Abstract Book
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Abstracts
Oral presentations
Abstract: O_01

Treatment issues --- HCV-HIV coinfection

Acute hepatitis C infection in HIV negative men who have sex with men

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Background: Acute hepatitis C (AHC) infection is now well recognised in HIV infected men who have sex with men (MSM) but risk of HIV negative MSM becoming infected remains unclear. We evaluated a population of MSM diagnosed with AHC attending a dedicated sexual health service.

Methods: From January 2010 to December 2013, all cases of HCV antibody positive (Ab) HIV negative MSM were identified. European AIDS Network (NEAT) criteria were applied to determine acute infection i.e. positive HCV Ab or HCV RNA with documented negative HCV Ab +/- negative HCV RNA within previous 12 months, or alanine aminotransferase (ALT) rise of > 10xULN/ > 5x ULN with previously documented normal ALT within the last 12 months.

Results: 45 individuals fulfilled the diagnostic criteria for acute hepatitis C. 10 were RNA negative at baseline and excluded and classed as previous spontaneous clearance. 3 had follow-up HCV PCR performed and remained PCR negative. 35 patients were diagnosed with AHC. 16 had a previously negative HCV Ab within 1 year, 16 had significant elevation in ALT levels, and 3 were clinically felt to have AHC from risk exposure. Median age at diagnosis was 38 years (range 24- 56). 13 identified as Caucasian, 1 as Asian. 82.9% reported unprotected anal sex. High risk sexual practices were reported- 34.3% engaged in group sex, 31.4% practiced fisting. 20.0% had a sexual partner with HCV. 28.6% had a coexisting sexually transmitted infection (STI) at HCV diagnosis- 4 episodes of gonorrhoea, 4 episodes of chlamydia, 1 gonorrhoea/chlamydia co-infection, 2 episodes of syphilis. 74.3% patients were hepatitis B immune. 57.1% of patients had documented recreational drug use. 25.7% and 42.9% admitted injecting and nasal use of drugs respectively. Drug use included cocaine, GHB, mephedrone, crystal methamphetamine and ketamine. 31.4% engaged in sex whilst under the influence of recreational drugs. Median HCV RNA was 5.42 log10 international units/mL (range 1.56- 6.97 log10 iu/mL). Median alanine aminotransferase was 84 international units/L (range 16- 2238 iu/L). Genotype was documented in 19 patients (16 genotype 1, 1 genotype 3, 1 genotype 4).

5 patients achieved spontaneous clearance of AHC, none of whom had documented evidence of subsequent reinfection. 10 patients received treatment for AHC (pegylated interferon +/- ribavirin), 7 of whom achieved SVR and remain undetectable at follow-up. We then selected a typical month to review HCV screening in HIV-negative MSM. In November 2013, 3811 HIV negative MSM attended sexual health services. Only 14.8% (565/3810) had HCV testing with either HCV RNA or HCV antibody.

Conclusions: Similar to the ongoing epidemic of AHC in HIV positive MSM, AHC is an issue for HIV negative MSM who have similar risks. Only one quarter of these patients report intravenous drug use, so other risk factors must be recognised as significant for HCV transmission. HCV testing must be considered as a part of sexual health screening in environments where risk factors or outbreaks of HCV exist. Accurate history taking, documentation of drug use and risk prevention messages are crucial in this high risk population.

Preliminary data from this work presented at the Third Joint Conference of British HIV Association with British Association Sexual Health and HIV (1st-4th April 2014, Arena and Convention Centre Liverpool).

No conflict of interest
Abstract: O_02

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

**Dutch Acute HCV in HIV Study (DAHHS): A study on the efficacy of 12 weeks of boceprevir peginterferon and ribavirin for acute HCV-1 in HIV+ patients**


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**Background:** Acute HCV emerged as a sexually transmitted disease among HIV+ men who have sex with men (MSM) with incidence rates between 0.1 and 1%. Relatively high cure rates (65-75%) are achieved with 24 weeks of peginterferon (+ribavirin). The addition of a direct-acting anti-viral drug (DAA) may lead to higher cure rates or alternatively allow for a shorter treatment duration. At Q4 2013 the DAHHS study network was implemented in 9 HIV treatment centers. These centers treat approximately 60% of all HIV positive MSM in care in the Netherlands. In DAHHS, 60 HIV+ MSM with an acute HCV genotype 1 infection will be treated with a 12-week boceprevir, peginterferon and ribavirin regimen (BocPegRBV).

**Materials & Methods:** HIV+ MSM with a new ALAT above the upper limit of normal are screened for the presence of HCV RNA. An acute HCV infection is defined as the period between date of diagnosis minus middle of first positive and last negative test < 6 months. Patients in which a 2log HCV RNA decrease 4 weeks after diagnosis is observed, initiate therapy only if no further decline of HCV RNA is observed 4 weeks later. BocPegRBV is discontinued after 12 weeks if HCV RNA is <25 IU/ml at w4 and HCV RNA undetectable at w8 (COBAS AmpliPrep/COBAS TaqMan HCV Test, Roche Diagnostics). Primary endpoint is SVR24 in patients with no HCV RNA detected at w4 (RVR4). Major secondary endpoints are SVR24 in all patients treated and SVR24 in patients with RVR at week 1. In this interim analysis we report on (1) the incidence of acute HCV among HIV+ MSM in the DAHHS network (2) the week 4 HCV RNA results.

**Results:** Throughout the first months of the study 53 new HCV infections were diagnosed in HIV+ patients during 3419 patient years of follow-up (PYFU) with an incidence of 1.55 per 100 PYFU. At the time of abstract submission, 30 patients were included in the study of which 25 started therapy, 3 had spontaneous clearance, 2 have only passed the screening visit. 5 are still in prescreening. 20 patients were excluded [genotype 4 (n=11), infection >6 months (n=6), spontaneous clearance without inclusion (n=2), refused participation (n=1)]. 17/19 patients with w4 data available at the time of abstract submission had HCV RNA <25 IU/ml of which 12 had no HCV RNA detected. 1 patient had 50 IU/ml HCV RNA and 1 patient had a 3 log decrease to 1.3E4 IU/ml at w4. No adverse event leading to discontinuation of therapy occurred. Updated RVR4 data of the first 30 or more patients will be presented.

**Conclusions:** HCV incidence among HIV+ MSM in DAHHS is extremely high at 1.55% per year. Treatment response at w4 was excellent. The DAHHS network allows for a fast and accurate evaluation of new DAA for the treatment of acute HCV in a significant number of patients.

Conflict of interest: This study received funding by Merck.
Abstract: O_03

Treatment issues --- HBV-HIV coinfection

Loss of hepatitis B surface antigen is not common among patients infected with HIV and hepatitis B virus

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Background. In patients chronically infected with hepatitis B virus (HBV), hepatitis B surface antigen (HBsAg) loss is considered the ideal therapeutic end-point, as it is associated with decreased viral activity and improved liver-related outcomes. Hepatitis B 'e' antigen (HBeAg) loss is another therapeutic and clinically-relevant end-point for patients with HBeAg-positive serology. The rates of both these outcomes among HIV-HBV co-infected patients have been reported either retrospectively or during antiviral treatment with a finite range of potency. The objective of this study was to examine the rate of HBeAg- and HBsAg-loss, and their determinants, in a large, prospective cohort of HIV-HBV infected patients.

Materials and Methods. A total 290 patients from the French HIV-HBV/Bi-LIVER cohorts were included if they had one visit at inclusion and at least one other visit during follow-up. A complete HBV serological battery (HBeAg, anti-HBe antibodies, HBsAg, and anti-HBs antibodies) was taken at inclusion and every yearly visit. Follow-up was divided into a series of consecutive 12-month periods. A piecewise exponential survival model was then employed to determine risk-factors associated with HBeAg- and HBsAg-loss in both univariable and multivariable analysis. Cumulative HIV-RNA and HBV-DNA were calculated as log10 copies/mL·year and log10 IU/mL·year, respectively.

Results. At baseline, patients were predominately male (84.1%) with a median age of 40 years (IQR: 35-45). Almost all patients were undergoing antiretroviral therapy (91.4%), over a median 5.6 (IQR: 2.8-7.4) years prior to inclusion. During a median 7.4 years (IQR: 3.1-8.0) of follow-up, rates of undetectable HBV-DNA viral load (<60 IU/mL) substantially increased, from 39.1% at the inclusion visit to 90.6% at the end of follow-up. Accordingly, tenofovir use became more frequent, with 19.0% at inclusion and 85.5% towards the end of follow-up, while 35 (12.1%) patients received concomitant pegylated-interferon therapy at some point during follow-up. CD4+ cell counts also increased from a median 400/mm3 (IQR: 268-554) at inclusion to 525/mm3 (IQR: 415-668) at the last cohort visit. In HBeAg-positive patients (N=151), the incidence rate of HBeAg-loss was 8.4/100 person-years after a median 3.0 years (IQR: 2.0-4.9) of follow-up. In multivariable analysis, higher cumulative HIV-RNA (HR=0.84, 95%CI: 0.71-0.99, \(p=0.04\)) and HBV-DNA replication (HR=0.73, 95%CI: 0.67-0.79, \(p<0.001\)) were significantly associated with decreased rates in HBeAg-loss. In the overall study population, the incidence rate of HBsAg-loss was 1.0/100 person-years after a median 4.6 years (IQR: 2.1-7.2) of follow-up. HBsAg-loss occurred at a consistent rate, with cumulative proportion of patients remaining HBsAg-positive at 99.3%, 97.8%, 95.8%, and 94.6% after 1, 3, 5, and 7 years of follow-up, respectively. Again, HBsAg-loss was much lower with increased cumulative HIV-RNA (HR=0.52, 95%CI: 0.31-0.87, \(p=0.01\)) and HBV-DNA replication (HR=0.75, 95%CI: 0.55-1.02, \(p=0.06\)). No specific anti-HBV treatment was associated with either HBeAg or HBsAg-loss.

Conclusions. Despite high rates of HBV virological suppression and increased use of potent anti-HBV therapy, HBsAg-loss remains uncommon in HIV-HBV co-infected patients. Suppression of HIV and HBV are pivotal in increasing the rate of this important therapeutic outcome.

No conflict of interest
Abstract: O_04

New anti-HCV agents

Sofosbuvir for the treatment of chronic hepatitis C: cost-effectiveness analysis including HIV co-infected patients

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Introduction The hepatitis C virus (HCV) is considered a major global public health problem. The combination of pegylated interferon-α and ribavirin (PegIFN/RBV) has been the current standard of care for chronic hepatitis C (CHC) patients, with the exception of HCV genotype 1 infected patients. For these patients triple combination therapy with PegIFN/RBV and boceprevir (BOC) or telaprevir (TVR) is also available. Recently, sofosbuvir – a new pan-genotypic inhibitor of the HCV NS5B RNA-dependent RNA polymerase – has been licensed for use in adult CHC patients, having shown high sustained virologic response (SVR) rates and an excellent safety profile in combination therapy with RBV or PegIFN/RBV. According to international clinical practice guidelines, HCV treatment recommendations for human immunodeficiency virus (HIV) co-infected patients are identical to those for HCV mono-infected patients. The objective of this study was to assess the cost-effectiveness of sofosbuvir based therapy for the treatment of CHC, including HIV co-infected adult patients, in Portugal.

Materials & Methods Results are based on a discrete-time, Markov-type cost-effectiveness model on sofosbuvir-containing regimens for CHC treatment accounting for different subpopulations in terms of HCV genotype, HIV co-infection status and previous treatment experience. The model incorporates 13 health states: 5 Metavir score states, 2 SVR states (with and without cirrhosis) and 3 advanced liver disease states (decompensated cirrhosis, hepatocellular carcinoma and liver transplant). For PegIFN eligible/tolerant, treatment naïve patients, the model allows for the comparison of the triple regimen sofosbuvir/PegIFN/RBV against combination therapy with PegIFN/RBV, irrespective of genotype, and BOC/PegIFN/RBV or TVR/PegIFN/RBV, in genotype 1 infected patients. For PegIFN ineligible/intolerant patients, comparison of combination therapy with sofosbuvir and RBV was performed against lack-of-therapy. Results are expressed in incremental costs per life year (LY) and quality-adjusted life year (QALY).

Results Overall sofosbuvir-containing regimens are expected to result in an increment of 3.49 LY (3.05 QALY) in Portuguese CHC patients population weighted for the different subpopulations assuming Portuguese epidemiologic data, when compared to PegIFN/RBV and lack-of-therapy where appropriate. On average treatment costs are expected to increase by 51,062€/patient, resulting in an incremental cost-effectiveness ratio (ICER) of 14,649€/LY (16,720€/QALY). In the comparison against the BOC and TVR containing regimens (genotype 1), ICER of 10,675€/LY (12,238€/QALY) and 14,618€/LY (16,495€/QALY) were obtained, respectively. For HIV co-infected and PegIFN eligible/tolerant patients, estimated ICER varied between 6.463€/LY (6.902€/QALY) and 21.281€/LY (28.245€/QALY), for genotype 1 and 2, respectively, when comparing against treatment with PegIFN/RBV. Additionally, in HCV/HIV coinfected patients ineligible/intolerant to PegIFN, the comparison against lack-of-therapy resulted in ICER of 15.656€/LY (17.756€/QALY) and 12.915€/LY (19.077€/QALY), for HCV genotype 1 and genotype 3, respectively.

