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ABSTRACT BOOK

I National Conference of the Group for the Study of Viral Hepatitis (GEHEP) of SEIMC

24-26 September 2015, Vigo, Spain

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24-26 September 2015, Vigo, Spain

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Valid suport

Presentation for registration no. 0336E/329/2015 - 13/01/2015
Generalitat de Catalunya, Health Department (Gran Via), Barcelona, Spain.

Oral Presentations

OR-01 **A single tablet regimen of ledipasvir/sofosbuvir for 12 weeks in HCV genotype 1 or 4 infected patients with HIV-1 co-infection: The phase 3 ION-4 study**

Luis Enrique Morano¹, Curtis Cooper², Susanna Naggie³, Michael Saag⁴, María Sainz⁵, Jenny Yang⁶, Luisa Stamm⁶, Philip Pang⁶, John Mchutchison⁶, Douglas Dieterich⁷, Mark Sulkowski⁸.

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Background & Aims: We evaluated the safety and efficacy of the IFN-free, RBV free, single tablet regimen of ledipasvir/sofosbuvir (LDV/SOF) in HCV genotype 1 or 4 patients co-infected with HIV-1 in the Phase 3 ION-4 study.

Methods: HCV treatment naïve and experienced HIV co-infected patients on stable, approved antiretroviral (ARV) regimens received LDV/SOF (90mg/400mg) once daily for 12 weeks. Patients with compensated cirrhosis were eligible. Permitted concomitant ARVs included tenofovir/emtricitabine (TDF/FTC) with raltegravir (RAL), efavirenz (EFV) or rilpivirine (RPV). Safety evaluations included enhanced renal toxicity monitoring, CD4 count and HIV-1 RNA levels. The primary endpoint was SVR12.

Results: 335 patients with GT1a (75%), GT1b (23%) and GT4 (2%) were enrolled in the study; 82% were male, 34% were black, mean age was 52 (range 26-72), mean baseline HCV RNA was 6.7 log₁₀ IU/mL (range 4.1-7.8), median baseline CD4 count was 662 cells/uL (range 106-2069), 20% had cirrhosis, 24% were *IL28B* CC genotype and 55% had not responded to prior HCV treatment. Most patients were taking EFV (48%) or RAL (44%). The table 1 shows SVR4 by ARV regimen. Overall, SVR24 was 96% (321/335); 2 patients had on-treatment virologic failure due to non-compliance and 10 had virologic relapse after discontinuing treatment. Overall, SVR24 (96%) among non-cirrhotic (F0-F3) patients was similar to SVR4 (94%) among cirrhotic (F4) patients. No patient had confirmed HIV virologic rebound (HIV-1 RNA ≥ 400 copies/mL). No patients discontinued study drug due to an AE. AEs occurring in ≥ 10% of patients were headache (25%), fatigue (21%) and diarrhea (11%). No significant lab abnormalities were observed.

Conclusions: The IFN-free, RBV-free, single tablet regimen of LDV/SOF administered once daily for 12 weeks is highly effective and well tolerated in treatment-naïve and experienced, genotype 1 or 4 HCV-infected patients with HIV-1 coinfection, including those with cirrhosis. Complete SVR24 data will be presented.

Table 1

Virologic Response	TDF + FTC + EFV (n = 160)	TDF + FTC + RAL (n = 146)	TDF + FTC + RPV (n = 29)	Overall (n = 335)
SVR24, n (%)	151 (94)	142 (97)	28 (97)	321 (96)
On-Treatment Failure, n (%)	1 (< 1)	0	1 (3)	2 (< 1)
Relapse, n (%)	8 (5)	2 (1)	0	10 (3)
Other, n (%)	0	2 (1)	0	2 (< 1)

OR-02 High efficacy and low relapse rates observed with 8 or 12 Weeks of LDV/SOF Single Tablet Regimen in GT1 HCV-infected treatment-naïve, non-cirrhotic patients with pretreatment HCV RNA < 6 Million IU/mL

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Background and Aims: A shortened duration of ledipasvir/sofosbuvir (LDV/SOF) for 8 weeks (+RBV) was compared to 12 weeks LDV/SOF in genotype 1 (GT1) treatment-naïve, non-cirrhotic patients in ION3, a Phase 3, randomized, open label study (n = 647). Overall sustained virologic response (SVR) rates were non-inferior between the 8 and 12 week LDV/SOF arms (94% and 96% respectively), however relapse was numerically higher in those treated for 8 weeks (5.1%) compared to 12 weeks (1.4%). Addition of RBV did not improve SVR. A post-hoc analysis of the ION3 trial was conducted to evaluate baseline factors that might be responsible for the differential in relapse rates between the 8 and 12 week arms of LDV/SOF.

Methods: Baseline historical negative predictors were evaluated in subjects who relapsed, including: age, gender, race, GT1 subtype, METAVIR fibrosis stage, BMI, IL28B status, and baseline HCV RNA. For baseline viral load, predefined Cutoff of 800,000 IU/ml and subsequently up to 10 million IU/mL were assessed.

Results: In the ION3 trial, approximately 60% of treatment naïve, non-cirrhotic subjects had baseline HCV RNA of < 6 million IU/mL. For these subjects, there was no difference in SVR rates (97% and 96%) nor relapse rates (1.6% and 1.5%) between 8 and 12 weeks of LDV/SOF treatment. SVR rates were identical for the 8 week and 12 week arms (96%) in patients with pretreatment HCV RNA < 10 million IU/mL, and relapse occurred in 3.1% vs. 1.2%, respectively. The majority of failures in ION3 who were treated for 8 weeks had a baseline HCV RNA greater than 10 million IU/mL. Although higher overall rates of relapse were observed for males and subjects who were IL28B nonCC, sex and IL28B status had no effect on outcome among those with a pretreatment HCV RNA < 6 million IU/ml.

Conclusions: A baseline HCV RNA < 6 million IU/mL in treatment naïve, non-cirrhotic GT1 patients correlated with similar SVR and relapse rates with 8 weeks

or 12 weeks of LDV/SOF single tablet regimen regardless of other patient characteristics. This shortened duration could improve adherence and affordability of HCV treatment.

OR-03 Evolution of strategies to treat chronic hepatitis C virus infection including direct-acting antivirals in Spain in a real-life setting: The GEHEP-MONO Cohort (GEHEP-001 Study)

María Mancebo¹, Luis Enrique Morano-Amado², Enrique Ortega³, Patricia Monje⁴, José Hernández-Quero⁵, Sergio Reus-Bañuls⁶, Francisco Vera-Méndez⁷, Josep Cucurull⁸, Antonio Rivero-Juárez⁹, Pablo Ryan¹⁰, Marcial Delgado-Fernández¹¹, Dolores Merino¹², Francisco Téllez¹³, María Tacias Pitarch¹⁴, Carlos Dueñas-Gutiérrez¹⁵, Diego Pérez-Parente¹⁶, Miguel García-Deltoro³, Karin Neukam¹⁷, Juan Antonio Pineda¹⁷.

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Background & Aims: Options for treatment against hepatitis C virus (HCV) infection have experienced rapid changes since the first commercialization of direct acting antivirals (DAA). DAA disposition not only depends on scientific advances, but also on restrictions given by international and national health authorities. In Spain, from April 1st, there is a National Strategy, which aimed to homogenize hepatitis C management across the different Spanish autonomous communities. The purpose of this study was to analyze the over-time changes of treatment strategies for DAA-based therapy against chronic HCV mono-infection within the GEHEP-MONO cohort.

Methods: This is a multicentric, prospective cohort study (ClinicalTrials.gov number NCT02333292) that registers all individuals who initiate any DAA-based treatment against HCV infection outside clinical trials in Units of Infectious Diseases throughout 13 Spanish hospitals. A descriptive analysis of the treatment regimens initiated according to Spanish autonomous communities, HCV genotype and the year of treatment initiation was conducted. Those communities in which 20 or less patients were registered, namely Madrid, Catalonia, Castile-Leon, and Murcia, were combined for the analysis.

Results: A total of 302 patients have been included to date, 208 (68%) subjects were male and median age (interquartile range) was 51 (45-59) years. 266 (87.1%) patients were infected with HCV genotype 1, 1 (0.3%) subjects carried HCV genotype 2, 17 (5.6%) individuals bore HCV genotypes 3 and 22 (7%) subjects carried HCV genotype 4. Cirrhosis at baseline was diagnosed in 136 (47%) patients. The numbers (proportion of the overall DAA-treated patients) of recruited patients treated with interferon (IFN)-sparing therapy according to autonomous communities and year of treatment initiation were: Andalusia: 2014: 1 (6%), 2015: 44 (88%); Valencia Community: 2014: 0, 2015: 23 (89%); Galicia: 2014: 0, 2015: 8 (44%); others: 2014: 2 (13%), 2015: 9 (64%). Among the patients infected with HCV genotype 1-4, the number of individuals treated with IFN-based DAA-containing therapy was 11 (100%) in 2011, 60 (100%) in 2012, 48 (100%) in 2013, 71 (97%) in 2014 and 17 (19%) in 2015. The corresponding numbers for individuals infected by HCV genotype 2-3 were: none between 2011-2013, 1 (50%) in 2014 and 7 (41%) in 2015.

Conclusions: Recently, a significant increase in the proportion of patients treated with IFN-sparing therapy is observed. However, in 2015, there are still an important proportion of patients who have been treated with IFN-based treatment throughout all HCV genotypes. There are remarkable differences in the strategies used across the communities.

OR-04 Impact of HIV coinfection on the efficacy and safety of direct-acting antiviral-based therapy against chronic hepatitis C under real-life conditions: Combined results from the HEPAVIR-DAA and the GEHEP-MONO (GEHEP-001) cohorts

Karin Neukam¹, Patricia Monje², Antonio Rivero-Juárez³, Luis Enrique Morano-Amado⁴, Purificación Rubio⁵, Francisco Téllez⁶, Dolores Merino⁷, Guillermo Ojeda-Burgos⁸, Antonio Collado⁹, Ignacio de los Santos Gil¹⁰, Marcial Delgado-Fernández¹¹, José Hernández-Quero¹², Sergio Reus-Bañuls¹³, Onofre Martínez-Madrid¹⁴, Francisca Cuenca-López³, Diego Pérez-Parente¹⁵, Enrique Ortega⁵, Juan Antonio Pineda².

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Background & Aims: The availability of direct acting antivirals (DAA) has changed the paradigm of treatment against hepatitis C virus (HCV) infection. However, no comparison between results from HIV/HCV-coinfected subjects and from HCV-monoinfected patients have been carried out in clinical trials. This study is aimed to evaluate the impact of HIV coinfection on the efficacy and safety of DAA-based treatment in the clinical practice in patients attending Infectious Diseases units.

Methods: In a prospective multicohort study, HIV/HCV-coinfected patients (HEPAVIR-DAA Cohort; ClinicalTrials.gov ID: NCT02057003) and HCV-monoinfected individuals (GEHEP-MONO Cohort; ClinicalTrials.gov ID: NCT02333292) who initiate any DAA-based therapy at the Infectious Disease units of 22 hospitals throughout Spain are included. The primary efficacy and safety outcome variables were the achievement of sustained virologic response 12 months after the scheduled end of therapy date (SVR12) and discontinuation of therapy due to adverse events.

Results: Of the 683 patients included in the cohorts, 336 (49%) subjects had achieved the SVR12 evaluation timepoint (Table 2). The majority initiated interferon-based therapy, mainly based on telaprevir (72.9%) or boceprevir (17.9%). Twenty-one (12.7%) HIV/HCV-coinfected patients and 5 (2.9%) HCV-monoinfected patients had received IFN-free therapy at the time of this analysis. Overall rates of SVR12 in subjects with and without HIV-coinfection were 54.2% (90/166 patients) versus 65.9% (112/170 subjects; $p = 0.029$) in an intention-to-treat analysis and 66.2% (90/136 subjects) versus 76.7% (112/146 patients) in an on-treatment approach ($p = 0.05$). Thirty-six (10.7%) patients discontinued therapy due to adverse events, 19 (11.4%) HIV/HCV-coinfected individuals and 17 (10%) HCV-monoinfected subjects ($p = 0.668$). In a multivariate analysis adjusted for age, sex, HCV and IL28B genotype, baseline HCV-RNA load, treatment regimen and previous response to therapy, HIV-coinfection [adjusted odds ratio (AOR): 0.548; 95% confidence interval (95%CI): 0.329-0.912; $p = 0.021$], bearing baseline cirrhosis (AOR: 0.528, 95%CI: 0.316-0.881; $p = 0.015$) and having received interferon-free therapy (AOR: 7.824, 95%CI: 2.12-28.87; $p = 0.002$) were independently associated with SVR12.

Table 2

Parameter	HIV (-) (n = 170)	HIV (+) (n = 166)	p
HCV genotype, no. (%)			0.157
1a	70 (41.9)	81 (51.3)	
1b	81 (48.5)	44 (27.8)	
1 (a/b)	0	2 (1.3)	
1 (undetermined)	16 (9.6)	31 (19.6)	
2	0	0	
3	3 (1.8)	5 (3)	
4	0	3 (1.8)	
Cirrhosis, no. (%)	87 (51.2)	114 (68.7)	0.001
Previously naïve to anti-HCV therapy	64 (37.6)	44 (26.5)	0.029

Conclusions: HIV-coinfection might worsen the response to DAA-based therapy, although this difference could be driven by a more advanced degree of liver damage. HIV/HCV-coinfected patients did not show higher rates of discontinuations due to adverse events.

OR-05 Direct-acting antivirals against HCV infection in elderly patients: are they so well tolerated and safe as we thought?

