of NCPH defined by Vispo et al. (Curr Opin Infect Dis 2011;24:12-18). Moreover, patients with HCV or HBV coinfection, alcohol abuse and/or evidence of cirrhosis were excluded. Three controls were chosen for each case, adjusted for gender, age, CD4 counts, plasma HIV-RNA and site. Tagging SNPs at 4 enzymes involved in the purine metabolic pathway (inosine triphosphatase, 5'-nucleotidase cytosolic II, purine nucleoside phosphorylase and xantine oxidase) was performed using SNPlex microarray technology.

Results: A total of 80 individuals were finally examined; 22 with NCPH and 58 matched controls. Overall, 67% were male, median age 47 years (IQR 44-53), >90% Caucasians, and median ddI exposure 66 months (IQR, 48-86). There were no significant differences comparing NCPH and controls. A total of 36 tagging SNPs were analysed. Two SNPs located at the 5'-nucleotidase gene were associated with NCPH: 48% of patients with rs11598702 CC/CT vs 9% with TT (p=0.003). Another two alleles located at the xantine oxidase gene were also associated with NCPH: 71% of patients with rs1429376 AA vs 23% with CC/AC (p=0.015) and again 71% of patients with rs1594160 AA compared to 23% with CC/AC (p=0.015). Interestingly, there was a cumulative risk of NCPH for these four SNPs: 7%, 26%, 42%, 50% and 100%, respectively, for none, 1, 2, 3 or all SNPs (p=0.001).

Conclusions: SNPs at the 5'-nucleotidase and xantine oxidase genes influence the risk of NCPH in HIV-infected patients with prior exposure to ddI. Hypothetically, endothelial damage at portal vessels caused by increased levels of harmful purine metabolites of ddI taken orally might explain this finding.

No conflict of interest
Abstract: O_02A

Liver cancer

Incidence of end stage liver disease (ESLD) in a cohort of HIV/HCV infected patients in France ‘HEPAVIH ANRS C013’

D. Salmon1, E. Pambrun2, M. Winnock2, E. Rosenthal3, M.A. Valantin1, C. Duvivier4, P. Sogni6, F. Bani Sadr1, K. Lacombe7

1Hôpital Cochin APHP Université Paris Descartes, Unité des Maladies Infectieuses et Tropicales, Paris, France; 2Université Bordeaux Segalen ISPED Centre INSERM U897, Epidémiologie - Biostatistiques, Bordeaux, France; 3Hôpital de L'Arche, Médecine Interne, Nice, France; 4Hôpital La Pitié Salpêtrière APHP Université Pierre et Marie curie, Maladies Infectieuses et Tropicales, Paris, France; 5Hôpital Necker APHP Université Paris Descartes, Maladies Infectieuses et Tropicales, Paris, France; 6Hôpital Cochin APHP Université Paris Descartes, Unité d'Hépatologie, Paris, France; 7Hôpital Saint-Antoine APHP Université Pierre et Marie Curie, Maladies Infectieuses et Tropicales, Paris, France

Background: The HEPAVIH ANRS C013’, implemented in 2005 aimed at describing the natural history of HIC/HCV co-infection in France. Our objectives were to assess the incidence of end-stage liver disease (hepatocellular carcinoma (HCC) or decompensated cirrhosis (ascites, variceal bleeding, hepatic encephalopathy) and the influence of anti-HCV bi-therapy on this incidence,

Methods: The study involved 1175 patients included in HEPAVIH ANRS C013’ and followed for a median duration of 38 months. Fibrosis stage was evaluated by liver biopsy or fibroscan, or fibrotest. For incidence of ESLD, the study focused on HIV/HCV-coinfected patients without decompensated cirrhosis or HCC at inclusion. Fibrosis stage was evaluated using an algorithm combining liver biopsy and non-invasive liver fibrosis tests. Time from enrollment to the first liver decompensation, HCC or death was reported as function of fibrosis stage at enrolment.

Results: Incidence of events was clearly dependent of fibrosis stage. In patients with HIV/HCV and compensated cirrhosis, the incidence rate of first ESLD or HCC was 4% at one year, 6.1% at two years, 11% at three years, 13% at four years, 16% at five years. Among ESLD events notified, 10 (27%) were hepatocellular carcinoma, 23 (62%) were decompensated cirrhosis and 4 (10%) were both. At five years, there was a trend for an lower incidence of ESLD in patients with SVR than in patients who remained chronically infected (5% vs 17%, p=0.1). However, two cases of HCC occurred in the group with SVR.

Conclusions: Incidence of liver-related deaths seems to be lower in cirrhotic patients who have cleared the virus than in those who remain chronically infected with HCV. Progression towards cirrhosis should be stopped by an earlier access to anti HCV therapy.

No conflict of interest
Abstract: O_02B

Liver cancer

Mortality risk and causes of death in a cohort of HIV/HCV infected patients in France: ANRS C013 HEPAVIH

E. Pambrun1, M. Winnock1, E. Rosenthal2, M.A. Valantin3, C. Duvivier4, P. Sogni5, F. Bani Sadr6, F. Dabis1, D. Salmon6

1Université Bordeaux Segalen ISPED Centre INSERM U897, Epidémiologie Biostatistiques, Bordeaux, France; 2Hôpital de l’Archet CHU de Nice, Médecine Interne, Nice, France; 3Hôpital La Pitié Salpêtrière APHP Université Pierre et Marie Curie, Maladies Infectieuses et Tropicales, Paris, France; 4Hôpital Necker APHP Université Paris Descartes, Maladies Infectieuses et Tropicales, Paris, France; 5Hôpital Cochin APHP Université Paris Descartes, Unité d’Hépatologie, Paris, France; 6Hôpital Cochin APHP Université Paris Descartes, Unité des Maladies Infectieuses et Tropicales, Paris, France

Background: The ANRS C013 HEPAVIH multi-centre cohort was implemented in 2005 and aims at describing the natural course of HIV/HCV co-infection in France.

Methods: Chronic HCV infection was defined as a positive HCV RNA. Chronically HCV- HIV co-infected patients were followed every year, if non cirrhotic, and every six months if cirrhotic. Specific additional visits were scheduled in case of anti-HCV treatment. The causes of death were regularly validated by an expert committee.

Results: 1175 patients have been enrolled in the cohort. HIV-HCV chronically co-infected patients presented mostly HCV genotypes 1 and 4 (56% and 22% respectively). Median age at baseline was 45 years; 70% were men; 95% had already received combination antiretroviral therapy (cART), 42% were naïve of anti-HCV treatment, and 11% had excessive alcohol consumption. To date, the overall median duration of follow-up is 38 months, 25% of patients are cirrhotic, 34% have initiated an anti-HCV treatment during follow-up, and 68 deaths have been notified overall. The 5-year cumulative mortality risk has been estimated at 9%, much higher in decompensated cirrhotic patients (66%) than in compensated cirrhotic patients (8%) and in non-cirrhotic patients (98%) (p<10-4). The causes of death were documented for 78 out of 82 deaths. Among those patients with documented cause of death (91%), the main underlying causes were (by decreasing frequency): liver-related (liver cancer excepted) (34%), hepatocellular carcinoma (13%), cancer not related to AIDS or HCV (13%), cardiovascular disease (10%), AIDS-related cause (10%), other infections (13%, half of them of the respiratory tract), overdose (4%) and suicide (3%). Overall, neoplasia-related deaths accounted for 27% of the causes of all documented deaths, whether AIDS-related or not.

Conclusions: Despite the availability of anti-HCV therapy, liver-related deaths remain predominant in HIV/HVC co-infected patients in France. Also, malignancies, whether AIDS-related or not, are a frequent cause of mortality among HIV/HCV co-infected patients. Appropriate actions in case management should be implemented in order to overcome the burden of malignancies in these patients.

No conflict of interest
Abstract: O_03

Liver stiffness predicts liver-related events and mortality in HIV/HCV-coinfected patients

J. V. Fernández-Montero1, E Vispo1, P. Barreiro1, P. Labarga2, L. Martin-Carbonero2, M. Arredondo 1, V. Soriano1

1Department of Infectious Diseases. Hospital Carlos III, Madrid (Spain)

Background: The widespread use of HAART has improved dramatically the survival of HIV-infected patients. Liver conditions frequently associated with HIV infection, especially chronic viral hepatitis, remain a major cause of morbidity and mortality in these patients. In this regard, non-invasive techniques used for the assessment of liver fibrosis could hypothetically play a role in the prognosis of the coinfected population.

Methods: A prospective program of liver fibrosis assessment using transient elastometry (TE) is ongoing in all HIV+ individuals at our institution since 2004. Data from HIV/HCV-coinfected patients with at least 2 TE separated >18 months were selected for the current analysis. Liver fibrosis progression was defined as an increase from ≤9.2 KPa (F0-F2 Metavir estimates) to >9.2 KPa (F3-F4) between TE1 and TE2, or an increase of >30% in liver stiffness values in patients with TE1 >9.2 KPa.

Results: Data from a total of 525 HIV/HCV-coinfected patients (mean age 41 years, 71% males, 81% IDU, mean BMI 23.3 kg/m2, HBsAg+ 4.2%, alcohol abuse 8.4%, mean CD4 count 519 cells/µL) was analyzed. The mean interval between TE1 and TE2 was 53 months (+/- 14 months).

During follow-up, 12 patients (2.2%) died. Liver-related events (defined as development of ascites, encephalopathy, esophageal varices or hepatocellular carcinoma) appeared in 53 patients (10%). Baseline liver stiffness was independently associated with mortality (OR 1.03-1.74, p=0.02), liver-related morbidity (OR1.23, 95% CI 1.12-1.34, p=0.0001) and overall mortality and morbidity (OR 1.2, 95% CI 1.11-1.3, p=0.0001). When assessing protective factors against liver-related conditions, achieving sustained virological response (SVR) following antiviral therapy (OR 25, 95% CI 1.51-333, p=0.02) or a higher BMI (OR 1.25, 95% CI 1.02-1.54, p=0.03) were both protective factors against liver morbidity, while in a joint analysis of morbidity and mortality, a higher BMI (1.28, 95% CI 1.03-1.56, p=0.02) showed a protective effect.

Conclusions: Liver stiffness, as measured by transient elastometry, predicts liver-related morbidity and mortality in HIV/HCV coinfected patients.
Abstract: O_04

Liver Steatosis

Steatohepatitis and fibrosis progression in HIV/HCV-coinfected patients

J. Macías1, J. Berenguer2, M.A. Japón1, J.A. Girón-González2, A. Rivero2, L.F. López-Cortés2, A. Moreno1, M. Márquez2, J.A. Inbarren2, E. Ortega10, P. Miralles1, N. Merchante1, J.A. Pineda1

1Hospital Universitario de Valme, Unit of Infectious Diseases and Microbiology, Seville, Spain; 2Hospital General Universitario Gregorio Marañón, Unit of Infectious Diseases, Madrid, Spain; 3Hospital Universitario Virgen del Rocio, Pathology Department, Seville, Spain; 4Hospital Universitario Puerta del Mar, Unit of Infectious Diseases, Cadiz, Spain; 5Hospital Universitario Reina Sofía, Unit of Infectious Diseases, Cordoba, Spain; 6Hospital Universitario Virgen del Rocio, Department of Infectious Diseases, Seville, Spain; 7Hospital Universitario Ramón y Cajal, Unit of Infectious Diseases, Madrid, Spain; 8Hospital Universitario Virgen de la Victoria, Unit of Infectious Diseases, Malaga, Spain; 9Hospital Donostia, Unit of Infectious Diseases, San Sebastian, Spain; 10Hospital General Universitario de Valencia, Unit of Infectious Diseases, Valencia, Spain

Background: Hepatic steatosis (HS) is a common condition in HIV/HCV-coinfected patients. HS has been associated with liver fibrosis progression in several studies. The role of steatohepatitis on fibrosis progression in HIV/HCV-coinfected patients needs clarification, as only one report, to our knowledge, evaluated steatohepatitis in HIV/HCV-coinfected patients. Furthermore, there is no data on the changes steatohepatitis over time in HIV/HCV coinfection.

Objective: To evaluate the rates of steatohepatitis in sequential liver biopsies and factors associated with thereof.

Patients and Methods: HIV-infected patients with detectable serum HCV RNA, who underwent two biopsies, separated at least by 1 year, were included in this retrospective study. The nonalcoholic fatty liver disease activity score (NAS) was calculated as the unweighted sum of steatosis, lobular inflammation, and hepatocellular ballooning scores. The Scheuer score was applied to stage fibrosis.

Results: Among 146 individuals, the median (IQR) NAS score was 3 (3-4) for the first biopsy and 4 (3-4) for the follow-up biopsy (p=0.002). The median (IQR) time between biopsies was 3.3 (2.0-5.2) years. The NAS score increased in 65 (45%) and decreased in 35 (24%) individuals between the initial and final biopsy. Steatohepatitis was detected in 24 (16%) patients in the first biopsy and in 27 (18%) subjects in the final biopsy (p=0.602). Steatohepatitis persisted in 9 (38%) of 24 patients. Among 122 individuals without steatohepatitis initially, 18 (15%) showed progression. Patients with steatohepatitis were exposed to dideoxynucleosides for a median (IQR) time of 5 (4-10) years vs. 3 (1-5) years for those not exposed to them (p=0.175). Eleven (14%) patients with ART for <4 years and 10 (25%) subjects with ART for ≥4 years showed steatohepatitis persistence or progression (p=0.119). Persistence of or progression to steatohepatitis was independently associated with progression ≥1 fibrosis stages between biopsies (OR [95% CI]=2.4 [1.01-5.7], p=0.047).

Conclusions: Steatohepatitis is frequently observed in HIV/HCV-coinfected patients and NAS score increases over time in these individuals. Steatohepatitis tends to be associated with more prolonged exposures to dideoxynucleoside analogs. The persistence of or progression to steatohepatitis is linked to fibrosis progression in HIV/HCV coinfection.