Conclusions: Sofosbuvir-containing regimens for the treatment of adult CHC patients, irrespective of HIV co-infection status, are expected to result in significant health gains at an incremental cost within the range of European Health Authorities acceptability.
10th International Workshop on HIV & Hepatitis Co-infection

Abstracts
Poster presentations
Abstract: P_01

Liver cancer

Anti-tumor activity of a miR-199-dependent oncolytic adenovirus

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Oncolytic virotherapy represents a growing field of experimental cancer therapy. For safe and effective virotherapy, restricted tissue expression and replication of the virus is desirable. Various methods have been developed to achieve such restricted expression. They included the engineering of viral genomes through the insertion of tissue-specific promoters or genes encoding for tissue specific binding proteins.

Here, we employed a new approach based on the use of microRNAs (miRNAs) to achieve tumor-specific viral expression and replication. miRNAs are approximately 22-nucleotide (nt)-long non-coding RNAs that are able to bind the 3’ untranslated regions (UTRs) of homologous target mRNAs and causing either their degradation or translation inhibition. Since miRNA are differentially expressed in cancer versus normal cells, it is theoretically possible to make virus expression restricted to cancer cells in a miRNA-dependent manner.

Several studies have shown that miR-199 is significantly down-regulated in primary hepatocellular carcinoma (HCC) tissue and HCC cell lines. With this notion in mind, we developed a conditionally replication-competent oncolytic adenovirus, Ad-199T, by introducing four copies of miR-199 target sites within the 3’ UTR of the E1A gene, which is essential for adenovirus replication.

In vitro studies of the properties of Ad-199T virus revealed that E1A expression was indeed tightly regulated both at RNA and protein levels depending upon the expression of miR-199. Consequently, Ad-199T could replicate in the HCC derived cells HepG2, negative for miR-199 expression, while its replication was strictly controlled in HepG2-199 cells, which were engineered to express high level of miR-199. A replication-competent miRNA independent Ad-Control was also generated. Thus, these in vitro studies proved that cytotoxicity of Ad-199T was effective in HCC derived cells, which lacks expression of miR-199, and could be successfully controlled in cells that express miR-199 at high level.

To assess in vivo properties of Ad-199T, we tested an orthotopic tumor model. HepG2 cells were implanted in the liver of newborn B6D2 mice. The cells could survive at least one week in this environment, enough for testing in vivo properties of Ad-199T. These studies revealed that intrahepatic delivery of Ad-199T led to virus replication in HepG2 derived xenograft tumors and a faster removal of cancer cells. Conversely, Ad-199T replication was not detected in normal, miR-199 positive, liver parenchyma.

These results demonstrate that Ad-199T is a conditionally replicative adenovirus (CRAd) miR-199 dependent, with antitumor activity in vivo. This system allows replication of the oncolytic virus in HCC cells and, at the same time, tightly control replication in normal liver tissues, thus avoiding or reducing hepatotoxicity.

No conflict of interest
Abstract: P_02

Liver cancer

Trends of Hepatocellular Carcinoma (HCC) in HIV-Infected Patients over Time, 1995 – 2013

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Background: The incidence of HCC overall has been rising worldwide. Cases of HCC in HIV-positive patients have only recently been reported, and their frequency over time as well as trends over time is unknown.

Methods: HIV-infected patients with HCC (AASLD criteria) were retrospectively identified from 1992-2011 in 38 centers in North and South America, Europe, and Australia. Time of diagnosis was divided into earlier (1995-2005) and later years (2006-2011).

Results: Among 221 HIV-infected patients with HCC, the number of cases rose steadily between 1995 and 2011. Compared to diagnosis pre-2006 (n=102), patients with a diagnosis 2006 or later tended to be diagnosed through screening more often (63% vs. 52%, p=0.097), were on antiretroviral therapy more often (90% vs. 79%, p=0.022), and had lower HIV viral load (mean, 1.98 vs. 2.80 log copies/mL, p=0.001), higher median CD4+ cells (356 vs. 272 per mm3, p=0.001), and lower median AFP levels (87 vs. 727 ng/mL, p=0.001). They also tended to have effective HCC therapy more often (64% vs. 51%, p=0.053), mostly because of more frequent use of surgical resection (16% vs. 5%) and of sorafenib, which became available in 2007 (12% vs. 0%). There was no difference in age (mean, 51 years), etiology of HCC (HCV, 77%; HBV, 22%, non-viral, 1%), and tumor staging (BCLC stages C&D, 56% vs. 54%). Survival was significantly longer 2006-2011 (median, 16.2 vs. 7.4 months, p=0.004). In multi-variable Cox regression analysis, only screening, log HIV viral load, AFP <200 ng/mL, BCLC staging, and effective HCC therapy were independently predictive of survival but not year of diagnosis before or after 2006.

Conclusion: In HIV-infected patients with HCC, a diagnosis in 2006-11 was associated with better survival than one in 1995-2005. This was explained by better HIV viral control, more frequent screening and HCC therapy, as well as a lower AFP level.

No conflict of interest
Abstract: P_03

Liver cancer

Comparative analysis of hepatitis C virus genotyping methods for discriminating rare subtypes in Venezuela

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Introduction: Infection by hepatitis C virus (HCV) is a public health problem and represents a major cause of chronic liver disease worldwide. This virus has an RNA genome and displays a high degree of genetic variability, classified in 7 genotypes and numerous subtypes. Genotype determination is important from a clinical point of view, for the selection of an appropriate antiviral treatment, as well as the dose and duration of it. In Venezuela, sequence analysis of the NS5B region allowed classifying the most common subtypes in the country as 1a, 1b and 2j. Due to the abundance of a rare subtype (G2j) and the presence of other minor subtypes of G2 in the country, the aim of this study was to evaluate the performance of common genotyping tests to discriminate this subtype.

Materials and methods: A total of 67 samples from individuals with HCV infection were analyzed, prior informed consent and approval of the Bioethics Committee of the National Institute of Hygiene 'Rafael Rangel'. HCV genotyping tests used were reverse line blot hybridization (Versant HCV Genotype 2.0 LiPA) and sequencing of the 5'NC and NS5B regions of HCV (5’NCS and NS5S). The degree of agreement between tests was carried out by calculating the kappa coefficient (κ), an instrument designed to adjust the effect of chance in the proportion of the observed concordance. A dendogram performed according to the band presence and intensity in the LiPA test was compared to the homology tress obtained from sequence analysis.

Results: The determination of genotype and subtype, taking as reference test the NS5S sequencing, showed a high degree of concordance (100% and 98%), in the genotype assignement, and 67% and 59%, in subtype assignment, when evaluating 5'NCS and reverse line blot hybridization, respectively. Discrepancies at subtype level were observed in 17 and 21 samples by 5'NCS and reverse line blot hybridization, respectively. The NS5S allowed for the identification of subtypes 2j and 2s, not discriminated by 5'NCS. However, PCR was more sensitive to amplify 5 'NC region (96% compared to LiPA), vs. 78% of for NS5B region PCR amplification. No specific band pattern was observed in LiPA for G2j isolates, and no good correlations were observed when comparing LiPA dendograms for each genotype with homology trees neither for 5NCS nor for NS5S.

Conclusions: The correlation between the studied methodologies, with respect to the reference test was: 'good' for 5NCS and 'moderate' for LiPA. The analysis of the HCV 5'NC region can lead to mistakes at the level of subtypes, so the presence of some subtypes may be underestimated, as is the case G2j and other G2 subtypes in our country.

No conflict of interest
Abstract: P_04

Liver Steatosis

Non- viral liver disease burden in HIV-positive individuals: an observational retrospective cohort study

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Introduction: Since the era of highly active antiretroviral therapy liver disease has emerged as a major contributor to morbidity and mortality amongst individuals with human immunodeficiency virus (HIV). This is often related to chronic viral hepatitis B and C, however potent antivirals have significantly improved long-term outcomes. In the UK non-alcoholic fatty liver disease (NAFLD) and alcohol-related liver disease (ALRD) have increased significantly over the last decade. There is very limited data in HIV-positive individuals regarding prevalence of both NAFLD and ARLD. Early diagnosis is important to ensure institution of timely interventions. Our aim was to assess chronic liver disease (CLD) excluding chronic viral hepatitis in HIV-positive individuals with emphasis on NAFLD, ARLD and antiretroviral-related hepatotoxicity.

Material & Methods: This was a retrospective cohort study between 2005 and 2012. We initially identified HIV-positive patients with negative hepatitis B and C serology and at least two aminoalanine transferase (ALT) >1xULN over a six month period. Patients with evidence of CLD on one or more of the following were included: abdominal imaging, Transient Elastography (TE) and liver biopsy results. CLD was defined as: abnormal imaging and/or histological or TE evidence of >F2 (METAVIR) fibrosis. Data collected included demographical information, antiretroviral history, patterns of alcohol use, liver panel, lipids, glucose, imaging, TE and liver biopsy results. Those with biliary, autoimmune or congenital liver disease were excluded. Univariate analysis was performed to assess independent predictors of chronic liver disease.

Results: We identified 1047 HIV positive individuals with at least two elevated ALT > 1X ULN over a six month period. Of these, 244 (23%) were investigated further. 147 patients (14%) met the criteria for CLD. The most common radiological finding was fatty liver in approximately 47% patients. NAFLD is implicated in the aetiology of CLD in approximately 68%, ARLD in 45% and antiretroviral therapy in 74%. In 69% there was more than one contributing factor. Overall 13% of patients had > F2 fibrosis, portal hypertension or evidence of decompensation.

Conclusions: A significant number of HIV-positive individuals have elevated ALT in the absence of chronic viral hepatitis, although only 23% are investigated further. A substantial proportion of patients had NAFLD as an underlying factor. Of those investigated about 13% have evidence of >F2 fibrosis/portal hypertension/hepatic decompensation. Our data underscores the need for increased awareness of non-chronic viral hepatitis related CLD amongst HIV-positive individuals and more aggressive investigations of elevated ALT in such a cohort, as well as appropriate lifestyle intervention. Our institution will be performing a prospective study using transient elastograpy to evaluate the 77% patients not originally investigated. With this data we hope to establish the overall prevalence of CLD as well as establish guidelines on appropriate referral and investigation in this population.

This data was presented at the BASHH/BHIVA conference in Liverpool, UK in April 2014.

No conflict of interest
Abstract: P_05

**Liver toxicity**

**Death related to end stage liver disease in HIV/HCV coinfected patients**

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**Introduction:** With the introduction of HAART liver related mortality has become the leading cause of non-AIDS deaths in HIV infected patients.

**Material & Methods:** Retrospective study of clinical, epidemiological and analytical characteristics of HIV/HCV co-infected patients that died due to liver decompensation in CHP – HJU, between January 2003 and December 2013. Patients that died elsewhere or with unknown causes of death were excluded. The aim of these study was to analyze the interval between the first liver decompensation and death due to this cause.

**Results:** A total of 291 HIV/HCV co-infected patients died during the analyzed period, 49 (17%) of end stage liver disease. Of these 83.7% were male, 91.8% with a history of intravenous drug use and with a mean nadir CD4 T-cell count of 105/mm3 (13%). A positive AgHBs was found in 25% of the patients. Genotype distribution was: 53.8% gen 1, 34.6% gen 3 a, 7.7% gen 4 and 3.8% gen 2. Ninety four percent of the patients never underwent HCV treatment, 39.2% due to sustained alcohol and drug abuse, 26.1% refused and 17.4 had clinical contraindication for PEG-INF+RBV treatment. Only one (33%) of the treated patients achieved SVR.

At the time of the first liver decompensation, 85.1% had AIDS, 63.3% were on HAART and 32.7% had an HIV RNA <50cop/ml. The mean duration of HIV diagnosis was 9 years (min 0, max 19) and of HCV infection was 19 years. Median liver stiffness was 42.2 Kpa, 68.9% had a Child Pugh score C and a median MELD score of 16. Presentation of ESLD was ascitis (36.7%), hepatic encephalopathy (30.6%) and non obstructive jaundice (20.4%). Two patients (4%) developed hepatocarcinoma. The mean time between the first liver decompensation and death was 7 months (median 1 month). During this period, the patients had a average of two decompensations (min 1, max 12) and died with a mean age of 42 years old.

**Conclusions:** There is a high percentage of patients that didn’t undergo treatment. Survival of HIV/HCV co-infected patients after the first liver decompensation is extremely poor.

No conflict of interest

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Abstract: P_06

**New anti-HCV agents**

**Clinical experience of Telaprevir for the treatment of chronic hepatitis C in HIV co-infection**

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**Introduction:** HIV and HCV co-infection is associated with excess morbidity and mortality. Telaprevir is available in combination with Pegylated Interferon alfa (PegIFNα) and Ribavirin (RBV) for the treatment of Genotype 1 hepatitis C in adults with compensated liver disease. We report outcomes of treatment with Telaprevir in hepatitis C genotype 1 co-infected individuals.

**Material & Methods:** 30 individuals received Telaprevir/PegIFNα/RBV for 12 weeks. PegIFNα/RBV was then continued until 24 weeks in non-cirrhotics with rapid virological response (RVR) and until 48 weeks in the remaining patients.

**Results:** 12 of the 30 were hepatitis C genotype 1a infected, 1 was genotype 1b infected and 17 were genotype 1a/1b infected.
21 were treatment naïve. In the treatment-experienced individuals, 3 had been partial responders, 2 null-responders and 4 had relapsed.

28 were on antiretroviral therapy and 24 had an undetectable HIV viral load. The median CD4 count was 530 cells/μL (range 153-1267 cells/μL). 27 patients were on a Truvada backbone and 1 on a Tenofovir-only backbone. Third agents were as follows: 14 Raltegravir (1 with additional Etravirine), 6 Rilpivirine, 4 Darunavir/r, 3 Atazanavir/r, and 1 Efavirenz.