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Background & Aims: New direct-acting antivirals agents (DAAs) highly safe and well tolerated are part of current available interferon-free regimens against HCV infection. Therefore, elderly patients, over 65 years old, in whom comorbidities and concomitant chronic medications exist, might benefit of these therapies. However, there is scarce data regard the effectiveness and safety of these new drugs among elderly population.

Methods: All HCV-infected patients over 65 years in clinical follow-up at a reference hospital in Northwest of Spain who initiated anti-HCV therapy since May 2014 until July 2015 were included. Epidemiological, clinical, laboratory, liver fibrosis status (measured by elastography), antiviral regimen and the pharmacotherapeutic profile were recorded. A descriptive analysis was done and t-Student test was performed to compare quantitative variables.

Results: A total of 32 HCVmono-infected patients over 65 years were recorded. Most were female (67%) with a mean age of 70 ± 11 years. All were HCV genotype 1 (79% subtype b), 70% were F4, 58% were previously exposed to anti-HCV therapy and 42% had a non favorable ILB28 genotype. Median HCV-RNA was 6.04 log UI/ml (5.44-6.54) at the time of treatment initiation. The table 3 depicted the specific treatment regimens. 61% included ribavirin (RBV), the RBV dose was based on body weight. It was necessary a dose reduction in 39% of them mainly at week 4 of treatment initiation. Only in 3 cases, the treatment regimens included interferon. 82% of patients had concomitant medication chronically and 27% needed adjustment. 55% of patients experienced adverse events. The main adverse events were: asthenia (36%), anemia

Table 3. Hepatitis C treatment regimes in the study population

Treatment regimen	n (%)
Sofosbuvir + Simeprevir + Ribavirin	7 (21.2%)
Sofosbuvir + Ledipasvir	6 (18.2%)
Ombitasvir + Paritaprevir/r + Dasabuvir	6 (18.2%)
Sofosbuvir + Ledipasvir + Ribavirin	4 (12.1%)
Ombitasvir + Paritaprevir/r + Dasabuvir + Ribavirin	4 (12.1%)
Sofosbuvir + Simeprevir	2 (6.1%)
Telaprevir + Interferon + Ribavirin	2 (6.1%)
Simeprevir + Interferon + Ribavirin	1 (3%)
Sofosbuvir + Daclatasvir + Ribavirin	1 (3%)

(33%), dryness (15%), hyperbilirubinemia (12%) and insomnia (9%). After therapy initiation transaminases were normalized on week 4 in all cases. Adherence was recorded in 13 patients (41%), being over 90% in all the visits. Only two patients required to stop therapy due to adverse events and this was associated to regimens including interferon (TVP/peg-IFN/RBV and SMV/peg-IFN/RBV). None patient had died.

Conclusions: Adverse events were frequent (55%) among HCV-infected patients over 65 years who initiate anti-HCV therapy using DAAs. The majority of these patients (82%) had concomitant medication that need to be adjusted in 27% of them. Moreover, in one third of patients receiving RBV a dose reduction was required. However, the rate of discontinuation due to adverse events was low (3%). These findings highlight that in patients over 65 years who initiate a DAAs therapy a special caution is recommended especially with RBV-doses adjustment and the management of concomitant medication.

OR-06 Short-term changes in liver function tests in patients with cirrhosis after DAA-based therapy in real life: Results from the HEPAVIR-DAA and the GEHEP-MONO (GEHEP-001 Study) cohorts

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Background & Aims: Improvements in biological markers of liver function, as well as in MELD and Child-Pugh-Turcotte (CPT) scores, have been found in clinical trials in patients with advanced liver disease receiving DAA-based therapy, mainly IFN-free combinations. However, a proportion of patients experience a worsening in liver function. No real-life data are currently available. This study was aimed to analyze changes in liver function parameters in subjects with cirrhosis receiving DAA-based therapy.

Methods: HIV/HCV-coinfected patients included in the HEPAVIR-DAA Cohort (ClinicalTrials.gov ID: NCT02057003) and HCV-monoinfected individuals enrolled in the GEHEP-

MONO Cohort (ClinicalTrials.gov ID: NCT02333292), who were given HCV therapy including at least one DAA at the Infectious Disease units of 6 Spanish hospitals, were selected for this retrospective analysis. All patients met the following criteria: 1) Baseline liver stiffness (LS) \geq 12.5 KPa; 2) Having reached the time-point for assessing SVR12; 3) Available measurements of baseline CPT and MELD scores. Changes in CPT, MELD, albumin, INR and total bilirubin from baseline to SVR12 time-points were evaluated.

Results: Seventy-five patients were included. Median age was 49 years, 58 (77%) were male and 39 (52%) HIV-infected. Thirteen (17%) received IFN-free combinations. Median (Q1-Q3) baseline LS was 22 (15-34) KPa. Seventy (93%) were at CPT class A and 5 (7%) at B. Fifty-one (68%) subjects (66% of those with IFN-based and 77% of those with IFN-free combinations) attained SVR12. Median (baseline vs. at SVR12 time-point) values of the liver function parameters were: Albumin 4.1 g/dL vs 4.4 g/dL ($p = 0.47$), INR 1.08 vs. 1.08 ($p = 0.83$), total bilirubin 0.8 mg/dL vs 0.6 mg/dL ($p = 0.001$), MELD index (available in 48 subjects at SVR12) 8 vs 7 ($p = 0.44$), CPT score (also in 48 patients) 5 vs. 5 ($p = 0.85$). In 15 patients (20%) MELD index increased 1-4 points, in 17 (23%) remained steady and in 16 (21%) declined 1-6 points. CPT score increased in 4 (8%), decreased in 5 (10%) and did not change in 39 (81%). Among 8 patients on IFN-free therapy, MELD increased in 5, remained the same in 1 and decreased in 2. When splitting the population according to SVR, no difference were observed between subgroups.

Conclusions: Overall, in patients with HCV-related cirrhosis and relatively spared liver function, DAA-based therapy leads to a mild improvement in liver function tests in the short term. However, there is a substantial proportion in whom major prognosis liver scores worsen. Predictors to identify those who develop functional impairment are required.

OR-07 Distribution of hepatitis C virus genotypes in Spain during the period 2011-2015 (GEHEP 005 Study)

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Background & Aims: In the era of direct antiviral treatment of chronic hepatitis C, HCV genotype and genotype 1 subtype (1a/1b) must be assessed prior to treatment initiation and is one of the major factors driving the choice of therapy. In Spain, studies assessing the distribution of HCV genotypes and major epidemiology, clinical and virological factors associated are still lacking. Here we report on molecular epidemiology of HCV genotypes in Spain during the period 2011-2015.

Methods: A retrospective study recruiting 15140 patients from 24 hospitals from 9 autonomous communities (Andalucía, Aragón, Castilla-León, Cataluña, Galicia, Islas Canarias, Madrid, Navarra y País Vasco) has been performed. Annual distribution of HCV genotypes and subtypes, as well as gender, age, transmission route, HIV and/or HBV coinfection, and treatment details were recorded. Data were anonymized into a SPSS data base, and proportions and chi square test were used for analysis.

Results: Throughout the study period, 15140 chronically infected HCV patients have been recruited. Baseline characteristics were: median age was 51.79 years (IQR, 56-44), 68.7% were male, 14.8% were HIV coinfecting, 28.2% were HBV coinfecting, and the most frequent transmission routes was parenteral (70.2%), followed by unknown (26.7%). Genotype distribution was: 68.8% HCV-1 (27% HCV-1a and 35.9% HCV-1b), 2.7% HCV-2, 16.5% HCV-3, 11.9% HCV-4, and 0.1% other genotypes (HCV-5, HCV-6). Line probe assay test (LiPA 2.0 Siemens) was the main method for HCV genotyping (42.9%), followed by Roche and Abbott methods 20.1% and 18.2% respectively. HCV genotypes 1a, 3 and 4 were closely associated with male gender, parenteral route, and coinfection by HIV and HBV; in contrast, genotype 1b was associated with female sex, non-parenteral route and mono-infection. In addition, age effect was observed in genotype distribution and different patterns of genotypic distribution was observed between different geographical areas of Spain (Center vs North/South).

Finally, prior to interferon-free era, we found overall rates of SVR of 45.2% for GT1 (GT1a 42% and GT1b 44.9%), 63.8% for GT3 and 38.6% for GT4.

Conclusions: We present the most recent data on molecular epidemiology of hepatitis C virus in Spain (GEHEP 005 Study). This study confirms that in Spain genotypic distribution varies with age, sex, HIV and HBV coinfection, and within geographical areas and epidemiological groups.

OR-08 Distribution of HCV genotypes in several European regions

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Background & Aims: Analysis of Hepatitis C virus (HCV) genotype (GT) distribution and transmission risk factors in a population of unselected patients in European regions.

Methods: Anonymised epidemiological information and viral genotype from HCV-infected patients who underwent HCV genotyping within the years 2011-2015 were collected from 53 European centres and analysed retrospectively.

Results: 36,995 patients were analysed. Among them, GT1 was predominant (66.1%) followed by GT3 (20.1%), GT4 (9.1%), GT2 (4.5%), GT5 (0.2%), GT6 (0.1%) and 3 cases of GT P. The genotype distribution was similar in all analysed countries, though some variations were observed in i) Russian samples, with lower proportion of GT1 samples (50.8%) and higher GTs 2 (11.2%) and 3 (37.9%); ii) Italy, with higher proportion of GT2 (Catanzaro 23.9%, Rome 13.6%); and iii) Spain, where GT4 was significantly more prevalent (11.9%; $f = 0.538$). Within the GT1, subtype 1a represented 41.6% of the samples, 1b 55.0%, and 3.4 were not assigned a subtype. No major deviations to this pattern were observed within the five years

No significant differences of genotype distribution were detected between genders. Patients ≥ 65 years of age, whose infection is mostly ligated to past infections through medical-related procedures, carried a significantly larger proportion of genotype 1b viruses than the general population. In younger patients, mostly infected by tattooing and/or drug abuse, genotype 1a infection prevailed, (33.5% for tattoo/piercing and drug abuse) followed by genotype 3 (30%). In infections in the context of sexual practices with or without concomitant drug abuse (8.4%), the proportion of genotype 3 was lower (12.4%) and that of genotype 4 higher (20.3%). Genotype 4 was mostly abundant in MSM (28.9%). HIV coinfection was significantly associated with higher proportions GT1a- (23.3%; $f = 0.2037$) and GT4-infections (16.6%; $f < 0.020$), while HBV did not.

Conclusions: We report the genotype distribution in European areas. The repartition is similar central European countries. Genotype prevalence largely depends on age, transmission route and HIV coinfection. Currently, intravenous drug use associated or not to sexual practices seem to be the major force shaping the GT distribution in Europe. Further analysis based on sequencing and phylogenetic analysis are required to refine the HCV geno/subgenotype map as well as to deliver more insights in HCV spread.

OR-09 Using NS5b sequencing for hepatitis C virus Genotyping reveals discordances with commercial platforms. The GEHEP-007 study

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Background & Aims: The availability of new antiviral drugs against HCV infection requires the highest precision for estimating HCV genotyping, including subtype differentiation especially in the case of genotype 1 infection. In the setting of the Spanish Group for Viral Hepatitis Study (GEHEP), we aimed to evaluate the correct assignment of HCV genotypes by three commercial methods, Trugene-HCV genotyping kit (Siemens), VERSANT HCV Genotype 2.0 assay (Siemens), and Real Time HCV genotype II (Abbott), compared to NS5B sequencing.

Methods: 308 clinical samples carrying HCV genotypes representing the most frequent geno/subtypes circulating in Spain were studied. Samples were stored at -80°C until sequencing of an internal fragment of 330 bp in the NS5B gene (nucleotide positions 7935 to 8266). Genotypes were assigned using Blast (http://hcv.lanl.gov/content/sequence/BASIC_BLAST/basic_blast.html), geno2pheno_{HCV} (hbv.bioinf.mpi-inf.mpg.de/) and phyML. Major discrepancies were defined as differences in the assigned genotype by one of the three methods and NS5b sequencing (including genotypes 1a and 1b misclassification). Minor discrepancies were considered when differences at subtype level were observed.

Results: The overall discordance with respect to the reference method was 34% for Trugene, and 17% for VERSANT HCV2.0. The Abbott assay correctly identified all 1a and 1b subtypes, and genotypes 2, 3, 4 and 5, but did not discriminate the subtype in these cases. Major discordances were found in 16% of the cases for Trugene HCV, being the majority of them 1a/1b related discordances; for VERSANT HCV 2.0, we found major discordances in 10% of the cases, being all except one 1b/1a cases. Minor discordances were found for Trugene in 18% of the cases, and for VERSANT HCV 2.0 in 8%. With NS5b sequencing, genotypes 2, 3, 4 and 5 by the Abbott HCV genotype Real Time II assay were resolved as 2a ($n = 1$), 2b ($n = 2$), 2c ($n = 3$), 3a ($n = 9$), 4d ($n = 3$) and 5a ($n = 2$).

Conclusions: When NS5b sequencing is used as reference, Trugene failed to correctly assign HCV genotype in up to a third of cases, with more than 15% of errors with

a high impact on clinical practice. VERSANT HCV Genotype 2.0 assay did not assign correctly HCV subtype in 10% of cases. Abbott Real Time HCV genotype II assay properly assigned all the genotypes 1 analyzed, although it was not able to discriminate subtype genotypes 2, 3, 4 and 5.

OR-10 No evidence of acute hepatitis C virus infection outbreak among HIV-infected patients from Southern Spain

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Background & Aims: A number of epidemics of acute hepatitis C virus infection (AHCVI) have been described recently within defined areas worldwide among HIV-infected men who have sex with men (MSM). This study aims to describe cases of AHC in the HIV-infected population in Southern Spain.