No conflict of interest
Abstract: O_05

New anti-HCV agents

Determinants of hepatitis C virus kinetics using direct acting antivirals

F. Rick1, I. Maida1, N. Rallón1, M.G. Floris2, P. Barreiro1, P. Labarga1, I. Perez1, E. Vispo1, S. Babudieri2, V. Soriano1, J.M. Benito1

1Hospital Carlos III, infectious diseases, Madrid, Spain; 2University of Sassari, infectious diseases, Sassari, Italy

Background: NS3A/4A protease inhibitors Boceprevir (BOC) and Telaprevir (TLV) are the first direct acting antivirals approved for the treatment of chronic hepatitis C genotype 1 virus infections. Triple combination therapy increases sustained virological response (SVR) rates to 65-70% compared to 30-40% using pegIFNα/RBV. Predictors of early viral kinetics in patients treated with DAA are not well defined yet.

Methods: A total of 37 individuals from two reference clinics in Spain and Italy, respectively, who had initiated triple therapy with TLV or BOC were evaluated. The influence of demographics, baseline HCV-RNA, HCV-1 subtypes, HIV coinfection and IL28B alleles on early viral kinetics using univariate and multivariate analyses were analysed. Rapid virological response (RVR) was defined as undetectable HCV-RNA (<10 IU/ml) at week 4 of treatment for TLV and week 8 in BOC patients (4 weeks of triple therapy after the lead-in phase).

Results: Median age, gender distribution, median baseline HCV-RNA, liver fibrosis stage, HCV-1 subtype and IL28B alleles did not differ significantly when comparing patients on BOC and TLV. HIV coinfection was present in 29% of subjects on BOC but in none on TLV (p=0.04). The rate of RVR in the whole study population was 64%. It was greater in HCV-1b than HCV-1a patients (86% vs 67%, respectively) and in patients treated with TLV than BOC (92% vs 71%, respectively), although differences did not reach statistical significance (p=0.3 and p=0.2, respectively). There was a trend for more pronounced HCV-RNA decay (represented by differences between baseline HCV-RNA and at week 4) in patients on TLV than BOC (5.15 vs 4.73 log IU/ml, p=0.07). Overall, patients on TLV experienced more pronounced HCV-RNA declines than those on BOC (1.28 vs 0.59 log IU/ml per week, p<0.001). A linear regression analysis confirmed the association between use of TLV and faster HCV-RNA decay (R=0.89; beta coefficient 0.70±0.07; p<0.0001) regardless any other variable (HIV coinfection and IL28B alleles). There was a trend for faster HCV-RNA decay in patients infected with HCV-1b vs 1a (p=0.08).

Conclusion: There is a faster HCV-RNA decline in patients treated with triple combination therapy including TLV than in those treated with BOC. The precedent 4-week lead-in phase with dual therapy in patients treated BOC may explain it. The impact of our observation on early selection of drug resistance might be relevant.

No conflict of interest
Abstract: O_06

Treatment issues --- HCV-HIV coinfection

Amino acid changes in Core D1 domain of Hepatitis C (HCV) may influence viral replication ability in HIV/HCV coinfected pts before anti-HCV therapy

M. Merli1, S. Bagaglio1, H. Hasson1, E. Messina1, A. Carbone1, A. Lazzarin1, C. Uberti-Foppa1, G. Morsica1

1San Raffaele Scientific Institute, Dept. of Infectious Diseases, Milan, Italy

Background and Aim: The HCV core is a basic and dimeric protein thought to oligomerize upon packaging of the genomic RNA in order to form the viral nucleocapsid. The N-terminal RNA binding domain D1 of mature core protein includes three highly basic clusters (BD1–BD3) and a tryptophan rich domain that are responsible for the nucleic acid chaperone activity of the HCV core protein. Viral replication may be influenced by amino acid (aa) changes in core D1 domain. The mutational profile of this region in HIV/HCV coinfected patients (pts) is yet unknown. We analysed the core D1 domain (aa 12-117) in 28 HIV/HCV coinfected pts [23 males/5 females, median age 43 years (IQR= 40-45)] before starting standard anti-HCV therapy (PEG-IFN and ribavirin).

Materials & Methods: Sustained virological response (SVR) was defined as maintenance of HCV-RNA negativity 24 weeks after anti-HCV treatment completion. All pts were infected by genotype 1 (25 pts) or 4 (3 pts). Amino acid sequence of HCV core region was analysed at baseline in all pts. Pts showing an aa sequence identical to genotype 1 D1 domain were considered wild type independently from the infecting genotype. The frequencies of mutated domain between SVR and NR were compared by Fisher exact test. Clinical and virological characteristics, including age, sex, HIV RNA level, CD4+ cells count and transaminases, were similar between pts harbouring mutated or wild type D1. Interestingly, HCV RNA viremia was significantly lower in pts harbouring mutations compared to pts showing wild type D1 domain (5.33 vs 6.28 median Log HCV RNA IU/ml, respectively, p=0.002), independently from response to standard of care treatment.

Conclusions: These data suggest that the presence of aa substitutions in N-terminal Core D1 domain may impair virus replication ability.

No conflict of interest
Abstract: O_07

Treatment issues --- HCV-HIV coinfection

IL28B variants association with sustained virological response and plasma cytokine levels in HIV/HCV coinfected patients


1Instituto de Salud Carlos III, Unidad de Coinfección HIV/Hepatitis, Madrid, Spain; 2Hospital Carlos III, Servicio de Enfermedades Infecciosas, Madrid, Spain; 3Hospital General Universitario Gregorio Marañón, Unidad de Enfermedades Infecciosas /VIH, Madrid, Spain

Introduction: Polymorphisms nearby and within IL28B gene are strongly associated with virological response to anti-HCV therapy in HCV monoinfected and HIV/HCV coinfected patients. However HIV/HCV coinfected patients show pronounced difficulty in achieving a full virological response. Scarce studies have analyzed the influence of these variants on plasma cytokine levels. Our aim was to identify how less studied IL28B SNPs predict sustained virological responses in a cohort of Caucasian HIV/HCV coinfected patients, and the effect on cytokine levels. We also study the effect of HCV genotype 1, 4 or 3.

Material & Methods: A retrospective follow-up study was carried out on 326 patients under anti-HCV therapy. Sustained virological response (SVR) to therapy was measured by plasma HCV viral load (HCV RNA-negative 24 weeks after cessation of treatment), and HCV genotype was also determined. Four IL28B SNPs were genotyped (rs12980275, rs8099917, rs7248668, and rs11881222) by GoldenGate® assay with VeraCode® Technology at Spanish National Genotyping Centre (CeGen). Thirteen cytokines were assessed on 57 plasma samples by using Human Th1/Th2/Th9/Th17/Th22 13plex FlowCytomix Multiplex™.

Results: The SVR rate for all patients was 54.6%, while 41.6% and 82.52% for HCV genotype 1/4 and 2/3 respectively. Strong linkage disequilibrium was detected for rs12980275/rs11881222 (r² = 0.94) and rs8099917/rs7248668 (r² = 0.99). All SNPs were strongly associated with SVR although only for HCV genotype 1/4. Haplotype showed no improvement on treatment outcome prediction. However, we performed a decision tree that allow us to improve the classification of HCV 1/4 subjects with poor responder genotypes for rs12980275 (AG+GG), by considering the genotype of rs8099917. Thus, we could improve in 15% the prediction of SVR. Regarding plasma cytokine levels, patients with favorable IL28B genotypes that achieves SVR showed reduced levels of Th1 (IFN-γ), Th2 (IL-6 and IL-9), and pro-inflammatory (TNF-α) cytokines. Moreover, we observed that IFN-γ expression seem to be mostly dependent on IL28B genotype, rather than virologic response of patients. In respect to IL-6 and IL-9, TNF-α, we found that all of them were dependent on virological response.

Conclusions: IL28B polymorphisms predict SVR in HIV/HCV genotype 1/4 coinfected patients. Haplotype do not improve SNPs prediction, nevertheless we were able to improve non responder patients classification by a decision tree with rs12980275 and rs8099917 polymorphisms. IL28B genotype affects IFN-γ plasma protein expression in HIV/HCV coinfected patients, where it was reduced in poor response patients. These results may help to increase the treatment success among coinfected patients.

No conflict of interest
Abstract: O_08A

12-Week Interferon-Free Regimen of ABT-450/r+ABT-333+Ribavirin Achieved SVR12 in More Than 90% of Treatment-Naïve HCV Genotype-1-Infected Subjects and 47% of Previous Non-Responders


1 Abbott, Abbott Park, IL, USA; 2 Cedars-Sinai Medical Center, Los Angeles, CA, USA; 3 Alamo Medical Research, San Antonio, TX, USA; 4 Digestive Disease Institute, Virginia Mason Medical Center, Seattle, WA, USA; 5 University of Colorado Denver and Hospital, Aurora, CO, USA; 6 Kansas City Gastroenterology & Hepatology, Kansas City, MO, USA

Background: ABT-450 is a potent NS3 HCV protease inhibitor identified as a lead compound by Abbott and Enanta (boosted with low-dose ritonavir, ABT-450/r), and ABT-333 is a non-nucleoside NS5B polymerase inhibitor. ABT-450/r and ABT-333 are being evaluated together, and in combination with other anti-HCV agents, for the treatment of HCV infection.

Methods: HCV genotype-1, non-cirrhotic subjects were enrolled in an open-label study of ABT-450/r QD + ABT-333 BID + weight-based ribavirin administered twice daily (1000-1200 mg total daily dose). Two different doses of ABT-450/r were evaluated in treatment-naïve subjects; treatment-experienced subjects were also assessed, as described in the table. Treatment duration was 12 weeks.

Results: Baseline demographics and virologic results are shown in the table. Eighty-eight percent of subjects were subtype 1a. One subject in Arm 1 discontinued due to isolated ALT/AST elevations at week 2, 1 subject in Arm 2 discontinued due to noncompliance during week 1. All remaining subjects in Arms 1 and 2 completed treatment and achieved SVR12. In Arm 3, 6 subjects experienced viral breakthrough while on treatment, and 3 subjects relapsed at post-treatment week 2. Forty-seven percent of subjects in Arm 3 achieved SVR12. Virologic responses appear to be independent of ABT-450/r dose and IL28B genotype in treatment-naïve subjects. There were no deaths or serious adverse events (AEs). The most common AEs were fatigue (42%), nausea (22%), and headache (20%). Most AEs were mild or moderate; 4 subjects experienced severe AEs (fatigue, pain, hyperbilirubinemia [maximum value: 106 mcg/mL, 6.2 mg/dL], and vomiting); none resulted in study drug interruption or discontinuation.

Conclusions: In this study, an interferon-free 12-week regimen of ABT-450/r+ABT-333+RBV was well tolerated and achieved SVR12 in 93-95% of treatment-naïve and 47% of previous non-responders infected with HCV genotype-1. ABT-450/r 250/100 mg and 150/100 mg doses show comparable efficacy in treatment-naïve subjects. The difference in SVR rates observed in naïve and previous non-responders suggest that extrapolation of results across these populations must be done with caution. Additional trials of ABT-450/r in 2 and 3 DAA regimens are currently underway.

Conflict of interest: B. B is employee of Abbott

Table: Baseline Demographics and RVR, SVR4, and SVR12 rates (Intent to Treat)

<table>
<thead>
<tr>
<th>Character</th>
<th>Arm 1: Treatment-naïve</th>
<th>Arm 2: Treatment-naïve</th>
<th>Arm 3: Prev. non-responders*</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>ABT-450/250/100 mg + ABT-333 400 mg + RBV</td>
<td>ABT-450/150/100 mg + ABT-333 400 mg + RBV</td>
<td>ABT-450/150/100 mg + ABT-333 400 mg + RBV</td>
</tr>
<tr>
<td>N=19</td>
<td>N=14</td>
<td>N=17</td>
<td></td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>10 (52.6)</td>
<td>14 (100)</td>
<td>11 (64.7)</td>
</tr>
<tr>
<td>White, n (%)</td>
<td>15 (78.9)</td>
<td>12 (85.7)</td>
<td>13 (76.5)</td>
</tr>
<tr>
<td>Age, Years, Mean ± SD</td>
<td>53.8 ± 9.78</td>
<td>50.9 ± 10.46</td>
<td>52.3 ± 9.03</td>
</tr>
<tr>
<td>BMI, kg/m², Mean ± SD</td>
<td>27.3 ± 3.84</td>
<td>24.6 ± 3.08</td>
<td>28.3 ± 5.11</td>
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<tr>
<td>HCV Genotype 1a, n (%)</td>
<td>17 (89.5)</td>
<td>11 (78.6)</td>
<td>16 (94.1)</td>
</tr>
<tr>
<td>IL28B CC Genotype, n (%)</td>
<td>10 (52.6)</td>
<td>5 (35.7)</td>
<td>0</td>
</tr>
<tr>
<td>Baseline HCV RNA, log10 IU/mL, Mean ± SD</td>
<td>6.25 ± 0.80</td>
<td>6.44 ± 1.15</td>
<td>6.93 ± 0.47</td>
</tr>
<tr>
<td>Virologic Results</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RVR: HCV RNA &lt;25 IU/mL at Week 4, n (%)</td>
<td>19 (100)</td>
<td>13 (92.9)</td>
<td>15 (88.2)</td>
</tr>
<tr>
<td>SVR4: HCV RNA &lt;25 IU/mL 4 Weeks After End of Treatment, n (%)</td>
<td>18 (94.7)</td>
<td>13 (92.9)</td>
<td>0</td>
</tr>
<tr>
<td>SVR12: HCV RNA &lt;25 IU/mL 12 Weeks After End of Treatment, n (%)</td>
<td>13 (94.7)</td>
<td>13 (92.9)</td>
<td>8 (47.1%)</td>
</tr>
</tbody>
</table>

*6 subjects were null responders and 11 subjects failed to achieve undetectable HCV RNA at the end of treatment (partial responders). 3/6 null responders and 5/11 partial responders achieved SVR12.

f1 subject discontinued due to ALT and AST elevation; f2 subject discontinued due to inability to comply with study drug regimen; f6 subjects had viral breakthrough; f3 subjects relapsed

Reviews in Antiviral Therapy & Infectious Diseases – Volume 5: 2012
Abstract: O_08B

A 12-Week Interferon-Free Regimen of ABT-450/r, ABT-072, and Ribavirin was Well Tolerated and Achieved Sustained Virologic Response in 91% Treatment-Naïve HCV IL28B-CC Genotype-1-Infected Subjects

D. E. Cohen1, E. Lawitz2, F. Poordad3, K. V. Kowdley4, D. Jensen5, S. Siggelkow1, K. Wikstrom1, L. Larsen1, R. M. Menon1, T. Podsadecki1, B. Bernstein1

1 Abbott, Abbott Park, IL, USA; 2 Alamo Medical Research, San Antonio, TX, USA; 3 Cedars-Sinai Medical Center, Los Angeles, CA, USA; 4 Digestive Disease Institute, Virginia Mason Medical Center, Seattle, WA, USA; 5 Center for Liver Diseases, University of Chicago Medical Center Chicago, Chicago, IL, USA

Background: ABT-450 is a potent NS3 HCV protease inhibitor identified as lead compound by Abbott and Enanta (dosed with low-dose ritonavir, ABT-450/r), and ABT-072 is a non-nucleoside NS5B polymerase inhibitor. Both are being developed for the treatment of HCV infection with other anti-HCV agents.