Pre-treatment liver fibroscans were performed on 24/30 patients: 9 4 values (cirrhosis).

At week 4, 25 individuals achieved RVR, 3 achieved Hep C PCR values <1000 iu/ml (2 log drop), 2 failed to achieve a 2 log drop and discontinued treatment. Both these individuals had genotypic resistance to Boceprevir and Telaprevir.

At week 12, 3 further individuals had ceased therapy due to relocation, intolerance (fatigue/nausea) and disengagement with services, respectively. All of the remaining 25 had extended RVR (eRVR).

At week 24, 14 of the remaining 25 maintained an undetectable viral load, of which 3 were cirrhotic and continuing therapy to 48 weeks. Data is awaited for 7 individuals. 3 individuals stopped therapy after week 12 due to refractory anaemia, non-adherence and disengagement with health services, respectively. One individual experienced a sustained virological breakthrough between week 12 and 24.

End of treatment: so far, 12 patients have achieved End of Treatment Response (ETR) (11 on 24-week treatment and 1 on 48-week treatment). Of the 24-week treatment group, Sustained Virological Response at 4 weeks (SVR4) was maintained in 9 individuals (1 relapsed and data is awaited for 1), SVR12 in 6 (data awaited for 3) and SVR24 in 2 (data awaited for 4). Of the 48-week treatment, 1 has completed treatment with ETR and 2 are receiving on-going treatment and achieving eRVR.

4 individuals required blood transfusions or EPO and 1 required GCS-F.

Conclusion: Telaprevir is an effective and well-tolerated treatment in individuals, who are unable or unwilling to wait for Interferon-sparing regimens.

No conflict of interest

Abstract: P_07

Non invasive assessment of liver fibrosis

Discordance between absolute CD4 count and percentage in relation to the degree of liver fibrosis in HIV patients coinfected with HCV

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Background: Clinical decisions such as the start of treatment or the indication of prophylactic measures in HIV infection are based on the CD4 lymphocyte count. Some studies have reported a downward tendency in absolute CD4 counts in patients with liver cirrhosis, possibly related to splenic sequestration, which could make it more useful to use percentage CD4 (%CD4) values in decision making. The present study examines whether the Fibroscan® (F) results are related to the existence of discordance between the absolute CD4 count and %CD4, and evaluates the possible existence of an F cutoff point indicating the use of %CD4 instead of the absolute count.

Material & Methods: A retrospective, cross-sectional, analytical observation study was made of HIV patients coinfected with HCV and subjected to Fibroscan® (F) exploration according to standard practice in our hospital during the year 2013. The exploration was made using a probe adjusted to patient body weight, with 10 valid measurements, and IQR 2/3 of the final exploratory result, and IQ > 60%. The patients were required to have a CD4 count in the three months before F. A sample size of 60 individuals was estimated to afford a sensitivity and specificity of 95% with a prevalence of 30%, a precision of 10% and a confidence level of 95%. The primary dependent variable was discordance between the absolute CD4 count and its percentage value, considering subjects with CD4% >28% and CD4 <500 cells or those with CD4%>20% and CD4 <350 cells. Information was also
collected referred to age, gender, transaminase levels, blood count, total lymphocyte counts, CD4 and HIV and HCV viremia. We analyzed the relationship of the discordance between CD4 and %CD4 with respect to the rest of the variables using the Student t-test in the case of quantitative parameters and the Fisher exact test in the rest of cases. A non-conditional multivariate logistic regression analysis was then performed, followed by calculation of the area under the ROC curve of F to assess its capacity to diagnose the discordance between CD4 and %CD4. Regarding the cutoff points, we chose the most sensitive and specific value among those that maximized the sum of sensitivity and specificity. A 95% confidence level was considered, with use of the SPSS version 18 statistical package.

Results: A total of 67 patients (mean age 45 years (SD 6); 31% females) were included in the study. Discordance was observed in 13 cases (19.4%). In the bivariate analysis, discordance was related to the degree of fibrosis and platelet and lymphocyte count, though statistical significance was only maintained for the degree of fibrosis in the multivariate analysis - the probability of discordance increasing 10% for every 1 Kp increase in F (OR 1.10; CI 1.03-1.16). The area under the ROC curve was 0.82 (CI 0.69-0.95), with sensitivity and specificity values for the identification of discordance of 90% and 65%, respectively, for 7 Kp, and of 60% and 98% for 32 Kp.

Conclusion: In HIV patients coinfected with HCV, the degree of fibrosis detected by F is related to discordance. Accordingly, above 7 Kp (with high sensitivity) and above 32 Kp (with high specificity), the clinical decisions should be based on %CD4 and not on the absolute counts.

No conflict of interest

Abstract: P_08

Non invasive assessment of liver fibrosis

Non-invasive fibrosis biomarkers in Hepatitis C virus infection: a correlation of APRI score, FIB 4 and Real Time Elastography

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Introduction: In recent years, the assessment of hepatic fibrosis by noninvasive methods has demonstrated a reasonable ability to identify significant fibrosis. FIB-4 and APRI are tests based on blood analysis results that have been used to estimate fibrosis in HCV-infected patients. Real-time tissue elastography (RTE) is a non-invasive method for the measurement of tissue elasticity using ultrasonography, allowing an estimate of liver fibrosis. The objective was to correlate the results of hepatic fibrosis evaluation by RTE with the results obtained by APRI and FIB-4 scores evaluation, in patients with HCV infection.

Methods: Retrospective revision of clinical files of HCV infected patients, currently followed in an Infectious Diseases outpatient clinic, submitted to a RTE for hepatic fibrosis evaluation. RTE was performed by a single investigator using an ultrasound machine. The corresponding APRI and FIB-4 scores were calculated. For APRI score, cut-offs of 1.0 and 0.7 were considered for cirrhosis and significant hepatic fibrosis, respectively (Hepatology 2011 Mar; 53(3):726-36). For FIB-4 score, values >3.25 and <1.45 were considered, respectively, for a F3-F4 and F0-F1 fibrosis grade (Hepatology 2007;46(1):32-36). The statistical analysis was done through IBM SPSS Statistics 20

Results: Eighty six patients were included, 54 male (63%) and 32 female (37%). HCV infection was diagnosed in a mean of 8 years (1-30). HCV genotypes were G1 (n=53; 63%)
Abstract: P_09

Non-invasive assessment of liver fibrosis

Non-invasive markers for liver fibrosis: comparison between Fibroscan® and serologic markers (APRI and Fib-4) in HCV/HIV co-infected patients

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Background: Hepatitis C infection is becoming of major concern in the HIV infected population, since now we can bring HIV under control and patients with HCV infection, as well as others with different causes of liver disease, are more frequently progressing for end-stage liver disease and liver failure, with significant implications regarding not only morbidity and mortality for the patients, but also producing high pressure in health care systems with the corresponding financial cost involved. Liver fibrosis assessment has its gold standard in the Liver Biopsy, but in the recent years, indirect methods, such as Transient Hepatic Elastography (Fibroscan®) have become validated for the follow-up of these patients. Nonetheless, this method may still be available in only a few limited centres. The serologic markers APRI (AST-to-platelet ratio index) and Fib4 can be calculated using simple formulas during patient’s visits to the clinic, and therefore could be useful in the management of these patients.

Materials & Methods: Liver fibrosis was assessed by Fibroscan®. The APRI and Fib-4 scores were calculated using Wai’s and Sterling’s formula, respectively. We considered as advanced fibrosis all stages further then F2. We applied Kendall rank correlation coefficient and the Spearman correlation test.

Results: We studied 132 HIV/HVC co-infected individuals, 82.6% were male, with a median age of 44 years [29 – 75]. The majority of them were Caucasian (97%). The most prevalent route of transmission was intravenous drug use (90.2%), followed by the sexual route in 5.3% of the individuals. The median time of...
exposition for the HCV infection was 16 years [1 – 41], 23.5% of the patients had a high HCV viral load (> 600 000 UI/ml) and the medium ALT was of 80 UI/L. The distribution of HCV genotypes was 61.4% for genotype 1, 23.5% for genotype 3, 11.4% for genotype 4 and 0.7% for genotype 2. The majority of the patients were under antiretroviral therapy (91.7%), but from these, 25.6% did not have HIV viral load suppressed. The median T CD4+ cell count was 457 cels/mm³ [27 – 1042]. The mean liver stiffness was 11.8 KPa (σ = 11.6). The mean value for Fib-4 was 2.8 (σ = 5.21) and for APRI was of 1.8 (σ = 7.2). The correlation between liver stiffness assessed by Fibroscan® and that calculated by Fib-4 was fair (Kendall Rank = 0.33, substantial correlation if Kendall Rank above 0.61). However, in our study, the comparison between Fibroscan® and APRI was not statistically significant (p = 0.176). The major differences were observed in the advanced stages of liver fibrosis in which more individuals were wrongly classified as having advanced fibrosis that was not confirmed by Fibroscan®.

**Conclusions:** After the analysis of the recovered data, we can conclude that serologic markers can be better used in monitoring the very early stages of liver fibrosis in co-infected patients. When sings of progression do occur, more accurate methods should be performed such as Fibroscan® or even a liver biopsy.

No conflict of interest

**Abstract: P_10**

**Non invasive assessment of liver fibrosis**

**Fibrosis stage evaluation in hcv monoinfected and hiv/hcv co-infected patients: real time hepatic elastography correlation with seromarkers fib4 & apri**

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**Introduction:** Hepatic biopsy and histopathologic findings continue to be the gold standard to evaluate fibrosis stage. The emergence of non-invasive methods such as elastography and seromarkers had changed the current clinical practice concerning fibrosis determination and hepatic disease progression monitoring.

**Objective:** to correlate the results obtained by real-time hepatic elastography (RT-HE) and concomitant seromarkers determination (APRI and FIB4) in a cohort of HCV chronic infected individuals.

**Materials & Methods:** HCV chronic infected patients, with or without HIV co-infection, who underwent RT-HE in the last 4 years (2010-2014) and concurrent routine laboratory evaluation. Demographic, epidemiological, clinical, laboratorial, immunologic, virologic and therapeutic response data were collected. METAVIR score was considered for fibrosis stage determination. Statistical analysis was performed with SPSS version 20. T-test, chi², Spearman, Kolmogorov-Smirnov tests and correlation analysis were performed.

**Results:** A total of 230 patients were included: male gender was predominant (74%); mean age was 47 years (25-81); mean time since HCV diagnosis was 11 years (0-33) and 78% acquired the infection by intravenous illicit drug use (IVDU). The main reasons to perform RT-HE were: fibrosis progression monitoring.
Non-invasive fibrosis biomarkers in HIV/HCV co-infection: a correlation of APRI score, FIB 4 and Real Time Elastography

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Introduction: Although liver biopsy still remains the reference standard for evaluation of hepatic fibrosis in chronic HCV infection, it is an invasive procedure with associated risks. The assessment of hepatic fibrosis by non-invasive methods has demonstrated a reasonable ability to identify significant fibrosis. Real-time tissue elastography (RTE) is a non-invasive method for the measurement of tissue elasticity, that has shown good correlation results with fibrosis grade evaluation by liver biopsy, in HIV/HCV coinfected patients. The purpose of this study was to correlate the results of hepatic fibrosis evaluation by RTE with the results obtained by APRI and FIB-4 scores, in patients with HIV/HCV coinfection.

Methods: Retrospective revision of clinical files of HIV/HCV coinfected patients, currently followed in an Infectious Diseases outpatient clinic, submitted to a RTE for hepatic fibrosis evaluation. RTE was performed by a single investigator; the corresponding APRI and FIB-4 scores were determined during the same trimester. For APRI score, cut-offs of 1.0 and 0.7 were considered for cirrhosis and significant hepatic fibrosis, respectively (Hepatology 2011 Mar; 53(3):726-36). For FIB-4 score, values >3.25 and <1.45 were considered, respectively, for a F3-F4 and F0-F1 fibrosis grade (Hepatology 2006 Jun; 43(6):1317-1325). The statistical analysis was done through IBM SPSS Statistics 20.
Results: One hundred and fifty eight patients were included, there was a male gender predominance (n=116, 73%). HCV infection was diagnosed in a mean of 8 years (1-30). HCV genotypes were G1a (n=69, 44%), G1b (n=20, 13%), G3 (n=29, 18%), G4 (n=20, 13%), 2 (n=3); 17 patients had G1 without specification of subtype. RTE evaluation considered 71 patients as having significant fibrosis of whom 18 had serious fibrosis or cirrhosis. The APRI-score >0.7 and FIB-4 >3.25 were related to a high-grade fibrosis and cirrhosis (p<0.05) by RTE evaluation. The AUROC of APRI and FIB-4 for cirrhosis was 0.84 and 0.81 (95% CI, 0.593-1 and 0.571-1), respectively. There was a poorer correlation of APRI and the expected grade of cirrhosis (Kappa coefficient of 0.286) and high grade fibrosis (Kappa coefficient of 0.068) by RTE. There were also a poor correlation factor between FIB-4 and significant fibrosis and cirrhosis (Kappa coefficient 0.089)

Conclusion: In our study, the APRI and FIB-4 scores have a poorer correlation with fibrosis grade evaluation by RTE in HIV/HCV co-infected patients. When evaluating liver fibrosis by noninvasive procedures, it is important to use more than one method and liver biopsy should be considered on an individual basis. Regarding hepatic fibrosis evaluation by RTE in HIV/HCV coinfected, more studies are needed to optimize its results value.

No conflict of interest

Abstract: P_12

Resistance --- Hepatitis C

HBV resistance mutations reviled at patients after liver transplantations in Belarus

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Background. In the last some years in the republic increase in quantity of cases of chronic hepatitis B is observed. So, if in 2010 457 cases, in 2012 already 753 new cases of chronic hepatitis B were registered.

