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Abstract Book

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HIV & Hepatitis

2 - 3 June 2016, Berlin, Germany

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Abstracts

Abstract: 1

Treatment issues --- HCV-HIV coinfection

Intensive monitoring in MSM with a high risk for Hepatitis C reinfection can impact the incidence of new infections

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Introduction: Hepatitis C (HCV) prevalence rises among HIV-infected men who have sex with men (MSM) since 2000. By 2014, more than 10% of HIV-infected MSM had evidence of being exposed to HCV. Direct-acting antivirals (DAA) available since 2015 have a >95% cure rate. Within 2 years of being cured, however, 33% of patients become reinfected. A previous infection is therefore a strong determinant for a new infection. Acute HCV infections are generally asymptomatic. Timely identification of new infections followed by immediate treatment may help to prevent onward HCV transmission. Current methods used for testing are an HCV-antibody test and alanine-aminotransferase (ALT) levels. Approximately 20% of all new infections are missed when these tests are done due to a slow appearance of antibodies and a low sensitivity of the assay. We developed a mathematical model to test whether alternative monitoring strategies haven an impact on the HCV epidemic.

Method: A deterministic mathematical model was constructed to represent the HCV/HIV co-infected epidemic among Dutch MSM from 2000 until 2015, using epidemiological data from the Dutch SHM HIV database. From 2015, all identified HCV infected MSM received DAAs immediately after diagnosis. Our baseline scenario, reflects current practice in Europe: all HIV-infected MSM are monitored every 6 months with an ALT test and every 12 months with an HCV-antibody test. Impact of increased frequency of testing to once per month for all HIV-infected MSM was evaluated. In addition, we also evaluated the impact of testing with a highly sensitive (92%) PCR test either monthly or every 3 or 6-months targeted to those MSM whom previously cleared or were cured from a HCV infection. This on the assumption that they are at higher risk for reinfection.

Results: Increasing the current monitoring strategy to a monthly ALT test in all HIV-infected MSM will have limited effect e.g. a decrease in HCV prevalence in HIV-infected MSM from 2.0% (interquartile range [IQR]1.3%-2.6%) at baseline to 1.8% (IQR 1.2%-2.5%) in 2030. This is results in a 3.4% (IQR 1.0%-5.9%) reduction in new infections between 2015 and 2030. Testing the target group every 6 months with a sensitive PCR test reduces prevalence to 1.5% (IQR 1.1%-2.0%) in 2030, with an overall reduction of 2.9% (IQR -1.0%-12%) of new infections. Monthly testing in the high-risk target group of previously infected patients using the PCR test will result in a strong prevalence reduction of 1.2% (IQR0.9%-1.7%) in 2030.This testing strategy prevents 10.3% (IQR 5.2%-19.4%) of new infections compared to the current monitoring strategy. Testing the target group every 3-months with a PCR test resulting in 1.3% (IQR1.0%-1.9%) prevalence and 6.7% (1.9%-16.3%) new infections prevented.

Conclusion: Intensive monitoring can help to reduce the HCV epidemic among HIV-infected MSM in the Netherlands. The most effective strategy is targeted testing within a group of previously HCV infected MSM with a sensitive PCR test. This strategy maximum results in preventing 10.3% of new infections compared to the current monitoring strategy.

Conflict of interest
financial relationship(s): Gilead

Abstract: 3

Drug Interactions --- Hepatitis ARTs

Glomerular Filtration Rate Change During HCV Treatment with Sofosbuvir/Ledipasvir in HCV/HIV Coinfected Patients Treated with Tenofovir ± Boosted Protease Inhibitor

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Background: Treatment of chronic hepatitis C (HCV) in HCV/HIV coinfected patients requires awareness to interactions between DAAs and antiretroviral (ART) medications. Tenofovir (TDF) associated renal toxicity may be increased due to concomitant exposure to boosted protease inhibitors (PIs) and sofosbuvir/ledipasvir.

Aim: Evaluation of the evolution of the glomerular filtration rate (GFR) during HCV treatment with sofosbuvir/ledipasvir in HCV/HIV coinfected patients treated with TDF ± boosted PIs compared to patients not receiving any of these drugs.

Methods: Prospective study of HCV/HIV coinfected patients treated with sofosbuvir/ledipasvir for chronic hepatitis C. The GFR using the Cockcroft-Gault equation was evaluated at baseline and at the end of HCV treatment. Patients were randomized in three groups based on their ART regimen: without TDF, with TDF but without PI, with TDF + PI.

Results: We included 101 HCV/HIV coinfected patients treated with sofosbuvir/ledipasvir. Overall, 89% were male, the mean age was 46 years old and the acquisition of HCV was by intravenous drug use in 93%. All patients were receiving ART: TDF was part of the regimen in 48 patients and of these 17 were receiving TDF + boosted PI. The mean CD4 cell count was 625/mm^3 and all had undetectable HIV RNA. The baseline characteristics of patients receiving ART regimens with and without TDF, and of patients receiving TDF with or without PI are shown in the following tables:

	Without (n=53)	TDF (n=48)	p	TDF without PI (n=31)	TDF + PI (n=17)	p
Mean Age (years)	45,9	46,4	0,64	46,3	46,8	0,78
Male	48 (87,5%)	42 (90,6%)	0,62	27 (87,1%)	15 (88,2%)	0,9
Body Mass Index (Kg/m2)	23,1	22,5	0,44	22,1	23,2	0,48
Diabetes	2 (3.8%)	2 (4,2%)	0,95	2 (6,5%)	0 (0%)	0,28
Hipertension	10 (18,8%)	7 (14,5%)	0,29	3 (9,6%)	4 (23,5%)	0,14
GFR (ml/min/1,73m2)	107,1	107,4	0,95	107,1	107,4	0,95

The following table shows GFR evolution in patients treated with ART regimens without TDF compared with patients treated TDF without PI and patients treated with TDF +PI, and the odds ratio of GFR decrease:

	Mean Baseline GFR	Mean End of Treatment GFR	Odds Ratio (95% confidence interval)	p
Without TDF (n=53)	107,5	101	0,371 (0,153 – 0,899)	< 0,05
TDF (n=31)	107,1	96,5	1,7 (0,525 – 5,530)	< 0,05
TDF+ PI (n=17)	106,6	96,4	3,69 (1,12 – 11,1)	< 0,05

Conclusion: We observed a decrease in the mean GFR in all patients treated with sofosbuvir/ledipasvir. However, there is an association between exposure to TDF and GFR decrease, particularly with concomitant use of a boosted PI. The GFR decrease, while small, should prompt clinicians to monitor renal function in HCV/HIV coinfected patients receiving TDF as part of their ART regimen, especially in the presence of a boosted PI.

No conflict of interest

Abstract: 4

Treatment issues --- HCV-HIV coinfection

Are risk factors still relevant for HCV treatment with directly-acting agents against HCV in HIV-HCV-coinfection results from the German hepatitis C cohort (GECCO)?

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Introduction: Directly-acting agents (DAA) against HCV have improved treatment of chronic hepatitis C in HIV-coinfected individuals due to higher efficacy, better tolerability and substantial reduction of contraindications. Despite this major progress treatment failure still occurs. Here we assessed the influence of traditional risk factors on treatment outcome in the German hepatitis C cohort (GECCO).

Methods: The GECCO cohort is a multicenter cohort from 9 sites in Germany (n=1353). All patients started on the following DAAs were included in the analysis: pegylated interferon (PegIFN) and ribavirin (RBV) and Sofosbuvir (SOF); SOF and RBV; SOF and simeprevir (SMV); SOF and daclatasvir (DCV) +/- RBV; SOF and ledipasvir (LDV); paritaprevir/ritonavir (PRT/r), ombitasvir (OMV) +/- RBV and +/- dasabuvir (DSV). Treatment outcome is measured as sustained virologic response at week 12 after end of therapy (SVR12) on an intent to treat basis. Most GECCO patients are part of the German hepatitis C registry.

Results: The analysis is based on the 283 HIV/HCV-coinfected patients documented in GECCO. Risk factors associated with lower treatment success (SVR12) were: treatment with PegIFN/RBV/SOF (86%) versus DAAs only (95%) (p=0.05), being treated for GT2/GT3 (82%) compared to GT1/GT4 (95%) (p=0.041) and having CD4+ cells <350/µL (85%) compared to ≥ 350/µL (94%) (p=0.076). Age (</≥ 60 years p=1.00), sex (p=1.00), HCV-RNA at baseline (</≥ 6 Mio IU/mL p=0.579), ALT level at baseline (normal range / > upper limit of normal p=0.418), patients treatment naïve or pretreated (p=0.353), being on opioid maintenance (p=0.38) and presence of liver cirrhosis (p=0.226) were not associated with lower SVR12.

Conclusions: Risk factors for treatment failure are the use of PegIFN in the regimen and being infected with GT2 and GT3. These factors are associated with higher toxicity or lower antiviral efficacy of antiviral therapy for specific genotypes. There was a trend for lower CD4+cells as a predictor of lower SVR12, as the only factor independent from antiviral therapy. In conclusion most traditional risk factors do not remain to be relevant for treatment success when using DAA regimen.

Conflict of interest
financial relationship(s): Advisory board, speaker honorarium or grants: AbbVie, BMS, Gilead, Janssen, MSD, ViiV

Abstract: 5

Treatment issues --- HCV-HIV coinfection

Daclatasvir + Sofosbuvir +/- Ribavirin in HIV/HCV co-infected patients with advanced liver disease: preliminary data from the Italian Compassionate Use Program

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Introduction: Combination of Daclatasvir (DCV) and Sofosbuvir (SOF) is widely used in HIV/HCV co-infection because of few drug-drug interactions with HAART. Anyway, data on safety and efficacy in co-infected population with advanced liver disease are still scarce. We report preliminary data from a cohort of co-infected patients treated with DCV+SOF in a compassionate use program (CUP) in Italy.

Methods: CUP enrolled adult patients with liver cirrhosis and/or high risk of death within 12 months without other treatment options. All patients received SOF 400 mg QD + DCV (dose depending on comedications); ribavirin (RBV) use was at physician's discretion.