Methods: Eleven treatment-naïve, non-cirrhotic HCV Genotype-1 (GT-1) infected subjects with IL28B rs12979860 genotype CC were enrolled in an open-label study assessing the safety, tolerability, pharmacokinetics, and antiviral activity of ABT-450/r 150/100 mg once-daily (QD) + ABT-072 400 mg QD + weight-based ribavirin 1000-1200 mg/day dosed twice-daily for 12 weeks.

Results: Of the 11 subjects, 8 (73%) subjects were male, 9 (82%) Caucasian, and 3 (27%) reported Latino ethnicity. At baseline (BL), median age was 56 years (range 41-66), mean BMI was 26.9 kg/m², and mean HCV RNA was 6.9 log_{10} IU/mL (100% with BL HCV RNA >800,000 IU/mL). Eight (73%) subjects were infected with GT1a. All 11 subjects completed 12 weeks of treatment and were followed for 24 weeks post-treatment. A rapid decrease in HCV RNA level was observed with treatment and all subjects had HCV RNA levels <25 IU/mL by week 3 (Figure 1). All subjects maintained HCV RNA <25 IU/mL from weeks 4 through 12 of treatment, and all had undetectable HCV RNA from week 5 to the end of treatment. One subject relapsed at post-treatment week 8, while 10 subjects (91%) achieved SVR_{24}. Analysis of resistance variants in the subject who relapsed is currently being performed. There were no deaths, serious or severe adverse events (AEs), or premature discontinuations. Most reported AEs were mild in severity; the most common were headache, fatigue, nausea, and dry skin.

Conclusions: ABT-450/r + ABT-072 + RBV is well tolerated and achieves SVR_{24} in 91% of treatment-naïve, non-cirrhotic HCV GT1-infected subjects with IL28B CC genotype after 12 weeks of treatment.

Conflict of interest: D.C is employee of Abbott

Figure 1. Individual Changes in Plasma HCV RNA (log_{10} IU/mL) Through 12 Weeks of Treatment
Abstract: O_09

Treatment issues --- HBV-HIV coinfection

Measurement of serum HBsAg in HIV/HBV coinfected patients predicts HBsAg clearance during long-term exposure to tenofovir

Z. Plaza1, A. Aguilera2, A. Mena3, L. Martin-Carbonero2, E. Vispo1, S. Tomé2, J. Pedreira1, C. Rodríguez1, V. Soriano1, E. Poveda1

1Hospital Carlos III, Infectious Disease, Madrid, Spain; 2Hospital Conxo-CHUS, Microbiology, Santiago de Compostela, Spain; 3Hospital Universitario de A Coruña, Infectious Disease, A Coruña, Spain; 4Centro Sanitario Sandoval, Centro Sanitario Sandoval, Madrid, Spain

Background: Achievement of HBsAg seroconversion is the closest outcome to clinical cure in chronic HBV infection. Several studies have suggested a role for periodic HBsAg monitoring to predict the chances of HBsAg seroconversion in response to anti-HBV therapy in patients with chronic hepatitis B infection. In HBV-monoinfected patients, interferon-based therapy results in a greater likelihood of achieving HBsAg clearance than nucleos(t)ide analogues (NA) therapy. However, very limited data have been reported up to date in HIV+ patients with CHB. The aim of our study was to examine the rate of HBsAg seroconversion and the role of periodic HBsAg quantitative monitoring in a large group of HIV/HBV-coinfected patients treated with tenofovir (TDF).

Methods: All HBsAg+ patients seen at 3 clinics in Spain were identified. Demographics, coinfections (HCV, HDV), antiviral therapy, and laboratory parameters (HIV-RNA, HBV-DNA, HBeAg, HBsAg, HBV genotype) were retrospectively recorded. Serum HBsAg levels were quantified using the Abbott ARCHITECT assay which depicts a dynamic range from 0.05 to 250 IU/ml.

Results: A total of 147 chronic HIV/HBV-coinfected patients were identified. Overall 45% were HBeAg+ and 20.2% were HCV-RNA+. HDV coinfection was recognized in 26.7% of patients. HBV genotypes A and D were the most common (36% and 28%, respectively). The rate of HBeAg and HBsAg loss during the study period was 7.4% and 6.8%, respectively.

Overall, 93% of patients were on TDF therapy (median length 47 months). Nearly 30% had initiated TDF having undetectable serum HBV-DNA (<200 IU/mL). Median HBV-DNA in patients with baseline detectable HBV-DNA was 6.4 [IQR: 4.8-8]. Overall, 60% of patients had received lamivudine before beginning TDF. Longitudinal follow-up (median, 5 years) could be performed in a subset of 51 patients with stored serum specimens. Patients who experienced HBsAg clearance had lower baseline HBsAg levels than those who remained HBsAg+ (1.4[0.3-2.1] vs. 4[3.2-4.6] log IU/ml, p<0.001). The former experienced more pronounced HBsAg declines than those with persistent HBsAg during follow-up (0.5 vs. 0.3 log IU/ml, p=0.027). Median baseline HBsAg levels were lower in HBV genotypes D than A (3.5[2.2-4.3] vs. 4.2[2.3-5] log IU/ml, p=0.03). HBeAg+ patients had at baseline greater HBsAg levels than HBeAg negative patients (4.4[4-5] vs. 3.4[2.4-4.3] log IU/ml, p=0.001). In the multivariate analysis, both baseline HBsAg levels and HBsAg declines >0.5 log/ml/year were independent predictors of subsequent HBsAg clearance.

Conclusions: Baseline measurement and periodic monitoring of serum HBsAg predicts HBsAg clearance at 5 years in HIV/HBV-coinfected patients treated with TDF.

No conflict of interest
Abstract: O_10

Hepatitis Delta in Spain - Main characteristics and influence of HIV infection

L. Martín-Carbonero1, E. Poveda1, A. Aguilera2, A. Mena3, E. Vispo1, J. García-Samaniego1, J. Pedreira1, F. Teixeira1, Z. Plaza1, A. Madejón1, V. Soriano1.

1Hospital Carlos III, Madrid. 2Hospital Conxo-CHUS, Santiago de Compostela. 3Hospital Juan Canalejo, La Coruña. SPAIN

Background: Hepatitis delta is the less common but the most severe form of chronic viral hepatitis. New HDV infections have declined in recent years in Europe mainly as result of a wide implementation of HBV vaccination and reduced intravenous drug use. Herein, we report the current profile of patients with delta hepatitis and examine the influence of HIV infection.

Methods: HDV infection was diagnosed in the presence of specific antibodies (anti-HDV IgG) in three different clinics in Spain. Epidemiological, clinical and virological characteristics were retrospectively assessed. Further analyses were performed on a merged database of all participating clinics.

Results: A total of 75 anti-HDV+ patients were identified, of whom 39 (52%) were coinfected with HIV. Most patients (89%) were native Spaniards and median [IQR] age was similar in both groups: 41 [37.5-46] and 42 [37.5-51.5] years in HIV-pos vs HIV-neg patients, respectively (p=0.2). HIV-pos patients were more often male (87% vs 64%; p=0.03) and had acquired HDV parenterally (95% vs 36%; p<0.01) than HIV-neg patients. Most HIV-pos patients (79% vs 8%; p<0.01) were on treatment with drugs active HBV, mainly TDF/FTC. By contrast, most HIV-neg patients had received interferon (19% vs 5%; p=0.06). Overall, HBeAg was positive in 18% and 11% (p=0.4) of HIV-pos vs HIV-neg patients. Serum HBV-DNA was undetectable in 58% and 57%, respectively. Anti-HDV IgM was positive in 80% and 72% (p=0.6), respectively. Serum HDV-RNA could be tested in 45 patients; it was positive in 92% (23/25) of HIV-pos and 90% (18/20) of HIV-pos and HIV-neg patients. Median HDV-RNA levels tended to be greater in HIV-pos than HIV-neg patients (6 [4.2-6.7] vs 4.2 [1.7-6.3] log IU/ml, p=0.2).

Conclusion: Hepatitis delta does not show significant differences in HIV-neg and HIV-pos patients as long as they are on antiretroviral therapy including anti-HBV agents. Advanced liver fibrosis is found in around a half of delta hepatitis patients. Moreover, suppression/clearance of HCV due to viral interference is seen in most patients with both anti-HDV and anti-HCV Ab, regardless HIV status.

No conflict of interest

(p<0.01). However, serum HCV-RNA was detectable in 7/8 (87%) and 13/22 (59%) of HCV-seropositive subjects, respectively. Using Fibroscan, significant (>7.5 KPa) and advanced liver fibrosis (>12 KPa) were found in 77% and 48% of HIV-pos and 86% and 54% of HIV-neg patients, respectively.
Abstract: O_11

Treatment issues --- HCV-HIV coinfection

Is the value of 350 CD4 cell the real cut-off to initiate HCV/HIV treatment?


1CHP-Joaquim Urbano Hospital, Infectious Diseases, Porto, Portugal; 2Hospital São João, Infectious Diseases, Porto, Portugal; 3Hospital Universitário de Coimbra, Infectious Diseases, Coimbra, Portugal; 4Centro Hospitalar de Coimbra, Infectious Diseases, Coimbra, Portugal; 5CHLO-Hospital Egas Moniz, Infectious Diseases, Lisboa, Portugal; 6Hospital Garcia da Horta, Infectious Diseases, Lisboa, Portugal; 7CHP-Hospital Santo Antonio, Internal Medicine, Porto, Portugal; 8CHLC-Centro Hospitalar Lisboa Central, Internal Medicine, Lisboa, Portugal; 9Hospital São João, Infectious Diseases, Porto, Portugal; 10Hospital Universitário de Coimbra, infectious Diseases, Coimbra, Portugal; 11Hospital Garcia da Horta, infectious Diseases, Lisboa, Portugal; 12CHLO-Hospital Egas Moniz, Infectious Diseases, Lisboa, Portugal; 13Centro Hospitalar de Coimbra, infectious Diseases, Coimbra, Portugal; 14CHP-Joaquim Urbano Hospital, infectious Diseases, Porto, Portugal

Background: When chronic hepatitis C is detected early in the course of HIV infection, treatment for chronic HCV is advised. However, if a coinfected patient has significant immunodeficiency (CD4 count < 350 cells/μl), the CD4 count should be improved using HAART prior to commencing anti-HCV treatment. It’s therefore assumed that patients with an high CD4 count are more likely to achieve SVR than lower CD4.

Material & Methods: We made a retrospective analysis of the Sustained Virological Response (SVR) in patients treated with Peg-IFN and Ribavirin according with the CD4 cell count. The patients were included in two groups, a group with a CD4 cell count > 200 cells/μl and < 350 cells/μl and a group with a CD4 cell count over 350 cells/μl. Statistical analysis was made using SPSS version 16.0.

Results: We evaluated a total of 602 patients. Of these, 482 (80%) were male. The mean age was 38 years old (min :19-max: 62). The majority of our patients (89%) had the intravenous drug use as the risk for the infection and 88% of them were under HAART. Distribution of genotypes: 58,4% genotype 1, 27,7% genotype 3, 12,3% genotype 4 and 1,9% genotype 2. The total SVR rate was 45,9% with 32,5% SVR in genotype 1 and 74,8% in genotype 3.

Conclusions: We found no differences in Rapid Virological Response (RVR), Early Virological Response (EVR) and Sustained Virological Response (SVR) rates in patients coinfected with HCV/ HIV treated with PEG-INF and ribavirin despite the CD4 cell count.

No conflict of interest

Table1: SVR according with HCV genotype and CD4 cell count.

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<th>≥350 CD4</th>
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<tr>
<td>RVS GLOBAL</td>
<td>44.1%</td>
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<td>RVS GEN 1/4</td>
<td>25%</td>
<td>34%</td>
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<tr>
<td>RVS GEN2/3</td>
<td>80%</td>
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Table2: RVR and EVR according with CD4 cell count.

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<th>&lt;350CD4</th>
<th>≥ 350CD4</th>
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<tr>
<td>RVR</td>
<td>33.8%</td>
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<td>RVP</td>
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Abstract: O_12

Treatment issues --- HCV-HIV coinfection

Ribavirin is Needed in Addition to Pegylated Interferon for Optimal Responses in the Treatment of Acute HCV Genotype 2 and 3 Infection in HIV

C. Boesecke1, P. Ingiliz2, H.J. Stellbrink3, M. Nelson4, S. Bhagani5, M. Guiguet6, M.A. Valantin7, T. Reiberger8, M. Vogel1, J.K. Rockstroh1

1Bonn University Hospital, Medical Department I, Bonn, Germany; 2MiB, Berlin, Germany; 3Infektionsmedizinisches Centrum Hamburg, (fCH), Hamburg, Germany; 4Chelsea and Westminster Hospital, London, United Kingdom; 5Royal Free Hospital, London, United Kingdom; 6UPMC-Pans06 UMR S943, Inserm U943, Paris, France; 7Hôpital La Pitié Salpêtrière, AP-HP, Paris, France; 8Medical University of Vienna, Vienna, Austria

Background: The ongoing epidemic of acute hepatitis C (AHC) infection among MSM highlights the need to identify factors allowing for optimal HCV treatment outcome in HIV co-infected individuals. Here we evaluate the impact of added ribavirin (RBV) on sustained virological response (SVR) rates in different HCV genotypes (GT).