Methods: In a retrospective study conducted in eight hospitals throughout Andalusia, Spain, the medical histories of all HIV-infected patients were examined. AHCVI was considered as hepatitis C virus (HCV) IgG antibody seroconversion and the time of infection was considered the moment between the last negative and the first positive HCV antibody determination. Here we report all AHCVI cases among HIV-infected patients diagnosed at the Infectious Disease Units of the participating hospitals from 2000 through 2014.

Results: A total of 23 cases of AHCVI were detected between 2004 and 2014 in Southern Spain: 3 patients between 2004-2005, 5 patients between 2006-2007, 4 patients between 2008-2009, 4 patients between 2010-2011,

5 patients between 2012-2013 and 2 patients in 2014. No case was reported before this date. Of the 22 (95.7%) male subjects, 21 (95.5%) individuals were MSM. Peak (interquartile range) ALT during AHCVI were 496 (291-656) IU/mL and peak bilirubin values were 1.15 (0.9-1.98) mg/dL, respectively. Thirteen (56.5%) patients presented symptoms of any kind, mainly asthenia (39.1%).

Conclusions: The number of cases of AHCVI in HIV-infected patients in Southern Spain is both low and there is no evidence of an increase over time. Prospective studies to determine the incidence of AHCVI, as well as the reasons for the lack of an epidemic outbreak in this setting, are necessary. These data are crucial for preventing AHCVI. In the meantime, awareness and sequential screening for HCV antibodies in seronegative patients should be mandatory.

OR-11 Uselessness of HBsAg levels to classify non-D genotype HBV carriers

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Background & Aims: HBsAg levels have been proposed as a useful marker to identify HBV inactive carriers. Levels below 1000 IU/mL along with HBV DNA < 2000 IU/mL have shown a diagnostic accuracy of 94% for genotype D patients [Brunetto MR, et al. Gastroenterology 2010]. However, there is scarce data regarding the HBsAg levels variability among the different genotypes. The aim of this study is to assess HBsAg levels according to the HBV genotype and the diagnostic accuracy of the HBsAg < 1000 IU/mL plus HBV DNA < 2000 IU/mL cut-off in non genotype D- HBV carriers.

Methods: 103 monoinfected chronic carriers were selected. Biochemical and virological characteristics were recorded and contrasted according to the genotype. Genotype were determine by direct sequencing.

Table 4.

	A (n = 17)	D (n = 37)	B (n = 2)	E (n = 25)	H + F (n = 18)	p
Mean HBV DNA (logIU/mL)	3.0	2.8	2.7	2.9	2.7	0.89
Mean HBsAg (logIU/mL)	3.5	2.7	2.3	3.4	4.1	< 0.001
HBsAg < 1000 IU/mL + HBV DNA < 2000 IU/mL*, n (%)	3/12 (25%)	18/27 (67%)	1/1 (100%)	5/17 (29%)	2/15 (13%)	0.007

*All patients included presented normal ALT levels.

Results: 53 (51.5%) were male and the mean age was 46 years old (SD 13). The mean ALT value was 25 IU/mL (SD 18), HBV DNA 650 IU/mL (2.8 log, SD 1) and HBsAg levels 2000 IU/mL (3.3 log, SD 1.1). HBsAg and HBV DNA levels according to HBV genotypes are shown in the table 4 (4 patients were not included in the analysis due to infection by mixture genotype A/E). Patients infected by HBV genotype D presented the lowest HBsAg levels. Less than 30% of non genotype-D infected patients met the cut-off proposed by Brunetto et al, in comparison with 67% for genotype D.

Conclusions: In chronic HBV carriers HBsAg levels were statistically greater in patients infected by genotypes A, E, H or F in comparison with genotype D. The cut-off of HBsAg levels < 1000 IU/mL plus HBV DNA < 2000 IU/mL does not allow for proper classification of non-D genotype HBV inactive carriers.

OR-12 **Role of hepatitis B virus infection as a cardiovascular risk factor**

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Background & Aims: the association between hepatitis C virus and insulin resistance, steatosis and dyslipemia is well established, mainly for those patients with severe fibrosis and aged over 55 years. However, there is scarce data concerning the possible role of hepatitis B virus (HBV) as a cardiovascular risk factor. The aim of the study was to assess the potential association between atherosclerosis and HBV infection in patients with mild liver disease.

Methods: in a cohort of 128 untreated chronic HBeAg negative patients the cardiovascular risk was assessed through carotid atherosclerosis (measure of intima-media thickness-IMT- and presence of atherome plaques by Doppler ultrasonography). Patients were evaluated using anthropometric, metabolic and analytical measurements. All patients presented FibroScan® below 9.2 kPa or liver biopsy with mild fibrosis. The results were contrasted with a Spanish cohort of healthy subjects, stratified by sex and age [Junyent M, et al. Med Clin (Barc) 2005].

Results: 128 monoinfected patients were included (56% male, mean age 48 years old) with the following risk factors: 32% former or active smokers, 19% arterial hypertension, 20% dyslipemia, 5% diabetes and 3% significant alcohol intake. Mean ALT levels were 28 IU/mL (SD 17), HBsAg 3.1 logIU/mL (SD 1.1) and HBV DNA 2.9 logIU/mL (SD 1). Greater IMT was observed in patients infected by HBV in comparison with healthy controls (Mean IMT

0.65 vs. 0.56, $p < 0.001$ and maximum IMT 0.82 vs. 0.66, $p < 0.001$, respectively), but only 19% presented carotid plaques, a similar rate to healthy subjects. Factors associated with atherome plaques in the univariate analysis were patients's age, tobacco use, abdominal diameter, GGT levels, insulin resistance, dyslipemia and arterial hypertension. However, in the multivariate analysis older age was the only variable associated. Neither the HBV DNA levels nor HBsAg levels were related to increased IMT or higher rate of carotid plaques.

Conclusions: Intima-media thickness was increased in patients infected by HBV with mild liver disease, suggesting a possible role of HBV as a cardiovascular risk factor. The presence of carotid plaques was similar to healthy subjects and related to age, in line with findings described in HCV infected patients [Petta S, et al. Hepatology 2012].

OR-13 **Bacterial translocation is not a predictor of clinical outcome in HIV/HCV-coinfected patients with compensated liver cirrhosis**

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Background & Aims: Bacterial translocation (BT) is a common phenomenon in patients with cirrhosis, irrespective of its aetiology. Previous studies have shown that HIV/HCV-coinfected patients exhibit increased levels of surrogate serum markers of BT. Besides, BT seems to increase with the severity of liver fibrosis in these patients. It is not known if BT impacts on the prognosis of HIV/HCV-coinfected patients with cirrhosis. This study evaluates if BT is a predictor of clinical outcome in HIV/HCV-coinfected patients with compensated cirrhosis.

Methods: Retrospective cohort study conducted in 3 tertiary care hospitals from Spain which included 248 HIV/HCV-coinfected patients with a new diagnosis of cirrhosis, based on the presence of a liver stiffness (LS) greater than 14 kiloPascals (kPa), no previous decompensation of liver disease and an available frozen sera sample from the time of the diagnosis of cirrhosis. The serum levels of the DNA sequences encoding the well conserved 16S rRNA subunit (DNAr 16S), the lipopolysaccharide (LPS) and the soluble CD14 (sCD14) at baseline were measured by real-time PCR and ELISA, respectively. The primary end-point was the emergence of a first liver decompensation (LD) and/or death of any cause. Secondary end-points were the

emergence of a first LD, liver related death (LRD) and death of any cause. The associations between these end-points and baseline factors, including serum markers of BT, were evaluated.

Results: After a median (RIQ) follow-up of 54 (33-72) months, forty-six (18%) patients developed a first LD. Forty-three (17%) patients died during follow-up, 24 of them due to liver disease. Sixty (24%) patients developed a first LD and/or died of any cause during follow-up. Baseline levels of DNAr 16S, LPS and sCD14 were not associated with the probability of developing the primary end-point of the study. The independent predictors of developing a first LD and/or death of any cause were CD4 cell count < 200 (adjusted hazard ratio [AHR] 3.1, 95% confidence interval (CI): 1.6-5.6; $p < 0.0001$), a baseline LS ≥ 40 kPa (AHR 3.1, 1.7-5.6; $p < 0.0001$), Child-Pugh stage B (vs A) (AHR 2.1, 95% CI: 0.9-6.5; $p = 0.059$) and, as a protective factor, achieving sustained virological response during follow-up (AHR 0.1; 95% CI: 0.04-0.4; $p = 0.002$). Baseline levels of BT serum markers were also not associated with any of the secondary end-points analysed in the study.

Conclusion: BT does not seem to be a relevant predictor of clinical outcome in HIV/HCV-coinfected patients with compensated cirrhosis.

OR-14 Liver stiffness predicts variceal bleeding in HIV/HCV-coinfected patients with compensated cirrhosis

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Background & Aims: A previous study has shown that a liver stiffness (LS) < 21 kiloPascals (kPa) has a 100% negative predictive value (NPV) to exclude the presence of esophageal varices (EV) at risk of bleeding in HIV/HCV-coinfected patients. Consequently, upper gastrointestinal endoscopy (UGE) for the screening of EV could be avoided in these patients. However, this strategy has not been widely accepted due to concerns about its safety. This study assess the predictive value of LS to predict the risk of variceal bleeding in HIV/HCV-coinfected patients with compensated cirrhosis.

Methods: Prospective cohort study of 446 HIV/HCV-coinfected patients with a new diagnosis of cirrhosis, based on the presence of LS ≥ 14 kPa, and no previous decompensation of liver disease. All patients underwent a UGE for the screening of EV at entry in the cohort before November 2009. From this date, UGE was not recommended by the cohort protocol in patients with LS < 21 kPa. The time from diagnosis of cirrhosis to the emergence of a variceal bleeding episode, as well as the predictors of this outcome were evaluated.

Results: In 305 (68%) patients, at least 1 UGE was done. VE at risk of bleeding were present in 26 (8.5%) of them. The median (RIQ) elapsed time between LS assessment and UGE examination was 21 (-12, 78) days. After a median (RIQ) follow-up of 49 (25-68) months, 16 (3.6%, 95% confidence interval: 1.9-5.3) patients developed a first variceal bleeding episode. In all cases, baseline LS was ≥ 21 kPa. Thus, the NPV of a LS < 21 kPa to predict a bleeding episode during follow-up was 100%. At the moment of the bleeding episode, LS was also above this threshold.

Conclusions: Baseline LS identifies HIV/HCV-coinfected patients with compensated cirrhosis with a very low risk of presenting a variceal bleeding episode. In fact, no individual with baseline LS < 21 kPa developed this outcome. Our results confirm that UGE can be safely spared in patients with LS < 21 kPa.

OR-15 Survival and prognostic factors of hepatocellular carcinoma in HIV-infected patients

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Background & Aims: The incidence of hepatocellular carcinoma (HCC) has notably increased in HIV-infected patients in the last years. The prognostic factors of HCC in this population are not well known, including the role of HIV specific factors. This study describes the clinical characteristics and to assess the survival and prognostic factors of HCC in HIV-infected patients.

Methods: The HCC-GEHEP cohort recruits HCC cases diagnosed in HIV-infected patients from 32 centers from Spain. HCC diagnosis was made following the AASLD criteria. The time from HCC diagnosis to death of any cause, as well as the predictors of this outcome, were evaluated.

Results: From January 1996, 281 HCC cases have been diagnosed in HIV-infected patients in the participant centers. HCC was related to hepatitis C virus (HCV) infection in 177 (63%) cases, HCV and alcohol in 54 (19%), hepatitis B virus (HBV) infection in 26 (9%), HCV/HBV infection in 20 (7%) and alcohol in 4 (2%). HCC was diagnosed within a screening program in 147 (52%) patients. One hundred and seventy-three (62%) received therapy against HCC, 81 (29%) potentially curative therapies and 92 (33%) non-curative therapies. Two hundred and one (72%) patients died, 188 of them due to liver disease. The median survival time after diagnosis was 5 (2-23) months. The independent predictors of mortality in a multivariate Cox model adjusted by age, sex and CD4 cell count were: diagnosis of HCC out of a screening program (adjusted hazard ratio [AHR] 1.38; 95% confidence interval [CI]: 1.01-1.89; $p = 0.042$), baseline alpha-fetoprotein level above 200 ng/dL (AHR 2.17, 95% CI: 1.58-2.98; $p < 0.0001$), detectable HIV viral load at HCC diagnosis (AHR 1.42; 95% CI: 1.01-2.01; $p < 0.0001$) and BCLC stage (B vs A: AHR 3.21; 95% CI: 1.81-5.74; $p < 0.0001$. C vs A: AHR 3.77; 95% CI: 2.45-5.81; $p < 0.0001$. D vs A: AHR 7.24; 95% CI: 4.43-11.85; $p < 0.0001$.)

Conclusions: Survival of HCC after diagnosis is very poor in HIV-infected patients. Besides liver-related factors, detectable HIV viral load is associated with worse outcome. Adherence to screening programs should be implemented, as screening is associated with better survival.

OR-16 **Real-life experience with Sorafenib for the treatment of hepatocellular carcinoma in HIV-infected patients**

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Background & Aims: Sorafenib is an oral multikinase inhibitor that has shown a survival benefit in patients with advanced hepatocellular carcinoma (HCC). To date, there is little information regarding the efficacy and safety of sorafenib in HIV-infected patients. The aim of this study is to report the experience with the use of sorafenib in a cohort of HIV-infected patients with HCC.

Methods: The HCC-GEHEP cohort recruits HCC cases diagnosed in HIV-infected patients from 32 centers from Spain. For this analysis, HCC cases receiving at least one dose of sorafenib were included. HCC diagnosis was made following the AASLD criteria. Tumor response was evaluated according to the Response Evaluation Criteria in Solid Tumors (RECIST). Patients who died before their first clinical reassessment were judged as having progressive disease. The overall survival after the start of treatment (OSaT) was defined as the time from sorafenib treatment initiation to the date of death from any cause or the date of the patient's last follow-up visit.