Results: 58 patients were enrolled; to date, 41 have data available for SVR12 analysis.
74.1% of patients were male; median age was 52 years (IQR 50-54).
20.7% had previous AIDS; baseline HIV-RNA was undetectable in 98.3%. HAART regimens were heterogeneous: the most used were 2NRTIs+INSTI (31.4%) and INSTI+PI (29.6%).
Most patients were infected by genotype 1a (46.6%) and 3 (31%); 8.6% were also HBV co-infected. Cirrhosis was present in 93.1% of subjects (CPT A 42.6%, B 42.6%, C 5.6%) with a median MELD of 12 (IQR 9-13). 13.8% were waitlisted for liver transplant (LT) and 12.1% were LT recipients.
All patients completed 24 weeks of treatment, except 3 (5.2%) who discontinued earlier: 1 at week 20 because of liver toxicity (and died 12 weeks later), 1 at week 13 (dead of cholestatic fibrosing hepatitis), 1 had LT at week 20 and reached SVR12. 1 patient died during follow-up for a car accident.
SVR12 rate in ITT analysis was 92.7% in the overall population (92% in GT1, 92.3% in GT3, 100% in GT4), 83.3% in LT recipients and 100% in LT candidates.
RBV was used in 74.1% of patients: of these, 24.3% developed haemoglobin levels <10 g/dl, 10.8% introduced erythropoietin and 35% discontinued RBV. 30% of patients developed total bilirubin >4 mg/dl. 1 patient had HIV virologic failure (>400 copies/ml), but was re-suppressed by switching HAART.

Conclusions: These preliminary data show that DCV + SOF +/- RBV is effective in this difficult-to-treat population, with high SVR12 rate and an acceptable safety profile, even if management of anemia and liver-related complications can be challenging. HAART management in combination with anti-HCV therapy was not a significant issue.

No conflict of interest

Abstract: 6

Treatment issues --- HCV-HIV coinfection

Rate and predictors of treatment failure to all-oral HCV regimens outside clinical trials in Spain

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Background: Cure rates above 90% have been reported in most phase 3 clinical trials using distinct all-oral direct-acting antivirals (DAA) in chronic hepatitis C patients. Preliminary results in real world patients have confirmed these good news, although efficacy tends to be lower. In Spain, nearly 45,000 hepatitis C patients had been treated with all-oral DAA regimens up to March 2016.

Methods: All consecutive chronic hepatitis C patients treated with all-oral DAA regimens at three hepatitis clinics in Spain were retrospectively examined. Host and viral factors were tested as predictors of treatment failure.

Results: A total of 363 chronic hepatitis C patients had completed a course of all-oral DAA therapy outside clinical trials up to the end of 2015. All but 11 (3%) patients achieved sustained virological response. Eight failures occurred after 12 weeks of sofosbuvir-ledipasvir, despite being on ribavirin 4 of them. All failures but one were relapses. The only patient with viral breakthrough selected NS5B L159F and NS5A Y93H. In multivariate analyses, only advanced liver fibrosis (Metavir F3-F4) and HIV coinfection were significantly associated with treatment failure. A trend towards lower response was seen for HCV genotype 4 (8% of G4 treated patients failed).

Conclusions: Treatment failures outside clinical trials are roughly seen in 3% of chronic hepatitis C patients that complete a course of all-oral DAA therapy, resembling what is seen in registration trials. In our series, outcomes were not significantly influenced by ribavirin addition, IL28B polymorphisms, HCV genotype, high baseline HCV-RNA neither prior interferon failure. However, advanced liver fibrosis and HIV coinfection were significantly associated with treatment failure. Our findings support that there is still room for individualization of current DAA therapy.

No conflict of interest

Abstract: 7

Liver Steatosis

Sustained virologic response in chronic HCV infected patients is associated with weight gain and decrease in controlled attenuation parameter (CAP)

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Introduction: Transient elastography (TE) has been established as a noninvasive method to assess liver stiffness (LS) in patients with chronic hepatitis C virus (HCV) infection. Recent studies have validated controlled attenuation parameter (CAP) with TE as a method to assess hepatic steatosis. LS has been demonstrated to decrease in chronic HCV patients that have achieved sustained virologic response (SVR). The aim of our study was to evaluate the impact of SVR on CAP as well as change in body weight.

Materials and Methods: In this retrospective study, patients treated at a single, tertiary medical center who underwent TE with CAP measurement were eligible for inclusion. Patients were included if they had HCV, achieved SVR 12, and had CAP scores pretreatment and post-SVR. The primary outcome of interest was weight change (post-SVR weight compared to pretreatment). The correlation between various demographic (age, gender, ethnicity) and clinical (diabetes, HCV genotype, platelets, albumin, ALT, CAP and BMI) variables were compared to weight change using Spearman's rank correlation. A multivariate, linear regression model was constructed using variables deemed to be clinically significant. All data were analyzed using SAS v9.3.

Results: 27 HCV monoinfected patients were included. The median age was 58 years (range 27-77). 70% (n=19) were male and 44% (n=12) were Caucasian. Fourteen patients (52%) had a BMI>25 kg/m^2. Nearly all patients (n=26) had genotype 1 infection; 16 had 1a, 10 had 1b. The average weight change post-SVR was a gain of 4.48 lbs (-7 to 14), and average change in CAP was -15.7 dB/m (-121 to 94). On univariate analysis, male gender and post-SVR CAP score were each independently correlated with a positive increase in weight (p=0.0159 and p=0.0324 respectively). A BMI>25 kg/m^2 was also correlated with an increase in weight change with a trend towards significance (p=0.1). Higher baseline albumin was associated with a decrease in weight change also with a trend towards significance (p=0.0838). Increase in CAP change was associated with decrease in weight change but did not achieve statistical significance (p=0.16). On multivariate analysis, after controlling for gender, age, pretreatment CAP, diabetes, pretreatment BMI, ALT, and ethnicity; Caucasian ethnicity was associated with a statistically significant increase in weight of 10.5 lbs (p=0.0411). Male gender trended towards a significant increase in weight change of 6.1 lbs (p=0.0549). Additionally, Hispanic ethnicity also trended towards a significant increase in weight change of 11.3 lbs (p=0.0561).

Conclusions: Patients that achieved SVR gained weight, and had a decrease in CAP. This might imply an increase in muscle rather than fat as the cause of weight gain. Further validation of post-SVR CAP and weight need to be done with a metric to investigate possible change in muscle mass. Males were far more likely to have a significant increase in weight post-SVR. Patients with a higher albumin at baseline were less prone to have weight gain, possibly related to better liver metabolic function. To our knowledge, our study is the first to describe post-SVR change in weight and CAP.

No conflict of interest

Abstract: 8

Non invasive assessment of liver fibrosis

The role of Presepsin (sCD14-ST) as an indirect marker of immune activation in HIV and HCV infections and in HIV/HCV co-infection

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Background: Presepsin, a newly discovered soluble fragment of CD14, has been studied as a sepsis biomarker. The mechanism of its secretion is involved in the TLR4 activation cascade and it is related to mCD14 and sCD14, which are monocyte activation markers, indirectly representing the presence of bacterial translocation. Presepsin is secreted by activated monocytes and the major stimulus for its production is phagocytosis. Therefore Presepsin could be employed as an immune activation marker, particularly innate immunity activation, and it could allow for the estimation of bacterial translocation rates. The aim of this study was to assess the correlations between Presepsin serum concentration and bacterial translocation, immune activation and fibrosis markers in subjects with HIV and HCV mono-infections and in HIV/HCV co-infection, compared to healthy controls.

Methods: This cross-sectional study included patients with hepatitis C virus (HCV) and human immunodeficiency virus (HIV) mono-infections, HIV/HCV co-infection, and healthy controls (20 subjects/group). Peripheral blood was analyzed to determine the levels of Presepsin, Forkhead box 3 (Foxp3+) T cells, TGF- β1, CD14 (soluble and surface isoforms), IL-17 and bacterial translocation products. These measurements were correlated to the severity of liver fibrosis, measured with the FIB-4 score and transient elastography.

Results: Presepsin is a biomarker of chronic immune activation, as demonstrated by its correlations with sCD14, mCD14 and CD4+CD25+Foxp3+ lymphocytes, particularly in HIV infection. Its concentration is correlated to liver fibrosis markers, such as FIB4, particularly in HCV mono-infected patients.

Conclusions: These findings open to the possibility of employing Presepsin as an indirect and easy-to-measure biomarker of immune activation and enhanced fibrogenic state, respectively in HIV and HCV infections.

No conflict of interest

Abstract: 9

Non invasive assessment of liver fibrosis

Hepatic Fibrosis 12 Weeks After the End of Treatment with Direct Acting Antivirals (DAAs) in HCV/HIV Coinfected Patients

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Background: In some studies, sustained virological response (SVR) after treatment of chronic hepatitis C (HCV) is associated with non progression, and sometimes regression of liver fibrosis in HCV/HIV coinfected patients.

Aim: To evaluate the effect of HCV treatment with DAAs on liver stiffness evaluated by transient elastography (TE) in HCV/HIV coinfected patients.

Methods: We evaluated HCV/HIV coinfected patients treated with DAAs containing regimens during 12 to 24 weeks. Liver stiffness was evaluated using FibroScan® at baseline and 12 weeks after the end of treatment. To assess the influence of advanced fibrosis on the results, patients were randomized in two groups (F1-F3 and F4).

Results: We included 89 patients with a mean age of 46.4 years old, 88.8% were male. Acquisition of HCV was by intravenous drug use in 93.3% (41% under substitution treatment with methadone), sexual in 3.4% and transfusion in 1.1%. Mean CD4 cell count was 615/mm^3 and all had undetectable HIV RNA. The most frequent genotype was G1 (82%), followed by G4 (11.2%), G3 (5.6%) and G2 (1.1%). Most patients had advanced liver fibrosis (52.8% were cirrhotic, 28.1% were F3) and 19.1% were F1-F2. The percentage of HCV treatment experienced patients was 48.3% (with pegylated interferon + ribavirin).
Sofosbuvir and ledipasvir ± ribavirin was prescribed in 89.9% of patients. Other regimens were sofosbuvir + ribavirin (5.6%), ombitasvir/paritaprevir/ritonavir + dasabuvir (3.4%) and sofosbuvir + daclatasvir + ribavirin (1.7%). SVR12 was achieved in 97.8% of the patients. Relapse was registered in two cases. The following table shows a decrease of fibrosis after treatment in all patients and in the groups of F1-F3 and F4.

	Mean Baseline Fibrosis (KPa)	Mean 12 Weeks After Treatment Fibrosis (KPa)	*P*
All patients	18.7	13.6	<0.001
F4 (n=47)	27.7	19.2	<0.001
F1-F3 (n=42)	9.02	7,4	<0.05

Conclusion: We observed a significant decrease in liver fibrosis in HIV/HCV coinfected patients who were treated with DAAs. The improvement of fibrosis was more pronounced in patients with advanced disease.