Methods: 284 HIV-infected patients from 4 European countries with diagnosed acute HCV infection were treated early with pegylated interferon (pegIFN) and ribavirin (RBV) (n=254) or pegylated interferon alone (n=30), followed prospectively and evaluated for virological response rates. Fisher's exact test, chi-square test and binary logistic regression model were used for statistical analysis.

Results: All patients were male, median age was 39 years. Main routes of transmission were MSM (95%) and IVDU (3%). In 75% of patients clinical signs of acute hepatic infection were missing. 68% of patients were infected with HCV GT 1, 4.6% with GT 2, 10.6% with GT 3 and 16.9% with GT 4. Median baseline HCV RNA was 939.249 IU/ml and median CD4 T cell count 471 cells/ul. 65% of all patients received HAART. By univariate analysis, there were no statistical differences at baseline for HCV or HIV characteristics between patients with GT 1/4 (group 1) and patients with GT 2/3 (group 2) infection. Median time from diagnosis to treatment start was 9.6 weeks, median treatment duration 26 weeks, median time to first negative HCV PCR 8 weeks. Ribavirin dose reduction occurred in 10.4%. Treatment was stopped in 17 patients (6%) due to toxicities. Overall SVR rate was 69.7% (198/284). Interestingly, SVR rates were significantly higher in group 2 receiving pegIFN and RBV (31/33) when compared with pegIFN mono-therapy (6/10) (94% vs. 60% respectively; p=0.02). In multivariate analysis, pegIFN/RBV combination therapy (p=0.037) and rapid virological response (RVR) (p≤0.0001) were significantly associated with SVR in group 2. In group 1, only RVR (p≤0.0001) was significantly associated with SVR.

Conclusions: Ribavirin is important in the management of AHC in HIV-positive patients; for GT 2/3 infections almost all patients clear virus with combination therapy. Treatment outcome data from this large cohort also confirm that early antiviral treatment of acute HCV infection in HIV co-infected individuals results in virological response rates which are significantly higher than those obtained in treatment of chronic HCV co-infection.

No conflict of interest
8\textsuperscript{th} International Workshop on HIV & Hepatitis Co-infection

30 May – 1 June 2012,
Madrid, Spain

Abstracts
Poster Presentations
Abstract: P_01

Liver cancer

Alphafetoprotein for the screening of HCC in HIV-positive patients: an obsolete or useful marker?

E. Angeli¹, A. Mainini¹, S. Landonio², G. Rizzardini³, G. Gubertini¹

¹Ospedale L. Sacco Universita di Milano, Il Dept Infect Diseases, Milano, Italy; ²Ospedale L. Sacco Universita di Milano, I Dept Infect Diseases, Milano, Italy; ³Ospedale L. Sacco Universita di Milano, II-I Dept Infect Diseases, Milano, Italy

Background. HCC is a quite rare complication of chronic liver disease, even in HIV-positive patients. Curative treatment is also related to early diagnosis, therefore screening with US is strictly mandatory in patients at high risk; in addition, routinely alphafetoprotein (αFP) determination might be helpful, even if with some limits related to sensitivity.

Materials and Methods. In a case-control study, we evaluated all HCC occurred in HIV-positive patients at the II-I Dept Infectious Disease, L. Sacco Hospital, Milan-Italy since 2003 up to date and compared to HIV-negative controls, considering clinical and epidemiological features (gender, age, duration and etiology of liver disease), haemato-chemical parameters (liver function tests, platelets and αFP serum level) and diagnostic characteristics (time between last US and HCC diagnosis, BCLC stage).

Results. Twenty-two cases of HCC have been diagnosed in our departments, among more than 3000 HIV-positive outpatients. We compared them to 42 HIV-negative controls. Cases significantly differed from controls, according to mean age (49.5 vs 68.3 ys, p=0.0001), mean platelets level (197727 vs 127243, p=0.045), mean αFP (1069.15 vs 68.17 µg/L, p=0.0135) and mean time between last US and HCC diagnosis (14.6 vs 6.9 months, p=0.003), but not for gender, mean duration and etiology of liver disease, Child-Pugh score, AST, ALT, total bilirubin, prothrombin time and albumin level, BCLC stage. In addition, HIV-positive patients had significantly more frequently αFP level above 2 x ULN than HIV-negative ones when HCC was detected (p=0.02).

Conclusions. Even in our experience, HCC is a rare event in HIV-positive patients, but adequate diagnosis is still lacking, sometimes also in relation to low patient’s adherence to screening program. Therefore, big efforts should be made to monitor these patients through routinely US examination. As we observed that αFP is more frequently elevated in HIV-positive patients, it might be a useful marker to address patients to further diagnostic procedures for its high feasibility, in order to achieve an early diagnosis and subsequently a successful treatment.

No conflict of interest

Abstract: P_02

Liver toxicity

Evaluation of hepatotoxicity in HIV naive patients on highly active anti-retroviral therapy after 1 year of follow-up

C. Valente¹, E. Ramos¹, N. Pereira², M.J. Aleixo³, S. Almeida³, I. Germano³, R. Pinho³, C. Figueiredo⁴, N. Neves⁵, J. Méndez⁵, N. Malaba¹, M. Aguias⁶, F. Lampreià³, D. Faría⁶, R. Sarmento e Castro⁶

¹Ctro Hosp. de Coimbra, Infectious Diseases Unit, Coimbra, Portugal; ²H S João, Infectious Diseases Unit, Porto, Portugal; ³H Garcia Orta, Infectious Diseases Unit, Lisboa, Portugal; ⁴CHLC, Internal Medicine, Lisboa, Portugal; ⁵CHB Barlavento Algarvio, Internal Medicine, Portimão, Portugal

Introduction: In HIV infected patients, liver toxicity is one of the most problematic adverse effects of anti-retroviral therapy (ART). Virtually every ART medication has been associated with liver enzyme elevations, although certain drugs may cause liver injury more frequently than others. The aim of this study was to analyse the prevalence of markedly elevated ALT and AST in HIV monoinfected and HIV/HCV coinfected patients and to determine possible interactions with host, viral factors and ART.

Material and Methods: This study was conducted in six portuguese centers in a population of HIV naïve positive patients on ART, randomly selected. Patients enrolled
were under the following drugs: Truvada (TRV)/Kivexa (KVX) and EFV/NVP or LPV/r/ATV/r/DRV/r. The definition of hepatotoxicity was based on the ACTG grading scheme and the evaluation of ALT and AST was performed at the 6th and 12th month. The considered normal basal level for ALT was 40 IU/ml.

Results: From the 290 subjects, 208 were males (71.7%) and the average age when starting ART was 42 years. The mean HIV-RNA was 273 084 cp/ml and the mean level CD4 cell count was 229 cel/mm3. Out of the total, 97 patients (33.4%) were HCV positive and from these 73.1% had a detectable viremia. The mean level of HCV-RNA was 2595054 IU/ml and the genotypic distribution was as follow: G1-40%, G2-2.6%, G3-34.6% and G4-22.6%. From the total, 183 patients (63.1%) had a baseline level of ALT <40 IU/ml (Group I) and 107 (36.9%) had an abnormal liver enzyme prior to therapy (Group II). Patients were under the following ART schedules: TRV/EFV-51%, TRV/NVP-3.7%, TRV/ATV/r-18.2%, TRV/LPV/r-9.3%, TRV/DRV/r-0.3%, KVX/EFV-10.6%, KVX/NVP-1.3%, KVX/ATV/r-3.1%, KVX/LPV/r-1% and KVX/DRV/r-0%. When evaluating ALT at 6th month after starting ART, in Group I, 27 patients (14.7%) had any grade of hepatotoxicity: grade 1 (>1.25-2.5-fold)-15pt; grade 2 (>2.5-5-fold)-7pt and grade 3 (>5-10-fold)-5pt; the same analyse performed at 12th month demonstrated hepatotoxicity in 26 patients (14.2%): 22 - grade 1, 2 - grade 2 and 2 - grade 3. In Group II and after 6 months of ART, 21 patients (19.6%) developed hepatotoxicity: 13 - grade 1, 4 - grade 2 and 1 - grade 3. At 12th month, only 14 patients had ALT elevation and from these only 1 had a moderate hepatotoxicity (>3.5-fold). Regarding the ART schedules and after evaluation at 12th month, those more often responsible for hepatotoxicity were: TRV/NVP (27.2%), TRV/ATV/r (15%), KVX/NVP (11.1%), TRV/LPV/r (7.4%) in Group I and TRV/NVP (18.15), TRV/LPV/r (7.4%), TRV/EFV (4.7%) and TRV/ATV/r (3.7%) in Group II. In those patients with hepatotoxicity, 67% and 76.1% had a CD4 nadir level <250 cel/mm3 respectively in Group I and Group II, and those found to be HCV positive were represented in 81.4% and 66.6% in Group I and II respectively.

Conclusions: Hepatotoxicity under HAART occurred in 14.9% of the patients (16.5% at 6th month and 13.4% at 12th month). Moderate liver injury ranged from 0.9 to 2.7% and no grade 4 was identified. Patients with abnormal level of liver enzymes previous to ART, had a higher grade of hepatotoxicity compared to those with normal levels at baseline (14.7% vs 19.6%); this fact was not significant at month 12 (12.1% vs 14.2%). In this study CD4 cell count <250 cel/mm3, HCV positivity and ART schedule, were identified factors associated with higher liver injury.

No conflict of interest

Abstract: P_03

Non invasive assessment of liver fibrosis

Concordance between transient elastography and ultrasonography in the assessment of liver fibrosis in HIV-infected patients with chronic liver disease

M. Merli1, M. Mandelli2, L. Galli1, A. Carbone1, E. Messina1, G. Morsica1, S. Bagaglio1, G. Gallotta1, G. Balconi2, A. Lazzarin1, C. Uberti-Foppa1, H. Hasson1

1San Raffaele Scientific Institute, Dept. of Infectious Diseases, Milan, Italy; 2San Raffaele Scientific Institute, Dept. of Radiology, Milan, Italy

Background Ultrasonography (US) and transient elastography (TE) are currently used in the management of patients with chronic liver diseases, especially for the assessment and monitoring of Advanced Liver Fibrosis (ALF) and Cirrhosis (C). TE has become a reliable non-invasive tool in assessing liver fibrosis, but few data are available concerning the concordance between TE and ultrasonographic parameters. In this study we investigated the agreement between US and TE in evaluating ALF or C in HIV-infected patients with chronic liver disease.

Material & Methods We conducted a monocentric retrospective study on 200 patients who underwent TE and abdominal US, performed between October 2007 and September 2011 within two-month maximum distance between each other, for the assessment of chronic liver disease. Four US parameters (liver surface (LS), portal vein...
Abstract: P_04

Non invasive assessment of liver fibrosis

Progression of hepatic fibrosis assessed by liver elastography in patients with HCV/HIV under treatment with Peginterferon and ribavirin.

J. Mendez1, M. Araujo Abreu1, A.R. Silva1, S. Boavida1, R. Sarmento e Castro1

1CHP-Joaquim Urbano Hospital, Infectious Diseases, Porto, Portugal

Background: Transient elastography (Fibroscan ®) is a non-invasive method for the assessment of hepatic fibrosis in patients with chronic liver diseases, which has been used to evaluate the chronic hepatitis C treatment response.

Objectives: To evaluate the stage of fibrosis before and after the treatment of chronic hepatitis C.

Methods: Prospective analysis of liver fibrosis in patients coinfected with HCV/HIV treated with peginterferon alpha-2a and ribavirin. The assessment of liver fibrosis by Fibroscan ® was performed in all patients prior to treatment (FS1), after the treatment (FS2) and 12 months after FS2 (FS3).

Results: We included 70 patients of whom fifty-five (78.6%) were male. The mean age was 38.1 years (min 23, max 52). The risk for HCV/HIV infection was intravenous drug abuse in sixty-three patients (90%). The mean pretreatment CD4 lymphocyte count was 568/mm3 and the HIV viral load of 2955 Cop/mL. The majority of patients (77.1%) were under HAART. The distribution according to HCV genotypes was: G1/G4 - 51 (72.9%) and G2/G3 - 19(27.1%). SVR was achieved in 48.6% of cases (G1/G4-37, 3%, G2/G3 - 78.9%). Patients with Sustained Virological Response (SVR) had a significant reduction of fibrosis after the treatment – 9.9 Kpa vs 7.5 Kpa (p <0.05) - and a non significant reduction 12 months after FS2 – 7.8 Kpa vs 7.3 Kpa (p=0.520). Regarding only the patients who achieved an SVR, it is concluded that patients infected with G2-G3 – 11.3 Kpa vs 8 Kpa (p<0.05) - and those with severe fibrosis – 14.2 Kpa vs 9.7 Kpa (p<0.05) - had a greater reduction in liver fibrosis.
Conclusions: There was only a significant reduction of liver fibrosis in patients with SVR and particularly in the cases of genotypes 2/3 and severe fibrosis. In patients with SVR the fibrosis reduction obtained at the end of treatment was maintained after two years (FS3). There was a reduction of fibrosis in patients relapsed, but stopping the treatment led to a new increase of liver fibrosis. There was an increase of liver fibrosis in non-responders.