Results: From January 1996, 281 HCC cases have been diagnosed in HIV-infected patients in the participant centers. In 48 (17%) patients, treatment with sorafenib was started. Complete information regarding sorafenib therapy was available in 35 of them at the moment of the present analysis. The median (RIQ) elapsed time between HCC diagnosis and sorafenib initiation was 45 (19-218) days. In 4 cases sorafenib was started after HCC recurrence with previous potential curative therapies whereas in 4 cases sorafenib was started after progression following transarterial chemoembolization. In the remaining 27 cases, sorafenib was the first treatment against HCC. BCLC stage at sorafenib initiation was distributed as follows: A 3 (9%), B 2 (6%), C 25 (71%) and D 5 (14%). Median (RIQ) duration of sorafenib treatment was 60 (27-127) days. Adverse events of any grade occurred in 20 (57%) patients. Diarrhea was the most common side effect occurring in 11 (31%) patients. Besides, 14 (40%) patients developed a liver decompensation of cirrhosis during treatment. Regarding HIV infection, antiretroviral therapy had to be modified before sorafenib initiation in one patient. HIV viral load remained undetectable during therapy in all cases. Twenty-nine (83%)

patients have died at the end of the study. The median (RIQ) OSaT was 3.2 (2.1-6.6) months.

Conclusions: The efficacy and tolerability of sorafenib in HIV-infected patients in real-life conditions is significantly lower than figures reported in the registration clinical trial. On the contrary, sorafenib does not seem to interfere with antiretroviral therapy.

OR-17 Impact of genetic polymorphisms associated with non-alcoholic fatty liver disease on HIV-infected individuals

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Background & Aims: Fatty liver disease (FLD) is frequently observed in HIV-infected patients and a cause of advanced liver disease. Genetic factors could play a role in determining risk for FLD development in those patients. The aim of this study was to evaluate the association of those single nucleotide polymorphisms (SNPs) previously found to be related to non-alcoholic FLD by genome wide association analyses in the general population with the presence of FLD, including steatohepatitis, in HIV-infected individuals.

Methods: 431 HIV-infected patients were included in this study. All of them underwent a transient elastography with the controlled attenuation parameter (CAP) examination and were genotyped for 19 selected SNPs. A CAP value higher than 238 dB/m was selected to define the presence of FLD. Elevated alanine aminotransferase levels plus presence of FLD was considered as a surrogate marker of steatohepatitis.

Results: 179 (41.5%) individuals showed FLD, including 122 (28.3%) with steatohepatitis. The rs12743824 and rs738491 SNPs were independently associated with FLD and steatohepatitis, respectively. For rs12743824, among 252 individuals without FLD 182 (72.2%) were A-allele carriers versus 111 (62%) out of 179 patients with this disease (multivariate $p = 0.006$, adjusted OR = 0.51, 95% C.I. = 0.33-0.83). For rs738491, 20 (16.4%) out of 122 patients with steatohepatitis were TT-carriers versus 18 (5.8%) out of 309 patients without this condition (multivariate $p = 0.005$, adjusted OR = 2.94, 95% C.I. = 1.39-6.20).

Conclusions: *LPPR4* and *SAMM50* allelic variants are independent risk factors for FLD and steatohepatitis development, respectively, in HIV-infected individuals.

OR-18 Relationship between variations in fat mass and obesity associated gene and fatty liver disease in HIV-infected patients

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Background & Aims: Fatty liver disease (FLD) is frequently observed in HIV-infected patients. Obesity and diabetes mellitus are strongly associated with FLD. Fat mass and obesity associated (*FTO*) gene has been identified as one of the main susceptibility genes involved in obesity and type 2 diabetes mellitus (T2DM). It has not been clarified whether the *FTO* gene could be related with FLD independently of obesity or T2DM in the setting of HIV infection. The aim of this study is to evaluate the association of single nucleotide polymorphisms (SNPs) within the *FTO* gene, previously related to obesity or T2DM, with FLD in HIV-infected patients.

Methods: 431 HIV-infected patients were included in this study. FLD was defined as a value of the controlled attenuation parameter (CAP) ≥ 238 dB/m, obtained by transient elastography. Four SNPs within *FTO* intron 1 (rs11642841, rs8050136, rs9939609 and rs9940128) were genotyped using a custom Golden Gate protocol.

Results: FLD was diagnosed in 179 (41.5%) individuals. All genotyped SNPs were associated with FLD, showing rs9940128 the strongest association. The frequency of FLD among rs9940128_AA carriers was 56.4% (44 out of 78 individuals) and that of patients without this variation was 38.2% (135 out of 353 individuals) ($p = 0.003$). After the multivariate analysis, rs9940128_AA genotype [adjusted odds ratio (AOR) = 2.20, 95% confidence interval (95%CI) = 1.26-3.85, $p = 0.006$], higher fasting plasma glucose levels (AOR = 1.83, 95% CI = 1.15-2.92, $p = 0.011$) and overweight (AOR = 3.44, 95% CI = 2.18-5.44, $p < 10^{-6}$) were associated with FLD.

Conclusions: Variations within the *FTO* gene are predictors of FLD in HIV-infected patients independently of metabolic factors.



Poster Oral Presentations

PO-19 **Effectiveness and safety clinic ombitasvir, paritaprevir, ritonavir practice with or without dasabuvir and ribavirin**

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Background & Aims: The last generation drugs for the treatment of hepatitis C, has brought a revolution in the treatment, achieved SVR rates above 95% in clinical trials. This work aims to evaluate the effectiveness and safety of these drugs in clinical practice.

Method: Retrospective observational study has taken place in a tertiary hospital which a health area that comprises a population of 440,000 inhabitants. All patients treated with ombitasvir, paritaprevir, with or without ritonavir and ribavirin dasabuvir between April 1 and July 10, 2015 were included.

Results: 93 patients were included, 70% male, mean age 54.01 ± 12.23 years. 18 patients had HCV-HIV coinfection. 31.2% of patients were pre-treated, of which, 47.7% were relapsers, 34.9% were partial responders and 17.9% null responders. 34.4% of patients had genotype 1a, 49.5% 1b, 16.1% genotype 4, and one of the patients has a mixed genotype (1b + 4). 69.6% of patients had no CC IL28B polymorphism, 65.6% a baseline viral load $> 800.000\text{UI/mL}$ and 24.7% cirrhosis. In Week 2 of treatment, 20.9% and 33.5% of patients had undetectable and unquantifiable ($< 15\text{ UI/mL}$) viral load respectively, data which changed to 80.2% and 8.9% of patients at week 4. All patients who finished the treatment did it with negative viral load. Only 12.5% of patients had anemia, all of which were treated with ribavirin. The modification of the ribavirin dose was performed in 36.7% of these patients, receiving only one of them erythropoietin and transfusional support.

Conclusions: Ombitasvir, ritonavir and paritaprevir, with or without dasabuvir and ribavirin shown in our group of patients excellent efficacy data, regardless of previous patient or disease characteristics, showing no serious adverse effects for patients which requiring to discontinuation of treatment.

PO-20 **Implications of starting HCV treatment in HIV/HCV-coinfected patients**

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Background & Aims: When both HIV and HCV treatments are indicated, the antiretroviral therapy (ART) regimen may need to be modified before HCV treatment is initiated to reduce the potential for drug-drug interactions and overlapping toxicities that may develop during the period of concurrent HIV and HCV treatment. In this study we describe the modifications on ART regimen when HIV/HCVcoinfected patients start HCV therapy with new direct acting antiviral (DAA) agents in our HealthCare Area and evaluate its economic impact on ART regimen costs.

Methods: Observational retrospective study. Gender, ART regimen and its cost-per-month (previous and after starting HCV therapy) and oral HCV regimen chosen are recorded of every HIV/HCVcoinfected patient who start therapy with new DAA agents (simeprevir, sofosbuvir, ledipasvir, daclatasvir, ombitasvir/paritaprevir/ritonavir, dasabuvir).

Patient data, regimens prescribed and treatment cost were collected from External Patients & Management Pharmacy's Database and analysed using SPSS statistical package.

Results: A total of 41 patients (17% female) started therapy with DAA agents during the time of the study. ART regimen was modified in 21 (51.2%) of them.

22 antiretroviral drugs were changed (in one patient 2 modifications were needed), 10 (45.5%) were due to the substitution of one non-nucleoside reverse transcriptase inhibitor (NNRTI) and the other 12 (54.5%) corresponded to a change of a protease inhibitor (PI) of the original regimen. The modifications from a NNRTI to avoid interactions with DAAs resulted in the prescription of another not-contraindicated NNRTI (rilpivirine) in 6 (60%) cases, an integrase strand transfer inhibitor (INSTI) in 3 (30%), and a PI (darunavir/r) in 1 case (10%). The modifications from an original PI resulted in the replacement by another not-contraindicated PI in 5 patients (41.6%), to an INSTI in 4 (33.3%), and to a NNRTI in 3 (25%).

The average ART cost-per-patient was 639.89€ monthly before starting HCV therapy, and 672.68€ later (variations from -121.36€ to +388.67€), which means an increase of 5.12% in the monthly cost per patient.

Conclusions: Original ART had to be modified in a high proportion of patients (more than half in our series) when started HCV therapy. All modifications were due to NNRTI and PI interactions with current DAA agents. These changes have led to a slight increase in the ART cost per patient, which can be considered manageable for public spending.

PO-21 Efficacy and tolerance of the new HCV treatments on genotype 4 patients

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Background & Aims: New direct-acting antiviral (DAA) have been extensively evaluated in pivotal clinical trials in which genotype (GT) 1 HCV infected patients were the biggest subgroup due to its major prevalence in the USA and Europe. Current data regarding the rest of GT, specially GT4, is very scarce, with few clinical trials, all involving small cohorts according to congress communications, having to resort and extrapolate the results from GT1 trials. The aim was to evaluate the effectiveness and safety of the latest DAA on our cohort of HCV GT4 patients with data from previous treatments and to the fourth week after the end of the treatment (SVR 4W).

Methods: Ambispective observational study in our centre including HCV GT4 mono and HIV coinfecting patients who recently started treatment, are currently on it or have finished it, using the latest generation DAA. Base analytic values and global efficiency and tolerance results are described.

Table 5. Virological response under treatment (Undetectable HCV viral load UI/mL)

4W viral response (n = 15)	12W viral response (n = 12)	4W Sustained virological response (n = 7)
80% (1 pt. 22 and 2 pts. < 15 detectable)	100%	100%

Results: From early January to late June 2015, 16 patients HCV GT4 have initiated latest generation DAA treatment: mean age (IQR) 50.5 (46-54) years, 75% male, 69% coinfecting, mean HCV load (IQR) 6.05 (5.56-6.49) Log₁₀ UI/mL, Metavir score fibrosis stage F0-1 (25%), F2 (19%), F3 (6%), F4 (50%), previous Peginterferon (P) + Rivabirin (R) treatment 66% (null response 78%, partial response 11%, relapser 11%). We worked with different treatment regimens: Sofosbuvir (SOF)/Simeprevir (SMP) ± R on 50% patients, SOF/Ledipasvir (LDP) on 25% patients, SOF/Daclatasvir ± R on 12% patients, Ombitasvir-Paritaprevir/R and PR + SMP on 6% patients each. The efficacy is shown on table 5. None of the 4 patients on LDP and antiretroviral therapy including on 3 out of them Tenofovir (1 + Protease inhibitor) had altered their filtration glomerular rate. Lastly, it is imperative to showcase the lack of secondary effects grade 3-4 or treatment withdrawal.

Conclusions: The efficacy and tolerance of the new HCV DAA is excellent in the daily practice as well, ascertaining the good response GT4 shows, in contrast to what happened with PR treatments.

PO-22 Efficacy and safety of therapy against hepatitis C virus infection including direct-acting antivirals in HCV-monoinfected patients in the clinical practice: Results from the GEHEP-MONO Cohort (GEHEP-001 Study)

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Background & Aims: In the last years, options for treatment against hepatitis C virus (HCV) infection have changed radically with the availability of direct acting antiviral (DAA). Data on safety and efficacy of regimens including a DAA are mainly derived from clinical trials. The aims of the GEHEP-MONO study is to evaluate the proportion of HCV-monoinfected patients who show SVR to treatment including DAAs in the clinical practice in patients attending Infectious Disease outpatient facilities, as well as to determine the frequency of adverse events that cause treatment interruption in this setting.

Methods: In this multicentric, prospective cohort study (ClinicalTrials.gov number NCT02333292) all individuals who initiate therapy against HCV including any DAA in Units of Infectious Diseases throughout 13 Spanish hospitals are included. The primary outcome variable for efficacy is the achievement of SVR 12 months after scheduled end of therapy (SVR12), while the primary outcome variable for safety is the discontinuation of therapy due to AE.

Results: A total of 302 individuals have been registered to date. Of these, 156 (51.7%) have reached the SVR12 evaluation point and were entered in the analysis. Median (interquartile range) age was 50.3 (44.7-58.5) years, 114 (73.1%) individuals were male, 76 (48.7%) presented cirrhosis at baseline and 58 (37.2%) subjects were naïve to treatment against HCV. 154 (98.8%) subjects initiated interferon-based therapy, the majority in combination with telaprevir (84%) or boceprevir (12.8%). SVR12 was achieved by 105 (67.3%) individuals, 11 (7.1%) patients did not respond to therapy, 7 (4.5%) suffered virologic breakthrough, 13 (8.3%) subjects discontinued therapy due to AE and 13 (8.3%) individuals presented relapse. The rate of SVR12 in an on-treatment approach was 77.2% (105/136 patients). In a multivariate analysis adjusted for age, sex, baseline HCV RNA levels, IL28B genotype and treatment regimen, bearing cirrhosis at baseline [AOR: 0.314, 95% confidence interval (95%CI): 0.132-0.747; p = 0.009] and previous null or partial response to therapy against HCV infection (AOR: 0.29, 95%CI: 0.109-0.773; p = 0.013] was independently associated with SVR12.