No conflict of interest

Abstract: 10

Resistance --- Hepatitis B

High incidence of lamivudine-resistant HBV mutants and presence of liver damages in HIV-positive eastern Indian patients harbouring HBV/D2 strains

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Introduction: Carrying the third largest population of HIV infection and the second largest population of chronic hepatitis B infection in the world, India is an important reservoir for HIV-hepatitis B virus (HBV) co-infection. Studies from the treatment-naive HIV-HBV co-infected individuals reveal a high frequency (11.3%) of chronic HBV infection among HIV-positive individuals from eastern India (EI) and the predominance of HBV sub-genotype D2 (HBV/D2) among the HBV variants. In India, HIV-HBV co-infected patients have received lamivudine (3TC) mono-therapy as the anti-HBV treatment since 2004 being a part of highly-active anti-retroviral therapy (HAART) and tenofovir (TDF, the recommended drug for the treatment of HIV-HBV co-infection) has been introduced from 2013. Information related to the molecular epidemiology of treated HIV-HBV co-infected individuals is limited. The present study was aimed to characterise the HBV infection and treatment response among chronic HBV infected HIV-positive patients from EI who did not show HBV DNA suppression during long-term HAART.

Materials & Methods: Thirty-six HIV-HBV co-infected patients who did not have HBV DNA suppression (<20 IU/ml) during long-term 3TC mono-therapy (mean duration 31.28±22.42 months) were investigated. These patients received 3TC as the sole anti-HBV treatment as a part of HAART from the Calcutta School of Tropical Medicine, the main ART centre in EI. A few patients having TDF add-on to their

treatment regimen were followed up for treatment response. Different virological parameters were studied- plasma HBV DNA load quantification by real-time PCR, hepatitis B e antigen (HBeAg) detection by commercial ELISA, 3TC-resistant mutation analysis by direct sequencing and HBV genotype/sub-genotype determination by phylogenetic analysis. Descriptive statistics for continuous and categorical variables were employed.

Results: During long-term HAART, 36 HIV-HBV co-infected patients (mean age 36.91±6.99 years and mean CD4 count 347.56±200.15 cells/mm^3) showed the presence of virological failure to anti-HBV treatment as indicated by the high percentage of HBV DNA load >2000 IU/ml (55.56%), HBeAg positivity (88.89%) and high mean HBV viremia (4.31±1.51 logIU/ml). HBV/D2 (41.67%) strains predominated over the other HBV variants-HBV/A1 (38.88%), HBV/D3 (11.11%), HBV/D1 (5.56%) and HBV/C1 (2.78%). Remarkably, 50% of the HBV/D2 strains showed the presence of 3TC-resistant double (rtL180M+rtM204V) and triple (rtV173L+rtL180M+rtM204V) mutations in the HBV polymerase gene region. Moreover among these drug-resistant HBV/D2 strains, 87.5% had the 3TC-resiatant triple mutation associated vaccine escape mutations (sE164D+sI195M), which was significantly higher than the prevalence in HBV/A1 strains (20%, P=0.023). The 3TC-resistant HBV/D2 strains demonstrated high mean HBV viremia (5.49±0.03 logIU/ml) and the signs liver damages (elevated mean serum alanine aminotransferase level and high fibrosis score). Upon TDF add-on, the 3TC-non-responder HBV/D2 strains (N=5) showed delayed HBV suppression as indicated by the persistence of 3TC-resistant mutations and an increase in mean HBV DNA load >2 logIU/ml (4.55±3.68 logIU/ml in 21.33±1.53 months vs. 2.34±2.33 logIU/ml in 10.33±5.03 months).

Conclusions: The high incidence of 3TC-resistant mutations in HBV/D2 strains, the major HBV variants among HAART experienced HIV-HBV co-infected patients in EI, retaining high infectivity and increased liver damage potency underscore the urgent requirement for proper management of these mutants from clinical and public health perspectives.

No conflict of interest

Abstract: 11

Treatment issues --- HBV-HIV coinfection

Hepatitis B and C viral infections in people who are at risk for, and living with, HIV in Bangladesh: prevalence and behavioral risk factors

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Introduction: Viral hepatitis and Human Immunodeficiency virus (HIV) are major public health concerns as co-infection with hepatitis B virus (HBV) and hepatitis C virus (HCV) results in increased risk for complications among people who are at risk for, or living with, HIV and has serious impact on treatment outcomes. We undertook this study to evaluate the presence of HBV, HCV & syphilis in people living with HIV and AIDS (PLWHA) and people who are at risk for HIV in Bangladesh.

Material & Methods: A cross-sectional survey was performed with 277 PLWHA, 308 female sex workers (FSWs) and 294 injecting drug users (IDUs) in Bangladesh recruited through time-located cluster sampling. Behavioral survey was conducted and blood samples were tested for hepatitis B surface antigen (HBsAg), antibody to HBV core antigen (anti-HBc), and anti-HCV antibodies (anti-HCV) and syphilis (both rapid plasma reagin-RPR+ and treponema pallidum hemagglutination-TPHA+). FSWs and IDUs were also tested for HIV infection. The survey data was analysed statistically using SPSS. Predictors of infection were explored using univariable and multivariable logistic regression.

Results: The prevalence of coinfection in PLWHA with hepatitis was: HBsAg 23.3%; anti-HCV 27.6% and both HBsAg and anti-HCV 6.8%. Alternatively, sero-prevalence of HBsAg, anti-HCV and both HBsAg/anti-HCV among FSWs & IDUs were 3.6%, 1.2%, 0.7% and 43.7%, 48.3%, 8.6%; respectively (P<0.001). The prevalence of HIV was 0% in FSWs and 3.2% among IDUs. Further, the prevalence rates of syphilis were also high among PLWHA

(6.7%), FSWs (11.4%) and IDUs (13.3%). Risk behaviors were common, and perception of risk and correct knowledge of HIV was extremely low. The most common mode of HIV transmission was sexual promiscuity (68%), followed by partner positivity (9%), injecting drug use (18%) and history of untested blood transfusion (5%). Multivariable analysis found a large number of factors associated with higher levels of infection (including age of first sex, marital status, poverty, living apart from spouse, exposure to risk factors, number of sex partners and level of unprotected sex) (P<0.001). Protection against risk was low, but those who reported using condoms at last sex had lower rates of infections.

Conclusions: Co-infection with HBV and HCV is a common problem in Bangladesh. Our study demonstrated presence of high level of HBV and HCV co-infections both in people who are at risk for, or living with, HIV. Interventions targeting risk reduction for HIV and other sexually transmitted infections in Bangladesh should screen for for markers of HBV and HCV infections and adequate attention must be given to the treatment and well-being of PLWHA to enable them live in a safe environment.

No conflict of interest

Abstract: 12

New anti-HCV agents

Treatment of Patients with Hepatitis B or C May Reactivate Suppressed Hepatitis B or C Coinfection Risking Decompensation

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Hepatitis B and C coinfection is common because of similar modes of transmission. Usually, there is a dominant virus with the other coinfected virus remaining undetectable. We describe 3 patients who had reactivation of the suppressed virus after treatment for the active virus. In the first case, a 45-year-old man with HCV and HBV coinfection presented for treatment of HCV. Initially, his HCV PCR was 600,000 IU/mL and he had an undetectable HBV DNA. He was started on ledipasvir and sofosbuvir for 12 weeks. After 4 weeks, his HCV viral load became undetectable; however, his HBV DNA increased to 1939 IU/mL. At 12 weeks, the HCV viral load remained undetectable, and the HBV DNA was also fortunately undetectable, without requiring HBV treatment. In the second case, a 37-year-old man also with coinfection of HCV and HBV presented for treatment of HBV with tenofovir. This patient had acute HBV suppressing chronic HCV. His HBV viral load trended down over 16 weeks of treatment; however, HCV RNA which was previously undetectable, became positive just as HBV DNA was decreasing to undetectable levels at 12 weeks. At 16 weeks, HBV DNA was trending towards being undetectable, and the HCV RNA was fortunately undetectable without requiring HCV treatment. In the third case, a 21-year-old man with coinfection of HCV and HBV presented for treatment of HBV with tenofovir. His HBV DNA trended down over 32 weeks of treatment; however, HCV RNA which was previously undetectable, became positive just as HBV DNA was decreasing to undetectable levels at 32 weeks. He was having worsening liver enzymes which initially prompted testing for HCV viral load, and now may need initiation of

treatment for HCV in the near future. New direct-acting antiviral-based therapy (DAAs) without the need for interferon are showing high treatment success with less toxicity and are becoming widely used. However, our cases show that patients with dual infection treated with DAAs for HCV can potentially reactivate HBV given the lack of anti-HBV activity with the new DAA regimens. Treatment of HBV can also result in reactivation of HCV. There are no current guidelines regarding monitoring of the reactivation of non-dominant virus in these patients undergoing treatment. Our patients fortunately have not yet required treatment of their reactivated virus, but patients with other medical comorbidities and cirrhosis may need early initiation of treatment to prevent acute decompensation. Close follow-up laboratory studies for viral reactivation and liver function may be a necessary addition to current guidelines as detecting a second active hepatitis virus can prevent hepatic decompensation by allowing for the timely initiation of another antiviral agent.

No conflict of interest

Partial data previously presented at the Ohio Gastroenterology Society 2015 Annual Meeting, Columbus, OH, September 19, 2015.

Abstract: 13

New anti-HCV agents

Rapid drop in serum glucose and risk of hypoglycemia in chronic hepatitis C patients with diabetes treated with DAA

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Introduction: Chronic HCV infection is associated with metabolic abnormalities, including insulin resistance. Up to 15-25% of chronic hepatitis C patients will develop diabetes lifelong. New DAA allow HCV suppression within a very short-time frame. Little is known on the rapid metabolic effects occurring in chronic hepatitis C patients treated with DAA.

Methods: All chronic hepatitis C patients that received DAA regimens during at least 4 weeks at two reference clinics in Madrid were retrospectively examined. A GEE (generalized estimation equation) analysis was performed several times, using Gaussian family with an identity link, in order to estimate the association between serum glucose as dependent variable and Diabetes Mellitus diagnosis and serum HCV-RNA changes.