Materials and Methods. 351 samples of blood serum/plasma from patients (202 male and 149 female) from different regions of Belarus were sequenced. The age of patients fluctuated from 6 months to 75 years. All samples were HBsAg and HBV DNA positive. Genotyping carried out on gene P region (reverse transcriptase), 750bp HBV DNA fragment was analyzed. For the analysis used programs: Sequencing Analysis v.5.1.1. SeqScape v.2.6, BioEdit, Geno2pheno, HBV-Grade 12/2008 and Stanford University HBV Database. The phylogenetic analysis carried out with MEGA 4.1 program use.

Results. In 290 (82.6±3.2%) samples HBV D genotype was defined. The genotype A was revealed in 55 (15.7 ± 3.9%), C genotype in 5 (1.4 ±3.1%) samples. The carried-out phylogenetic analysis of the sequences received DNA fragments allowed to establish that all isolates of a genotype A belonged to the A2 subtype, and a genotype C – to the HBV C2 subtype. Thus all samples with a HBV A genotype were received from inhabitants of Belarus, and the genotype C was defined at citizens of Vietnam and China which has arrived to work in our country. Among samples with a HBV D genotype all known 4 subtypes
were revealed: D1, D2, D3 and D4. 129 patients (44.5%) of all cases HBV D genotype, were carriers D2 subtype. In 88 (30.3%) cases HBV D3 subtype was defined. The D1 and D4 subtypes were defined in 69 (23.8%) and 4 (1.4%) samples, respectively. For the first time in the Republic at the patient from Vietnam HBV B4 subtype was defined. At 5 patients with chronic hepatitis B the resistance mutations were revealed. Among these patients there were 3 women (age of 18, 40 and 61 years) at two from which D1 and at one D2 the HBV subtype was revealed, and 2 men (22 and 56 years), both were HBV D2 subtype carriers. Three patients were after the liver transplantation, one kidney and one patient without organ transplantation. At four patients 204V mutation at one - 204I was revealed. Two patients had the major mutations 180M and 204V, one 173LV, 180V, 204V. It is known that the mutation 204V defines virus resistance to Lamivudin, Entecavir and Telbuvidine. Two patients in addition had HBsAg mutations, one – P127T and A128V, the second – P127T.

Conclusion. In 2013 in the country 97 cases acute (2012 – 116) and 923 chronic (2012 - 753) hepatitis B, or 9.71 and 7.95 on 100 thousand of population, respectively were registered. In this regard definition of genotypes/subtypes of a virus and resistance of a virus to anti-virus preparations is very actual for purpose of adequate schemes of therapy and their timely replacement.

No conflict of interest

Abstract: P_13

Resistance --- Hepatitis C

Resistant Associated Variants are Detectable at Baseline in Direct Acting Antiviral Naïve Hepatitis C NS3 and NS5A but not NS5B in Acute and Chronic HIV Co-infected Patients

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Introduction: The current standard of care for acute HCV is pegylated-interferon plus ribavirin (pIFN/RBV). If chronicity develops, newer direct antiviral drugs (DAAs) targeting HCV NS3, NS5A and NS5B may be combined with pIFN/RBV. HCV resistance associated variants (RAVs), associated with poorer outcomes may exist at baseline. We investigated the prevalence of RAVs by population sequencing in 79 subjects from three cohorts of HIV/HCV co-infected patients: (1) acute HCV (n=25), (2) chronic treatment naïve (n=20) (3) chronic treatment failure (pIFN/RBV) (n=34) and compared their prevalence in 85 HCV mono-infected patients.

Methods: HCV sequences were amplified from plasma viral RNA, using one-step RT-PCR, followed by a nested PCR. PCR amplicons covering amino acids 1-181 of HCV NS3 (gt1 only), 1-213 of domain I NS5A (gt1, 2, 3 and 4) and 219-347 of NS5B (pan genotypic)were sequenced and aligned against reference sequences.

Results: Baseline RAVs were observed in all cohorts in NS3 and NS5A, with baseline NS5B S282T not detected. NS3 Q80K polymorphism was present in HCV gt1a, and the frequency increased from acute to chronicity, ie: 5.3% vs 11.1% in the co-infected. NS5A variant at codon 30 did not differ markedly in HCV gt1a in acute vs chronic, whilst the Y93H variant present at 33.3% in gt1b chronic naives was absent in failures. Conversely, NS5A L31M variant was observed in a single gt1a failure.
Both NS3 I132V and NS5A L30R minor variants were common in HCV gt 1b and gt4 respectively with major RAVs absent for HCV gt3 in the co-infected. We observed a significant increase in NS3 variants for HCV gt1a mono-infected patients compared with gt1a co-infected p<0.0001 (Fisher’s Exact test). The NS3 R155K, and NS5A L31M and A30K major variants were detected in individual mono-infected patients infected with HCV gt1a, 2 or 3 respectively.

Conclusions: RAVs conferring low to moderate resistance to HCV NS3 and NS5A DAAs were frequently encountered in acute and chronics, and more prevalent in NS3 for the HCV gt1a mono-infected. Baseline resistance testing may be warranted in an era of IFN-free DAA therapy.

No conflict of interest

Abstract: P_14

Resistance --- Hepatitis C

Temporal dynamic of NS3 protease domain in HIV/ Hepatitis C genotype 1 coinfected individuals naïve to anti-HCV therapy or under triple therapy including boceprevir

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Background Hepatitis C protease inhibitors (HCV-PI) drove selection of unique mutations and cross-resistant mutations in the NS3 protease catalytic domain. Recently, the phylogenetic analysis of the complete genome has shown that HCV subtype 1a isolates can be separated into two distinct clades, designated 1 and 2.

Aim To evaluate temporal dynamic of NS3 protease domain in sequencial plasma samples of HIV/HCV genotype (G)1 coinfected individuals naïve to anti-HCV therapy or under triple therapy including boceprevir.

Methods 14 HIV/HCV coinfected individuals: 10 naïve to anti-HCV treatment and 4 on triple therapy, were included. The median interval between specimens examination in naïve patients was 36 months (range: 6-84) for a total of 24 points of observation. Sequential plasma samples in patients under triple therapy were analysed at baseline, week (W)4, W8 and W10 (based on HCV RNA detectability). The specimens from the unique non-responder patient were analysed until W24 post-treatment. Inflicting subtype and resistance associated mutations (RAM) against HCV-PI were investigated by population analysis of NS3 protease gene and by use of Geno2Pheno algorithm.

Results Sequence evaluation at baseline showed that 3 patients naïve to anti-HCV treatment were infected by G1b, 3 were infected by G1a clade1 and 4 by G1a clade2. Interestingly, specimens follow-up analysis showed that 2/3 G1b patients had a different subtype (G1a clade1) from that detected at baseline. In 5 G1a patients was mantained the same genotype and the same clade detected at baseline; in one patient a switch from clade1 to clade2 and in the other one patient a switch from clade 2 to clade1 was revealed. 3/10 naïve patients, had RAM at baseline: one G1a patient infected by clade1 harboured Q80K, one G1a clade2 had R155K, one G1b patient showed V36L+A156T+D168V mutant. Reversion to wild-type was observed in follow-up samples in these patients. Interestingly, the disappearance of Q80K in one patient was associated with switch from clade1 to clade2. In 2 patients infected by a wild-type G1a at baseline, RAM Q80K and R155K, were detected during follow-up. Of 4 patients under PI based anti-HCV treatment, 2 individuals infected by G1a clade1 and 1 patient infected by HCV G1b mantained the same virological pattern during treatment, while in one other patient infected by G1b, a different genotype was revealed as dominant (G1a clade2) at W4. Two responder patients, infected by G1b at baseline, showed a wild-type during treatment, 1 responder patient infected by G1a clade1 developed T54S variant at W10 of treatment.
The unique non-responder patient showed Q80K at baseline, that was maintained under treatment and during post-treatment period, showing also the presence of V36M+R155K mutant from W10 treatment to W4 post-treatment.

**Conclusions** The complex dynamic of HCV infection (assessed by switch to different clades in G1a infected patients, the alternance of HCV subtype 1a and 1b, and the emergence of PI resistant mutant in naive as in under HCV-PI patients) suggests the presence of mixed infection in some patients, with the dominance of a specific variant probably related to enviromental condition and/or drug induced pressure.

No conflict of interest

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**Abstract: P_15**

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

**Mutations Associated with Occult Hepatitis B in HIV-Positive South Africans**

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**Introduction:** Occult hepatitis B is defined by the presence of hepatitis B virus (HBV) DNA in the absence of hepatitis B surface antigen (HBsAg). Occult HBV is associated with the development of hepatocellular carcinoma, reactivation during immune suppression, and transmission during blood transfusion and liver transplant. Viral mutations are likely a significant contributor to the occult HBV phenotype. We identified occult-associated mutations in a population of HIV-positive South Africans and examined the effect of selected mutations on HBsAg production *in vitro*.

**Materials & Methods:** Serum was collected from 394 HIV-positive South Africans and tested for HBV DNA and HBsAg. For patients with detectable HBV DNA, the surface and polymerase open reading frames (ORFs) were sequenced and occult-associated mutations were identified. Selected mutations were inserted into replication-competent wild-type HBV and transfected into hepatocytes. HBsAg was measured by ELISA.

**Results:** Ninety patients (22.8%) had detectable HBV DNA (37 HBsAg positive and 53 HBsAg negative). Sequencing the surface and polymerase ORFs identified 235 occult-associated mutations. Five mutations were analyzed for their effect on HBsAg production *in vitro.* Two mutations resulted in decreased supernatant HBsAg in both HBV constructs tested, while the remainder had a construct-specific reduction in HBsAg.

**Conclusions:** Occult-associated mutations were common and found in all regions of the overlapping surface and polymerase ORFs. All mutations tested led to decreased HBsAg expression in at least one wild-type HBV construct, suggesting these mutations may play a role in the occult HBV phenotype. Further study is underway to determine the mechanism through which these mutations decrease HBsAg production.


No conflict of interest
Abstract: P_16

Treatment issues --- HBV-HIV coinfection

STaR: Rilpivirine/emtricitabine/tenofovir DF is non-inferior to efavirenz/emtricitabine/tenofovir DF in ART-naive adults co-infected with HBC at Week 96


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Introduction: Viral hepatitis B progresses faster among persons with HIV infection, and persons who are infected with both viruses experience greater liver-related morbidity than those not infected with HIV. Co-infection with viral hepatitis may also complicate the management of HIV infection.

Methods: STaR is a 1:1 randomized, open-label, 96-week study to evaluate the safety and efficacy of the STR RPV/FTC/TDF to the STR EFV/FTC/TDF in treatment-naive, HIV-1 infected subjects. The primary endpoint was the proportion of subjects with HIV-1 RNA <50 copies/mL (virologic suppression) at W48 using Snapshot algorithm (12% non-inferiority margin). Secondary endpoints included W96 results. Ad hoc analyses of efficacy and safety in subjects co-infected with HBV were also done, though the study was not powered to look at statistical differences within these subpopulations.

Results: A total of 786 subjects were randomized and received at least one dose of study drug (394 RPV/FTC/TDF; 392 EFV/FTC/TDF). Of these, 23 were co-infected with HBV (13 RPV/FTC/TDF; 10 EFV/FTC/TDF). There were two subjects in the RPV/FTC/TDF arm who were co-infected with both HBV and HCV and one subject in the EFV/FTC/TDF co-infected with HBV at baseline and acquired HCV during the study. In the overall population, RPV/FTC/TDF was non-inferior to EFV/FTC/TDF (85.8% vs 81.6%) at Week 48 for HIV RNA <50 copies/mL (difference 4.1%, 95% CI [-1.1%, 9.2%]). Non-inferiority was maintained at Week 96 (77.9% vs 72.4%; difference 5.5%, 95% CI [-0.6%, 11.5%]). For subjects co-infected with HBV, the rate of virologic suppression was 84.6% (11/13) with RPV/FTC/TDF vs 80.0% (8/10) with EFV/FTC/TDF at Week 48 and 69.2% (9/13) vs 40.0% (4/10) at Week 96. In the RPV/FTC/TDF arm at Week 96, one subject experienced virologic failure, one discontinued due to AE, and two discontinued due to other reasons with their last HIV-1 RNA <50 copies/mL. In the EFV/FTC/TDF arm, one subject experienced virologic failure, three discontinued due to AE, and two discontinued due to other reasons with their last HIV-1 RNA <50 copies/mL. No discontinuation due to AE in either arm was of hepatic etiology. Treatment emergent adverse events (TEAEs) included one report of abnormal liver function test in each arm, one report of immune reconstitution inflammatory syndrome HBV flare in the RPV/FTC/TDF arm, and one report of increased AST with EFV/FTC/TDF. The proportion experiencing Grade 3-4 ALT elevation through Week 96 in the overall population was 4.3% RPV/FTC/TDF vs 4.1% EFV/FTC/TDF and in the HBV co-infected population was 23% (3/13) vs 40% (4/10). For Grade 3-4 AST elevation, rates were 4.3% RPV/FTC/TDF vs 4.1% EFV/FTC/TDF in the overall population and 15% (2/13) vs 30% (3/10) in the HBV co-infected population.

Conclusions: In the overall study population, RPV/FTC/TDF was non-inferior to EFV/FTC/TDF at both Weeks 48 and 96. In subjects co-infected with HBV, both arms had lower rates of virologic suppression than in the mono-infected population at Week 96. There were few TEAEs related to liver function and no discontinuations due to hepatic etiology and low rates of Grade 3-4 elevations in AST and ALT.