Conclusions: Rates of SVR12 and its predictors to DAA-based therapy in HCV-monoinfected patients are similar to what has been reported for these drugs in clinical trials. Likewise, the rates of discontinuations due to AE reflect the described profile of these drugs.

PO-23 European mitochondrial DNA haplogroups impact on liver fibrosis progression among HCV and HIV/HCV co-infected patients from Northwest Spain

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Background: Mitochondrial DNA haplogroups are associated with the clinical outcome of several chronic diseases (i.e. Alzheimer, Parkinson, osteoarthritis, multiple sclerosis). Moreover, mtDNA haplogroups might be also related with the outcome of liver disease among HCV-infected patients.

Methods: This is a retrospective study in a large cohort of HCV and HIV/HCV co-infected patients in clinical follow-up at two hospitals in Northwest Spain. Epidemiological, clinical and virological data were recorded. The European mtDNA haplogroups were determined using Single Base Extension techniques.

Results: A total of 258 HCV and HIV/HCV co-infected patients were recorded. From these, 5 patients without Caucasian ethnicity and 6 in which mtDNA haplogroup could not be determined were excluded. Finally, the analysis was performed in 247 (34.8% HCV and 65.2% HIV/HCV co-infected). The mtDNA haplogroups was as follows: H (53%), U (10%), J (6%), K (6%), T (9%), V (3%), SHV (3%) and others (I, W, X, M) (10%).

For further analysis, individuals were pooled into the European clusters (HV, KU, JT and others). Overall, we did not find differences between mtDNA haplogroups and median age, gender, IL28B polymorphism, HCV G1-subtypes or HCV-RNA viral load levels at diagnosis. A higher prevalence of HCV G4 was observed in patients belonging to cluster HV (G4 76%; G3 64%; and G1 54%).

A higher prevalence of cluster HV was observed among patients with low fibrosis (F0-F2 63% vs. F3-F4 54%). Clusters HV and KU had lower liver stiffness values than JT and others (8.8 and 8.5 vs. 10.1 and 12.5, respectively). Finally, a lower prevalence of cluster HV (28.6%) was observed among patients with cirrhosis (> 12.5 Kpa), compared with clusters KU, JT, and others (38.2%, 37.9%, 47.6%, respectively). The multivariate analysis showed a

trend to higher level of fibrosis in clusters JT [OR = 1.59 (0.65-3.89)] and others [OR = 2.4 (0.85-6.79)] compared with cluster HV. Furthermore, HCV genotype 4 [OR = 0.37 (0.13-1.07)] was associated with lower likelihood of having cirrhosis compared with genotype 1. Advanced age was identified as risk factor for the development of liver fibrosis. Multivariate analysis was adjusted by age, gender, HCV-diagnosis time and HIV/HCV co-infection.

Conclusions: The mtDNA cluster HV was more prevalent among HCV genotype 4 and patients with lower fibrosis. Cluster HV and HCV genotype 4 seems to confer a lower risk for the development of liver fibrosis. These results might be useful for prioritization of treatment strategies among HCV-infected patients.

PO-24 High frequency of drug-drug interactions between direct acting antivirals and concomitant medications among HIV/HCV-coinfected patients

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Background & Aims: All available direct antiviral agents against HCV (DAA) can exhibit drug-drug interactions (DDI). Switching antiretroviral therapy (ART) because of DDI with DAA is not without risk of adverse events. Central nervous system acting drugs, commonly prescribed to persons who injected drugs (PWID), may be difficult to discontinue. Because of these, we analyzed the frequency and degree of potential DDI between DAA and concomitant medication used by HIV/HCV-coinfected patients.

Methods: All HIV and HCV genotype 1 or 4-coinfected patients, with liver stiffness ≥ 7.6 KPa, attended at a single Unit (November/14-June/15) were retrospectively analyzed. DDI were classified as major, i.e. do not co-administer, or minor, i.e. close monitoring, dosage alteration or change in timing may be required, following the <http://www.hep-druginteractions.org> database.

Results: 109 patients were included, 99 (91%) were PWID. The table 6 summarizes DDI. Major DDI were found in: paritaprevir-r/ombitasvir + dasabuvir (3D), 45 (41%); sofosbuvir/ledipasvir (SOF/LDV), 1 (1%); simeprevir (SMV), 88 (81%); daclatasvir (DCV), 3 (3%). Minor DDI were

Table 6.

	DDI N (%)							
	3D		SOF/LDV		SMV		DCV	
	Minor	Major	Minor	Major	Minor	Major	Minor	Major
NRTI	-	-	54 (49)	-	-	-	-	-
NNRTI	14 (13)	34 (31)	18 (16)	-	-	34 (31)	34 (31)	-
PI/r	51 (47)	9 (8)	-	-	-	60 (55)	14 (13)	-
CCR5 antagonist	6 (5)	-	6 (5)	-	-	-	-	-
Integrase inhibitors	-	3 (3)	3 (3)	-	-	3 (3)	3 (3)	-
Analgesics	12 (11)	-	-	-	12 (11)	-	-	-
Anticonvulsants	4 (4)	1 (1)	2 (1)	1 (1)	4 (4)	1 (1)	2 (2)	1 (1)
Anxiolytics	53 (49)	1 (1)	1 (1)	-	43 (39)	-	-	-
Antidepressants	15 (14)	-	4 (4)	-	15 (14)	-	6 (5)	-
Antipsychotics	6 (5)	2 (2)	-	-	5 (5)	-	-	-
Antidiabetics	1 (1)	-	4 (4)	-	4 (4)	-	4 (4)	-
Gastrointestinals	33 (30)	-	39 (36)	-	6 (5)	-	4 (4)	-
Antihypertensives	14 (13)	-	1 (1)	-	1 (1)	-	1 (1)	-
Lipid agents	1 (1)	11 (10)	13 (12)	-	13 (12)	-	13 (12)	-

found in: 3D, 96 (88%); SOF/LDV, 83 (76%); SMV, 67 (61%); DCV, 65 (60%).

Conclusions: DDI between DAA and ART or commonly prescribed medications are frequently found among HIV/HCV-coinfected patients. Major and minor DDI were more prevalent for 3D and SMV.

PO-25 Hepatitis C virus reinfection after sustained virological response in HIV-infected patients with chronic hepatitis C

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Background & Aims: The chance of hepatitis C virus (HCV) reinfections has led some clinicians to be reluctant to treat hepatitis C in specific settings where reinfections might be particularly common, such as in people who inject drugs (PWID). However, data on the frequency of HCV reinfections in HIV-coinfected PWID, particularly in the setting of subjects who attained sustained virological response (SVR) after therapy for chronic hepatitis C are scarce. The aim of this work was to assess the incidence of HCV reinfections after therapy-induced clearance in HIV-coinfected patients with prior chronic hepatitis C.

Methods: Eighty-four HIV-infected subjects, who had previously achieved SVR after being treated because of chronic hepatitis C, were analyzed. In all of them, at least yearly HCV RNA determinations were carried out during a median (range) of 34 (12-146) months.

Results: Seventy-two (86%) subjects were former PWID of whom 11 (15%) continued to use snorted or injected drugs during the follow-up. Four (4.76%) patients showed HCV reinfection (incidence 1.21 [95% Confidence Interval: 0.3-3.09] cases per 100 person-years). These patients maintained risk factors for HCV infection. In three cases, HCV genotype switched. Phylogenetic analysis of the remaining case suggested reinfection.

Conclusions: The incidence of HCV reinfection in the overall population of HIV-coinfected patients who achieved SVR after being treated against chronic hepatitis C is low. A low frequency of risk behavior is the main factor accounting for this modest rate of reinfection. The possibility of reinfection should not be considered a reason against treatment of HCV infection with direct acting antivirals in PWID.

PO-26 Liver stiffness predicts clinical outcome in HIV/HCV-coinfected patients with compensated cirrhosis

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Background & Aims: To assess if liver stiffness (LS) predicts clinical outcome in HIV/HCV-coinfected patients with compensated cirrhosis.

Methods: Prospective cohort study of 446 HIV/HCV-coinfected patients with a new diagnosis of cirrhosis and no previous liver decompensation (LD). The time from diagnosis to the first LD and liver-related death, as well as the predictors of these outcomes, were evaluated. Besides, the ability of LS to predict outcomes was compared to that of other classical prognostic scores, by means of the comparisons of the AUROC and the integrated discrimination improvement (IDI) between models.

Results: After a median (Q1-Q3) follow-up of 49 (25-68) months, 80 (17.9%) patients developed a first LD. The probability of LD at 3 years was 5% in patients with LS < 21 kPa, 13% in those with LS between 21 and 39.9 kPa and 28% in patients with LS ≥ 40 kPa (p < 0.0001). After multivariate analyses, the variables independently associated with LD were age (HR 1.06, 95% CI: 1.02-1.10; p = 0.001), HBV coinfection (HR 6.93, 95% CI: 2.17-18.76; p = 0.001), consecution of SVR (HR 0.34, 95% CI: 0.13-9.87; p = 0.024), clinical AIDS (HR 1.67, 95% CI: 1.05-2.66; p = 0.028), CTP stage B (vs A) (HR 4.18; 95% CI: 2.38-7.32; p < 0.0001) and baseline LS (comparison group: LS < 21 kPa) (LS 21-39.9 kPa: HR 2.48, 95% CI: 1.31-4.66, p = 0.005; LS ≥ 40 kPa: HR 3.68, 95% CI: 1.88-7.19, p < 0.0001). Comparisons of the ability of LS to predict a LD with that of CTP or MELD scores yielded a better performance of LS than MELD (IDI 3.3%; p = 0.01) and a similar performance of LS and CTP (IDI 0.13%; p = 0.9). By contrast, the combination of LS and CTP stage in a new predictive variable improved the ability to predict outcomes, being the AUROC of the model including this new variable higher than that of the model only based on the CTP stage (AUROC 0.612 vs

AUROC 0.575; $p = 0.06$). Sixty-one (13.6%) patients died during follow-up. In 37 (8.3%) patients, death was liver-related. The variables independently associated with liver related death and/or liver transplant were platelet count $< 50.000/\text{mm}^3$, baseline LS ≥ 21 kPa and consecution of SVR.

Conclusions: LS is an independent predictor of LD and liver-mortality in HIV/HCV-coinfected patients with compensated cirrhosis and provides additional prognostic information to that provided by CTP or MELD scores. The combination of LS and CTP stage in a new predictive index improves the ability of CTP to predict outcome.

PO-27 Increased incidence of cancer and cancer-related mortality among HIV/HCV coinfected patients, 1993-2014

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Background & Aims: Cancer is an increasing problem in HIV-infected patients. Hepatitis C virus infection is frequent among HIV patients and it could modified the incidence and spectrum of malignancies in this population. The aim of this study is to describe the clinical and epidemiological characteristics and the prognosis of HIV/HCV patients who developed a malignancy.

Methods: A cohort of HIV-infected patients was followed at our institution between 1993-2014. Cancer diagnosis and cancer-related mortality were obtained through the hospital coding department. Epidemiological, clinical data and mortality were recorded. A comparative analysis between HIV-monoinfected and HIV/HCV-coinfected population was carried.

Results: A total of 185 HIV patients (117 HIV-monoinfected [63.2%] and 68 HIV/HCV-coinfected [36.8%]) were diagnosed with 192 incident malignant tumors. Mean age at tumor diagnosis was 44 ± 11 years, 81.1% were males, 67% C-CDC and 60% were on antiretroviral treatment. Of the coinfected patients, 32.7% were cirrhotics, only 6 (8.8%) were previously treated against HCV. Cancer incidence increased in HIV-monoinfected from 4.5 cases/1000 patients in 1993 to 11.4 cases/1000-patients in 2014; in HIV/HCV-coinfected: from 2.4/1000-patients in 1993 to 23.3/1000-patients in 2014; it was a relative increase of 1.5 in HIV-monoinfected and 8.8 in coinfected, $p < 0.001$.

Non Hodgkin Lymphoma (NHL) (32.7%), Kaposi (25.7%) and Lung Cancer (16.8%) were the most frequent cancers in HIV-monoinfected patients; in HIV/HCV-coinfected: hepatocarcinoma (27.1%), lung cancers (23.7%) and NHL (18.6%) were the most representative. Globally, in HIV/HCV-coinfected, non-AIDS-defining malignancies were more frequent (76.5%) than in HIV-monoinfected (47.0%), $p < 0.01$. Immunovirological status at diagnosis of tumor did not differ among mono and coinfected patients (301 ± 246 CD4+/mcl in monoinfected vs 321 ± 257 CD4+/mcl in coinfected).

Global mortality was similar in both groups (65.5% in HIV vs 70.1% in HIV/HCV, $p = 0.6$). Survival was lower in coinfected (58.9 ± 10.9 months vs 66.6 ± 8.5 months, $p = 0.02$); excluding hepatocarcinoma, this survival difference still remained. Cancer-related mortality among HIV/HCV increased significantly in the 2004-2014 period (53.1%) vs in 1993-2003 (20.0%), $p = 0.008$.

Conclusions: Incidence of cancer was higher among HIV/HCV-coinfected patients than HIV-monoinfected, not only due to hepatocarcinoma, and it is increasing much faster in coinfected; this population has also lower survival. There is a high risk of NHL with a predominantly B-cell type in coinfected. Preventive actions and eradication of HCV-infection must be considered, and its impact evaluated.