Results: A total of 174 chronic hepatitis C patients who begun oral DAA regimens were identified. Overall, 71.3% were male, median age 54.5 years-old, and baseline serum HCV-RNA 6.17 log IU/mL. Prescribed regimens were as follows: SOF+ledipasvir (104), SOF+daclatasvir (29), SOF+simeprevir (22), 3D (9) and other interferon-free (10). At week 4, serum HCV-RNA <15 IU/mL was achieved by 84% of patients. All were undetectable at week 8. A total of 48 (27.6%) patients were diabetic, being insulin used by 25 of them. Median baseline glucose in diabetics was 134.9 mg/dL and declined to 125.7 mg/dL at week 4 of DAA (p=0.03). There was a major statistical interaction between glucose levels and diabetes mellitus. On average, glucose declined 8.04 mg/dL at week 4 of DAA treatment (p=0.053) whereas come back to baseline levels at week 8. Two individuals experienced symptomatic hypoglycemic episodes within the first month of DAA therapy that required reductions on insulin administration.

Conclusion: Given that no drug-drug interactions exist between insulin and either SOF, LDV, DCV or 3D, rapid suppression of HCV replication could lead to a rapid improvement of insulin sensitivity in DAA treated patients. Thus, diabetic patients on insulin treated for hepatitis C with DAA should be informed on the potential risk of hypoglycemic episodes during hepatitis C therapy.

No conflict of interest

Abstract: 14

New anti-HCV agents

Impact of ITPA polymorphisms on the risk of anemia using DAA in chronic hepatitis C patients

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Background: Single nucleotide polymorphisms (SNPs) at the inosine triphosphatase (ITPA) gene are associated with hemolytic anemia in chronic HCV patients treated with peginterferon-ribavirin (RBV). Information on the influence of ITPA polymorphisms on RBV-induced anemia in patients treated with new oral HCV direct acting antivirals (DAA) is scarce.

Methods: All patients treated with DAA plus RBV at one tertiary hospital in Madrid were examined. ITPA variants rs1127354 and rs6051702 were genotyped by allelic discrimination using real time PCR assays. ITPA genotypes rs1127354 CC and rs6051702 AA were considered as "unfavorables". Data were recorded at baseline and at week 4 of therapy.

Results: A total of 55 individuals initiated DAAs+RBV. HIV coinfection was present in 57%. The most frequent regimen was SOF-LDV+RBV (27; 49%) followed by SOF-DCV+RBV (12; 22%). Most individuals (48, 87.3%) harboured the unfavorable rs1127354CC genotype, whereas 29 (52.7%) carried the unfavorable rs6051702AA genotype. Of note, all patients with rs6051702AA had rs1127354CC. At baseline, median Hb was 14.8 g/dL. At week 4, median Hb drop was greater in patients with rs1127354CC than those with CA/AA (1.8 vs 0.7 g/dL, respectively; p=0.029). Similarly, patients with rs6051702AA experienced greater median Hb declines than those with AC/CC (2.2 vs 1.06 g/dL, p=0.016). Median Hb drop in patients who exclusively carried rs112354CC did not differ significantly from those with "favorable" ITPA genotypes (1.2 vs 0.7 g/dL; p=0.4). Eleven (20%) patients experienced at week 4 significant Hb drops (reduction >3 g/dl and/or to <10 g/dl). It developed in 39% of patients carrying rs6051702AA versus in none of the rest (p<0.001). There was no significant difference in Hb reductions according to HIV status.

Conclusions: Although both ITPA SNPs are associated with Hb drops in HCV patients treated with RBV, rs6051702AA seems to predict the best the risk of anemia. Baseline testing of this SNP might help to identify the subset of patients at greatest risk for RBV-induced anemia.

No conflict of interest

Abstract: 15

New anti-HCV agents

Testing efficacy of synthesized SiRNA on HCV viral replication in PBMC in-vitro

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Introduction and Aims: HCV infection and its complications are among the leading public health challenges, Sustained virological response of chronic HCV infection have improved recently by the use of DAAs. However, the emergence of drug-resistant variants is expected to be a major problem especially to those relapsers or non-responders. A novel combinatorial small interfering RNA (siRNA) could be a novel triple therapy that could be suitable for genotype 4, so there is a great demand for new therapies with high percentage of viral clearance for genotype 4. HCV was

originally thought to be strictly hepatotropic, but there is mounting evidence that it can also replicate in peripheral blood mononuclear cells (PBMC) from chronically infected HCV patients. These cells represent an extra-hepatic reservoir that can be implicated in virus recurrence and persistence. The patients with HCV RNA in PBMC showed a significantly lower response to therapy that support to be one of the factors influencing response to IFN-therapy. Almost all regions of HCV show potential for siRNA target with relative efficiencies of individual siRNA sequences, So the aim of this study to test the efficacy of SiRNA against HCV-4 replication in PBMC *in-vitro*, in order to introduce an alternative therapeutic option for HCV-4 suitable to eradicate it from its reservoir.

Methods: In the present study, efficacy of synthesized siRNA molecule that target 5′UTR of domain IIIC within IRES of HCV RNA (nt 59–79 from the 5'UTR and nt 109–129 from the core area) to eradicate HCV intra-PBMC in-vitro was tested and compared with traditional IFN/RBV *in vitro* by using both qRT-PCR and western blot. Forty genotype 4 chronic HCV patients who are naïve for any HCV treatment were enrolled and tested for presence of HCV intra-PBMC using qRT-PCR before and after siRNA treatment *in-vitro*.

Results: Our study shows that HCV RNA level significantly absent in PBMC on Day3 post-transfection, and the vitality of cells was up to 95%.

Conclusions: RNA-targeting approach might provide an effective therapeutic option for intra-PBMC HCV infection as we prove its role in HCV eradication in PBMCs 'as extrahepatic reservoir'. We suggest that siRNAs targeting 5'UTR represents a future therapy that could eradicate viral RNA from either hepatic or PBMCs reservoirs and due to that it will potentially cure patients with HCV with no relapsing state.

No conflict of interest

Abstract: 16

New anti-HCV agents

Chronic Hepatitis C Treatment in Monoinfected and HCV/HIV Coinfected Patients with Direct Acting Antivirals

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Background: Several clinical trials have shown similar sustained virological response (SVR) rates in HCV mono and HCV/HIV coinfected patients treated for chronic hepatitis C (HCV) with direct acting antivirals (DAAs).

Aim: Comparison of the response to HCV treatment with DAAs in HCV mono and HCV/HIV coinfected patients in real life setting.

Methods: Prospective study of HCV mono and HCV/HIV coinfected patients treated with DAAs for 12 to 24 weeks. We compared the baseline characteristics and the SRV12 rate using SPSS version 20.0.

Results: Of the 246 patients included, 121 (49.1%) were HCV/HIV coinfected. S The baseline characteristics of both groups are shown in the following table:

	HCV (n=125)	HCV/HIV (n=121)	p
Mean Age (years)	54	46	<0.001
Male	94 (75.2%)	105 (86.8%)	<0.05
Treatment Experienced	55.4%	44.6%	<0.05
Genotype 1	76 (60.8%)	91(81%)	<0.001
Genotype 2	3 (2,4%)	1 (0,8%)	0.33
Genotype 3	33 (26.4%)	8 (6.6%)	<0.001
Genotype 4	13 (10,4%)	14 (11,6%)	0.76

Cirrhosis	63 (50.4%)	64 (52.9%)	0.69
Mean Fibrosis (KPa)	16,9	19,2	0,22
Interleukin 28B – CC	12 (23.1%)	37 (35.9%)	0.10
Mean RNA HCV (UI/mL)	3.610.354	4.708.651	<0.05
Body Mass Index (Kg/m^2)	25.6	22.8	0.69
Sofosbuvir/ledipasvir	114 (91,2%)	108 (89,3%)	0.76

In intention to treat analysis, the global SVR12 rate was 93% in the HCV mono-infected group (seven relapses and two deaths) *vs* 95.0% in the HCV/HIV coinfeted group (three relapses and three deaths), p = 0.46. The rate of SVR12 in G1 was 96% in HCV *vs* 97% in HCV/HIV and in G3 the SVR12 was 90,9% in HCV *vs* 75% in HCV/HIV.

Conclusion: We observed high rates of SVR12 in both HCV mono-infected and HCV/HIV coinfected patients. Mono-infected patients had a higer proportion of treatment experience, genotype 3 infection and non-CC interleukin 28B polymorphism which may account for the slightly lower response rate in this group. HIV coinfection no longer appears to be a negative response factor for HCV treatment.

No conflict of interest

Abstract: 17

New anti-HCV agents

Treatment Of Chronic Hepatitis C with Direct Acting Antivirals in Patients Coinfected with HIV: Results in Real Life Setting

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Background: The new direct acting antivirals (DAAs) for the treatment of chronic hepatitis C (HCV) have shown high rates of SVR12 in clinical trials in HCV/HIV coinfected patients that must now be confirmed in the more complex patients from real life.

Aim: Evaluation of SVR12 in HCV/HIV coinfected patients treated with DAAs.

Methods: Prospective study of HCV/HIV patients treated with DAAs for HCV during a period of 12/24 weeks with an intention to treat analysis. All patients were under antiretroviral therapy. SPSS Version 20.0 was used for statistical analysis.

Results: Of the 121 patients included, 86.8% were male and the mean age was 46 years old. The acquisition of HCV was by intravenous drug use in 93.4%. Overall, 55.4% had received previous HCV treatment and 52.9% were cirrhotic. The most frequent genotype was G1 (81%), followed by G4 (11.6%), G3 (6.6%) and G2 (2%). All patients were receiving HIV treatment: the mean CD4 count was 597/mm^3 and all had undetectable HIV RNA.
Sofosbuvir and ledipasvir ± ribavirin was prescribed in 89.3% of patients. Other regimens were sofosbuvir + ribavirin (5.8%), ombitasvir/paritaprevir/ritonavir + dasabuvir (3.3%) and sofosbuvir + daclatasvir + ribavirin (1.7%).
Overall, 115 patients had SVR12 (95%), three patients relapsed and three patients died (two from complications of advanced liver disease and one of inoperable hepatocellular carcinoma). Patients with G1a had 96.6% SVR12 rate and patients with G1b had a 100% SVR12 rate. SVR12 rates were similar regardless of cirrhosis (92.2% for cirrhotic *vs* 98.2% for non-cirrhotic patients, p=0,125) or previous treatment (92.6% for treatment experienced *vs* 97% for treatment naïve patients, p=0.265).
The most common side effects were headache (17.6%), nausea (13.4%) and fatigue (8.4%). No patient discontinued treatment because of adverse effects.
At the end of treatment, two patients had a slight increase in HIV RNA and a third stopped HIV treatment temporarily. All patients had viral suppression after a short period.