No conflict of interest

Abstract: P_05

Non invasive assessment of liver fibrosis

Reproducibility of transient elastography between an experienced operator and an inexperienced one

M. Araújo Abreu1, J. Mendez2, R. Sarmento e Castro3

1CHP-Joaquim Urbano Hospital, Infectious Diseases, Porto, Portugal

Background: Transient elastography (FibroScan®, TE) is a non-invasive method for the assessment of hepatic fibrosis in patients with chronic liver diseases, by measuring liver stiffness. It is a rapid and user-friendly technique that can be easily performed at the bedside or in an outpatient clinic with immediate results. The objective of our work was to analyze the interobserver agreement of elastography measurements as well as to evaluate how the measurements of an experienced operator can be correlated with the measurements of an inexperienced one.

Material and Methods: Over a four month period, 131 patients underwent a transient elastography measurement by two different operators consecutively. The first operator was a very experienced one, with over 5000 exams made and the second operator had no prior experience. Each operator made 10 measurements per patient, the results where then compared using the intraclass correlation coefficient (ICC).

Results: There were realized 262 exams to 131 patients, 85.5% of which were men and 14.5% women. The mean age was 44.4 (min: 25, max: 76). Over half (55%) of the patients who underwent the exam were co-infected with HCV/HIV, 34.3% were infected with HCV and 10.7% were infected only with HIV. The global interobserver agreement (ICC) was of 96.6%. The ICC of the first 50 exams (one for each operator) was of 88.1%, compared with an agreement of 97.8% of the last 232 exams. The same was observed when compared the first 100 exams (ICC of 90.9%) with the last 162 exams (ICC of 98.3).

Conclusion: Transient Elastography is a highly reproducible and user-friendly technique for assessing liver fibrosis. In this work we can conclude that the interobserver agreement between operators is high and grows with the number of realized exams of the inexperienced operator.

No conflict of interest

Abstract: P_06

Non invasive assessment of liver fibrosis

Non-invasive diagnosis of liver fibrosis by fibroscan, blood tests, and their combination in HIV-HCV co-infected patients

J. Boursier1, K. Lacombe2, M. Winnock3, F. Degos4, M.A. Loko5, P. Sogni6, P. Calès1, D. Salmon7

1University Hospital, Hepato-Gastroenterology Department, Angers, France; 2INSERM, UMR-S707, Paris, France; 3Université Victor Segalen, Isped, Bordeaux, France; 4Hôpital Beaujon, Hepatology Department, Clichy, France; 5INSERM, U897, Bordeaux, France; 6Institut Cochin, Hepatology Department, Paris, France; 7Université Paris-Descartes, Faculté de Médecine, Paris, France

Background: Combination of non-invasive fibrosis tests increases their accuracy for the diagnosis of liver fibrosis and reduces the rate of liver biopsy (LB) in chronic hepatitis C, but has never been evaluated in human immunodeficiency virus (HIV)/hepatitis C virus (HCV) co-infection. We aimed to evaluate fibrosis tests, alone or in combination, in HIV-HCV co-infection.
Abstracts

Material & Methods: 116 HIV-HCV co-infected and 729 HCV-monoinfected patients with LB, Fibroscan (FS), and blood fibrosis tests (Fibrotest [FT], FibroMeter [FM], APRI, Fib4, and CirrhoMeter [CM]) were included. Combinations of fibrosis tests evaluated were: SAFE (APRI and FT; Sebastiani, Hepatology 2009), Bordeaux algorithm (BA, FT and FS; Castera, J Hepatol 2010), and FM+FS classification (FM and FS; Boursier, Am J Gastroenterol 2011). 'Successive algorithm' corresponded to the use in clinical practice of SAFE (or BA) for F≥2 and then, in case of F≥2 diagnosis, of SAFE (or BA) for F4 to differentiate F2/3 from F4 patients. 'Successive SAFE' included thus 3 diagnostic classes (F2/3, F4, LB) and 'Successive BA' 4 classes (F0/1, F2/3, F4, LB). FM+FS classification included 6 classes (F0/1, F1/2, F2±1, F2/3, F3±1, F4) without any LB required.

Results: In the HIV-HCV cohort, prevalence of significant fibrosis (Metavir F≥2) and cirrhosis were 41.4% and 11.2%. AUROCs for F≥2 were: FS: 0.874±0.033, FT: 0.852±0.034, FM: 0.843±0.036, APRI: 0.737±0.047, Fib4: 0.741±0.048, CM: 0.826±0.039. AUROCs for cirrhosis were: FS: 0.918±0.029, FT: 0.776±0.058, FM: 0.785±0.049, APRI: 0.701±0.082, Fib4: 0.826±0.061, CM: 0.876±0.041. Rates of well-classified patients by fibrosis classifications were: FM: 74.8%, FS (de Ledinghen, GCB 2008): 66.4% (p=0.054 vs FM), FT: 84.5% (p <10^-3 vs FS or FM). Rates of well-classified patients by Successive SAFE, Successive BA, and FM+FS classification were, respectively: 80.2%, 85.3%, 84.9% (p=0.412). Successive SAFE required LB in 62.9% patients, successive BA in 44.0% (p=0.007 vs SAFE), and FM+FS classification provided the best performance profile (rate of well-classified patients): F0/1: 79.4%, F2: 100.0%, F3: 70.0%, F4: 92.3%. Accuracies of single fibrosis tests and combinations of fibrosis tests were not significantly different between HIV-HCV and HCV cohorts.

Conclusions: The accuracy of non-invasive tests for the diagnosis of liver fibrosis in HIC-HCV co-infection is not significantly different than in HCV mono-infection. Fibrosis tests combinations developed in chronic hepatitis C improve the diagnostic accuracy of single fibrosis tests in HIV-HCV co-infected patients. The new FM+FS classification combining Fibroscan and FibroMeter allows for a more precise and accurate diagnosis than SAFE or Bordeaux algorithms, without any liver biopsy.

No conflict of interest

Abstract: P_07

New anti-HCV agents

Suboptimal response rates to pegylated interferon and ribavirin is in patients with IL28B genotype CC and detectable HCV RNA at treatment week 4

K. Neukam1, P. Barreiro1, A. Rivero-Juárez2, A. Caruz3, J.A. Mira1, A. Camacho4, J. Macías1, A. Rivero3, V. Soriano2, J.A. Pineda1

1Hospital Universitario de Valme, Unit of Infectious Diseases, Seville, Spain; 2Hospital Carlos III, Department of Infectious Diseases, Madrid, Spain; 3Hospital Universitario Reina Sofia, Instituto Maimónides de Investigación Biomédica (IMIBIC), Cordoba, Spain; 4Faculty of Sciences University of Jaen, Immunogenetics Unit, Jaen, Spain; 5Hospital Universitario Reina Sofia, Unit of Infectious Diseases, Cordoba, Spain

Background: Some experts consider that HCV genotype 1-infected patients harboring interleukin 28B (IL28B) genotype CC should be treated with bitherapy including pegylated interferon (Peg-IFN) plus ribavirin (RBV). However, since not all HCV-infected patients with IL28B genotype CC respond in the same manner, it is important to identify those patients with a low likelihood of sustained virological response (SVR) in this population. These patients could be candidates for therapy with novel direct-acting antivirals (DAA). The aim of this study was to assess the rate of SVR in these subjects, according to whether they achieve rapid virological response (RVR) or not.

Patients & Methods: Two hundred and twenty-two treatment-naive, HCV genotype 1-infected patients harboring interleukin 28B (IL28B) genotype CC should be treated with bitherapy including pegylated interferon (Peg-IFN) plus ribavirin (RBV). However, since not all HCV-infected patients with IL28B genotype CC respond in the same manner, it is important to identify those patients with a low likelihood of sustained virological response (SVR) in this population. These patients could be candidates for therapy with novel direct-acting antivirals (DAA). The aim of this study was to assess the rate of SVR in these subjects, according to whether they achieve rapid virological response (RVR) or not.

Patients & Methods: Two hundred and twenty-two treatment-naive, HCV genotype 1-infected patients, 160 of them with HIV/HCV coinfection, who initiated bitherapy with peg-IFN plus RBV at the Infectious Diseases Units of three tertiary care centers in Spain were included in this prospective cohort study. Patients were analyzed in an on-treatment approach. RVR was defined as undetectable plasma HCV-RNA at week 4 after treatment initiation. Undetectable plasma HCV-RNA 24 weeks after end of therapy was considered as SVR.

Results: Twenty-nine (18%) HIV/HCV-coinfected and 14 (23%) HCV-monoinfected (p=4.4*10^-3) individuals developed RVR. In the overall population, 32 (39%) patients with

No conflict of interest
IL28B genotype CC versus 11 (8%) bearing genotype non-CC achieved RVR (p=4.1x10^{-4}). In HCV-monoinfected patients with IL28B genotype CC, SVR was observed in 12 (92%) of those who achieved RVR and in 3 (30%) of those who did not (p<10^{-6}). The corresponding figures for HIV/HCV-coinfected individuals were 19 (100%) and 14 (35%), respectively (p<10^{-6}).

**Conclusion:** Treatment-naïve HCV-genotype 1-infected patients, with or without HIV-coinfection and bearing favorable IL28B genotype, should not be treated with bitherapy including Peg-IFN plus RBV, if they do not achieve RVR. These subjects clearly represent candidates for more effective therapy with DAAs.

No conflict of interest

**Abstract: P_08**

**Drug Interactions --- Hepatitis ARTs**

**Co-infection(HCV/HBV) in an HIV-2 population**

C. Afonso1, M. Doroana1, J. Fernandes1, C. Silva1, F. Antunes1

1Hospital Santa Maria, Research Unit and Integrated Management of HIV Infection/Hepatitis, Líbano, Portugal

**Background:** Portugal is a country with a close relationship with countries where HIV-2 infection is endemic. HIV-2 is characterized by a slower disease progression, low viremia, and a different response to antiretroviral therapy, when compared to HIV-1. Our objective was to characterize HBV and HCV co-infection in patients with HIV-2 infection, and to determine if the response to the therapy was like the one found in HIV-1 infection.

**Materials & Methods:** Retrospective analysis of the clinical records of all patients with HIV-2 infection admitted to our outpatient clinic since January 2001 to July 2011. Demographic characteristics and response to therapy were determined. The statistic analysis was descriptive.

**Results:** From a total of 1850 patient clinical records analyzed, 91 (5%) were HIV-2. There were two patients with dual infection (HIV-1/HIV-2) who were not taken in to account. HBV infection was present in 11 (12%) patients. Mean age at diagnosis was 35 years, seven (64%) were male, eight (73%) were of African origin and the mode of transmission was mostly (73%) by heterosexual sex (two cases of MSM and one of IDU). Distribution according with the CDC stage was: 2 A1, 2 A2, 3 B2 and 4 in CDC stage C3. All patients were AgHbs positive, 4 were AgHBe positive, 4 were AbHBe positive and 8 were AcHbc positive. None had delta hepatitis. DNA-VHB was positive in seven (64%) patients but genotype was only determined in three: 2 A and one E. Only nine patients were on antiretroviral therapy. Seven patients were under TDF plus 3TC/FTC, from these 5 had undetectable HBV-DNA and two had detectable HBV-DNA (one had detectable viral load but had a history of non adherence and no mutations of HBV on the resistance test performed; other had a viral load of 42 Ul/ml). Two patients were treated only with 3TC; one became undetectable and seroconverted to HBs Ab positive.

HCV infection was present in 6 (6.5%) patients. Mean age at diagnosis was 35 years, half were male, half were of African origin and the mode of transmission was by heterosexual sex (50%) or by IDU (50%). Distribution according with the CDC stage was: 2 A1, 2 A2 and 2 in CDC stage 3. All the patients had HCV Ab positive; only one had undetectable viral load of HCV without treatment. The other five patients: two were genotype1 and three had genotype 2. Only two patients had been treated: both with pegylated interferon 2alfa and ribavirin, both had genotype 2 and none had responded (IL 28B was not performed). None of these patients was co-infected with HBV and HCV.

**Conclusions:** In our cohort of HIV-2 patients co-infection with HBV was more prevalent than co-infection with HCV, probably related with the mode of transmission. Most of the patients co-infected with HBV had HBV-DNA undetectable. None of the patients treated for HCV had any viral response. Treatment of HIV-2 poses challenges that are even hard to overcome when these patients are co-infected with HBV or HCV.

No conflict of interest
Abstract: P_09

Treatment issues --- HCV-HIV co-infection

Human immunodeficiency virus (HIV) and hepatitis C virus (HCV) co-infections in Cameroon: seroprevalence and epidemiology

V. Dada Feubit1

1REDS/Université de l’Équateur, Programme éthique et recherche, Yaounde, Cameroon

Background: Viral infectious diseases are a substantial threat to global public health. Human immune-deficiency virus/Acquired immuno-deficiency syndrome (HIV/AIDS) ranks as one of the most prevalent infectious diseases facing making in the 21st century. Sub-Saharan Africa remains the most critically affected region with AIDS being the principal cause of mortality. To the pandemic of AIDS is associated HCV infection another public health problem throughout the world especially in sub-Saharan Africa. In order to determine the Seroprevalence and to understand the epidemiology of human Human immunodeficiency virus (HIV) and hepatitis C virus (HCV) co-infection in Cameroon a prospective cohort study was carried out in a public hospital in Douala, Cameroon.

Methods: From January 2005 to February 2006 a total of 14,742 familial blood donors and 311 people living with HIV/AIDS were screened both for antigens/antibodies to HIV and HCV using ELISA techniques. Statistical analysis was done using the chi square test at the threshold of 5% with SIGMA STAT software.

Results: The result obtained show that 851 (5.77%) of the 14,742 blood donors enrolled were positive for HIV; 362 (2.45%) were positive for HCV; and 22 (2.58%) were positive for both HIV and HCV. Moreover from 311 people living with HIV/AIDS 14 (4.50%) were positive for HCV. Means age for HIV positive participants was significantly lower compared to HCV positive participants. In addition HIV mono-infected patients were younger than HIV/HCV co-infected patients. Therefore HIV infection was more prevalent in Douala than HCV infection. HCV infected people were older than HIV mono-infected patients.