PO-28 HLA-B18 as risk factor of fast progression to severe liver fibrosis in HIV/HCV co-infected patients with minimal or moderate fibrosis: Implications for timing of therapy

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Background & Aims: Treatment is currently prioritized for patients with severe stages of fibrosis (F3-F4), although patients with no or minimal fibrosis are not exempt from rapid progression. However, the risk factors of accelerated progression remain unclear. The aim of our study was to analyze the influence of HLA-B molecules on liver fibrosis progression in HIV/HCV patients.

Methods: A retrospective longitudinal study included HIV/HCV patients in follow-up between 2007 and 2014. Inclusion criteria were: a) at least two determinations of Liver Stiffness Measurement (LSM); b) ≥ 12 months of total follow-up; c) active HCV infection. Exclusion criteria were: a) HCV treatment previous to follow-up; b) cirrhosis at baseline, defined as an LSM ≥ 14.6 kPa. Analytical, demographic and clinical variables were collected. LSM

cutoffs applied were: < 6.5 kPa (F0-F1); 6.5-9.4 kPa (F2); 9.5-14.5 kPa (F3) and \geq 14.6 kPa (F4). Outcome variables were: 1) fibrosis stage progressed at least one stage; 2) fibrosis progressed up to severe liver fibrosis (F3-F4). Patients were censored at: a) an event of interest; b) initiation of HCV treatment; c) loss of follow-up; d) end date of study.

Results: A total of 306 HIV/HCV patients were tested and 104 patients fulfilled the criteria. HLA-B*18 allele (B18^{pos} n = 15; B18^{neg} n = 89) was the only factor associated with progression of liver fibrosis [n = 11 (73.3%) vs. n = 34 (38.2%); p = 0.011]. 9 of 13 (69.2%) B18^{pos} patients with no or mild-to-moderate (stages F0-F2) developed advanced or severe fibrosis (F3-F4) during the follow-up period, while only 20 of 71 (28.2%) B18^{neg} patients with stages F0-F2 progressed to F3-F4. Survival analysis compared the probability of the degree of liver fibrosis increasing among B18^{pos/neg} patients and found differences at 1, 2, 3 and 5 years (log-rank; p < 0.001) and also showed a higher probability of progression to severe fibrosis in B18^{pos} patients at 1, 2, 3 and 5 years (log-rank; p < 0.001). Multivariate Cox regression showed that HLA-B*18 was the only independent risk factor associated with liver fibrosis progression, adjusted for other clinical variables (p < 0.001; HR = 6.62, 95%CI[2.74-16]).

Conclusions: HIV/HCV patients carrying allele HLA-B*18 were more likely to progress more rapidly to developing advanced and severe fibrosis (F3-F4) than HLA-B*18^{neg} patients. These results could help make decisions about the timing of HCV therapy in F0-F2 patients at risk of accelerated progression.

PO-29 Analysis of the effect of NS5A resistance associated variants in the response to daclatasvir-based therapy and their kinetics after virological failure

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Background & Aims: New direct acting antivirals targeting hepatitis C virus (HCV) NS5A gene are currently one of the mainstays of HCV treatment. NS5A resistance associated variants (RAVs) could reduce the efficacy of combinations including NS5A inhibitors. Because of this,

the aim of this study was to analyze the effect of baseline NS5A RAVs in the response to daclatasvir (DCV)-based therapy and the kinetics of RAVs emerging after virological failure.

Methods: All HCV genotype 1 (HCV-1)-infected patients who received therapy with DCV plus pegylated-interferon and ribavirin (PegIFN/RBV) were selected for this study. NS5A RAVs at aminoacidic positions 28, 30, 31, 32, 58 and 93 at baseline and at virological failure were analyzed by population and ultradeep sequencing methods. RAV kinetics after treatment failure were only analyzed by population sequencing methods.

Results: A total of 10 HCV-1-infected patients treated with DCV plus PegIFN/RBV were included in the study. Among them, 4 did not achieve sustained virological response (SVR): 2 HCV-1a infected patients relapsed and 2 HCV-1b infected patients experienced a viral breakthrough (HCV-1b). RAVs identified at baseline in HCV-1a infected patients showed a frequency < 1% in both patients with and without SVR. In HCV-1b infected patients, three variants were identified with high frequency (> 15%). Two RAVs (R30Q and Y93H) in patients who achieved SVR, whereas one variant at RAV aminoacidic position 31 (L31I) was detected in a patient with virological failure. At virological failure, RAVs at aminoacidic positions 30 (Q30R/E) and 32 (P32del) were detected as majority variants (> 80%) in the three available patients. NS5A RAVs detected as main variants at virological failure persisted at a frequency > 80% at least during 24 weeks and up to 48 weeks after the treatment discontinuation. Subsequently, treatment emergent RAVs were detected at less frequency and in combination with other variants at these positions up to 120 weeks after the discontinuation of the treatment. In addition, in one case we did not find a reversion to wild-type strain (Q30). Instead new RAV (Q30R) with the NS5A region was detected during the follow-up and persisted after the clearance of the previous one (Q30E).

Conclusions: RAVs at baseline do not seem to predict the response to DCV plus PegIFN/RBV treatments. However, NS5A RAVs are detected as majority variants in all virological failures included in this study. These RAVs persisted during the period of observation after virological failure, up to 120 weeks.

PO-30 Baseline NS3 resistance associated variants to Simeprevir and Paritaprevir and viral phylogeny of genotype 1 patients in Spain

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Background & Aims: Simeprevir and paritaprevir are two NS3/4a inhibitors currently being used in Spain for HCV treatment. Although still unclear, some baseline resistance associated variants (RAVs) in NS3 may compromise their antiviral activity. We have investigated the prevalence of NS3 baseline RAVs in patients infected by HCV genotype 1 across Spain, and investigated viral phylogeny of HCV-1 strains from Spanish patients in relation to other circulating in other parts of the world.

Methods: Observational retrospective study including patients from Andalucía, Levante, Galicia and Navarra. HCV NS3 (1-181) was Sanger sequenced and analysed using geno2pheno HCV (<http://hcv.bioinf.mpi-inf.mpg.de>). HCV-1a clade, RAVs (Lontok E-doi:10.1002/hep.27934) and geno2pheno resistance to simeprevir and paritaprevir were recorded. Maximum-likelihood (ML) phylogenies were estimated using NS3 sequences from Spain, North America, and Europe.

Results: We have studied 254 patients. Median baseline \log_{10} viral load was 6.39 (IQR 6.12-6.76) UI/ml, median age was 46 (IQR 41.25-53.75) years and 80% were male. 219 patients were HCV-1a genotype, and 35 HCV-1b. For HCV-1a, baseline NS3 RAVs were detected in 60 patients (27.4%): V36A, n = 1 (0.5%); V36M, n = 7 (3.2%); Y56H, n = 1 (0.5%), Q80K, n = 21 (9.6%); S122G, n = 16 (7.3%); S122R, n = 2 (0.9%); R155K, n = 4 (1.8%); D168A, n = 4 (1.8%); D168E, n = 8 (3.7%); D168 H, n = 2 (0.9%); D168V, n = 2 (0.9%); D168Y, n = 2 (0.9%), and V170T, n = 2 (0.9%). HCV-1a patients were infected mostly by clade II (n = 172, 78.2%). Q80K was significantly more prevalent (p < 0.001) in clade I than in clade II (37.5% vs 2.3%). No other RAV was associated to HCV-1a clade. For HCV-1b baseline NS3 RAVS were detected in 5 patients (14.3%): Q80R, n = 1 (3%); S122A, n = 1 (3%); S122T, n = 3 (8.6%) and D168E, n = 1 (3%). Using geno2pheno interpretation, 25/254 patients (9.8%) showed resistance to paritaprevir, all HCV-1b infected patients, and 60 patients (23.5%) showed resistance to simeprevir (56 HCV-1a patients and 4 HCV-1b patients). HCV_1a clade I sequences were highly interspersed between Spanish isolates, and with sequences from Italy, Germany and North America, while HCV_1a clade II were highly interspersed with sequences from Italy, Germany and Switzerland.

Conclusions: Baseline RAVs in NS3 are more frequent in HCV-1a genotypes, and Q80K prevalence is low in the Spanish population, possibly due to a spread of clade II HCV-1a isolates. Caution must be made when interpreting resistance, as clinically validated algorithms for RAVs interpretation have not yet been implemented. Multiple

introductions from different geographic regions can add to explain the high variability found in Spain.

PO-31 Prevalence of baseline NS5A resistance associated variants in genotype 1 patients in Spain

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Background & Aims: Baseline resistance associated variants (RAVs) in the NS5a region of HCV have been related to a poorer Sustained Virological Response (SVR) in cirrhotic patients. Recent updates of HCV treatment guidelines (AASLD-IDSA) highlight the importance in this subset of patients, or those with an urgent need for retreatment to test for NS5a RAVs. In this study we have investigated the prevalence of NS5a baseline RAVs in patients infected by HCV genotype 1 naïve to antiviral treatment in the south of Spain.

Methods: We have performed an observational study including patients with a previous HCV-1a or HCV-1b genotype, tested with NS5b sequencing from November 2014 to July 2015 in our laboratory. HCV NS5a (codons 1-96) was Sanger sequenced. All sequences were analysed using geno2pheno (g2p) HCV (<http://hcv.bioinf.mpi-inf.mpg.de>) and RAVs at positions 28, 29, 30, 31, 32, 58, 62, 92 & 93 were evaluated according to the g2p algorithm and to the recent consensus of Lontok E, et al (doi: 10.1002/hep.27934). Resistance to daclatasvir, ledipasvir, and ombitasvir (g2p) was also recorded.

Results: We have studied 105 patients. Median baseline \log_{10} viral load was 6.26 (IQR 5.75-6.59) UI/ml, median age was 53 (IQR 46-59) years and 69 (66%) were male. 54 patients were infected by HCV-1a genotype, and 51 were infected by HCV-1b. For HCV-1a, baseline NS5a RAVs were detected in 9 patients (17%) using g2p (28T, n = 1; 28V, n = 4; 30H, n = 1; 31Q, n = 1; 58L, n = 1; 58P, n = 2; 58Q, n = 1) and 5 patients (9%) using the Lontok consensus (28T, n = 1; 28V, n = 3; 30H, n = 1); One patient showed resistance to daclatasvir, two to ledipasvir, and one to ombitasvir. For HCV-1b infected patients, NS5a RAVS were detected in 12 patients (24%) (non significant differences from HCV-1a) using g2p (30Q, n = 2; 31F, n = 1; 31I, n = 1; 31M, n = 4; 32S, n = 1; 58S, n = 1; 92T, n = 1; 93H, n = 2) and 10 patients (20%) using the Lontok consensus (30H, n = 1; 30Q, n = 1; 31F, n = 1; 31M, n = 4; 58S, n = 1; 93H, n = 2). Two HCV-1b infected patients showed resistance to daclatasvir, six patients to ledipasvir and two to ombitasvir.

Conclusions: Baseline RAVs to NS5a were equally distributed (absolute numbers) across HCV-1a and HCV-1b

genotypes. Attention should be paid on which mutations must be considered relevant, as different algorithms may score them in different ways. Using g2p for interpretation, NS5a RAVs showed a lower impact on resistance to dactatasvir and ombitasvir (3 cases each; 2.8%), than to ledipasvir (8 cases; 7.6%).

PO-32 Detection of Q80K polymorphism in NS3 protease of HCV genotype 1a by a Real Time allele-specific PCR

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Background: Currently, direct Sanger sequencing of NS3 protease is used to detect Q80K. The Optimist-2 trial shows an impact on SVR12% of Sofosbuvir + Simeprevir 12 week treatment in genotype 1a cirrhotic patients. In our study we have designed an Allele-Specific Real Time PCR assay for the detection of Q80K and compared it with Sanger sequencing.

Methods: We have conducted an observational, ambispective study of all genotype 1a samples from patients attended at Complejo Hospitalario Universitario Granada, Spain, from 2011 to 2015. These samples were used as training set. As a validation set, we have used a blinded panel of samples previously sequenced at the University of Cologne. HCV NS3 viral protease (codons 10 to 181) were Sanger sequenced and analysed using geno2pheno_[HCV] (<http://hcv.bioinf.mpi-inf.mpg.de>). Q80K polymorphism was also investigated by a homemade allele-specific real time PCR protocol. Briefly, the RT-PCR product of NS3 viral amplification was 1/25 diluted and subjected to AS-PCR reactions aiming to detect AAA/AAG (mutant) and CAA/CAG (wild type) alleles.

Results: The training set consisted of 132 HCV 1-infected patients [median age (years), 46 (IQR 41.25-53.75), 108 males (82%), median HCV viral load (Log IU/ml) 6.39 (IQR 6.12-6.76). Q80K mutation was detected in 10 patients making a prevalence of 7.6%; AS-RT PCR successfully detected all Q80K polymorphisms detected by Sanger (AAA allele in 90% of the Q80K positive cases and AAG in 10%). HCV 1a Clade II was the most prevalent (n = 106; 80%). Two cases of Q80K were detected in the Clade II population and 8 in the Clade I (p < 0.001). The validation set consisted of 48 samples, 26 carrying Q80K positive (22 AAA; 3 AAG; 1 AAR); our AS-PCR successfully detected all but one AAA positive case. Using Sanger as reference, sensitivity, specificity, positive predictive

value and negative predictive values of the AS-PCR test were 97%, 99%, 97% and 99% respectively.

Conclusions: We have developed an allele-specific real time PCR for the detection of Q80K NS3 protease mutation in HCV 1a genotypes that can be easily performed in routine diagnostic laboratories without the need of DNA sequencing facilities.