No conflict of interest
Abstract: P_17

Treatment issues --- HBV-HIV coinfection

Prevalence of Hepatitis B Virus, Hepatitis C Virus and Human Immunodeficiency Virus infections among blood donors in Western Kenya

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Introduction: Hepatitis B virus (HBV), Hepatitis C virus (HCV) and Human Immunodeficiency Virus (HIV) infections are transfusion transmissible infections that cause fatal and chronic life threatening infections. The prevalence of these infections is not well reported among the blood donor population. This study aimed to determine the sero-prevalence of HIV, HCV, HBV and the trend over a three year period among donors in Western Kenya's Regional blood transfusion center located in Eldoret.

Materials and Methods: A retrospective cross sectional study was conducted on consecutive blood donor records from the Eldoret Regional Blood Transfusion Centre (RBTC) over a three-year period: 2010-2012. After collection of donated blood, samples are taken for screening of HIV, HBV and HCV infections using ELISA technique for anti HIV-1 antibody, HBsAg, and anti HCV-antibody

Results: A total of 70,971 assumed healthy blood donors aged between 16-60 years (mean: age 24 years) in western Kenya donated blood between 2010 and 2012. The male to female ratio was 3:1. 1,068 donors had HBV, HCV or HIV infection. 736 (69%) of those infected were students. The prevalence of HBV, HIV and HCV was 1.1%, 0.2% and 0.3% for the three years. There was no demonstrable rise in the prevalence of all three infections over the three year period. About 3.3% (36) of the infected donors had co-infection with the most (56%) diagnosed co-infection being HBV/HIV.

Conclusion: Blood donors are a highly selected population with low risk of HBV, HIV and HCV

No conflict of interest

Abstract: P_18

Treatment issues --- HBV-HIV coinfection

Outcomes of HBV therapy in HIV/HBV co-infected patients in British Columbia, Canada


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Background: We evaluated HBV treatment response to sequential lamivudine (3TC) monotherapy then 3TC/emtricitabine with tenofovir (TDF) combination when compared to immediate combination therapy in HIV+ patients.

Methods: Patients positive for either HBsAg or HBV DNA in the BC HIV Drug Treatment Program were included in this study. HBV DNA viral loads (HBVL) were followed after initiation of ART 01/1997 and 06/2012. Time to virologic suppression, was assessed using Cox models adjusted for age, gender, IDU and time on combination therapy. For individuals with baseline APRI ≥1.5, time to APRI <1.5 was assessed.

Results: Overall 509 patients were included, n=452 (89%) were male with median age at first ART 39 years (interquartile range [IQR] 33 - 45 years), 43% were MSM and 39% IDU while 44% were HCV+. Baseline median CD4 count was 240 cells/ul (IQR 100-330 cells/ul). Of 509 patients, 231 (45%) had sequential
therapy and 153 (30%) began combination therapy. Median time to HBV viral suppression was 63 (IQR 15 – 121 months), and 15 (5 – 26 months) for sequential and immediate combination groups respectively (p< 0.001). In adjusted Cox analysis receipt of immediate combination therapy was associated with virologic suppression (adjusted Hazard Ratio 5.91; 95%CI 2.81 – 12.44). Median time to APRI reversion was 4 (IQR 2-11 months) and 3 (IQR 2-7 months) for sequential vs. immediate combination groups respectively (log rank p = 0.313).

Conclusions: HBV/HIV co-infected patients had faster time to HBV virological suppression when using immediate combination therapy with 3TC/FTC and TDF compared to those treated with initial monotherapy but had similar time of APRI reversion.

Conflict of interest: Honararia for attending advisory boards for Gilead - paid to institution

Abstract: P_19

Treatment issues --- HCV-HIV coinfection

HCV genotypes at HIV infected patients

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Background. Now in Belarus steadily high increase of quantity of HIV infection and chronic hepatitis C cases is observed. For 2013 more than 1500 new cases of HIV infection and about 3000 cases of chronic hepatitis C are officially registered in the country.

Materials and methods. ELISA, 'in-house' HIV & HCV RT-PCR. Sequencing on gag, env, pol HIV-1 and core/E1 and NS5 HCV genes

regions have been carried out. The analysis of the received fragments carried out with use of software products 'Sequencing Analysis v.5.1.1', 'BioEdit', 'SeqScape v.2.6'. The phylogenetic analysis carried out by means of the Mega 4.1 (NJ & Kimura methods).

Results. From July 2012 till January, 2014 438 blood serums/plasma samples on the hepatitis C virus (HCV) genotype definition received from patients from different Republic of Belarus regions have been tested. Of 438 specimens 106 were from HIV infected IDUs. Of 106 samples 71 was from males, middle age of 36.6±0.7 years and 35 from females, middle age of 37.2±2.1 years. 95 (89.6%) patients had HIV+HCV and 11 (10.4%) HIV+HCV+HBV co-infections. 29 specimens (18 males middle age of 36.6±3.6 years and 11 females middle age of 34.3±3.2 years) there were from Minsk and the Minsk region, 2 (1 male aged 37 years and 1 female at the age of 38 years) from Vitebsk and Vitebsk area, 10 (6 females middle age of 37,1±2.1 years and 4 females middle age of 34.5±3.5 years) from Mogilyov and the Mogilyov area, 7 (3 males middle age of 39,0±1.3 years and 4 females middle age of 40,3±3.6 years) from Gomel and the Gomel region, 10 males (middle age of 38,3±4.3 years) from Brest and the Brest region, 48 (from 33 males middle age of 37,7±4.8 years and 15 females middle age of 38,0±7.7 years) from Grodno and the Grodno region. The conducted researches allowed to establish that at the HIV-infected patients with HCV and/or HBV co-infection, HCV 3a and 1b 38 (35,5±4,0%) and 37 (34,6±4,6%) genotypes, respectively, practically with an identical frequency have been defined. 1a was found in 25 specimens (23,4±4,0%), 2a genotype in 3 samples (2.8%±2.4%) was defined and 2k (1,9±1,3%) and 2c (0,9±0,9%) genotypes in 2 and 1 specimens, respectively. The conducted researches on HCV genotyping showed that more than 80% of all cases are caused 1b (53,8%) and 3a (28,8%) virus genotypes in Belarus.

Conclusion. Thus, received results show that both in IDUs group, and in group of patients with HCV-monoinfection 1b HCV genotype dominates on the territory of Belarus. On the other hand our data confirm also the results, received early other researchers about high prevalence of HCV 3a genotype in IDUs group.

No conflict of interest
Abstract: P_20

Treatment issues --- HCV-HIV coinfection

Extended rapid virologic response in inmates at Spanish prisons treated with Telaprevir, Peg-Interferon Alfa and Ribavirin for chronic Hepatitis C

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Introduction: The extended rapid virologic response (eRVR) in patients treated with Telaprevir (TVR), Peg-Interferon (PegIFN) and Ribavirin (RBV) ranges approximately from 58-65% in the general population, but data on convicts is limited. The aim of this study is to determine the eRVR in prisoners at Spain with and without HIV infection treated with TVR, PegIFN and RBV.

Material & Methods: Multicenter, descriptive study conducted in seven prisons in Spain (five in Catalonia, one in the Basque Country and one in the Levant region). The study includes prisoners who began Hepatitis C treatment with TVR, PegIFN and RBV during 2013. Viral load was determined in International Units (IU) at week 4 and 12. Complete Rapid Virologic Response (cRVR) was defined as a negative viral load at week 4, and Partial Rapid Virologic Response (pRVR) as detectable viral load, but less than 1000 IU. Extended Rapid Virologic response (eRVR) refers to undetectable viral load at both week 4 and week 12. An intention-to-treat analysis was performed. Age, history of intravenous drug use (IDU), opioid substitution treatment (OST), HIV co-infection, CD4+ T lymphocytes level, fibrosis stage, IL28B polymorphism, baseline HCV-RNA and HCV genotype were the variables studied. High HCV-RNA viral load was defined as > 400,000 IU / mL. The degree of fibrosis was determined by transient elastography. Mean and standard deviation were used for continuous variables and percentage and 95% confidence interval for discrete variables. Differences between groups were evaluated using t-test for independent samples with continuous variables and c² tests for discrete variables.

Results: A total of 24 patients were treated, all male, with a mean age of 43.7 ± 5.8 years. 87.5% showed previous history of IDU and 25% were under OST treatment (5 with methadone and 1 with buprenorphine / naloxone). 45.8% had HIV-coinfection. High baseline HCV-RNA was found in 87.5%, ILB28 polymorphism was CT or TT in 75%, and stage 4 fibrosis (cirrhosis) was present in 45.8%. 75% were treatment-naïve (100% in the HIV-coinfection group vs. 53.8% in the HIV-negative (p=0.01). There were two treatment virologic failures, one follow up lost due to prison release, one triple treatment stop due to adverse events and a case of TVR withdrawal due to skin rash, which remained under PegIFN and RBV treatment. cRVR was obtained in the 83.3% and eRVR in the 62.5%. In the HIV-coinfected, eRVR was 45.5% vs 78.6% in the monoinfected (p = 0.11). The only variable associated with eRVR was age (100% eRVR in the under 40 group vs. 52.6% in those 40 years old or older; p=0.03).

Conclusions: In prisoners treated with TVR, PegIFN and RBV for HCV chronic hepatitis, extended rapid virologic response (eRVR) was similar to the one obtained in non-prisoners in the TVR pivotal studies. These data suggest that treatment of HCV chronic hepatitis with TVR, PegIFN and RBV in prisons is feasible and effective.

No conflict of interest
Abstract: P_21

Treatment issues --- HCV-HIV coinfection

Suboptimal Virological Response to Pegylated Interferon-Ribavirin-Boceprevir: Treatment Intensification by Adding Sofosbuvir as Salvage Therapy

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Background: The addition of the protease inhibitor, Boceprevir (BOC), to Pegylated Interferon alfa (PegIFN) and Ribavirin (RBV) significantly increases the probability of achieving SVR. However, treatment failure is likely if HCV PCR is detectable beyond 8 weeks of triple therapy.

Aim: We describe two patients undergoing therapy with PegIFN -RBV-BOC who had detectable HCV PCR beyond 8 weeks of treatment where Sofosbuvir (SOF) was then added for 12 weeks as salvage therapy.

Methods: Patients were initially treated with PegIFN-RBV lead-in. BOC was added after week 4. HCV PCR was measured by Cobas AmpliPrep TaqMan, LLQ 15 IU/mL. SOF added when HCV PCR detectable despite ongoing therapy with PegIFN-RBV-BOC. SVR4 data will be presented.

Results: Case 1: 62 year old man with Hepatitis C (HCV) and HIV co-infection. HIV controlled with Emtricitabine-Tenofovir-Rilpivirine: CD4 655 (59%), HIV viral load <50 copies/mL. HCV was genotype 1, previously treated with PegIFN-RBV Jun 2007 x 48 weeks: nadir HCV viral load 2.61E2 IU/mL. Cirrhosis present (Fibroscan 21.3 kPa, Fibrotest 0.82). Retreated May 2013 with the following response: Baseline HCV 3.80E5 IU/mL, week 4 (double therapy): 2.02E5 IU/mL, week 8: 8.13E1 IU/mL, week 12: <15 IU/mL (detected), week 16: undetectable, week 32: <15 IU/mL (detected). SOF added at week 34. HCV PCR undetectable from week 38 onwards.

Case 2: 59 year old man with HCV mono-infection. Cirrhosis present (Fibrotest 0.87). Treated Oct 2013 with the following response: Baseline HCV 2.93E7 IU/mL, week 4 not done, week 8: 4.39E1 IU/mL, week 12: <15 IU/mL (detected). SOF added at week 14. HCV PCR undetectable from week 18 onwards.

Conclusion: To our knowledge, these are the first cases where SOF was added as intensification therapy when on-treatment response to PegIFN-RBV-BOC was suboptimal. Addition of SOF did not result in significant new side effects.

No conflict of interest

Abstract: P_22

Treatment issues --- HCV-HIV coinfection

Efficacy and tolerability of Telaprevir-based triple therapy in HIV-HCV-coinfected patients

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Introduction: Clinical trials on triple therapy against HCV infection in HIV-infected patients including telaprevir (TVR) plus pegylated interferon and ribavirin (PR) have reported considerably higher response rates than with PR alone. However, there is little information about the response to triple therapy used in clinical practice in these patients. This study was aimed to evaluate the efficacy and safety of triple therapy including TVR in HIV/HCV-coinfected patients in real-life conditions.

Material and Methods: HIV/HCV genotype 1-coinfected patients seen at 4 Hospitals in
Madrid (Spain) who received therapy including TVR plus PR for at least 2 weeks were included in this study. The response was evaluated at treatment week 4 and 12, and sustained viral response (SVR) was evaluated 12 and 24 weeks after the end of the treatment.