Conclusions and Recommendations: HIV/HCV co-infection represents a significant threat to people living with HIV/AIDS therefore the monitoring of the disease progression is necessary in co-infected patients

No conflict of interest

Abstract: P_10

Treatment issues --- HCV-HIV co-infection

IL-28 SNP Genotype and Treatment Outcome in HIV-1/Hepatitis Co-Infected Patients

R. Metcalf1, E. Page1, K. Gedela2, P. Pantelidis1, P. Kelleher3, M. Nelson1

1Imperial College London, immunology, London, United Kingdom; 2Chelsea & Westminster NHS Foundation Trust, HIV & Sexual Health, London, United Kingdom; 3Imperial College NHS Foundation Trust, Infection & Immunity, London, United Kingdom; 4Imperial College London, Immunology, London, United Kingdom; 5Chelsea & Westminster NHS Foundation Trust, HIV & Sexual Health, London, United Kingdom

Background: Current therapy for Hepatitis C in HIV-1 sero-positive individuals is poorly tolerated and less successful compared with HCV mono-infected patients. Two single nucleotide polymorphisms (SNPs), rs12979860 and rs8099917, near the IL28B gene are strongly associated with treatment outcomes in HCV mono-infected patients, however there is less data for use of IL-128 SNP in predicting treatment outcomes in HIV-1/HCV co-infected patients. The aim of this study was to determine whether the IL-28B associated SNPs rs12979860 and rs8099917 were associated with treatment outcome in HIV-1/HCV co-infected patients. The aim of this study was to determine whether the IL-28B associated SNPs rs12979860 and rs8099917 were associated with treatment outcome in HIV-1/HCV co-infected individuals

Material & Methods: 59 HIV-1/HCV co-infected patients who had completed interferon-a and ribavirin treatment were recruited to the study. DNA was isolated from whole blood using a Qiagen blood and tissue DNeasy kit. Applied Biosystems TaqMan® SNP Genotyping Assays were used for the detection of the 2 SNPs. Real-time PCR was performed and the genotype of each SNP was determined by the presence or absence of the
specific alleles, detected by fluorescently labeled probes. Fisher's exact test, odd ratios and the Mann-Whitney test were used to test for statistical differences between patient groups.

**Results:** Patients consisted primarily of male (91%) Caucasian (78%) with a median age of 45 years (range: 27-70) and HCV genotype-1 or 4 infection (86%). At the time of treatment commencing the median CD4 count was 519/ml (116-1271); median HIV viral load was <50-copies/ml (<50-32533) and median HCV viral load was 879,333 IU/ml (1534-16,889,250). 41 patients expressed either of the favourable IL-28 genotypes; rs8099917 TT rs12979860 CC. There was a significant increase in frequency of the rs8099917 TT genotype (82%, 32 of 39) compared with the GT/GG genotypes (18%, 7 of 39, p< 0.01, OR: 5.587) among individuals who were treated successfully. The CC genotype of rs12979860 SNP was also more frequently observed (59%, 23 of 39) among the successfully treated patients, compared with the CT/TT genotypes (41%, 16 of 29, p=0.05, OR: 3.354). Median HCV viral load was significantly lower in successfully (627,247Iu/ml) treated patients compared to those that failed (2,307,159. p<0.05). 85% of patients expressing TT and/or CC with a baseline HCV viral load of less than 10^7IU/ml had successful treatment compared with 42% that had a viral load greater than 10^7IU/ml (p<0.05). No differences in treatment outcome were seen for baseline CD4 T count, HIV viral load or duration of HCV infection.

**Conclusions:** A combination of IL28 SNP genotypic analysis and HCV baseline viral load may be useful to predictive treatment outcome in HCV/HIV-1 co-infection. Prospective studies in larger numbers of patients are needed to confirm the clinical utility of this simple, rapid, inexpensive assay in the management of HCV/HIV-1 co-infection.

No conflict of interest

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**Abstract: P_11**

**Treatment issues --- HCV-HIV coinfection**

**A pilot study to evaluate the safety, efficacy and pharmacokinetics of once daily lopinavir-ritonavir monotherapy in HIV-HCV co-infected patients**

H. Tossonian1, B. Conway1, C. La Porte2, L. Wong1, J. Sampalis3, N. Ackad4, C. Cooper2

1University of British Columbia, Downtown Infectious Diseases Clinic, Vancouver, Canada; 2University of Ottawa, Ottawa Hospital Research Institute, Ottawa, Canada; 3McGill University and JSS Medical Research, Montreal, Canada; 4Abbott Laboratories, Montreal, Canada

**Background:** Safe, effective, easy to dose antiretroviral therapy that minimizes hepatic complication risk is essential in optimizing HIV treatment in patients co-infected with hepatitis C virus (HCV) infection. Once-daily (QD) nucleoside-sparing boosted protease inhibitor monotherapy may achieve this goal.

**Material and Methods:** A prospective, open-label pilot simplification study of QD lopinavir/ritonavir (LPV/r) monotherapy in HIV-HCV co-infected patients was conducted in Canada. Patients on highly active antiretroviral therapy (HAART) with undetectable HIV RNA for ≥6 months were eligible for inclusion in this study. The primary outcome was maintenance of HIV-RNA <50 c/mL through week 48. HIV-RNA, immune measures, metabolic markers and pharmacokinetics (PK) were assessed.

**Results:** Twenty participants received QD LPV/r monotherapy. Mean baseline age and CD4 count was 46.9 years and 467 /μL respectively, and mean duration of virologic suppression pre-switch was 146 weeks. Six participants interrupted therapy prior to week 48 (n=3 viral breakthrough, n=3 for other issues). By per protocol analysis, 10 of 14 participants [71.4% (95% CI 45.4, 88.3)] completed 48 weeks of therapy, remained on QD LPV/r monotherapy without re-intensification with nucleosides and were virologically suppressed at week 48. Virologic breakthrough (HIV RNA >50 c/mL on 2 consecutive measures) occurred in 7 patients [mean standard error (SE) time to breakthrough = 38.3 (4.8) weeks]. Re-suppression occurred with improved
adherence in 2 participants. Of the remaining five participants with virologic breakthrough, three discontinued the study for drug intolerance and poor adherence to study drug prior to week 48 and two had detectable HIV-RNA levels at week 48 despite being on triple antiretroviral therapy. LPV Cmin was <1 mg/L in 8 patients at week 24, consistent with non-adherence around the time of this measurement. This was associated with virologic breakthrough in 2 cases but no development of LPV/r resistance. No clinically significant changes in CD4 cell count, or metabolic parameters were noted. Three participants developed transient, unsustained grade 3 liver enzyme elevations. None of 9 severe adverse events (SAEs) were causally associated with LPV/r or related to progression of HCV disease.

Conclusions: QD LPV/r monotherapy in HIV-HCV co-infected individuals offers a safe and effective approach to the management of the HIV infection, with a predictable pharmacokinetic profile. Failure of this strategy is most often associated with non-adherence and has no effect on the long-term efficacy of antiretroviral therapy in participants who experienced a virologic breakthrough. This approach, in concert with careful adherence and virologic monitoring, may be considered to optimize the long-term management of HIV/HCV co-infected individuals, especially in patients with genotype 2 & 3 infection, where interferon and ribavirin will remain the standard of care in the short and medium term.

No conflict of interest

Abstract: P_12

Treatment issues --- HCV-HIV coinfection

Epidemiological, clinical and laboratorial characterization of HIV-infected patients co-infected with HCV and HBV in 11 HIV clinics in Portugal


1CHLC HCC, Infectious Diseases, Lisboa, Portugal; 2CHSJ EPE, Infectious Diseases, Porto, Portugal; 3CHP HU, Infectious Diseases, Porto, Portugal

Background: The management of chronic viral hepatitis in HIV-infected patients is currently one of the most challenging clinical management issues in infectious diseases clinical practice. The objectives of this study is to describe epidemiological, clinical and laboratorial data of HIV-infected patients co-infected with HBV and HCV in 11 HIV clinics in Portugal.

Material & Methods: Retrospective analysis of clinical files of HIV-HCV-HBV co-infected patients. HIV-infected patients with positive anti-HCV antibody and HBs Ag positive were included.

Results: HIV/HCV/HBV triple infection was identified in 125 patients; 117 (93.6%) male; risk behavior was IVDU in 121 (96.8%). HIV diagnosis was done by screening analysis in 76 (60.8%) patients, prior diagnostic of OI in 20 (16%) and prior diagnostic of NOI in 25 (20%). Median duration of HIV-infection was 12 years (1-25) and 108 patients (86.4%) were under ARV treatment. Median CD4 count (cells/mm³) at diagnosis and time of analysis were respectively 350 (1-1705) and 420 (3-1680). Median duration of HCV infection was 11.5 years (1-25); 23 and 39 patients respectively had undetectable HCV RNA at diagnosis and time of current analysis. HCV genotype was available for 66: G1 in 44 (66.7%), G3 in 12 (18.2%) and G4 in 10 (15.1%). Median duration of HBV infection was 11 years (<1-25) and 14/125 (11.2%) had undetectable HBV DNA at diagnosis; HBe antigen was positive in 40 (32%) and non available (NA) in 12 (0.8%); Hepatitis Delta antibody was positive in 47 (37.6%), negative in 36 (28.8%) and NA in 42 (33.6%). ARV regimens were 2NRTI+IP/r in 55/108 (50.9%), 2NRTI+NNRTI in 39/108 (36.1%), 2NRTI+integrase inhibitor in 5 (4.6%), other in 9 (8.4%). Background regimens including 3TC, FTC, tenofovir or combination of two of these were used in 107/108 (99.1%) patients. Median duration of ARV treatment was 9 years (0-29). HIV RNA was available for 87/108 (80.6%) patients, undetectable in 50/87 (57.5%), and detectable on 37/87 (42.5%). Median duration of hepatitis B treatment was 5.75 years (0.75-18) in 112/125 (89.6%)
Abstract: P_13

Treatment issues --- HCV-HIV coinfection

Can haemoglobin drop replace rapid virological response in predicting a sustained virological response?

D. Awoyemi1, S. Mandalia1, M. Bower1, M. Anderson1, M. Nelson1

1Chelsea and Westminster Hospital, St Stephen’s AIDS trust, London, United Kingdom

Background: Hepatitis C treatment with peginterferon and ribavirin can lead to bone marrow suppression, haemolysis and anaemia. A drop in haemoglobin (3 >g/dL) during the first 8 weeks of treatment has been associated with higher sustained virological response (SVR- 6 months post-treatment) rates. Here we measure the change in haemoglobin with peginterferon and ribavirin treatment and establish whether this predicts SVR rates.

Method: This was a retrospective cohort of all HIV and hepatitis C co-infected patients started on interferon for hepatitis C treatment between January 2007 and September 2010. The clinic prescribing database identified 69 patients started on peginterferon and ribavirin treatment. Patients were separated into two groups according to their SVR at 6 months, and the change in haemoglobin from baseline (+/-2weeks) to week 4 (+/-2weeks) was measured for patients in both groups. A Mann-Whitney u-test, a Yate’s corrected chi-squared test and unpaired t-tests were used to test for associations between the sustained or rapid virological responders and non-responders and the mean change in haemoglobin.

Results: Patient demographics: Mean age was 45 (range 31-71), 63 (91%) were male, 38 (55%) had acute hepatitis and 50 (72 %) with HCV genotype 1. Of 69 patients; 44 (64%) had a SVR at 6 months, and 25 (36%) did not have a SVR. 28 patients (40%) had a RVR and 37 (54%) did not have a RVR, 4 (6%) patients had missing data. Of those that had a RVR; 21 (75%) had a SVR and 7 (25%) did not have a SVR (p=0.044). The average haemoglobin (hb) drop (n=69) was -1.3g/dL (-2.3g/dL to -0.3 g/dL), and the mean drop in haemoglobin in the “ no SVR group” (n=25) was -1.2 g/dL(-1.9 to -0.6) and -1.3g/dL(-2.5 to -0.3) in the “SVR group” (n=44). The mean drop in haemoglobin did not differ significantly between the two groups (p =0.401).In the “no RVR group” the mean hb drop was -1.0 (-2.4 to -0.5), n=37 and the mean hb drop was -1.4 (-2.1 to -0.2), n=28 in the “RVR group”. There was no significant difference between mean Hb drop in the “RVR” and “no RVR” group (p=0.942).

Conclusions: A rapid virological response at 4 weeks and a haemoglobin drop > 3g/dL have both been shown to predict SVR rates. In this study we establish whether a drop in Haemoglobin could predict SVR rates and therefore negate the need for a HCV RNA polymerase chain reaction at 4 weeks which may be useful due to cost and unavailability in some clinical settings. RVR did show a significant associated with SVR ( p=0.044) but the drop in haemoglobin was not associated with SVR (p=0.401) or RVR (p=0.942).

No conflict of interest
Abstract: P_14

Treatment issues --- HCV-HIV coinfection

Effect of the treatment of HCV with interferon (IFN) and ribavirin (RBV) in the body composition measurement by DXA in HIV-HCV coinfected patients

I. De Los Santos Gil¹, M. Manzano Luque¹, J. Sanz Sanz²

¹Hospital Universitario de la Princesa, Infectious Diseases, Madrid, Spain

Background: HIV infection and the antiretroviral therapy (ART) have been associated with lipodystrophy (LD), and IFN has been shown to be associated with weight loss, sometimes of difficult recovery once completed. We unknown the effect of this treatment on the body composition, mainly body fat, in a group of patients, as HIV-infected, already with a degree of LD. Our objective is to assess the body composition in HIV-HCV patients that start treatment with IFN/RBV and the changes at its ending.

Material and Methods: Pilot and prospective study of HIV-HCV patients. We performed (baseline and at the end of treatment) clinical and laboratory parameters, HIV and HCV-related, as well as HCV-PCR 24 weeks after the completion of treatment to assess SVR. Total and regional body fat contents were measured in the same periods with DXA (Dual energy X-ray absorptiometry) scanners. For LD diagnostic we used the definition of fat/mass ratio (FMR): absence, when is <1, obvious when is >1.5, and between 1-1.5 it could have LD but is better to see the evolution. Data are expressed in median.