PO-33 Dimension of chronic hepatitis C virus in HIV-infected patients in the interferon-free era: an overview from southern Spain

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Background: The implementation of direct-acting antiviral drugs against hepatitis C (HCV) is prioritized for several populations where application will provide the most immediate and impactful benefit, such as HIV co-infected patients. In this scenario, a precise knowledge of the situation of HIV/HCV chronic co-infection is required to properly address this disease.

Methods: A prospective cross-sectional study was performed in 21 hospitals in Andalusia (Spain). The study population consisted of HIV-infected patients with active HCV chronic infection who were not receiving HCV treatment at the time of inclusion.

Results: A total of 13,506 HIV-infected patients were included in the study, 2561 (18.9%) of whom presented active chronic HCV infection. The majority of patients included were on HAART (96.2%), showed plasma levels with an undetectable HIV viral load (92.5%), and had good immunological status (median CD4+ cell count of 486 cells/mL). The main HCV route of transmission was injection drug use (87.7%). The HCV genotype distribution was as follows: 58.1% were genotype 1; 1.1% were genotype 2; 16.1% were genotype 3, and 22.1% were genotype 4 (2.6% were missing data). In total, 24.8% of the patients showed liver fibrosis stage F0-F1, 27.9% were stage F2,

16.7% were stage F3, and 21% were stage F4 (9.6% were missing data). With regards to previous HCV treatment experiences, 68.05% of patients were naïve, and 31.95% had failed to respond to a previous treatment. The percentage of F4 patients was higher among patients who had received treatment compared to previously untreated patients (30.4% vs. 16.6%, $p < 0.001$).

Conclusions: The burden of HCV/HIV co-infected patients in our population was reported as one in five HIV-infected patients requiring HCV treatment. Implementation of extra resources to face this important health challenge is therefore mandatory.

PO-34 High incidence and prevalence of hepatitis C in Europe's largest shantytown

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Background & Aims: The Cañada Real Galiana is a shantytown on the outskirts of Madrid, it concentrates 90% of the sale and consumption of illicit drugs in Madrid. The aim of this study was to evaluate the prevalence and incidence of HCV in this population.

Methods: A harm reduction facility followed active drug users during a two-year period (2013-2014).

Results: An HCV test was performed on 325 active drug users who were seen at the harm reduction facility during the study period. Two hundred and eleven (65%) drug users had a reactive HCV antibody test. HCV RNA testing was performed on only 129 patients of whom 110 (85%) had an active infection when tested. According to the HCV genotype, 57%, 36%, 4% and 3% harboured genotypes 1, 3, 4 and 2 respectively. The estimated rate of spontaneous clearance of the virus after infection in this population was around 15 percent. None of the outreach drug users had ever received follow up or therapy for HCV infection.

Fifteen individuals acquired HCV infection during the follow up period (12 new infections and 3 reinfections). The incidence rate of HCV infection in active drug users was 10.3%. All the new infected patients were active injecting drug users, 50% on methadone, 2 individuals injected cocaine and the rest of them injected heroin and cocaine. All except one were Spaniards, median age 36 years IQR (28-47); 60% male; 2 (13%) patients had HIV coinfection (one patient on antiretroviral treatment and undetectable); the median time to seroconversion was

10 IQR (1.7-19) months from follow up; median injections per person/day was 11 IQR (7-20); 20% had a symptomatic hepatitis, 84% were HCV genotype 1 infections and 2 patients had an spontaneous clearance.

Conclusions: In Cañada Real, the largest shantytown in Western Europe, the incidence and prevalence of HCV infection in active drug users is high. With the availability of newer and shorter duration therapies for HCV, treatment as a prevention approach could be feasible as a harm-reduction strategy.

PO-35 Identification of HCV genotype 3 by a commercial assay challenged by natural polymorphisms in isolates circulating in Spain

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Background & Aims: HCV genotyping is required in clinical practice in order to determine the type and duration of antiviral therapy. From 2009 to 2014, an indeterminate genotype result was obtained for 26 out of 1338 patients (1.94%) with the Real-Time HCV Genotype II assay (Abbott) at a tertiary care centre (HUGTiP). The reference genotyping method (NS5B Sanger sequencing and phylogenetic analysis), classified 24 cases as genotype 3 (20 as 3a and 4 as 3k), representing 7.95% of all HCV-3 detected cases ($n = 302$). One patient was from Belarus, 15 (62.5%) from Pakistan, and 8 (33.3%) from Spain. HCV-3 is the second most prevalent worldwide and in Spain, it has been associated with a higher risk for liver disease progression and a lower response to the latest antivirals. Given the relevance of accurately identifying HCV-3, we aimed to characterize the genetic diversity in the HCV 5' untranslated region (5'UTR) by ultra-deep pyrosequencing (UDPS), in order to find out whether these indeterminate results were due to the presence of mutations in the binding site of the HCV-3-specific probe of the genotyping assay.

Methods: For the 24 indeterminate samples the 5'UTR was amplified and subjected to UDPS with the 454/GS-Junior platform (Roche) following a recently published

methodology. For all identified haplotypes within each sample, the genotype/subtype was assigned by phylogenetic analysis. For comparison, three additional samples that were correctly identified as HCV-3 by the real-time assay were also analyzed.

Results: A median UDPS coverage of 591x (IQR,141-1830) was obtained per patient. For the highly conserved 5'UTR only one major sequence was identified in 11 patients. In the rest of patients, 1-3 additional minor sequences were found (representing < 6.5% of all sequences). HCV genotyping based on 5'UTR UDPS was in agreement with NS5B Sanger sequencing in all cases, confirming the absence of mixed infections and recombination events between different genotypes/subtypes. The alignment of the 5'UTR sequences evidenced the presence of 1-3 polymorphisms at the probe-binding site differentiating indeterminate from correctly genotyped HCV-3 samples.

Conclusions: The sequences generated in this study could help to improve the ability to detect HCV-3 by this commercial assay through a product change. This improvement would be relevant in Spain and in many countries where HCV-3 is highly prevalent or receive significant immigration from these areas. Additionally, these sequences will be useful for the assessment of HCV-3 detection by other assays, and for the design of new genotyping assays.

PO-36 Related factors to advanced liver fibrosis in HIV/HBV co-infected patients on antiviral therapy

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Background: There are few data of fibrosis development in HIV/HBV chronic infected patients on antiretroviral treatment (ART). This study evaluates the prevalence of advanced fibrosis measured by transient elastography (TE) and investigates the relationship with virological, epidemiological and metabolic factors.

Methods: Cross-sectional cohort study including all HIV/HBV co-infected patients on ART followed in a reference Hospital in the Northwest of Spain. Advanced fibrosis was defined as TE > 7.5 kPa, and Metabolic Syndrome (MS) according to the criteria of the International Diabetes Federation. Factors associated with advanced fibrosis were explored by univariate and multivariate adjusted logistic regression analyses. Statistical analysis was performed with the SPSS (v19.0).

Results: A total of 65 HIV/HBV co-infected patients were included; 61 (93.8%) had an optimal TE (8.8 ± 4.7 kPa);

mean age 46 ± 9 years-old and 70.5% were male, 95.1% were from Europe; 68.8% were smokers and 9.8% had an alcohol consumption > 40g/day. Mean time of HBV/HIV co-infection follow-up: 13 ± 5 years. All were on ART with 9.8 ± 5.8 years of exposure: 95.1% containing tenofovir/emtricitabina and 4.9% entecavir and lamivudine; 95.1% had undetected HBV-DNA viral load and 95.1% HIV-RNA load. Mean CD4 count was 534 ± 210 cells/ μ L, 41.0% were CDC-C category.

HBV genotypes distribution were: A-43.4%, B-9.4%, D-26.4%, E-7.5%, F-3.8%, G-3.8% and H-5.7%. Anti-HDV-Ab was positive in 19.7%, anti-HCV-Ab in 27.9% and HBeAg+ in 45.9%. The prevalence of MS was 32.8% (22.3-45.3), and it increased with age (18.4% in < 40 years-old, 28.3% in 41-60 years and 60.0% in > 60). Regardless to cardiovascular treatments: 32.3% received hypolipidemic therapy, 13.1% anti-diabetics agents and 10.8% anti-hypertensives.

The prevalence of advanced fibrosis was 57.4% (44.9-69.0). The multivariate analyse identified the following factors associated with fibrosis (OR, CI95%, p): presence of anti-HDV-Ab+ (4.88, 1.90-15.76, 0.01), HBeAg persistence (4.04, 1.50-17.16, 0.01), MS (3.35, 1.20-11.40, 0.04) and time of follow-up (2.10, 1.10-4.60, 0.04). There was no association with the transaminases levels, platelets count nor HBV genotypes or age.

Conclusions: In patients HIV/HBV co-infected with a complete control of HIV and HBV replication a rate of 57.4% of advanced liver fibrosis is recognized. The HDV co-infection and the persistence of HBeAg are the strongest factors associated with it. MS also plays an important role in the development of fibrosis among well-controlled HIV/HBV co-infected patients. Therefore, in HIV/HBV co-infected patients, with complete control of HIV and HBV viremia, liver fibrosis and metabolic disorders should be monitored, especially for those patients HDV co-infected and HbeAg+.

PO-37 Incidence of acute hepatitis E virus in HIV-infected patients and associated risk factors

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Background: Although hepatitis E virus (HEV) seroprevalence has been well described, its incidence in developed countries has not been properly documented. This represents the first step towards quantifying the extent of this emerging disease in developed countries.

Methods: The study population of this prospective longitudinal study consisted of HIV-infected patients who were seronegative for HEV antibodies at the start of the study. All patients included were followed up every 3-6 months during the study period. Patients underwent clinical examination and routine hematological, biochemical, immunological and virological assessments at each visit. The outcome variable was HEV seroconversion, defined as the development of detectable anti-HEV antibodies (IgG and/or IgM) and the risk factors for infection. ELISA to determine anti-HEV IgG and IgM was performed for all patients at every visit. Cumulative incidence and incidence rates of HEV were calculated, and bivariate analysis compared cumulative incidence between groups to identify variables related to HEV seroconversion.

Results: 698 patients who tested negative for anti-HEV IgG and IgM constituted the initial study population. 627 (89.9%) of these agreed to participate in the study and became the final study population. Median follow-up (IQR) was 11.96 months (8.52–14.52), with a median (max-min) of 3 (4–2) anti-HEV antibodies per patient. During the study period, forty-one patients developed detectable anti-HEV antibodies (cumulative incidence: 6.5%); thirty-six (87.8%) patients tested positive for anti-HEV IgG, and five (12.2%) for IgM. No patient tested positive for both IgG and IgM antibodies. The incidence rate was 7.2 cases per 100 patients/year (95% CI: 5.04–9.16 cases per 100 patients/year). Of the factors related to clinical HIV or hepatitis virus co-infection, bivariate analysis identified only a rural habitat as a risk factor for HEV seroconversion in the study. The rate of incidence of HEV seroconversion among patients living in rural areas was 17.4 cases per 100 patients/year; among patients living in urban areas it was 5.8 cases per 100 patients/year (log rank tests: $p < 0.001$).

Conclusions: We found a relatively high rate of incidence for HEV seroconversion in HIV-infected patients (7.2 HEV seroconversions per 100 patients/year). The rural habitat is the main risk factor for infection. The clinical implications of HEV seroconversion should be studied in HIV-infected patients.

PO-38 Changeable etiology of acute viral hepatitis: current role of hepatitis E virus

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Background & Aims: A progressive decrease in the incidence of hepatitis A (HAV), B (HBV), C (HCV) and D (HDV) has been observed over the last two decades. Regarding hepatitis E virus (HEV), new features have recently been discovered about its epidemiology. The importance of HEV as a cause of acute hepatitis is not as well-known as other viral agents, because it is not often included in the routinely serological diagnostic of acute liver diseases. The aim of the study was to determine the prevalence of hepatitis viruses (HAV, HBV, HCV, HDV and HEV) in the cases of acute liver disease in the Southwest area of Madrid.

Methods: A two-year study was conducted starting in January 2013. All pediatric and adult patients admitted to Emergency Department and Primary Care centers attached to Hospital 12 de Octubre (Madrid) with serum alanine aminotransferase (ALT) levels 10 times higher than the upper normal values and with a requested serological profile for viral hepatitis (HAV, HBV and HCV) were enrolled. Active search was performed with LIS (Laboratory Internal System). Serum bank samples of the enrolled patients were recovered to retrospectively determine markers for viral hepatitis that were not initially included (HEV). The following markers were determined in all samples: anti-HAV IgM, HBsAg and anti-HBc IgM, anti-HCV IgG, HCV Ag (Architect, Abbott), and anti-HEV IgM (DS-EIA-Anti-HEV-M, Diagnostics Systems Italy). Positive samples for anti-HEV IgM were confirmed with HEV-RNA (HEV RT-PCR, RealStar, Altona). Anti-HDV IgG (antiHD-EIA, Diasorin) was performed in positive samples for HBsAg.

Electronic medical records were reviewed (Including serological background and follow-up)

Results: 269 samples from patients with a requested serological profile for viral hepatitis were studied. According to serological markers and medical history a total of 52 acute viral hepatitis were detected: 15 (28.8%) HAV, 10 (19.2%) HBV, 7 (13.5%) HCV, 0 (0%) VHD and 20 (38.5%) HEV (12/20 HEV-RNA positive). Median age was 19 years (2-49) for HAV, 37 years (19-53) for HBV, 36.5 years (32-79) for HCV and 58.5 years (23-80) for HEV.

Conclusions: In view of the results, HEV can be considered a more frequent cause of acute viral hepatitis than previously documented. Therefore, serological testing for HEV might be included in the routine study of acute liver disease in adults in cases of high clinical suspicion.