**Results:** 58 patients have been included in this study; 79% were male, median age 48 y.o. (range 21-63); 38% were IL28B rs12979860 genotype CT or TT, 58.6% of patients presented cirrhosis and 24.1% presented fibrosis F3. Infection with HCV genotype 1a was observed in 53.4% and the median baseline HCV RNA load was 3.282.263 IU/mL (77.5% had viral load >800,000 IU/mL). The most commonly used ARV drugs were tenofovir/emtricitabine [36 (62%) patients], etravirine [21 (36%) patients], abacavir/lamivudine [18 (31%) patients], boosted protease inhibitors [16 (27.5%) patients] and raltegravir [12 (20.6%) patients]. Of the 42 (72.4%) patients who had received previous HCV treatment, 13.7% had been null responders, 25.8% partial responders and 31% had relapsed. In an intention-to-treat approach, proportions of patients with undetectable HCV RNA, according to the time-point of follow-up were 67.8% (38/56) at TW4, and 83.3% (40/48) at TW12, 80% (36/45) at TW24, 79.4% at TW36 (31/39) and 72% (26/36) at TW48. 15 (25.8%) patients discontinued HCV therapy [8 (13.8%) because they fulfilled stopping rules, 5 (8.6%) individuals due to adverse events and 2 (3.4%) were lost to follow-up. Rash associated with TVR (grade 1) was observed in 2 cases (3.4%) and all the patients showed anaemia at some point of treatment. RBV dose was decreased in 17 patients (29.3%) mainly in the first 12 weeks of treatment, and the same proportions needed erythropoietin, while G-CSF was administered in 6 patients. Also, blood transfusions were required in 5 patients. In an analysis by intention to treat in the 31 patients who had a 60 week follow-up after starting therapy, SVR 12 weeks after treatment discontinuation was observed in 21 (67.7%) patients. And in the analysis by intention to treat in 28 patients who had had a 72 week follow-up after starting therapy, SVR 24 weeks after treatment discontinuation was observed in 17 (60.7%) patients.

**Conclusions:** Response rates to triple therapy with TVR plus PR in HIV/HCV-coinfected patients under real-life conditions, and therefore, including a high proportion of difficult to treat patients (39.5 % of poor responders, pre-treated and 58.6% of subjects with cirrhosis), are similar to that found in patients in clinical trials. The safety profile of TVR-based therapy is also comparable to that shown in clinical trials, with only a rate of discontinuation of 8.6% of individuals related to toxicity.

No conflict of interest

**Abstract: P_23**

*Treatment issues --- HCV-HIV coinfection*

**Hepatic safety profile of elvitegravir/ cobicistat/ emtricitabine/ tenofovir DF (Stribild) in HIV/HCV co-infected subjects in the STRATEGY switch trials**


**Introduction:** Virologically suppressed HIV-infected subjects who switched to single-tablet regimen elvitegravir/ cobicistat/ emtricitabine/ tenofovir DF (Stribild, STB) from a ritonavir-boosted protease inhibitor (PI+RTV) or non-nucleoside reverse transcriptase inhibitor (NNRTI) combined with emtricitabine/tenofovir DF (TVD) maintained high rates of virologic suppression (HIV-1 RNA < 50 copies/mL) at week 48 in the STRATEGY-PI trial (STB 94% vs PI+RTV 87%) and STRATEGY-NNRTI trial (STB 93% vs NNRTI 88%). STB may also be a safe and effective switch option for Hepatitis C co-infected subjects.
**Materials & Methods:** At study entry, subjects had hepatic transaminases (AST and ALT) ≤5 x upper limit of normal and were not on HCV treatment. Chronic HCV infections, confirmed by positive screening serology and an ongoing history of HCV infection, were included in this co-infection analysis. Liver safety endpoints were grade 3 or 4 transaminase elevations and hepatic adverse events. Cases of acute HCV infection identified as adverse events were also reviewed. HIV viral suppression (HIV-1 RNA <50 copies/mL) at week 48 in co-infected subjects were also assessed.

**Results:** A total of 867 subjects were randomized and treated (584 switched to STB; 140 continued PI; 143 continued NNRTI). Baseline rates of chronic HCV co-infection were STB 3.9% (23/584), PI 6.4% (9/140), and NNRTI 0.7% (1/143). No subject had a treatment-emergent grade 3 or 4 ALT elevation. One subject in the PI group had a grade 3 AST elevation. The only hepatic adverse event reported was an increased in transaminase (grade 2 ALT elevation) that occurred in one subject on STB, which did not lead to study drug discontinuation. At week 48, all subjects (23/23) in the STB with chronic HCV co-infection maintained HIV-1 RNA <50 copies/mL. There were five cases of acute HCV infection in the STB group versus none in comparator groups. All five subjects continued STB therapy without subsequent hepatic adverse events and maintained HIV-1 RNA <50 copies/mL at week 48. One subject with acute HCV infection received HCV therapy with pegylated interferon and ribavirin after week 48.

**Conclusions:** STB was well-tolerated in this small group of HIV/HCV co-infected subjects who switched from a PI+RTV or NNRTI-containing regimen.

**Abstract: P_24**

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

**Influence of nevirapine therapy on HCV viral load among HIV/HCV-coinfected patients: Results from the HELICON study**


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**Background:** A retrospective study including a small population of subjects under nevirapine (NVP) has reported that individuals who receive NVP-based antiretroviral therapy (ART) have lower HCV-RNA levels than those who are taking efavirenz (EFV)-or protease inhibitor (PI)-based ART. This finding, if true, is very relevant, since a lower HCV viral load have a positive impact on the response to HCV-therapy among coinfected individuals. However, prospective studies with a different design are needed to clarify this issue. The aim of this study was to compare changes in plasma HCV viral load in HIV/HCV—coinfected patients starting NVP-containing regimens with those maintaining EFV or PI-based ART.

**Materials & Methods:** HIV/HCV-coinfected patients followed at six hospitals in Spain who started a three-drug antiretroviral regimen including two nucleos(t)ide retrotranscriptase inhibitors (NRTI) along with NVP due to adverse events related to EFV or PI-based ART or maintained a three-drug antiretroviral regimen including two NRTIs along with EFV or PI were included in this prospective observational post-authorization study. Cases
(NVP group) and controls (non-NVP group) were matched according to HCV genotype, duration of ART before beginning study, hospital and liver stiffness. The main outcome variable of the study was the difference in mean HCV-RNA levels between baseline and at 24 and 48 weeks after beginning treatment between both groups. Comparison of continuous measures between both groups was performed with the Wilcoxon signed-rank test.

**Results:** A total of 16 individuals in the NVP group and 16 patients in the non-NVP group (10 under PI and 6 under EFV) were included in this study. Three cases and 3 controls had only HCV-RNA determination at beginning therapy and at week 24 because antiretroviral regimen was stopped or switched before week 48 of treatment. Among those individuals receiving NVP, 12 and 4 patients started this antiretroviral drug due to adverse events associated with EFV and PI, respectively. At baseline, the mean HCV-RNA level in the NVP group was 6.31±0.59 log10 IU/mL and 5.96±1.27 log10 IU/mL in the non-NVP group (p=0.53). The mean HCV-RNA determination at week 24 was 6.36±0.49 log10 IU/mL and 6.0±1.12 log10 IU/mL in the arms with NVP and non-NVP (p=0.42), respectively. At week 48, the mean HCV-RNA level in the NVP group was 6.37±0.46 log10 IU/mL and 5.97±0.91 log10 IU/mL in the non-NVP group (p=0.31). There were no differences in HCV-RNA reduction by the treatment group between weeks 0 and 24 (NVP: -0.04±0.39 versus non-NVP: -0.07±0.41 log10 IU/mL, p=0.73) and between weeks 0 and 48 (NVP: 0.08±0.38 versus non-NVP: -0.17±0.76 log10 IU/mL, p=0.46) in both groups.

**Conclusions:** According to this pilot study, changes in plasma HCV viral load in HIV/HCV–coinfected patients starting NVP-containing regimens are not different than in those individuals maintaining EFV or PI-based ART.

Conflict of interest : This study was supported by a grant from Boehringer Ingelheim.

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**Abstract: P_25**

*Treatment issues --- HCV-HIV coinfection*

**Behaviour of HCV/HIV coinfected patients: spontaneous clearance and IL28b genotypes**

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**Introduction:** It is known that spontaneous clearance of Hepatitis C virus (HCV) is related to female sex (hazard ratio 2:1) and protective genetic variations of IL28b (hazard ratio is 2.25 in rs12979860 for C/C genotype against C/T and T/T genotypes). Our aim is to prove whether our co-infected patients behave as previous research does.

**Material & Methods:** Retrospective study of 170 HIV/HCV co-infected patients attended as outpatients in the Infectious Diseases Section of our hospital. Host genetic variation of IL28b has been performed to these patients.

**Results:** Persistent infection is found in 147 patients (86.4%). Within them: 114 (77.55%) are male; their mean age is 49.37 years (median 49, standard deviation [SD] 5.04). Alcohol abuse is seen in 40 (27.21%). 121 (82.33%) are former intravenous drug users; 11 (7.5%) are men who have sex with men (MSM); 13 (8.85%) had heterosexual sex behavior. HCV diagnosis was performed between 1992 and 2013. Serology status for HBV showed spontaneous clearance in 115 (78.23%), persistent infection in 5 (3.4%) and no contact with HBV in 27 (18.36%). Nadir average CD4 cells count is 210 (median 188, SD 167). HAART is been carried out by 142 patients (96.6%). HCV genotype distribution was as follows: HCV genotype 1a in 39 (26.53%); 1b in 21 (14.29%); 1 non-serialotypable in 22 (14.96%); 2 in 2 (1.36%); 3 in 31 (21.10%) and 4 in 25 (17%). Genetic variation of IL28b was performed for rs12979860 and rs8099917 loci: for rs12979860, C/C genotype was found in 56 (28.1%), C/T in 70 (47.62%) and T/T in 21
HCV natural clearance was noted in 23 patients (13.6%). 15 of them (65.21%) were male; mean age was 44.56 years (median 45, SD 11.3). Alcohol abuse was seen in 6 (26.09%). Mode of transmission: 14 (60.87%) were former intravenous drug users; 4 (17.4%) were MSM; 5 (21.74%) had heterosexual transmission. HBV serologic status showed spontaneous clearance in 17 (73.91%), persistent infection in 1 and no contact with HBV in 4 (17.41%). Nadir CD4 cells average was 189 (median 175, SD 179). HAART is been carried out by 18 patients (78.26%) at the time of the natural clearance detection. Genetic variation in rs12979860 was C/C in 19 (82.6%) and C/T in 4 (17.4%); in rs8099917 was T/T in 21 (91.3%) and T/G in 2 (8.7%). Adverse genotypes (T/T in rs12979860 and G/G in rs8099917) were not detected. Coexistence of protective genotypes (C/C in rs12979860 and T/T in rs8099917) is found in 19 (82.6%) of the patients with natural clearance.

Conclusions: In our HIV/HCV-coinfected cohort, when comparing patients with natural clearance to those with chronic infection, male sex is less frequent but MSM transmission is more frequently found. Whilst protective IL28b genotype is seen in 38.1 % of chronically infected patients, we could find this genetic variation in 82.6% of natural clearers.

No conflict of interest

Abstract: P_26

Treatment issues --- HCV-HIV coinfection

Etravirine-based ART in HIV/HCV co-infected cirrhotic patients receiving triple therapy against HCV with Telaprevir


Introduction: HCV triple therapy with telaprevir (TPV) increases SVR in HCV-G1 patients. To date, there is a lack of data on the use of TPV with antiretrovirals other than boosted atazanavir, efavirenz, raltegravir, or NRTIs. Etravirine (ETRA), a nonnucleoside reverse transcriptase inhibitor (NNRTI) in vivo it is a weak inducer of CYP3A and a weak inhibitor of CYP2C9, CYP2C19, and P-glycoprotein, that could allow its safe use with TPV. Moreover, ETRA shows a low risk of hepatotoxicity in HIV-1 subjects with viral hepatitis, even in those with severe fibrosis.

Material & Methods: The aim of the present report is to describe for the first time the safe co-administration of ETRA-based ART during a full 12-week course of TPV. This was a multicenter retrospective cohort study in Spain. Forty-four subjects who received a HCV triple therapy with TPV with ETRA-based ART were included in the cohort. Clinical and laboratory data of the first 12 weeks of HCV triple therapy were collected;

Results: Forty-four HIV-infected patients with advanced liver fibrosis or cirrhosis started HCV triple therapy with TPV in eight centers. The majority of patients (78%) received HAART consisted of a fixed combination of NRTIs plus ETRA. The median baseline CD4 count was 479 cells/ml (235-1000), and all subjects had baseline undetectable HIV-RNA. During the HCV treatment period HIV-RNA remained undetectable in all subjects, and the percentage of CD4 counts remained stable or decreased slightly. Regarding outcomes of HCV therapy, 34 patients had received prior HCV therapy with peg-IFN/RBV: partial response (at least 2 log10 IU/ml decrease within
the first 12 weeks) in 23 %, relapse 32%, null response in 22%. 68% of subjects had liver cirrhosis diagnosed on the basis of liver stiffness measurement (by Fibroscan™). 48% of patients were infected with HCV genotype 1a and the subtype was not available in 25% of them. Median baseline HCV-RNA was 6.2 log10 IU/ml (5.2-7). Forty-two subjects completed 12 weeks of triple therapy (one subject withdrew at 6 week due to intolerance and one at week 8 due to breakthrough). Three subjects stopped anti-HCV therapy at week 12, 2 following futility rules and 1 due to adverse events or intolerance of the HCV treatment. Thirty-eight patients (86%) achieved negative HCV-RNA and one subject had HCV-RNA lower limit detection (15 UI/ml) at week 12. The Peg-IFN dose was not adjusted in any subject; RBV dose was adjusted in 8 (18%) at week 4 and 14 (32%) at week 12. 14% of the subjects received G-CSF, EPO and/or blood transfusions were required in 11 patients (25%). Haematological adverse events were the most frequent collected and caused the withdrawn of the HCV therapy in one patient. Two mild liver decompensations (ascites) occurred during triple therapy period not requiring discontinuation of HCV or HIV therapy. There were not severe skin reactions or grade 4 anaemia cases

**Conclusion:** HAART therapies including ETRA were safe in HIV/HCV coinfected patients with advanced liver fibrosis/cirrhosis receiving peg-IFN/RBV plus TPV, with no safety issues and a 12-week rate of negative HCV RNA of 88%

**No conflict of interest**

**Abstract: P_27**

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

**Telaprevir decreases eGFR in HIV-HCV Coinfected Patients**

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**Background:** A decrease in estimated glomerular filtration rate (eGFR) during telaprevir (TVR) treatment was recently reported, particularly in patients with risk factors for renal impairment. The inhibition of organic cation transporter 2 by TVR has been suggested as the mechanism responsible for elevations in plasma creatinine. In HIV/HCV coinfected patients, the decrease in eGFR with TVR has been correlated with higher ribavirin (RBV) plasma levels and increased risk of anemia.