Results: We have included 10 male patients; age 45 yo; time on ART 115 months. HIV VL<20 in 9; CD4 count 577/mm³. Genotype 1 in 8, and 3 in 2. Time on IFN/RBV: 10 months. SVR in 6 patients. At the end of the treatment we observed a decrease in the level of total, HDL and LDL-cholesterol (expressed in percentage: 4, 16 and 1.5 respectively) and a slightly increase in the level of TGR (9%). The total body mass decreased 7% (from 76.2 kg to 70.6), the total body fat decreased 18.4% (from 21.060 g to 17.172) and the total lean mass decreased only 3%. When the results are expressed in percentage and by regional parts we observed also a decrease in all the parameters: 11% in total body fat (from 26.3 to 23.4), 6% in the fat in arms (21.9 to 20.5), 10% in total fat in legs (22.5 to 20.3) and 12.5% in total trunk fat (30.3 to 26.5). The FMR also decreased from 1.5 to 1.4.

Conclusions: In these patients, due to ART, we observed a trend to LD at baseline, as the FMR was 1.5. After 10 months on treatment with IFN/RBV there was a decrease in the total body mass (7%), mainly due to the loss of total body fat and less in the lean mass. Regarding the percentage of fat loss, we observed the biggest decrease in the trunk fat and the lesser in the limbs fat. So, the FMR also decreased. This effect doesn’t get worse the baseline LD, on the contrary it improves it, although very slightly (decrease of 0.1 in FMR), and could serve to advise the patients and not to be afraid of a possible worsening of LD. The study is ongoing and the next objective will be to perform DXA one year after the end of treatment and to expand the cohort to study clinical or laboratory factors related with these results.

No conflict of interest

Abstract: P_15

Treatment issues --- HCV-HIV coinfection

Clinical experience of boceprevir for the treatment of chronic hepatitis C in HIV co-infection.

A. Ahmed¹, E. Page¹, M. Bower², M. Nelson¹

¹Chelsea and Westminster Hospital NHS Foundation Trust, HIV/GUM, London, United Kingdom

Background: Co-infection of hepatitis C virus (HCV) and HIV is associated with excess morbidity and mortality. Recently two new treatments for HCV have been licensed; telaprevir and boceprevir. Prior to licensing boceprevir was available to HIV infected individuals co-infected with HCV as part of an expanded access programme (EAP).
Methods: We have reviewed the outcomes of individuals who received boceprevir within a designated EAP at week 24. To gain access to the EAP individuals had to have failed previous therapy and have bridging fibrosis or cirrhosis. All individuals received a lead in therapy of 4 weeks pegylated interferon weekly and weight based ribavirin daily. At week 5 boceprevir was added for a total of 44 weeks triple therapy.

Results: 5 individuals (4 male and 1 female) were recruited into the boceprevir EAP. All were on stable antiretroviral therapy (ART) for treatment of HIV. 4/5 were receiving a protease inhibitor as part of their ARV HIV treatment and 1 was on raltegravir with truvada. All had an undetectable HIV viral load at entry and median CD4 count was 368 (range 222-742). HIV viral load remained undetectable and median CD4 count at week 24 was 226 (range 158-574). 2 individuals were classified as null responders, 2 partial responders and 1 relapser to previous HCV therapy. 4/5 achieved a greater than 1 log drop in HCV PCR after the lead in phase. At week 12 all 5 individuals had an undetectable HCV PCR and remained undetectable at week 24. 1 patient stopped boceprevir at week 8 because of infection related neutropenia but continues with an undetectable HCV PCR at week 24 on pegylated interferon and ribavirin alone. 5 patients had a haemoglobin drop below 10g/dl and 4 required treatment with epoetin. 3 of those individuals required dose reduction of ribavirin and 2 also required blood transfusions. 4 patients had a neutrophil count below 1 (10^9/l) with 2 requiring treatment with G-CSF. Commonly reported side effects were depression (4/5), dysgeusia (4/5), fatigue (4/5) and anaemia (4/5).

Conclusion: In this small cohort of co-infected patients who had previously failed treatment for HCV, treatment with boceprevir was associated with a high rate of initial treatment success and toxicity.

Abstract: P_16

Treatment issues --- HCV-HIV co-infection

Predictors of sustained virological response to PegIFN-RBV in HIV/HCV coinfected patients differ according to baseline liver fibrosis stage

P. Barreiro1, P. Labarga1, E. Vispo1, I. Maida1, E. Poveda1, N. Rallón1, J.M. Benito1, J.V. Fernández-Montero1, V. Soriano1

1Hospital Carlos III, Infectious Disease, Madrid, Spain

Background: Baseline liver fibrosis stage influences response to hepatitis C therapy, including triple therapy with pegIFN-RBV plus HCV NS3 protease inhibitors. Whereas other factors have shown to influence treatment outcomes as well, no information exists regarding a different impact of predictors of treatment response according to liver fibrosis stage.

Methods: Retrospective analysis of all consecutive HIV+ patients coinfected with HCV genotype 1 and IFN-naïve that had received pegIFN alfa-2a (180 µg weekly) plus RBV (1,000-1,200 mg daily) at our institution. Factors associated with sustained virological response (SVR) were analyzed by baseline liver fibrosis stage as assessed by transient elastometry (FibroScan). Advanced liver fibrosis was defined for TE values >9.5 kPa (equivalent to Metavir scores F3-F4).

Results: A total of 211 patients were examined (76% males, mean age 42 years-old, 98% on HAART, 86% with HIV-RNA <50 copies/mL, mean CD4 count 516 cells/µL, mean HCV-RNA 6.3 log IU/mL, HCV subtype 1b 36%, IL28B CC alleles 35%). There were no significant differences in these variables when comparing 81 (38%) patients with advanced liver fibrosis versus the remaining 130 (62%) patients. SVR was achieved in 25 (31%) patients with advanced liver fibrosis versus the remaining 130 (62%) patients. SVR was in 25 (31%) patients with advanced liver fibrosis versus 57 (44%) with null/moderate liver fibrosis (p=0.06). In patients with advanced liver fibrosis, those with SVR vs non-SVR had respectively mean baseline HCV-RNA of 6.0 vs 6.7 log IU/mL (p=0.001), baseline HCV-RNA >800,000 IU/mL in 64% vs 94% (p=0.001), rapid virological response in
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37% vs 2% (p<0.001), HCV subtype 1b in 48% vs 63% (p=0.2) and IL28B CC alleles in 50% vs 31% (p=0.1). In contrast, baseline HCV-RNA was the single predictor of SVR (OR, 0.22 per log IU/mL (95% CI, 0.05-0.85), p=0.02) in patients with null/moderate liver fibrosis. In the multivariate analysis, predictors of SVR in patients with null/moderate liver fibrosis were lower HCV-RNA (OR, 0.14 per log IU/mL (95% CI, 0.05-0.38), p<0.001), HCV subtype 1b vs 1a (OR, 3.22 (95% CI, 2.63-20), p=0.04) and IL28B CC vs non-CC alleles (OR, 7.17 (95% CI, 2.0-25.6), p=0.002).

Conclusions: In HIV patients with chronic hepatitis C G1 and advanced liver fibrosis (F3-F4), baseline HCV-RNA is the most important predictor of SVR to pegIFN/RBV. In contrast, in HIV/HCV G1 patients with null/moderate liver fibrosis, all baseline HCV-RNA, IL28B alleles and HCV-1 subtype predict treatment outcomes.

No conflict of interest

Abstract: P_17

Treatment issues --- HCV-HIV coinfection

Importance of Prometheus Index in predicting sustained virological response (SVR) in patients co-infected with HCV/ HIV

M. Araújo Abreu1, A.R. Silva1, C. Oliveira1, J.C. Machado2, J. Mendez2, R. Sarmento e Castro2

1CHP- Joaquim Urbano Hospital, Infectious Diseases, Porto, Portugal; 2IPATIMUP, Pathologie, Porto, Portugal;
3CHP: Joaquim Urbano Hospital, Infectious Diseases, Porto, Portugal

Background: Since therapy with pegylated interferon and ribavirin induces several adverse effects, and the response is lower in patients HIV/HCV is important to find factors wich can predict the treatment outcome. Based on the four variables (HCV viral load, HCV genotype, liver fibrosis assessed by Fibroscan® and IL28B genotype), the recently developed Prometheus Index can be used to predict the probability of SVR.

Objectives: To determine the Prometheus index in a group of patients infected with HCV/HIV who were treated with pegylated IFN and ribavirin and evaluate the relationship between it and RVS.

Material & Methods: We made a retrospective analysis of patients who underwent treatment with pegylated IFN and ribavirin in which it was possible to determine the four variables necessary to calculate the Prometheus Index.

Results: We analyzed 76 patients, of whom 63 were male (82.9%) and 13 female (17.1%). The mean age was 41.1 years and the mean duration of time exposure was 18.6 years. Seventy patients (92.1%) were previous intravenous drug abusers, 33 (47.1%) of which were in methadone substitution therapy. The mean pre-treatment HCV viral load was 2,776,544 IU / ml. The median prior fibrosis was 7.6 kPa. The most common genotype was genotype 1 (67.1%). Genotype 3 occurred in 21.1%, genotype 4 in 10.5% and genotype 2 in 1.3% of patients. Thirty patients (39.5%) had CC genotype, 32 had CT genotype (42.1%) and 14 (18,4%) had TT genotype. Thirty-one patients (40.8%) achieved SVR. The calculated Prometheus index value was 76.4% for patients with SVR versus 45.2% in patients who did not achieve SVR (p <0.001). For the seventeen patients with genotype 1 who achieved SVR the mean Prometheus index was 65.46% compared with the value of 50.76% calculated to the ones in wich the treatment failed (p <0.05). For the fourteen patients with genotype 3 who achieved SVR the average value of the Prometheus index was 89.6% vs 98.6% in non responders (p = 0.531).

Conclusions: The probability of achieving SVR with pegylated IFN and ribavirin can be assessed with the Prometheus Index. This new tool can be very useful, particularly in genotype 1 patients.

No conflict of interest
Abstract: P_18

Treatment issues --- HCV-HIV coinfection

Different impact of IL28B polymorphisms on response to peginterferon-alfa plus ribavirin in HIV-positive patients infected with HCV subtypes 1a or 1b

E. Vispo¹, J.A. Pineda³, N.I. Rallón¹, P. Barreiro¹, K. Neukam², A. Rivero³, A. Rivero-Juarez³, P. Labarga¹, V. Soriano³

¹Hospital Carlos III, Infectious Diseases Department, Madrid, Spain; ²Hospital de Valme, Infectious Diseases Unit, Seville, Spain; ³Hospital Reina Sofia, Infectious Diseases Unit, Cordoba, Spain

Background: HCV subtype 1a has emerged as a predictor of poor response to triple hepatitis C therapy including boceprevir or telaprevir, which largely has been attributed to a lower resistance barrier in HCV-1a compared to -1b. However, a lower efficacy of pegIFN/RBV on HCV-1a than HCV-1b could alternatively contribute to explain it. Abnormal immune responses in the HIV setting could further contribute to unmask any differential effect of IFN on HCV-1 subtypes.

Methods: All chronic hepatitis C patients who had completed a course of pegIFN/RBV therapy at three referral clinics in Spain were identified. For this study, only individuals that were IFN-naive and had been successfully subtyped as 1a or 1b were examined. Moreover, only HIV-coinfected patients were included as they represented a more uniform population in terms of demographics and treatment exposure at our clinics. The IL28B rs12979860 alleles were typed using the 5' nuclease assay.

Results: A total of 176 HIV+ individuals were examined (mean age 42 years, 79% males, median HCV-RNA 6.61 log cop/mL), 105 of whom harbored HCV-1a and 71 HCV-1b. IL28B allele distribution was as follows: 64 CC and 109 CT/TT. SVR was achieved by 59% of CC vs 24% of CT/TT patients (p<0.001). On the other hand, SVR was 45% in HCV-1b vs 29% in HCV-1a (p=0.04). Interestingly, the effect of IL28B variants on SVR was mainly recognized in HCV-1a (64% in CC vs 16% in CT/TT; p<0.001), being less important on HCV-1b (63% in CC vs 40% in CT/TT; p=0.06).

Conclusions: The rate of SVR to pegIFN/RBV therapy is lower in HIV-infected patients with chronic hepatitis C due to HCV-1a than HCV-1b; being the impact of IL28B variants significantly stronger on HCV-1a than HCV-1b.

No conflict of interest

Abstract: P_19

Treatment issues --- HBV-HIV coinfection

Results from the implementation of occult hepatitis screening in the Spanish Cohort of HIV-infected pediatric patients (CoRISpe)

M. Archiles¹, A. Noguera-Julian³, C. Fortuny², M.I. de José³, M.J. Mellado³, C. Gavilán³, O. Neth³, M.L. Navarro³, L. Mayol³, M. Mendoza³, L.M. Ciria², M.T. Coll³, L. Garcia³, E. Núñez³, P. Soler-Palacín³

¹Hospital Universitari Vall d'Hebron, Pediatric Infectious Diseases and Immunodeficiencies Unit, Barcelona, Spain; ²Hospital Sant Joan de Déu, Pediatric Infectious Diseases Unit. Department of Pediatrics, Esplugues de Llobregat Barcelona, Spain; ³Hospital Universitario La Paz, Pediatric Infectious Diseases Unit. Department of Pediatrics, Alicante, Spain; ¹Hospital Virgen del Rocio, Pediatric Infectious Diseases Unit. Department of Pediatrics, Sevilla, Spain; ¹Hospital Gregorio Marañón, Pediatric Infectious Diseases Unit. Department of Pediatrics, Madrid, Spain; ¹Hospital Josep Trueta, Pediatric Infectious Diseases Unit. Department of Pediatrics, Girona, Spain; ¹Hospital Germans Trias i Pujol, Pediatric Infectious Diseases Unit. Department of Pediatrics, Badalona Barcelona, Spain; ¹Hospital Miguel Servet, Pediatric Infectious Diseases Unit. Department of Pediatrics, Zaragoza, Spain; ¹Hospital Asil de Granollers, Pediatric Infectious Diseases Unit. Department of Pediatrics, Granollers Barcelona, Spain; ¹Hospital de Mataró, Pediatric Infectious Diseases Unit. Department of Pediatrics, Mataró Barcelona, Spain; ¹Hospital Carlos Haya, Pediatric Infectious Diseases Unit. Department of Pediatrics, Málaga, Spain

Background: diagnosis of occult B (HBV) and seronegative C hepatitis virus (HCV) infection can be missed in immunocompromised patients when using regular screening methods; leading to an increased risk of severe liver damage in case of viral...
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reactivation. Data about these entities in HIV-infected children and adolescents are lacking.