Conclusion: We observed high rates of SVR12 in HCV/HIV coinfected patients treated with new DAAs, in spite of the high percentage of cirrhotic patients (52.9%). There was no association between SVR12 and conventional predictors of HCV treatment response.

No conflict of interest

Abstract: 18

Resistance --- Hepatitis C

Baseline NS5A Resistance Associated Variants (RAVs) Does Not Predict Virological Failure In HCV Genotype 1

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Background: Drug resistance may hamper the complete success of DAA in chronic hepatitis C patients. RAVs present both at baseline (as natural polymorphisms) and after DAA failure may confer reduced DAA susceptibility. This phenomenon is particularly relevant for NS5A inhibitors.

Methods: All HCV genotype 1 infected individuals treated with interferon-free DAA combinations at our institution were examined. Baseline NS5A polymorphisms were analyzed by bulk sequencing. Changes at positions M/L28, P29, Q/R/L30, L31, H/P58, E62, A92 and Y93 were considered as NS5A RAVs. The NS5B region was further sequenced in patients with virological failure.

Results: A total of 45 patients were analyzed (23 G1a and 22 G1b). All but 7 were treated with sofosbuvir with either ledipasvir (73.3%) or daclatasvir (8.9%). Overall, 43 (95.5%) achieved sustained virological response 12 weeks after treatment. At baseline, 8 (34.8%) G1a had RAVs at the NS5A (2 M28L; 1 Q30R; 1 H58L; 4 H58P). They were present in 15 (68.2%) G1b (1 L28V; 3 R30Q; 5 P58H; 1 P58T; 1 Y93H; 1 L28T+R30Q; 2 L28M+R30Q; 1 L28M+R30Q+L31M). Only 2 (4.5%) patients experienced virological failure.
Pt-1. He was coinfected with G1a and HIV, and received sofosbuvir/ledipasvir during only 8 weeks. Baseline HCV-RNA was 6.5 log IU/mL. Despite end-of-treatment virological response, HCV-RNA rebounded to 1,890 IU/mL 4 weeks thereafter. No RAVs were found at baseline neither upon failure.

Pt-2. He was a G1b treated with sofosbuvir+ledipasvir+ribavirin for 12 weeks. Baseline HCV-RNA was 6.3 log IU/mL. He achieved undetectable viremia at week 4 but experienced viral breakthrough by week 12 (139 IU/mL), being HCV-RNA of 89,300 IU/mL 4 weeks after drug discontinuation. He harbored Y93H at baseline that persisted after failure, adding L159F at the NS5B region.

Conclusions: HCV gene polymorphisms associated with resistance to NS5A inhibitors are relatively common in HCV genotype 1 infected individuals (roughly 50% in our series). However, their impact on sustained virological response to sofosbuvir-ledipasvir seems negligible if any. The only exception to this rule could be the presence of Y93H at baseline in patients with high baseline HCV-RNA.

No conflict of interest

Abstract: 20

Treatment issues --- HCV-HIV coinfection

Seroreversion of HCV Antibodies in HIV+ Patients with Acute Hepatitis C Following Sustained Virological Response

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Background: The recognition of epidemics of acute hepatitis C in HIV+ MSM has prompted to recommend periodic screening of HCV antibodies (HCV-Ab) in this population. Early treatment may provide high rates of viral clearance even using peginterferon-ribavirin therapy. Whereas HCV-Ab generally remain detectable for more than a decade in most chronic hepatitis C patients that achieve SVR (Toyoda et al. CID 2005), little is known on HCV-Ab dynamics and persistence in patients cured following acute hepatitis C, either

spontaneously or with antiviral therapy. Moreover, this information is anecdotal in persons with HIV coinfection (García-Costa et al. CID 2009).

Methods: All 2,328 HIV+ individuals attending a large HIV clinic in Madrid during the last decade were examined. Acute hepatitis C was diagnosed based on HCV seroconversion and/or positive serum HCV-RNA in a previous negative individual with compatible symptoms and/or elevated liver enzymes.

Results: A total of 32 cases of acute hepatitis C were diagnosed during the 10-year study period, all in HIV+ MSM. Median age 37 (range 27-55) years-old. Syphilis was concomitantly diagnosed in 13 (40.6%). Most subjects were on antiretroviral therapy, had undetectable plasma HIV-RNA and CD4 counts >350 cells/mm^3. HCV genotypes 1a and 4 were recognized in most subjects (36% and 51%, respectively). All but one depicted HCV-RNA+/HCV-Ab+. One individual with isolated HCV-RNA at presentation became HCV seroreactive one month later. Peginterferon-ribavirin was given for 24 weeks to 17 acute hepatitis C patients, of whom 15 (89%) achieved SVR. Median time for therapy onset was 14 (range 4-32) weeks. Of the remaining 17 untreated patients, 4 achieved spontaneous HCV clearance at weeks 6, 8, 16 and 144 since diagnosis.
At last control, serum HCV-Ab were tested in this population using a commercial EIA HCV-Ab assay (Abbott). HCV-Ab seroreactivity persisted in all but 3 individuals, being achieved the latest SVR with antiviral therapy after a median of 49 (38-95) months.

Conclusion: Seroreversion for HCV-Ab seems to be very rare. It may occur following acute hepatitis C in some HIV+ subjects that cure the infection with antiviral therapy but not in those that clear the virus spontaneously. Thus, any suspicion of HCV re-infection should be based on HCV-RNA or HCV antigen testing.

	No.	Median follow-up (months)	HCV-Ab seroreversion
Progression to chronicity	13	57	0
Spontaneous clearance	4	49	0
SVR with antiviral therapy	15	34	3

No conflict of interest

Abstract: 21

Treatment issues --- HCV-HIV coinfection

High serum HCV-RNA in chronic hepatitis C patients coinfected with HIV despite successful antiretroviral therapy

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Background: Baseline serum HCV-RNA predicts treatment success in chronic hepatitis C patients. Thresholds at 0.8, 2, 4 and 6 million IU/mL discriminate treatment outcomes using distinct antiviral regimens. Compared to the general population, immunosuppressed individuals exhibit greater viral load values. This has been confirmed in HIV-HCV coinfected patients, although little is known about the influence of antiretroviral therapy.

Methods: Serum HCV-RNA results recorded from all chronic hepatitis C patients consecutively attended at our clinic were analyzed.

Results: A total of 813 patients with detectable HCV-RNA were identified. HIV coinfection was present in 78.7%, of whom 91% were on antiretroviral therapy. Overall, 467 (57%), 273 (34%), 170 (21%) and 127 (16%) had HCV-RNA >0.8, >2, >4 and >6 million IU/mL, respectively. These high viral load values were found in 60%/36%/23%/18% of HIV-positive versus 43%/25%/11%/6% of HIV-negatives ($p<0.01$). In multivariate analysis, the greatest HCV-RNA values were only significantly associated with HIV coinfection and HCV genotypes 1 or 4. Greater HCV-RNA values were found in HIV patients on than off antiretroviral therapy.

Conclusion: Serum HCV-RNA values above 0.8, 2, 4 and 6 million IU/mL are roughly seen in 43%, 25%, 11% and 6% of chronic hepatitis C monoinfected patients, respectively. The corresponding figures are 1.3 to 3.0-fold greater in HIV-HCV coinfected patients, who may benefit less frequently from shorter oral HCV treatment lengths.

No conflict of interest

Abstract: 22

Treatment issues --- HCV-HIV coinfection

Evolution of CD4 Cell Count During Treatment of Chronic Hepatitis C with Direct Acting Antivirals (DAAs) in HCV/HIV Coinfected Patients

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Background: Treatment of chronic hepatitis C (HCV) with interferon based regimens was associated with a decrease in the CD4 cell count of HCV/HIV coinfected patients. Lower CD4 counts are associated with faster liver fibrosis.

Aim: To assess CD4 count evolution during HCV treatment with DAAs in HCV/HIV coinfected patients.

Methods: Prospective study of HCV/HIV coinfected patients treated with DAAs for chronic hepatitis C. CD4 cell counts at baseline and 12 weeks after treatment were compared. The patients were randomized based on CD4 count lower or equal and higher than 350CD4/mm^3.

Results: We included 105 patients: 92.4% were male, the mean age was 46 years old and the acquisition of HCV was by intravenous drug use in 94.3%. The most frequent genotype was G1 (81.9%), followed by G4 (12.4%), G3 (4.8%) and G2 (1%). Overall, 43.8% were treatment experienced. Mean value of fibrosis was 19.2KPa and 53.3% of patients were cirrhotic. All patients were receiving antirretroviral treatment and all had undetectable HIV RNA. The mean CD4 count was 601/mm^3. Of the patients with <350CD4/mm^3, 77% were cirrhotic. Sofosbuvir and ledipasvir ± ribavirin was prescribed in 90.5% of patients. Other regimens were sofosbuvir + ribavirin (4.8%), ombitasvir/paritaprevir/ritonavir + dasabuvir (3.8%) and sofosbuvir + daclatasvir + ribavirin (1.0%). The SVR12 rate was 98.1% (two patients relapsed).
The evolution of the CD4 count during treatment is shown on the following table:

	Mean Baseline CD4 Cell Count (mm^3)	Mean 12 Week After Treatment CD4 Cell Count (mm^3)	p
Total (n=105)	601	635	0.07
≤350CD4/mm^3 (n=23)	232	312	<0.05
>350CD4/mm^3 (n=82)	705	725	0.37

Conclusion: There is a global increase in the mean CD4 cell count after HCV treatment. The increase is greater in patients with less than 350 CD4 cells/mm^3 possibly due to the high proportion of cirrhotic patients (77%) in this group.

No conflict of interest

Abstract: 23

Treatment issues --- HCV-HIV coinfection

Electrical heart safety of sofosbuvir-based anti-HCV regimens in a cohort of HIV/HCV co-infected individuals.

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Background. Sofosbuvir (SOF) is generally well tolerated: no major serious adverse events emerged during clinical trials. Recently, a warning was raised about co-administration with amiodarone because of serious electrical heart adverse events, but its pathophysiology has not been established. HIV-infected patients are at increased risk of cardiovascular events and some antiretroviral drugs, such as atazanavir (ATV) and rilpivirine (RPV), have a not-negligible risk of QTc interval prolongation. The present study assessed QTc trend over treatment according to different antiretroviral (HAART) regimens and severity of liver disease.