**Methods:** Eighteen chronic hepatitis C genotype 1 patients coinfected with HIV received TVR in combination with pegylated-interferon and RBV for 12 weeks followed by treatment with PEG-IFN and RBV. Renal function of these patients was retrospectively evaluated; eGFR was estimated by the CKD-EPI formula. Wilcoxon’s signed -rank test for repeated measures was used for comparisons between follow-up and baseline results. The association between the antiretroviral drug used and the presence of any baseline comorbidity with eGFR changes was investigated.

**Results:** Mean age was 48.6 years and 94.4% were male, 14/18 (78%) had severe fibrosis/cirrhosis, 61% had genotype 1a, 55.6% were treatment naive, 16.7% prior relapsers, 22% prior non-responders and 1 patient had prior viral breakthrough. Baseline HIV RNA was <40 copies/mL in 88.9% of patients; mean baseline CD4 count was 695 cells/µL. Statistically significant reduction in eGFR (mL/min/1.73m²) was seen between baseline (93.6 [73.0-109.0]) and weeks 4 (90.0 [34.0-112.0], p-value 0.018), 8 (90.0 [56.0-111.0], p-value 0.032) and 12 (90.0 [58.0-113.0], p-value 0.011). Changes in eGFR were reversible after TVR discontinuation (week 24 104.2 [80.0-120.0], p-value 0.507). Consequently, serum creatinine significantly rose during TVR phase and lowered after week 12. None statistically significant association was found between the change in eGFR during TVR phase and lowered after week 12. None statistically significant association was found between the change in eGFR between baseline and week 12 and the presence of any baseline comorbidity nor the class of ARV drug used. Changes in hemoglobin were not correlated with the magnitude of the decrease in eGFR during TVR phase.

**Conclusion:** Even though the short number of patients evaluated, treatment with TVR was significantly associated with a reversible decrease in eGFR. The improvement of renal
function after discontinuation of the HCV protease inhibitor argues strongly for a causal relationship. The effect of TVR on renal drug transporters and its related clinical implications deserve further investigation.

Conflict of interest
financial relationship(s): Boehringer Ingelheim, GSK, Viiv, Pfizer, BMS, Abbott, Gilead, Janssen and Merck

Abstract: P_28

Treatment issues --- HCV-HIV coinfection

Efficacy and tolerability of telaprevir-containing triple therapy in HIV-HCV coinfected subjects


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Background: The efficacy of a telaprevir (TVR)-containing triple therapy for hepatitis C (HCV) in the context of HIV-coinfection has been analysed in patients with low grade fibrosis and not previously treated for HCV infection. Hence, the objective of the present study was to analyze the virological efficacy and tolerability of a TVR-containing triple therapy in HIV-coinfected patients in routine clinical practice.

Methods: Between March 2012 and December 2013, an observational multicenter study included 79 HIV-HCV-genotype 1 coinfected patients starting TVR (2250 mg/day), pegylated interferon (135-180 mcg weekly) and ribavirin (15 mg/kg). Efficacy analysis was performed according to time on treatment of each patient, as follows:

a) Patients not currently on treatment: sustained virological response (SVR) if undetectability 12/24 weeks after treatment interruption was achieved, independently the total time on treatment; end of treatment response (EOT) if undetectable HCV-RNA viral load after 48 weeks on treatment was shown.

b) Patients on follow up: undetectability at week 24 and/or 36; if less than 24 weeks, undetectability at both 4 and 12 weeks (extended rapid virological response, eRVR).

Tolerability was assessed considering: treatment interruption due to triple therapy intolerance and treatment-related side effects.

Results: Regarding baseline characteristics of patients, it should be noticed that, apart from HIV-coinfection and HCV genotype 1, many other negative predictor factors of treatment response (advanced fibrosis, non-CC IL28B genotype, previous non response to dual therapy, high baseline HCV viral load) were present. Antiretroviral therapy (cART) combined with HCV treatment was based on clinical decision. Besides, cART and triple therapy for HCV infection modifications were permitted.

Regarding efficacy, final data about treatment response were available in 57/79 patients: 24 patients experienced confirmed treatment failure (24/79, 30.4%), while 30 patients fulfilled criteria of EOT response or SVR (33/79, 41.8%). For patients on follow up (N=22): 13/22 maintained undetectable HCV-RNA after 36 weeks follow up, while 7/9 patients with less than 24 weeks have achieved eRVR.

Along the observational period, 25/79 (31.6%) patients interrupted promptly triple therapy: 8/25 due to futility rules, while 16/25 developed drug-related adverse events (11 of them were due to unspecific intolerance); finally, 1 patient died due to urinary sepsis. Interestingly, 8/16 patients with treatment interruption due to tolerability issues fulfilled criteria of SVR.

Grade 3-4 hematological side effects were observed in one patient; haematological disorders grade 1-2 occurred in nearly 60% of patients and mainly in first weeks of triple therapy, driving to ribavirin dosage reduction or EPO administration in 23% of patients. Rash and pruritus grade 1-2 was observed in 19% of patients, while one case of grade 3 rash drove to treatment interruption.
Conclusion: this difficult-to-treat HIV-coinfected population showed rates of virological efficacy around 70%, although SVR for patients on follow up needs to be confirmed and a close vigilance of serious adverse events is required mainly in the first weeks of treatment. The high rate of treatment interruption is mainly due to intolerance issues more than a real virologic failure. Selected patients could be benefited from shortened therapy.

No conflict of interest

Abstract: P_29

Treatment issues --- HCV-HIV coinfection

In HIV/HCV Coinfected Patients, an Antiretroviral Therapy Based on Atazanavir/Ritonavir Reduces Glucose Abnormalities and Liver Fibrosis (COAT Study)

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Introduction: It is known that insulin resistance (IR) is related with higher risk of steatosis, liver fibrosis progression and hepatocellular carcinoma in patients (pts) with chronic hepatitis C. The COAT Study is a 96-week, open label, multi-centre, controlled and randomized trial to compare the change in metabolic and hepatic toxicity of atazanavir/ritonavir (ATV/r) containing regimen versus a current boosted protease inhibitor (PI/r) in HIV/HCV co-infected patients.

Material & Methods: HIV-1/HCV-RNA positive individuals on antiretroviral regimen (ARV) based on PI/r plus two NRTIs, with HIV-RNA <50 copies/ml, with a functional liver Child Pugh classification ≤A5, never exposed to ATV and anti-HCV treatment naive, are enrolled in this study and randomized 1:1 to maintain the current PI/r or to switch to ATV/r (300/100mg QD). The primary end point was the rate of pts with any glucose abnormalities (GA) between two groups at 48 and 96 weeks. Secondary end points were: 1) change in liver fibrosis progression defined with FibroTest®; 2) change in Hyaluronic acid (HA) plasma level at week 96. Chi-Square or Fisher's Exact test and t-test for unpaired samples were used for statistical analysis. A p value <0.05 was considered to be significant. Multivariate logistic analysis has been adjusted for the following covariates: gender, age, CDC stage C, HCV genotype, didanosine, stavudine and zidovudine previous exposure, years of PI exposure, alcohol intake, total cholesterol and triglycerides plasma level and platelets cells count.

Results: A total of 127 pts were enrolled and 76 (39 in the switch arm and 37 in the maintaining arm) were included in the 96th week analysis; 70% was co-infected with HCV genotype 1 or 4 and 30% with genotype 2 or 3. The most baseline characteristics was similar in two groups. At 96 weeks, patients who maintain PI/r or switch to ATV/r had the following glucose abnormalities: absence of insulin resistance was in 29% vs 66% (p value 0.0013), absence of glucose intolerance 68% vs 89% (p value 0.02), presence of diabetes 21% vs 8% (p value 0.02). At the logistic regression analysis the variables related with the absence of any GA were: to switch to ATV/r [HR 9.2 (IC 95% 1.9-44.6) p value 0.006], absence of glucose intolerance 68% vs 89% (p value 0.02), presence of diabetes 21% vs 8% (p value 0.02). At the logistic regression analysis the variables related with the absence of any GA were: to switch to ATV/r [HR 9.2 (IC 95% 1.9-44.6) p value 0.006], HCV genotype 1 or 4 vs 2 or 3 [HR 0.2 (IC95% 0.07-0.8) p value 0.03] and didanosine previous exposure [HR 0.2 (IC 95% 0.5-0.7) p value 0.01]. Liver fibrosis stage, defined with FibroTest®, improved in 61.3% pts who switch to ATV/r and increased in controls (-40 ng/ml vs +110 ng/ml p value <0.001).

Conclusion: Our results suggest that an antiretroviral therapy based on ATV/r has lower
impact on glucose metabolism and reduced the non invasive markers of liver fibrosis progression such as FibroTest® and Hayluronic Acid plasma level in subjects with an HIV-1/HCV co-infection.

No conflict of interest

Abstract: P_30

Treatment issues -- HCV-HIV coinfection

Impact of HCV coinfection on HIV-1 progression and treatment outcome

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Background: Currently nearly 20% of HIV infected individuals are infected with the hepatitis C virus (HCV) and hepatitis-related liver disease is the leading cause of non-AIDS-related deaths among HIV patients. The negative impact of HCV in HCV hepatitis is well established with viral hepatitis showing faster progression and worse outcomes in the presence of HIV coinfection. However the impact of HCV on HIV disease progression is still controversial. Therefore, we aim to assess the role of HCV on HIV-1 progression and treatment outcome.

Materials & Methods: The patient dataset contained 301 HIV-1 infected patients, from which 85 where co-infected with chronic, non-treated HCV (HCV+ group) and 216 were monoinfected by HIV (HCV-). All patients were receiving triple antiretroviral therapy, and blood samples were collected at steady state. Among the therapeutic scheme, only one antiretroviral drug was quantified by RP-HPLC-UV, which resulted in the separation of patients into 5 different subsets: efavirenz (600mg qd), nevirapine (200mg bid), lopinavir/ritonavir (400/100 mg bid), atazanavir/ritonavir (300/100 mg qd), or darunavir/ritonavir (600/100 mg bid). Clinical and treatment data was retrieved from clinical files.

Results: The HCV+ group appeared to have worse outcome regarding immunological recovery and viral load evolution, when compared to the HCV-group. In terms of the HCV effect on HIV replication, despite no differences being observed between overall viral loads in both groups, the presence of HCV revealed to significantly contribute to higher risk for detectable viral load (OR = 2.3 and relative risk = 2.075). In terms of impact on immunological evolution, the TCD4+ cell count was significantly lower in the co-infected group (p=0.0013). As expected, HCV coinfection was associated with significantly elevated hepatic function markers (AST and ALT). Confounding brought by differences in renal function was ruled out due to similar creatinine clearances between groups. From the pharmacokinetic evaluation of patients by drug subset, it was possible to observe considerable variability in all classes, with efavirenz and lopinavir showing the highest variability with highly scattered plasma concentration curves. However, the observed/expected concentration ratios showed no difference between mono and coinfected patients despite marked visual differences in group mean ratios, which could be partly due to wide standard deviations. Furthermore the great majority of patients had AST and ALT bellow grade 3 hepatotoxicity level. All the statistical evaluation of the data was performed using GraphPad Prism, using the t-student test for normally distributed variables and a non parametric test (Mann-Witney) was applied when normality was not found. For contingency analyses the Fisher test was used.

Conclusions: Our results appear to support a significant impact of the HCV infection on the HIV disease evolution, showing higher risk for detectable levels of HIV DNA and lower TCD4+ cell count in the coinfected group. However no significant differences were found in the pharmacokinetic profiles between mono-infected and co-infected patients. Ongoing work of genetic characterization of our patient population suggests a possible correlation between drug levels and genetic polymorphisms.

No conflict of interest
Abstract: P_31

Treatment issues --- HCV-HIV coinfection

The Picture of HCV in Portugal - analysis of 2095 patients


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Introduction: Hepatitis C Virus (HCV) infection is a major cause of chronic liver disease, cirrhosis and hepatocellular carcinoma in European countries. In spite of an estimated prevalence of 1%, epidemiological features are scarce and the real number of HCV infected patients that remain to be treated is unknown.

Material and Methods: With the aim of describing these patients across different regions of Portugal, several hospitals were proposed to collect this information during a six month period between 2013 e 2014. Information available was recorded regarding gender, age, HCV genotype, IL28B, fibrosis stage, HIV coinfection, if treatment was done and rate of sustained virological response (SVR).

Results: The sample included information from 2095 patients, from 8 Portuguese hospitals (north-27,3%, center-21,7% and south 51%) 79,9% were male with an average age of 45 years. Genotypic test was available in 1830 individuals with the following distribution: G1 - 60%, G2- 1,25%, G3 - 23,4%, G4 - 14,4% and mixed genotypes 0,87%. The HIV infected patients represented the majority (79,9%), with no differences regarding age or genotype. IL28B was performed in 442 patients: CC 41,4%, CT 43,6% and TT 14,9%.