**Objective:** to assess the prevalence of these entities within CoRISpe Cohort.

**Methods:** cross-sectional study including demographic, clinical, immunologic and virologic data, as well as antiretroviral treatment and vaccination status. HBV and HCV infection markers (HBsAg, anti-HBs, anti-HBc IgG and IgM, and PCR DNA test for HVB; ELISA and RIBA antibodies and PCR-RNA tests for HCV) were performed.

**Results:** overall 254 patients were included (55.51% female, 69.2% Caucasian, median age 14 years, most of whom vertically-infected (94.8%)). Occult HBV infection was seen in 2.4% (6 children) of our cohort (anti-HBc alone' pattern). Nevertheless, DNAemia was negative in all cases. Acute HBV infection markers were not detected and two patients (0.8%) showed chronic HBV infection markers. Fifteen patients (5.9%) had chronic HCV infection markers. In addition, two patients (0.8%) had seronegative HCV infection. Regarding to HBV vaccination status, almost 50% did not show an antibody protective response.

**Conclusions:** occult HBV infection was seen in 2.4% of our cohort (anti-HBc alone' pattern). The anti-HBc alone pattern appears to be as common as previously described but its significance remains unknown. Seronegative HCV may be underdiagnosed and this fact has implications for prognosis. On the other hand, vaccinal response seems to be suboptimal and revaccination should be considered in this population.

No conflict of interest

**Abstract: P_20**

**Treatment issues --- HBV-HIV coinfection**

**HIV/HBV co-infection in a Portuguese clinic**

J. Fernandes1, C. Afonso1, C. Silva1, M. Doroana1, F. Antunes1

1Hospital Santa Maria, Research Unit and Integrated Management of HIV infection/AIDS and Hepatitis, Lisboa, Portugal

**Introduction:** Hepatitis B virus (HBV) and human immunodeficiency virus (HIV) share similar routes of transmission, so co-infection is common. The study is aimed to determine the prevalence of HBV/HIV co-infection in the population that visits our clinic.

**Methods:** A retrospective review was performed of charts of currently active HIV infected patients that visit our clinic since January 2001 to July 2011. We analyzed and compared epidemiologic characteristics related to the total patients and the sub group of HBV co-infected patients. The statistical analysis was descriptive.

**Results:** From the total of 1850 patients, 71% were less than 50 years old, 63% were male, 25% were black and the route of transmission was predominantly sexual (82%) with only 18% related to intravenous drug user (IDU). HBsAg co-infection prevalence was 4.1% (77/1850). The majority of these patients were less than 50 years old (80%), 78% were male, 45% were black, and the main route of transmission was sexual (82%) and IDU represented only 18%. Four patients were super infected with HDV (7.7%). HBV genotype was only determined in 20 patients, with genotype A being more prevalent (13). The HBV DNA before treatment was only available for 47 patients. In concerns of treatment, eight patients received no treatment, and 69 received treatment (89%); from these seven were treated only with 3TC and 62 with 3TC/FTC plus TDF. Evaluation of viral load after treatment revealed 41 patients with undetectable HBV DNA (5 received only 3TC and 36 received 3TC/FTC plus TDF); 10 patients had no viral load evaluation after treatment initiation.

**Conclusions:** There are a good correlation related to epidemiologic characteristics between the total patients and the sub-group of HBV co-infected patients, with emphasis on the small proportion associated with IDU. There is some lack of information related to HBV genotype and HBV DNA before and after treatment initiation. Nevertheless we observed a good response to HBV treatment, even in the patients treated only with 3TC, since the majority of patients under treatment (59%) had undetectable HBV DNA (41/69). This was also observed in the four cases of HDV super infection.

No conflict of interest
Abstract: P_21

Treatment issues --- HCV-HIV coinfection

Comparison of demographic characteristics in HIV patients related to HBV and HCV co-infections in a Portuguese clinic

M. Doroana¹, C. Afonso¹, C. Silva¹, F. Antunes¹, J. Fernandes¹

¹Hospital de Santa Maria, Research Unit and Integrated Management of HIV infection/AIDS and Hepatitis, Lisbon, Portugal

Background: HBV/HCV and HIV infection share a similar route of transmission so they are common as a co-infection. This study aims to determine the prevalence of HBV and HCV in a specific HIV population that belongs to our clinic.

Materials & Methods: A retrospective analysis of 1850 HIV patients that came actively to our clinic from January 2001 until July 2011. We have analysed and compared the demographic characteristics related to the total HIV patients and the two subgroups: HBV and HCV coinfected patients. The statistical analysis was descriptive.

Results: From a total of 1850 patients (1757 HIV-1 and 93 HIV-2), 71% were less than 50 years old, 63% were male, 25% were black and the route of transmission was predominantly sexual (82%), from these, 60% heterosexual and 22% homosexual, with 17.8% related with Intravenous Drug Users (IDU). From the 1850 patients, 384 (20.7%) had HCV Ab+, the majority of them (76.8%) were less than 50 years old, 77% were male, 30% were black and the route of transmission was predominantly by IDU (72%), but we have also registered the importance of sexual route (heterosexual 18% and homosexual 10%). Regarding the prevalence of HBs Ag+ it was 4.1% (77/1850), of which 80% were less than 50 years old, 78% were male, 45% were black and the main route of transmission was sexual (82%) with the IDU representing only 18%. In regards to treatment we have observed that for the 77 patients with HBV co-infection, 69 (89.6%) have received treatment, whereas from 348 patients with HCV co-infection, only 121 (34.7%) have been submitted to treatment.

Conclusions: As in other series, we have realized that in our study there was a prevalence of HCV co-infection (20.7%) versus 4.1% of HBV co-infection. The route of transmission was predominantly by IDU in HCV and sexual in HBV. There was a great difference between the number of patients treated with HBV versus HCV; this lack of treatment could be due to the erroneous notion that the IDU are very difficult to treat.

No conflict of interest

Abstract: P_22

Treatment issues --- HCV-HIV coinfection

HCV treatment in coinfected patients. Is it possible to identify factors of non response?

C. Fernandes¹, J. Cortez¹, E. Ramos¹, A. Speidel¹, N. Malaba¹, C. Valente¹

¹University Hospital of Coimbra, Infectious Diseases, Coimbra, Portugal

Introduction: Due to the shared pathways of transmission, co-infection with HCV and HIV is common. As these patients have a faster liver fibrosis progression and a poor response to therapy, HCV treatment is crucial and should be started as soon as possible and focus should be given to factors that lead to a worse response.

Material & Methods: From 2002 to 2010, the authors have identified 66 HIV/HCV coinfected patients treated with Peginterferon alfa 2a/2b once a week plus ribavirin. The primary endpoint was to evaluate the Sustained Virologic Response (SVR) and secondly, to identify possible factors that contributed to a worse response to treatment.

Results: A total of 66 patients were included; they were predominantly male (78.8%) with an average age of 35 years (19 to 51 years). The main route of transmission was Intravenous Drug Use (87.8%) followed by sexual transmission (10.6%) and in one case blood transfusion was the identified route of transmission. The distribution of HCV genotypes (G) was the following: G1 43.9%,
Abstract: P_23

Treatment issues --- HCV-HIV coinfection

Genetic variation in IL28B in chronic hepatitis C infected patients studied in Centro Hospitalar Lisboa Norte (CHLN) from October 2011-February 2012

N. Gomes1, N. Patrício1, G. Marques1, T. Meira1, L. Sêco1, A. Bandeiras1, M.S. Malta Vacas1

1Hospital Santa Maria, Laboratório de Biologia Molecular - Serviço de Patologia Clínica, Lisboa, Portugal

Introduction: Considering the fact that chronic hepatitis C is a major cause of cirrhosis and hepatocellular carcinoma worldwide and in accordance with international studies that consider the analysis of rs12979860 polymorphism, located upstream of the IL28B gene, a strong predictor of sustained virological response (SVR), it became imperative the implementation of this new parameter to improve the treatment in chronic HCV infected patients, particularly in patients with HCV genotype 1.

Material and Methods: The study included 65 HCV patients. The genotype determination was performed with Siemens technology (RNA extraction, amplification and LiPA). The polymorphism of IL28B was determinate by LightCycler® System FastStart DNA Master HybProbe with RNA extraction, using Magna Pure Compact (Roche) and LightMix® IL28B kit (TIB Molbiol).

Results: A total of 65 patients were evaluated, 48 males (73,8%) and 17 females (26,2%). According to the IL28B genotype the distribution was: CT genotype - 33 patients (50,8%), CC genotype - 24 (36,9%) and TT - 8 patients (12,3%). The most common IL28B genotype on both genders was genotype CT: 21 male (63,6%) and 12 female (36,4%). Considering the HCV genotypes the results were: in patients with genotype 1, 62,5% were CT, 31,3% CC and 6,2% TT. In patients with genotype 3, 50% were CC, 28,6% TT and 21,4% CT and in patients with genotype 4, 66,7% were CT and 33,3% TT.

Conclusions: According to our study, which covers the period of five months, and which

Conclusions: In this subset of patients there were no differences in response to HCV treatment attributable to basal CD4 level, basal HIV viral load, HAART or HCV-RNA level. The NR had lower ALT basal level and all of them had G1 or G4. In this group of patients the absence of early virologic response (EVR) had a negative predictive value.

No conflict of interest
reflected the implementation of this new parameter in our Laboratory, patients with genotype 1 have higher prevalence of IL28B genotype CT and CC, the latter being the most likely to achieve a sustained virological response. For better approach to this issue we propose to continue the study of patients with chronic hepatitis C, in order to evaluate the prevalence of CC, CT and TT genotypes in our patient population.

No conflict of interest

Abstract: P_24

Treatment issues --- HBV-HIV co-infection

Chronic HBV infection and HBV/HIV co-infection: a retrospective evaluation of 152 Portuguese patients

V. Moneti1, D. Afalaiate1, N. Luis1, D. Fernandes1, A.C. Miranda1, T. Baptista1, S. Peres1, K. Mansinho1

1Hospital Egas Moniz, Infectious Diseases, Lisboa, Portugal

Background: Human immunodeficiency virus (HIV) and hepatitis B virus (HBV) are acquired through the same routes. HIV/HBV co-infection can influence the natural course of HBV infection and efficacy of therapy. Due to recent development in therapy and improve in understanding the natural history of infection, it was imperative to characterize the population with HBV infection followed in our department.

Methods: We identify 152 patients with chronic HBV infection, 107 mono-infected and 45 HIV co-infected, followed at our clinic, between 2001 and 2010. Inclusion criteria were presence of surface antigen (HBsAg-positive).

Demographic characterisation, HBV infection features, co-infection with other viruses, risk factors for hepatic disease and therapeutic strategy were investigated.

Results: The mean age was 43.9 years, 59% of patients were males; 44% of patients had African origin, 30% were European. Considering factors predisposing to liver injury, alcohol consumption was reported in 12%. Seven percent of patients presented IgG anti-HDV antibodies, two of them were also IgM anti-HDV positive. Considering chronic hepatitis C infection, 10 patients had anti-HCV antibodies, 7 presented triple infection (HIV/HBV/HCV). Diagnosis was made between 2001-2010 in 65% of patients and before 2001 in 35%. Route of transmission was not possible to determine in 72% of cases, sexually transmission was reported in 14%, intravenous drugs users were 7% and transfusion was the source of infection in 4%. Seventeen percent of patients presented positive HBeAg at time of diagnosis and 79% had negative AgHBe. Comparing the two different population, mono vs co-infected: HBeAg was positive in 10% and in 33% of patients, respectively. At the time of diagnosis ALT levels was above upper normal limit (cut off 52 UI/L) in 22% of patients: 17% mono-infected and in 35% co-infected. (p=0.01). Hepatic fibrosis evaluation with liver biopsy or non-invasive methods was performed in 19%. Focusing on serum HBV DNA levels, it was above 2000 IU/ml in 28% of cases: 29% mono-infected and in 28.6% co-infected patients. (p=0.22). Thirty-seven percent of total patients received treatment for chronic HBV infection: 33% were mono-infected and 77% co-infected.

Considering the 19 mono-infected patients under treatment, 3 started a therapeutic regimen with interferon alpha and 16 with a nucleoside. Considering the 45 co-infected patients, 82% were simultaneously treated for both HIV e HBV with therapeutic regimen including at least one reverse transcriptase nucleoside inhibitor (tenofovir, emtricitabine and lamivudine). Sixty percent of total patients did not receive treatment for chronic HBV infection, all of them were mono-infected or inactive carriers. At time of present evaluation 22 patients discontinued follow-up, they were all mono-infected.

Conclusions: There was a high prevalence of mono-infected patients in our evaluation. Our population present a high rate of follow-up discontinuation, mostly in mono-infected patients probably related to the frequently asymptomatic and inactive carrier status of infection. The early start of treatment in co-infected patients and the availability of drugs that are common for both treatments is reflected in a much higher proportion of co-infected patients being treated. Due to high prevalence of co-infection with multiple hepatotropic viruses, systematic screening is imperative.

No conflict of interest
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