Material & Methods. QTc corrected according to Bazett was assessed in patients treated with SOF-based regimens at baseline, after 1 and 4 weeks and at the end of therapy. Heart and general adverse events were collected. Descriptive statistics and non-parametric Kruskal-Wallis test were used.

Results. 49 HIV/HCV co-infected patients (males 74%, median age 52 years) were treated with different SOF-based regimens (20% only with SOF, 47% in combination with daclatasvir, 14% with simeprevir, 19% with ledipasvir,); 92% received also ribavirin. The majority was infected by genotype 3 (39%) and 1a (27%); 75% was cirrhotic (Child-Pough class A 87%, class B 8%, class C 5%; median MELD score was 8). All patients were HAART-experienced: 12% of them was receiving RPV and 22% ATV (either ritonavir-boosted or unboosted); 16.3% was taking also other drugs active on QTc interval such as methadone. Median baseline cardiovascular risk assessed with Framingham score was 11.2% (moderate risk).
In the overall analysis, QTc interval did not change sigificantly over treatment (p=0.14). Patients receiving RPV or ATV showed a median increase of 12 msec at week 4, but such difference was not significant (p=0.18), while no changes were observed with the other HAART regimens. Stratifying according to the liver disease severity, no changes were observed in F3 subjects, while in Child-Pough class A individuals there was an increase of 8,5 msec at week 4 (p<0.001). No major heart events and no QTc values above 500 msec were recorded; 2 patients developed asymptomatic extra-systolic rhythm at week 1 without QTc changes. Four patients discontinued ATV at week 1 because of jaundice; one patient stopped anti-HCV treatment because of hepatocellular carcinoma progression and was directed to palliative care.

Discussion. This analysis showed an increase of QTc from baseline to week 4, but this trend was generally not significant except for patients with class A cirrhosis (no strong conclusions could be drawn for patients in class B/C because of small sample size). No serious heart events were observed in this cohort of subjects at increased risk of cardiovascular events, even though rare rhythm abnormalities with undefined clinical significance were observed. Therefore, SOF-based regimens might need an electrocardiographic assessment in cirrhotic patients irrespective of HAART regimen.

No conflict of interest

Abstract: 24

Treatment issues --- HCV-HIV coinfection

Directly acting agents (DAA) against HCV, results from our coinfected patients one year after availability in clinical practice.

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Background: DAA against HCV have meant a revolution in chronic HCV hepatitis management, as we aim to eradicate the virus nowadays. After the clinical essays, we have to evaluate the AAD effectivity in our patients in real clinical practice.

Materials & Methods: Analysis of our 102 co-infected patients (HIV/HCV) who started treatment during the first year of availability of the DAA (17/2/15-17/2/16) at our hospital. Description of baseline parameters (age, sex, fibroscan® -kP and degree of fibrosis–,MELD score, CD4 count and HIV-viral load [VL], HCV

VL and genotype) with mean (M) medium (med) and deviation standard (SD) /interquartile range (IQR) for quantitative variables and count and percentage in qualitative ones. Ratio of each regime of AAD, and percentage of undetectable HCV VL at the 4th, 8th and 12th weeks of treatment; 'end of treatment' (EOT) rate, and sustained virological response at week 12 (SVR12) rate in those patients who have completed 3 months since the end of the treatment. We measured the rate of adverse effects (AE) and the number of treatment discontinuations because of them. SPSS22.

Results: 102 patients. M Age 50 years (SD-0,636); 80 males (78.4%); Fibroscan: med 8.65kPa (SD8.5) that determines F≤2 in 58 (57%); F2 in 28(28%) and F>2 in 44(43%). Med MELD of 6.5 points (2); med CD4 count: 664cel/ml (515); undetectable VIH VL in 87%. HCV genotype: G1a 46(45%), G1b 16(16%), G3 14(14%), G4 25(24%), G1+4 1(1%). Med HCV VL in log of 6.13 cop/ml (SD 6.76). Treatment with Simeprevir (SIM) in 5(5%); with SIM/sofosbuvir (SOF) in 3(3%), with 3D in 21(21%), with 2D in 9(9%), with SOF/ledipasvir (LDP) in 52(51%), and SOF/Daclatasvir (DAC) in 12(12%). Undetectable HCV VL at 4th week in 57/87 patients (65.5%); at 8th week in 69/77(89,6%); EOT response in 71/71 (100%) and SVR12 in 38/40 (95%). AE reported in 34/78 (43.6%), quitting the treatment 2 of the patients.

Conclusions: Our patients' are on average 50 years old and are mostly males. They have significant fibrosis in more than 40% and cirrhosis in nearly one-third of them; nevertheless they still do not have a very advanced MELD score with few cases of advanced liver disease (one patient with 20 points in MELD score, the others less than 15). Inmunovirological HIV control is achieved in most of patients during the HCV treatment.
Despite having data only from 40% of patients, we already have SVR12 rates of 95%, similar to that of clinical trials and studies in real life. We have initially treated the most complex patients (more advanced liver disease), with some treatments which are not considered as eligible anymore (as they were the ones available at the time). As we complete the current treatments (in patients with a lower degree of liver disease) we expect that the SVR12 rate will improve even more. The EA are common, only being serious in a timely manner.

No conflict of interest

Abstract: 25

Treatment issues --- HCV-HIV coinfection

Analysis of the drug-drug interactions (DDI) between directly acting agents (DAA) against HCV and antiretroviral treatment (ART) in our clinical practice.

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Objectives: HIV/HCV-coinfected patients are a complicated group due to DDIs; data are limited to the permitted combinations in clinical assays, with little information in 'real life'. Our study aims to assess the frequency and impact of these DDIs in clinical practice.

Methods and Materials: Coinfected patients starting AAD during the first year of availability at our hospital. We describe the HCV-characteristics, the prior ART to prescribe the AADs, the AADs used and the DDIs analysis (according to the 'University of Liverpool DDI tool' available online: category 1 (C1) without DDI;C2: Potential DDI; C3: contraindicated coadministration; C4: no data). We describe changes on ART to avoid DDIs, and the HIV-RNA evolution at the end of treatment. Analysis by SPSS22

Results: 102 patients; Fibrosis: F≤2 in 58 (57%), F3-4 in 44 (43%). HCV-genotype: G1a-46(45%),G1b-16(16%), G3-14(14%), G4-25(24%), G1+4-1(1%). 97 patients were on TAR, 59 with a TDF-FTC/ABC-3TC backbone plus a third agent, 18 on monotherapy (IP/r), 7 on bitherapy, 13 with other combinations.
We foresaw C3 DDIs in the 5 patients on Simeprevir (SIM); 20 DDIs (9 C2, 11 C3)in 21 patients with 3D; in 9 with 2D, 9 DDIs (5 C2, 4 C3); 55 on Sofosbuvir (SOF)-Ledipasvir (LDV), 12 DDIs (9 C2, 3 C3); and in the 12 with SOF/Daclatasvir we foresaw 9 DDIs (C2). ART was switched in 37 patients, 22 (60%) because of C3 DDIs, 13 (35%) because of C2 DDIs and 2(5%) without DDIs. 23 of 37 switches were made to avoid DDIs with NNRTI; 5 with a PI; and 4 with an INSTI.

27 patients who change the ART and have completed DDA treatment haven't showed any HIV-virological failure.

Conclusions: We have foreseen DDIs in half of the patients, of which 50% were because of contraindicated coadministration, specially with NNRTI and some PI when combined with SIM, 3D or 2D. Severe DDIs have been avoided by modifying the ART and switching has been safe.

No conflict of interest

Abstract: 26

Treatment issues --- HCV-HIV coinfection

Improving results of sofosbvir based HCV treatment in PWID population co-infected with HIV/HCV in Ukraine

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Introduction: HCV/HIV co-infection is registered in 38,4% of all newly detected HIV cases in Ukraine. HCV prevalence among PWID in Ukraine exceeds average international rates, reaching 71%. Among OST patients HCV rates are 56% and HIV– 42%. Introduction of sofosbuvir based treatment regimens should improve treatment outcomes for HIV/HCV co-infected PWID.

Materials & Methods: 87 patients (99% co-infection HIV/HCV) have initiated treatment with combination of sofosbuvir, peg interferon and ribavirin respectively to genotype within June-September 2015. Multidisciplinary approach was applied in order to achieve high retention rate. On the monthly basis clinical monitoring was established which enabled to obtain the data on main treatment indicators at baseline, 2, 4, 12, 24 weeks of treatment, end-of treatment results and 12 weeks after end-of-treatment response.

Results: Patients cohort consists of 80% of male, median age 37 yr. (range 24 - 61). Experience of drug use: 5% are active users, 7% have remission less than 6 month, 10% have less than year remission, 77% over 1 year, 7% OST (methadone and buprenorphine) patients. ARV treatment is receiving 97 %. Genotypes distribution is 41% (G1), 14% (G2), 45% (G3). SVR 12w among PWID cohort is achieved on 91%. Among naïve patients SVR 12 W is 89% and for treatment-experienced patients it is 81%.The
highest SVR was achieved in naïve patients with G3 – 100%.

Conclusions: Sofosbuvir in combination with peg-interferon and ribavirin showed high cure rates among HIV/HCV co-infected population of PWID within the multidisciplinary treatment model. High SVR rates among HIV/HCV co-infected patients can be reached by applying of combination of effective HCV treatment regimens with sofosbuvir and multidisciplinary treatment model with enhanced social support.

No conflict of interest

Abstract: 27

Treatment issues --- HCV-HIV coinfection

Sofosbuvir-based treatment in HCV/HIV co-infected patients: A "real-life" experience in an infectious diseases department

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Background and Aims: The prevalence of HCV infection is high among HIV-infected patients, since both virus share the same routes of transmission. Co-infection, even under antiretroviral therapy (ART), increases the overall risk of progression to cirrhosis and hepatocellular carcinoma.

The new HCV direct-acting antivirals (DAAs) created a new paradigm in the treatment of the infection, with high rates of efficacy and safety in clinical trials.
The aim of this study was to evaluate the efficacy and safety of sofosbuvir (SOF)-containing regimens in HCV/HIV co-infected patients, in a real-life setting.