Liver assessment (elastography or histology) was available in 50,5% of cases: F0 and F0/F1-27%, F1 and F1/F2-23,4%, F2 and F2/F3-19,7%, F3 and F3/F4-10,5% and F4-19,2%. Among the total of patients, 935 (44,7%) were treated with Peginterferon (P) and Ribavirin (R) and from these 43,3% achieved SVR, with the following results according to genotype: G1-32,7%, G3-66,5% and G4-34,8%. SVR was achieved in 46,7% in patients with F0-F2 and in 36,5% in those with F3-F4 and in 61,2% of CC genotype versus 47,2% in non-CC. Those who were not treated were mainly HIV+ (89,7%) and reason for contraindication to P/R was the barrier to treatment in 25,9% of the patients. Those who did not achieved SVR together with those who were never treated were infected mainly with G1 in 69,7%, followed by G4 in 16,3% and G3 in 12,8%.

Conclusions: The authors conclude that there is a very high proportion of HCV patients that are potential candidates to new HCV therapies (DAAs), specially G1 and G4 and HIV infected individuals, where IFN-free regimens could be a very good option for those with contraindication to P/R and those less motivated due to the poor tolerability of current therapies.

No conflict of interest

Abstract: P_32

Treatment issues --- HCV-HIV coinfection

Eligibility to triple therapy for hepatitis C in HIV/HCV-coinfected patients with advanced liver fibrosis or cirrhosis

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Background: We aimed to evaluate the eligibility to triple anti-HCV therapy including interferon (IFN), ribavirin (RBV) and telaprevir...
(TVR) or boceprevir (BOC) in HIV/HCV-coinfected patients with advanced liver fibrosis or cirrhosis (ALF-C), who require careful evaluation for the risk of adverse events and drug-drug interactions (DDI).

**Materials & Methods:** HIV-positive patients coinfected with HCV genotype 1 and showing ALF-C (liver stiffness ≥10kPa and/or clinical/ultrasonographical cirrhosis), followed at our centre between January and September 2013, were included. Eligibility to triple therapy was defined by the absence of absolute contraindication to any anti-HCV drug (IFN, RBV, TVR/BOC), the availability of antiretroviral regimen without significant DDIs and the patient’s wish to start triple therapy. Categorical and continuous variables were described by absolute (%) values and median (interquartile range) values, respectively. Mann-Whitney and Chi Square/Fisher’s exact test were applied to compare variable among eligible and ineligible subjects (patients who refused treatment were not included in the comparison analysis).

**Results:** Among 313 HIV-infected subjects with HCV genotype 1-coinfection, 95 (30%) showed ALF-C. Most of them were males [77 (81%)], median age was 46 (45-49) years old. Forty-three (45%) were naïve to antiviral therapy. Eight (8%) patients refused treatment. Thirty-two (34%) were eligible to triple therapy, though 24/32 (75%) showed relative or minor contraindications to antiviral drugs (requiring adjustment of antiretroviral regimen or adequate management of comorbidities, especially neuropsychiatric, cardiovascular or endocrine disorders). Fifty-five (58%) patients were ineligible to therapy because of absolute contraindications to IFN, as decompensated cirrhosis [36/55 (66%)] or inadequate control of comorbidities/previous severe adverse event related to IFN [19/55 (34%)]. Ineligible subjects showed lower platelets count [8 (64-132) vs 142 (109-179) 10^3/mcL; p<0.001], haemoglobin [13.2 (12.1-15.0) vs 15.5 (14.1-16.2) g/dL; p=0.003], white blood cells count [4.4 (3.5-5.4) vs 5.7 (4.8-6.8) 10^3/mcL; p=0.001], plasma albumin [3.6 (3.4-4.1) vs 4.2 (4.0-4.5); p=0.001] and absolute CD4 count [392 (247-563) vs 563 (375-846) cells/mcL; p=0.002]. Moreover, they were more frequently naïve to anti-HCV treatment [ naïve/ relapsed/ non responder/ intolerant/ unknown: 26(47%)/ 1(2%)/ 16(29%)/ 5(9%)/ 7(13%) vs 10(31%)/ 5(16%)/ 13(41%)/ 3(9%)/ 1(3%); p=0.046]. No significant differences were observed in terms of relative CD4 count [27 (22-32) vs 28 (22-40) %; p=0.094], plasma HCV RNA [5.3 (4.7-5.9) vs 6.1 (4.4-6.4) IU/mL; p=0.270], HIV undetectability [<50 cp/mL: 44 (80%) vs 30 (94%); p=0.120] and age [47 (45-49) vs 46 (45-49) yrs; p=0.292]. DDIs between TVR/BOC and antiretrovirals were predictable in 11 ineligible subjects, but were not the main reason of exclusion in any of them. Fourteen eligible subjects were on antiretroviral regimens with potential DDIs with HCV protease inhibitors, but in all cases a modification of the regimen was available.

**Conclusions:** Triple therapy with TVR/BOC in coinfected subjects with ALF-C is limited by comorbidities and poor liver function, but does not appear to be substantially affected by antiretroviral regimen and immunovirological status.

No conflict of interest

**Abstract: P_33**

Treatment issues --- HCV-HIV coinfection

HCV Genotype 4: treatment barriers and predictors of virological response in HIV patients

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Background: The prevalence of genotype 4 chronic hepatitis C (G4-CHC) is increasing in the context of HIV and is, until new direct antiviral agents (DAA) are widely available, affected by a low rate of response to peg-Interferon based treatment. The aims of this study were to outline treatment barriers and to investigate predictors of sustained virological response (SVR24) predictors in this setting.

Methods: HIV/G4-CHC patients seen at the Infectious Diseases departments of 2 French Hospital in 2010 were evaluated; patients who spontaneously cleared HCV virus before 2010 were excluded. The outcome variables explored were the treatment deferral and the achievement of an SVR 24 weeks after peg-interferon / ribavirin (PR) treatment cessation.

Results: Overall, 73 of 151 (48.3%) included patients did not receive PR-based treatment. Risk factors for treatment deferral were CD4-T cell count higher than 500/mm3 (adjusted OR=2.79, 95%CI 1.30-6.02, p=0.009), African origin (aOR=7.35, 95%CI 2.34-23.08, p=0.001) and longer history of HIV infection (aOR=1.13, 95%CI 1.06-1.19, p<0.0001), while female gender and cirrhosis were associated with a higher probability for patients to receive treatment (aOR=0.27, 95%CI 0.09-0.79, p=0.016 and aOR=0.19, 95%CI 0.06-0.64, p=0.007, respectively). Of 78 treated patients, 26 (36.6%) attained an SVR24. The only predictor of SVR24 was a baseline CD4-T cell count higher than 500/mm3, (aOR=5.84, 95%CI 1.650-20.68, p=0.006), while a history of previous intravenous drug use (IVDU) and the use of pegIFNalpah2b compared to pegIFNalpah2a were independently associated with the absence of HCV clearance (aOR=0.11, 95%CI 0.02-0.58, p=0.009 and aOR=0.09, 95%CI 0.01-0.69, p=0.039, respectively).

Conclusions: In this population of HIV/G4-CHC patients, PR-based treatment led to a poor response rate affected by IVDU and type of interferon. However, those with CD4-T cell count higher than 500/mm3 and no cirrhosis were more prone to face delay in treatment access, maybe in perspective of new DAA-based treatment.

No conflict of interest

Abstract: P_34

Treatment issues --- HCV-HIV coinfection

Pegylated interferon and ribavirin for hepatitis C genotype 1 treatment in mono and co-infected naive patients: A Portuguese centre experience

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Introduction: Since the early 2000s, chronic hepatitis C treatment was based on the combination of pegylated-interferon-α (PEG-INF) and ribavirin (RBV), with sustained virological response (SVR) obtained in more than 50% of patients. However, SVR rate has been consistently lower for genotype 1 (G1) infection. The main objective of our real life study was to evaluate SVR rate in HCV G1 infected naive patients treated with PEG-INF and RBV and identify predictors of SVR. Additionally, we compared the SVR rate in patients with and without infection by the human immunodeficiency virus (HIV).

Material and Methods: Retrospective cohort study of all naïve patients with hepatitis C G1 submitted to treatment with PEG-INF and RBV between 2001-2013. Continuous variables were summarized by mean and standard deviation or median and interquartile range, while categorical variables were expressed as proportions. For comparison of patients’ groups (with SVR versus without SVR; HIV infected versus non-HIV infected) Fisher exact test, Chi-square, Mann-Whitney and Student t were used. Differences were considered statistically significant when p <0.05.

Results: We identified 227 patients, 172 (75.8 %) were male and the mean age was 40 ± 9 years. HCV co-infection was present in 117 patients (51.5%). All together SVR was achieved in 42.3 % of patients. Age (p=0.001), HIV co-infection (p<0.0001), pre-treatment HCV RNA > 400000UI/mL (p=0.011) and lower
levels of pre-treatment aspartate aminotransferase (0.04) and alanine aminotransferase (0.016) were all associated with a lower likelihood of obtaining SVR. Analysis of the subset of patients that completed treatment or stopped based on stopping rules showed a slightly increased RVS rate of 47.1%. In those patients, male sex (0.038), HIV co-infection (p<0.0001), pre-treatment HCV RNA > 400000UI/mL (p=0.007) and lower levels of pre-treatment aspartate aminotransferase (0.049) and alanine aminotransferase (0.022) were all related to treatment failure. Stratified analysis by HIV infection status revealed a SVR rate of 24.8% for patients with HIV infection comparing with 60.9% SVR rate in those without HIV infection.

Conclusion: SVR rates observed in this study were low and strongly influenced by HIV co-infection. Factors such as age, high pre-treatment HCV viral load and low transaminase levels were also predictive of treatment failure. Nowadays, new and more effective treatments for hepatitis C are available but knowledge of response predictors to treatment with PEG-INF and RBV still is useful for selecting patients that will benefit most from these new treatments, particularly in settings where access to new treatment options is limited.

No conflict of interest

Abstract: P_35

Treatment issues --- HCV-HIV coinfection

STaR: Rilpivirine/emtricitabine/tenofovir DF is non-inferior to efavirenz/emtricitabine/tenofovir DF in ART-naive adults co-infected with HCV at Week 96


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Introduction: Co-infection with HCV and HIV is related to more rapid progression of HCV-related liver disease and greater liver-related morbidity than those with HCV monoinfection. Co-infection with viral hepatitis may also decrease immune recovery and complicate the management of HIV infection.

Methods: STaR is a randomized, open-label, 96-week study to evaluate the safety and efficacy of the STR RPV/FTC/TDF compared to the STR EFV/FTC/TDF in treatment-naive, HIV-1 infected subjects. Subjects were randomized 1:1 to receive either RPV/FTC/TDF or EFV/FTC/TDF. The primary endpoint was the proportion of subjects with HIV-1 RNA <50 copies/mL (virologic suppression) at W48 per FDA snapshot algorithm (12% non-inferiority margin). Secondary endpoints included W96 results. Ad hoc analyses of efficacy and safety in subjects co-infected with HCV were also done, though the study was not powered to look at statistical differences within these subpopulations.

Results: A total of 786 subjects were randomized and received at least one dose of study drug (394 RPV/FTC/TDF; 392 EFV/FTC/TDF). Of these, 33 were co-infected with HCV (15 RPV/FTC/TDF; 18 EFV/TDF/FTC) at screening based on surface antigen serology. There were two subjects in the RPV/FTC/TDF arm who were co-infected with both HBV and HCV. In the overall population, RPV/FTC/TDF was non-inferior to EFV/FTC/TDF (85.8% vs 81.6%) at W48 for HIV RNA <50 copies/mL (difference 4.1%, 95% CI [-1.1%, 9.2%]) per FDA snapshot analysis. Non-inferiority was maintained at W96 (77.9% vs 72.4%; difference 5.5%, 95% CI [-0.6%, 11.5%]). For subjects who were co-infected with HCV, the rate of virologic suppression was 80.0% (12/15) with RPV/FTC/TDF vs 61.1% (11/18) with EFV/FTC/TDF at Week 48 and 66.7% (10/15) with RPV/FTC/TDF vs 55.6% (10/18)
with EFV/FTC/TDF at Week 96. At Week 96, in the RPV/FTC/TDF arm three patients experienced virologic failure, one discontinued treatment due to an AE, and one discontinued for other reasons with last HIV-1 RNA <50 c/mL. In the EFV/FTC/TDF arm, three patients experienced virologic failure and five discontinued due to AE. No discontinuation due to AE in either arm was of hepatic etiology. The proportion experiencing Grade 3-4 ALT elevation was 20.0% (3/15) with RPV/FTC/TDF vs 11.1% (2/18) with EFV/FTC/TDF and Grade 3-4 AST elevation, 13.3% (2/15) vs 5.6% (1/18). HIV/HCV co-infected subjects had higher rates of Grade 3-4 TEAEs, serious adverse events, and discontinuations due to adverse event than the overall population. There was one report of elevated liver function tests and elevated GGT in each arm, one report of acute HCV in the RPV/FTC/TDF arm, and one report of HCV flare in the EFV/FTC/TDF arm.

**Conclusions:** In the overall study population, RPV/FTC/TDF was non-inferior to EFV/FTC/TDF at Weeks 48 and 96. In subjects co-infected with HCV, both RPV/FTC/TDF and EFV/FTC/TDF were associated with lower rates of virologic suppression. There were low rates of Grade 3-4 elevations in AST and ALT. There were few TEAEs related to liver function reported and no discontinuations due to hepatic etiology.

No conflict of interest
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