Methods: An observational study was conducted in an Infectious Diseases department including all co-infected patients who started a SOF-containing regimen, with ledipasvir (LDV) and/or ribavirin (RBV), between January 1st and December 15th 2015. Data on demographic, clinical and virological features was collected until March 15th 2016.

Results: In total, 225 patients, 166 (74%) male, 59 (26%) female, were included. The genotype (Gt) pattern was: Gt1 n=150 (67%), Gt2 n=4 (2%), Gt3 n=32 (14%), Gt4 n=39 (17%). Liver cirrhosis was present in 18% of the patients (40/225). Three SOF-containing regimens were used: SOF/LDV Gt 1 65% (146/225), Gt4 17% (39/225); SOF/RBV Gt2 2% (4/225), Gt3 7% (16/225); SOF/LDV + RBV Gt1 2% (4/225), Gt3 7% (16/225).
Sustained virological response 12 weeks after treatment completion (SVR12) was evaluated in 138 patients who reached this phase of treatment. Non-cirrhotic patients: Gt1 100% (83/83), Gt2 67% (2/3), Gt3 100% (9/9), Gt4 94% (17/18). Cirrhotic patients: compensated (Child-Pugh A) – Gt1 100% (12/12), Gt4 80% (4/5); decompensated (Child-Pugh B) – Gt1 100% (7/7), Gt4 0% (0/1).
Twenty-one patients reached 24 weeks after treatment completion. All but one had SVR24. Five patients failed to achieve an SVR, 3 were naïve and non-cirrhotic and 2 were treatment experienced and had cirrhosis, Child-Pugh A and B, respectively.
APRI score was available in 81 patients. The average of APRI score was 1,26 before treatment; 0,51 after 12 weeks of treatment and 0,49 at SVR12.
Treatment was overall well tolerated and no treatment discontinuations were reported. 89 (40%) patients reported at least 1 adverse event (AE). The most common AEs were asthenia (39%) and headache (31%). Proximal renal tubulopathy was observed in 4 patients, resulting in changes on ART regimens. Hyperbilirubinemia was reported in 10% of patients.

Conclusions: SOF-containing regimens are highly efficient and fairly tolerated in HCV/HIV co-infected patients. In our study, 61% (138/225) of the patients reached 12 weeks after treatment completion. Of these, 97% (134/138) achieved an SVR12.

No conflict of interest

Abstract: 28

Treatment issues --- HCV-HIV coinfection

Treatment of chronic HCV infection with DAA in co-infected HIV patients: a real life setting Portuguese experience

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Introdution: The treatment paradigm of chronic HCV infection has recently changed to the use of all oral interferon free regimens. Unfortunately, direct antiviral agents (DAA) widespread use is not uniform in all clinical settings, namely in Europe. Since early 2015, Portugal is living an advantageous opportunity allowing the use of reimbursed DAA regimens, that includes sofosbuvir (SOF) or sofosbuvir/ ledipasvir (SOF/LDP)coformulation, with or without ribavirin (RBV). HIV coinfection is considered a priority to engage HCV treatment.

Material and methods: At our Infectious Diseases Center, since 1st January 2015 until late February 2016, 238 HCV/HIV coinfected patients started treatment with a DAA based regimens. Epidemiological, demographic, clinical, laboratorial and therapeutic data was collected.

Results: Our cohort presents a male predominance of 77%, mean age of 47 years old and Portuguese origin in 92%. Mean time since HCV diagnosis was 15 years and the vast majority presumably acquired infcetion by intravenous drug use. Genotype distribution showed: 50% G1a; 13% G1b; 1,3% G2; 15% G3 and 21% G4. IL28B gene polymorphism was available for 94% of the study population revealing CT predominance (49%).
Hepatic fibrosis evaluation was performed by real time elastography in all patients showing the following distribution (METAVIR): F1 0,4%; F2 40%; F3 48% and F4 13%. Mean HCV plasma RNA was 3.339.480 UI/mL and only 16% presented with baseline values above 6 MIU/mL. Most patients (63%) were naïve for HCV treatment and 99% were on antiretroviral therapy. Mean TCD4 count at baseline was 649 cel/mm^3 and 88% had undetectable plasma HIV RNA.
DAA regimens more often prescribed were SOF/LDP (79%) and SOF/RBV (16%). Until late February, 38% of patients completed treatment and 20% were evaluated at 12 weeks after treatment completion. Sustained virologic response at week 12 was confirmed in 99% of patients and 2 patients relapsed. Death was notified in one of the relapse cases, a patient that developed sudden hepatic carcinoma. Mean TCD4 count after HCV treatment evidenced no significant change (666 cel/mm^3). Adverse events were reported by 29% of patients but in any case led to treatment interruption.

Conclusion: High treatment response rates corroborates the present clinical and scientific enthusiasm. New standard of care and predictive factors need to be defined to optimize the best use of available resources.

No conflict of interest

Abstract: 29

Treatment issues --- HCV-HIV coinfection

Treatment of chronic HCV genotype 3 infection in a Portugueses clinical cohort of co-infected HIV patients: is sofosbuvir and ribavirin enough ?

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Introduction: Recent use of new direct antiviral agents (DAA) for the treatment of HCV chronic infection has defined new difficult to treat population groups that includes genotype 3 infected patients. Besides, HIV coinfection is considered a priority to engage HCV treatment related to the faster progression of liver disease. DAA widespread use is not uniform in all clinical settings, namely in Europe. Since early 2015, Portugal is living an advantageous opportunity allowing the use of reimbursed DAA regimens, that includes sofosbuvir (SOF) or sofosbuvir/ ledipasvir (SOF/LDP) coformulation, with or without ribavirin (RBV).

Material and methods: At our Infectious Diseases Center, since 1st January 2015 until late February 2016, 36 HIV/HCV genotype 3 coinfected patients started treatment with SOF/RBV for 24 weeks. Epidemiological, demographic, clinical, laboratorial and therapeutic data were collected.

Results: All patients were born in Portugal, showing a male predominance (78%) and a mean age of 47 years old. Mean time since HCV diagnosis was 12,5 years and 83% presumably acquired infection by intravenous illicit substance use in the past. IL28B gene polymorphism was performed in 97% of patients, revealing CC genotype in 66%. Hepatic fibrosis was evaluated by real time

elastography in all patients showing the following distribution (METAVIR): F2 44%; F3 50% and F4 6%. Eighteen patients evidenced F3, 61% with APRI score above 0,7 cutt off and 28% with FIB4 score above 3,25, concordant data with advanced fibrosis. Mean baseline HCV plasma RNA was 4.203.657 IU/ml and 25% presented more than 6 MIU/mL. The vast majority was naïve for HCV treatment (86%) and all were on antiretroviral therapy, showing a mean baseline TCD4 count of 530 cel/mm^3 and undetectable plasma HIV RNA in 89%. Adverse events were reported by 31% of patient but did not lead to treatment discontinuation. Until present time, 42% of patients completed treatment with SOF/RBV and 14% were evaluated at 12 weeks after treatment completion, revealing a preliminary sustained virologic response rate (SVR12) of 100%.

Conclusion: As clinical real life setting data is becoming available new predictive response factors should be determined, especially directed to those considered as difficult to manage patients, enabling the profitability of existing resources.

No conflict of interest

Abstract: 30

Treatment issues --- HCV-HIV coinfection

End-of-treatment HCV negativization following direct-acting antivirals (DAAS) leads to the expansion of CD8/CD127+ T-cells in a cohort of HIV/HCV patients

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Introduction: Recent studies have shown a positive role of DAAs in the recovery of innate immunity but little is known on their role on T-cell immunity. We investigated the impact of HCV elimination with DAA in the reconstitution of T-cell phenotype in a cohort of HCV/HIV patients (pts).

Materials and Methods: We enrolled 16 HIV/HCV cART-treated pts with HIV-RNA<40cp/ml who underwent a complete 12 weeks-course of IFN-free DAA. Pts were stratified according to HCV-genotype,cirrhosis and anti-HCV regimen (sofosbuvir/simeprevir–SOF/SIM vs paritaprevir/r-ombitasvir-dasabuvir-3D).We evaluated CD4/CD8 frequency, activation(CD38), differentiation (CD127) and naive/memory markers (CD45RA/RO) on peripheral blood by flow cytometry before (BL) and at the end of anti-HCV therapy (EoT). Statistical analyses: Mann-Whitney, Wilcoxon,Spearman tests. Cirrhosis were defined by transient elastography (FibroScan).

Results: Median CD4 T-cell count at BL was of 547 cell/mmc (IQR 488-679). HCV genotypes displayed were 1 and 4 (11 vs 5 pts),with only 5 pts showing liver cirrhosis. Pts underwent DAA with 3D (8),SOF/SIM (7) or LDV/SOF (1). Following anti-HCV therapy all 16 pts achieved EoT response (undetectable HCV-RNA) and a significant reduction of transaminases compared to BL(AST, p=0.0005; ALT, p=<0.0001).Interestingly we found a significant expansion of CD8 frequency (p=0.007),with an increase in CD127 expression on CD8 (p=0.03) at EoT. Furthermore CD8 exhibited a trend towards higher CD45RO+ expression (p=0.053),whereas no differences in frequency of CD45+CD8+/CD4+ naïve cells were found at EoT. No significant loss of activated CD38 and CD38/RO+CD8 was shown following DAA (p=0.5) despite HCV elimination. In detail, we found a BL to EoT raise of CD8 frequency in both cirrhotic and non-cirrhotic pts (p=0.052 vs p=0.057) but no significant increase of CD8/CD127 according to cirrhosis. Pts who underwent SOF/SIM showed an higher expansion of CD8 (p=0.03) and a trend towards higher CD8/CD127 frequency compared to those who underwent 3D(p=0.09 vs p=0.48); finally,no differences in T-cell phenotype were found according to genotype.

Conclusions: DAA-mediated EoT HCV negativization is associated with an increase of CD8 proportion,especially due to an expansion of CD8 expressing CD127 allowing to speculate a possible role of DAA in recovering T-cell antiviral response even in the context of HIV coinfection.

No conflict of interest

Abstract: 31

Treatment issues --- HCV-HIV coinfection

Efficacy and renal safety of sofosbuvir-based regimens in HIV/HCV-coinfected patients - experience from a portuguese center

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Introduction: Sofosbuvir have become of upmost importance when designing regimens for Hepatits C treatment. If before concerns about efficacy dominated physicians' attention, today we focus much of our attention in the side effects and drug-drug interactions, especially in the co-infected population.

Materials & Methods: Retrospective analysis of clinical data from HIV/HCV co-infected patients that have completed HCV treatment with a Sofosbuvir containing regimen and that have at least a 12 week follow-up after completion of the treatment.

Results: From a total of 120 patients in whom Sofosbuvir containing regimens have been prescribed, 92 (76,7%) have completed treatment and 78 (65%) have at least a 12 week follow-up.
From the total, 84,6% were male, with a median age of 47 years old [33 – 77]. Genotype 1 was the most prevalent (78,2%), mainly genotype 1a (65,4%), followed by genotype 4 (14,1%), genotype 3 (6,4%) and genotype 2 (1,3%). Median RNA HCV was 6 921 128 UI/ml [1236 – 229 466 791]. Regarding fibrosis (transient elastography), 42,3% had absent-to-mild fibrosis and 30,8% had cirrhosis. In the cirrhotic group, average fibrosis was 27,9 kPa. The majority of the patients were naïve for HCV therapy (57,7%). Sofosbuvir/Ledipasvir 12 weeks was the most common regimen used (75,6%) and Ribavirin was prescribed in 18,6%. The median T $CD4^+$ cell count was of 550 cells/mm^3. From those under HAART, 89,5% had HIV viral load undetectable. The regimens were: 44,7% NRTI + PI; 35,5% NRTI + NNRTI; 10,5% NRTI + II. In 18,4% patients, a switch in the HAART regimen was done. In these an II was the drug of choice, in patients previously under a PI or a NNRTI based regimen (64,3%). After HCV therapy, 2 patients were lost for follow-up, 1 was dead and only one patient (1,3%) relapsed (he is HBV co-infected with stage F3 10 kPa).
Regarding adverse events, there was a significant decrease in haemoglobin levels in 3 patients, all of them with advanced fibrosis. Other important issue was the decrease in renal function (by one stage) in 23,1% of the patients. From those, 38,9% had advanced fibrosis. All but one had a FTC/TDF based regimen. Three patients had their HAART regimens changed during HCV treatment. In those whom ribavirin was prescribed, 22,2% also experienced a one-grade reduction in renal function. Before HCV treatment was initiated, 56,2% of the patients had stage 1 kidney function and none patient was classified as stage 3b. By the end of treatment, only 48% remained at stage 1, 8,2% at stage 3a and 2,7% achieved the 3b stage.

Conclusions: Sofosbuvir containing regimens are effective and safe in most patients. However, special attention should be given to those with advanced fibrosis, with regimens including TDF or a diminished renal function, which apparently are in a greater risk of developing complications during treatment. Further analysis is warranted in order to understand if those changes are transient during treatment or represent long-lasting complications.

No conflict of interest

Abstract: 32

Treatment issues --- HCV-HIV coinfection

Safety and effectiveness of Sofosbuvir/Ledispavir ± Ribavirin in HIV/HCV co-infected patients. A real life experience.

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Objective: We assessed safety and effectiveness of combination with a single tablet regimen including SOF/LDV ± RBV in HIV/HCV$^+$ subjects in clinical practice.

Methods: This is a retrospective analysis by intention to treat whose primary objective is the assessment the sustained viral response in HIV/HCV$^+$ patients. We included all the subjects who were treated with SOF/LDV ± RBV in our hospital from April to December 2015.

Results: 94 subjects were included: 74,5% male; median age: 50,6 (±6,4 years); 33% with prior anti-HCV therapy (telaprevir n=2, simeprevir n=3). 34% with cirrhosis (Child-Pugh score A: n=29 and Child-Pugh score B: n=3). Median baseline HCV RNA $\log_{10}$ UI/mL was 4,5 (±3,3); 62% genotype-1a; 27% genotype-4; 10% genotype-1b and 1% genotype-3. Median baseline CD4 cell counts was 544 (±358) and 96% with plasma HIV-RNA<50 copies/mL. 42,5% had to change prior ART (PI/r n=30, NNRTI=6). Others comorbidities: 34% psychiatric disorders, 7% cardiovascular disorders, 4% chronic obstructive pulmonary disease (COPD), 3% diabetes type-2 and 10% were taking methadone. Duration of therapy was 12 weeks for 66% of the subjects and 24 weeks for the rest of them, and only 11 individuals were treated with RBV. No significant differences were found between the different groups of treatment in terms of baseline characteristics. The most common adverse events were grade 1-2: asthenia 7,4%; headache 6,3%, anemia 3,2%, sickness/vomiting 1% and pruritus 1%. Of the 94 subjects included, only 67 individuals ended the study (71,3%), one patient died due to COPD and two patients dropped out before ending the therapy. Of the 67 individuals who ended the study, 65 showed sustained viral response (93%) and only 2 patients failed (3%).

Conclusions: The SOF/LDV ± RBV combination in HIV/HCV+ subjects with genotype 1 and 4 show a high efficiency. The safety of treatment was also high; there were no discontinuations due to toxicity.

No conflict of interest

Abstract: 33

Treatment issues --- HCV-HIV coinfection

Simeprevir and Sofosbuvir with modified doses of Ribavirin therapy on Telaprevir experienced Co infected (with HIV) cirrhotics with chronic hepatitis C: STOP C

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Background: Cirrhotics with CHC still remains a challenge. Co-infected cirrhotics (HIV+CHC) are at a greater risk for rapid decompensation affecting QOL and have a higher transplant risk burden. Interferon based therapy entails a longer duration with an increased susceptibility of infections and marrow suppression warranting use of growth factors and even discontinuation of therapy/treatment failure. Telaprevir; a protease inhibitor (PI) based therapy have proved efficacious in co-infected patients. Newer generation PI coupled with polymerase inhibitors and adjusted doses of RBV have shown favorable outcomes.

Aim: To evaluate the efficacy of Simeprevir, Sofosbuvir with RBV in prior Telaprevir experienced co-infected cirrhotics.

Methods: Fifty (n=50) co-infected (HIV+CHC, non AIDS) cirrhotics with mean MELD 16, HIV RNA undetectable, mean CD 4 count 439, Hb 10.7, HCV RNA 1.7 million copies, mean platelet count 104, albumin 2.9 and WBC 4600. 18 genotype 1a and 32 genotype 1b. Exclusion criteria: HBV, decompensated cirrhosis, hemolytic disease, heart failure, AIDS, Alcohol consumption > 30 gms/day, CrCl <50%, uncontrolled diabetes, portal hypertension, Patients on any herbal medications.

Group A: Simeprevir 150 mg + Sofosbuvir 400 mg + RBV for 24 weeks
Group B: Simeprevir 150 mg + Sofosbuvir 400 mg + RBV 1000 mg for 16 weeks

Results:

	GROUP A (n=22)	**GROUP B (n=28)**
48 hours	2/22 (9%) 4 log 11/22(50%)	4/28 (14%) 4 log 19/28
1 week	3/22 (14%) 6 log 8/22 (36%)	(68%)
4 weeks	16/22 (73%)	7/28 (25%) 6 log 22/28
8 weeks	17/22 (77%)	(78%)
12 weeks	17/22 (77%)	19/28 (68%)
16 weeks	17/22 (77%)	22/28 (78%)
24 weeks	18/22 (83%)	23/28 (82%)
40 weeks	18/22 (83%)	23/28 (82%)
		23/28 (82%)

Conclusion: The combination of Interferon free regimen in special population with prior experienced PI demonstrated no difference of SVR in 16th week over 24th weeks. Group A- 83% compared to Group B- 82% responders were noted. This regimen was well tolerated and has a better safety profile than conventional trials.

No conflict of interest

Author	Abstract Title	Abst#	
Badia, L.	Daclatasvir + Sofosbuvir +/- Ribavirin in HIV/HCV co-infected patients with advanced liver disease: preliminary data from the Italian Compassionate Use Program	O_05	6
Basu, P.	Simeprevir and Sofosbuvir with modified doses of Ribavirin therapy on Telaprevir experienced Co infected (with HIV) cirrhotics with chronic hepatitis C: STOP C	P_33	27
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Bruno, R.	The role of Presepsin (sCD14-ST) as an indirect marker of immune activation in HIV and HCV infections and in HIV/HCV co-infection	P_08	9
Cerrone, M.	End-of-treatment HCV negativization following direct-acting antivirals (DAAS) leads to the expansion of CD8/CD127+ T-cells in a cohort of HIV/HCV patients	P_30	25
Chen, A.	Treatment of Patients with Hepatitis B or C May Reactivate Suppressed Hepatitis B or C Coinfection Risking Decompensation	P_12	12
Filippovych, S.	Improving results of sofosbuvir based HCV treatment in PWID population co-infected with HIV/HCV in Ukraine	P_26	22
Garcia Fraile Fraile, L.	Directly acting agents (DAA) against HCV, results from our coinfected patients one year after availability in clinical practice.	P_24	20
Garcia Fraile Fraile, L.	Analysis of the drug-drug interactions (DDI) between directly acting agents (DAA) against HCV and antiretroviral treatment (ART) in our clinical practice.	P_25	21
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Miranda, A.	Treatment of chronic HCV genotype 3 infection in a Portugueses clinical cohort of co-infected HIV patients: is sofosbuvir and ribavirin enough ?	P_29	24
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Pal, A.	High incidence of lamivudine-resistant HBV mutants and presence of liver damages in HIV-positive eastern Indian patients harbouring HBV/D2 strains	P_10	10
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Ribeiro, A.	Efficacy and renal safety of sofosbuvir-based regimens in HIV/HCV-coinfected patients - experience from a portuguese center	P_31	26
Rodríguez-Da Silva, A.	Safety and effectiveness of Sofosbuvir/Ledispavir ± Ribavirin in HIV/HCV co-infected patients. A real life experience.	P_32	27
Rossotti, R.	Electrical heart safety of sofosbuvir-based anti-HCV regimens in a cohort of HIV/HCV co-infected individuals.	P_23	19
Roy, T.	Hepatitis B and C viral infections in people who are at risk for, and living with, HIV in Bangladesh: prevalence and behavioral risk factors	P_11	11

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Sarpel, D.	Sustained virologic response in chronic HCV infected patients is associated with weight gain and decrease in controlled attenuation parameter (CAP).	P_07	8
Soeiro, C.	Hepatic Fibrosis 12 Weeks After the End of Treatment with Direct Acting Antivirals (DAAs) in HCV/HIV Coinfected Patients	P_09	9
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