Poster Presentations

P-39 **KIR2DS2 is a strong predictor of thrombocytopenia secondary to pegylated interferon-alpha treatment: a lesson from HIV/HCV co-infected patients**

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Background: Thrombocytopenia is the leading cause of dose reduction of interferon, early therapy discontinuation and worse clinical outcomes like bleeding complications. We evaluate the role of the natural killer cell (NK) killer immunoglobulin-like receptor (KIR) in developing thrombocytopenia secondary to Peg-IFN therapy in HIV/HCV co-infected patients.

Methods: Caucasian HIV-infected patients with chronic hepatitis C, genotype 1, naïve to HCV treatment and receiving their first course of Peg-IFN/RBV combination therapy, were enrolled in the study. Whole blood samples were collected at baseline for genetic determination. KIR genotyping was performed using sequence-specific primers able to detect the presence of 16 different KIR genes. KIRs associated with decline in total platelet count were selected. Reductions in platelet count were analyzed by KIR genotype between baseline and weeks 1, 2, 4, 8 and 12. The association between KIR genotype and time to development of thrombocytopenia was assessed.

Results: Fifty-eight HIV/HCV infected patients who started treatment with Peg-IFN/RBV were enrolled in the study. KIRs 2DL2, 2DL5, 2DS1, 2DS2, 2DS3, 2DS4_{FULL}, 2DS5 and 3DS1 were included in the analysis. Every patient who lacked KIR2DL2 (n = 25), except one, also lacked KIR2DS2 (n = 24). Platelet count decline was analyzed at

different weeks of treatment according to KIR genotype and only lack of KIR 2DS2 was associated with platelet decline. Baseline median platelet counts were similar among patients bearing KIR2DS2 (171,500 cells/mL (122,000-215,250 cells/mL) and those lacking KIR2DS2 (189,000 cells/mL; IQR: 137,500-216,500 cells/mL) (p = 0.199). Absence of KIR2DS2 was strongly associated with the development of thrombocytopenia during Peg-IFN treatment (Absence of KIR2DS2: 13/24 [54.2%]; Presence of KIR2DS2: 7/34, [22.5%], p = 0.012). Patients with KIR2DS2 were free of thrombocytopenia longer than those without KIR2DS2 (Log-rank test = 0.008) (Figure 2), with mean time to development of thrombocytopenia being 6.6 weeks (5.7-9.43 weeks) and 10.3 weeks (9.05-11.71 weeks) among patients with presence and absence of KIR2DS2, respectively.

Conclusions: In conclusion, we found that lack of KIR2DS2 was associated with a greater decline in platelet count during HCV treatment with Peg-IFN in HIV co-infected patients. Determination of this genetic marker before starting HCV treatment could identify those patients with a high chance of developing thrombocytopenia during the first 12 weeks of therapy and help individualize treatment regimen. Studies are needed to confirm our results.

P-40 **Impact of baseline liver stiffness on the response to therapy against chronic hepatitis C virus infection including a direct-acting agent in patients with cirrhosis. HEPAVIR-DAA and the GEHEP-MONO (GEHEP-001 Study) cohorts**

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Background & Aims: The presence of cirrhosis is uniformly associated with a poorer response to DAA-based therapy against HCV infection. Consequently, specific clinical trials or substudies within clinical trials in cirrhotics patients are usually conducted. In these patients, different level of liver stiffness is strongly associated with the clinical outcome. However, whether the degree of liver stiffness has also an impact on the likelihood of sustained virological response (SVR) in such patients or not still remains unclear. Therefore, the aim of this study was to evaluate the impact of the grade of liver stiffness on SVR to DAA-based therapy in patients with cirrhosis.

Methods: This is a retrospective analysis of all patients included in the prospective HEPVIR-DAA and GEHEP-MONO cohorts (clinicaltrials.gov ID NCT02057003 and NCT02333292) who presented cirrhosis at treatment initiation and who completed a course of therapy against HCV infection including a DAA. Cirrhosis was defined as a liver stiffness (LS) equal or above 12.5 kPa measured by FibroScan®. The outcome variable was SVR twelve weeks after the scheduled end-of-therapy (SVR12).

Results: A total of 177 patients were included, 103 (58.5%) were HIV coinfecting and 167 (94.4%) individuals received an interferon-based regimen. The overall median liver stiffness (interquartile range) at baseline was 21.5 (16.8-32.7) kPa. SVR12 was achieved by 96 (54%) subjects in an intention-to-treat analysis. Patients who achieved SVR12 had a median (interquartile range) LS of 20.7 (16-29.1) kPa versus 25.1 (17.3-35.6) kPa in those without SVR12 ($p = 0.07$). The numbers of patients who achieved SVR12 according to baseline LS were: 49/80 (61.3%) patients with a LS of 12.5-20.9 kPa, 37/72 (51.4%) subjects with a LS of 21-39.9 kPa and 10/25 (40%) patients with a LS above or equal to 40 kPa (p for linear trend = 0.05). In an on-treatment analysis, 29/128 (22.7%) patients with a LS below 40 kPa versus 8/20 (40%) with a LS equal or above 40 kPa did not respond to therapy or showed a virologic breakthrough ($p = 0.096$). The numbers of patients who discontinued due to adverse

events with LS below 21 kPa versus LS equal or above 21 kPa were 6/80 (7.5%) versus 14/97 (14.4%), respectively ($p = 0.147$).

Conclusions: Cirrhotics patients with higher LS respond more poorly to DAA-based therapy against chronic HCV infection in the clinical practice, at least when interferon-based regimens are used. This should be considered when designing clinical trials in cirrhotics, so that results are interpreted according to the degree of LS.

P-41 Serum FGF21 level predicts lack of moderate and severe hepatic steatosis in HIV/HCV co-infected patients

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Background & Aims: Hepatic steatosis (HS) is a common condition in HIV and HCV co-infected patients. Since HS is a curable condition that can progress to end-stage liver disease, early identification is paramount in the context of HIV/HCV co-infection. In humans, high serum levels of fibroblast growth factor 21 (FGF21) have been linked to insulin-resistant states, obesity and non-alcoholic fatty liver disease. Our aim was to assess the usefulness of serum FGF21 levels for detecting HS in HIV/HCV patients.

Methods: Co-infected patients were included in the study and stratified according to their controlled attenuation parameter (CAP) values ($S0 \leq 237.7$; $237.7 > S1 \leq 259.3$; $259.4 > S2 \leq 292.3$; $S3 > 292.3$ dB/m). Serum was tested for FGF21 levels and positive (PPV) and negative predictive values (NPV) for detecting HS and degree of HS were calculated. Predictive accuracy was assessed by calculating the area under the receiver operating characteristic (AUROC) curve.

Results: A total of 127 HIV/HCV patients were enrolled in the study. Sixty-eight (53.5%) of these had HS and 59 (46.5%) did not. Subjects with HS showed higher liver stiffness values ($P = 0.005$), BMI ($P < 0.001$), serum GGT ($P = 0.007$), triglycerides ($P = 0.014$) and FGF21 levels ($P < 0.001$) compared with non-steatosis patients. The AUROC values of serum FGF21 concentrations for predicting HS, $HS \geq S2$ and $HS \geq S3$ were 0.72 (95% CI: 0.628–0.813), 0.787 (95% CI: 0.706–0.867) and 0.751 (95% CI: 0.653–0.848), respectively. When patients were stratified by degree of HS, serum FGF21 levels varied among groups ($P < 0.001$). The serum FGF21 cut-off value of 200 pg/mL had the highest NPV for $HS \geq S2$ (89.3%; 95% CI: 78.5–95%).

Conclusions: Serum FGF21 levels are increased in HIV/HCV patients with HS. We also report a serum FGF21 value with a high NPV for predicting the lack of moderate and severe HS. Since HS is highly prevalent in HIV/HCV patients, this minimally invasive biomarker could be used for diagnosis and follow-up of the disease.

P-42 Hepatitis C virus Core variations are associated with sustained virological response to combinations including NS3/4A protease inhibitors

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Background & Aims: Different Core variations have been associated with sustained virological response (SVR) in genotype 1b hepatitis C virus (HCV-1b)-infected patients treated with pegylated interferon plus ribavirin (PEG-IFN/RBV) in different ethnicities. Similarly, Core variations at position 70 have been associated with SVR in Asian HCV-1b-infected patients treated with telaprevir plus PEG-IFN/RBV. Thus, our aim was to analyze the impact of Core variations on SVR in Caucasian patients infected with HCV-1 who were treated with a HCV protease inhibitor (HCV-PI) plus PEG-IFN/RBV regimen.

Methods: Caucasian HCV-1 infected patients who received HCV-PI/PEG-IFN/RBV from June 2010 to October 2014 were included in this study. Core variations at aminoacidic positions 62, 70, 75, 91 and 110 were analyzed by population sequencing. Association analyses between Core variants and SVR were carried out separately for HCV-1a and HCV-1b subgroups of patients. Only those variants with prevalence > 10% were selected.

Results: A total of 56 patients were included in the study, 37 (66.1%) infected with HCV-1a and 19 (33.9%) infected with HCV-1b. Among them, 34 (60.7%) were treated with telaprevir, 13 (23.2%) with boceprevir, 8 (14.3%) with faldaprevir and 1 (1.8%) with simeprevir. There were almost no variations at Core selected positions among patients harbouring HCV-1a. In HCV-1b-infected patients, Core variants at aminoacidic positions 70, 75 and 110 were identified in 11 (57.9%), 17 (89.5%) and 7 (36.8%) individuals, respectively. Among HCV-1b-infected patients, the proportion of individuals who achieved SVR according to Core variations were: 8 (72.7%) for R70Q carriers and

8 (100%) for those without the variation ($p = 0.228$); 15 (88.23%) for T75A carriers and 1 (50%) for those without the T75A variant ($p = 0.298$); 4 (57.1%) for T110N carriers and 12 (100%) for patients without the variation ($p = 0.036$).

Conclusions: Core T110N variation is associated with a lower rate of SVR in Caucasian HCV-1b-infected patients receiving a HCV-PI plus PEG-IFN/RBV.

P-43 Hepatitis C genotype influences post-liver transplant outcomes in chronic infected patients in Santiago de Compostela District (Northwest Spain)

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Background: Recurrence of HCV infection after liver transplantation (LT) is characterized by an accelerated progression to cirrhosis. As many of the factors known to be associated with more aggressive recurrence and faster fibrosis progression cannot be modified, graft reinfection remains a major problem for most LT programs worldwide. The influence of HCV genotype (particularly genotype 1b) on the severity of disease recurrence following LT is also controversial.

Methods: The genotype and subtype of the HCV were studied by line probe assay (INNO-LIPA HCV II, Siemens Healthcare Diagnostics Inc., Germany) in 107 patients with recurrent HCV infection following LT. There were 85 males and 22 females with a mean age of 63 years (range 35-83). Frequency of different genotypes among patients was assessed according to gender and age at the time of sampling.

Results: Among 107 recipients (12 [11.2%] genotype 1a, 72 [67.3%] genotype 1b, 2 [1.9%] genotype 2, 13 [12.1%] genotype 3, and 8 [7.5%] genotype 4. Graft reinfection occurred in 7 recipients genotype 1a, 52 genotype 1b, 2 genotype 2, 8 genotype 3 and 7 genotype 4.

Conclusions: The risk of recurrence of HCV infection after liver transplantation can be influenced by genotype, compared to other studies where they have not found significant differences between genotypes. Of note, HCV recurrence after liver transplantation occurred in 7 HCV genotype 4 (87.5%) recipients.

P-44 Phylogeography of hepatitis C virus strains circulating in Spain

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Background: Current knowledge of HCV molecular epidemiology in Spain is limited to genotype distribution. Phylogeography and phylodynamics are new molecular epidemiology tools that may allow improving knowledge on viral distribution and migration. In this study we present data on molecular phylogeography of HCV strains circulating in Spain.

Methods: We have studied 251 patients from Andalucía, Galicia & Levante. A fragment of the HCV NS5b gene (8307-8614 nt) from 113 HCV-1a genotype, 68 HCV-1b, 6 HCV-2, 39 HCV-3 and 25 HCV-4, were Sanger sequenced for this study. In addition, NS5b sequences from Los Alamos database (8307-8614 nt), were downloaded [2021 HCV-1a genotype, 2613 HCV-1b, 960 HCV-2, 1078 HCV-3 and 978 HCV-4]. Redundant sequences or those without geographic information were discarded. Fasta sequences were edited with PhyDe (Phylogenetic Data Editor) and aligned with CLUSTAL W. For each genotype we built phylogenetic trees using maximum verosimilarity in RaxML following GTR + G + L evolutionary model. We analysed phylogenetic relationship of Spanish HCV isolates with those from other regions, by analysing clusters with bootstrap values > 70%.

Results: Clustering was rare among Spanish HCV-1 and HCV-3 isolates: for HCV-1a and HCV-3, we only found one cluster comprising two patients each, and none of the Spanish isolates were phylogenetically related with sequences from other geographic areas. This was also true for HCV-1b isolates, though intra-Spain clustering was more frequent than for HCV-1a, as we found 17 small clusters [11 (n = 2 patients), 3 (n = 3), 1 (n = 4)]. Clustering was more frequent for HCV-2 and HCV-4 isolates: for HCV-2 genotype, all our 6 isolates clustered into 3 different clusters, and 4 isolates joined two wide inter-country clusters [cluster 2.1, bootstrap = 74%, comprising 70 isolates from Spain, France, Burkina-Faso, Venezuela, UK, Netherlands and Canada; cluster 2.2 (bootstrap = 94%), 62 isolates from Spain, France, Netherlands, Canada, Morocco and Vietnam]; 12 HCV-4 Spanish isolates clustered into an inter-country cluster (n = 102; bootstrap = 89%), from France, Canada, United States, Ireland, Belgium and China.

Conclusions: HCV clustering is a rare event across HCV-1 and HCV-3 genotypes isolated in Spain, and from other geographical areas, suggesting a higher viral diversity and genetic distance for isolates from these genotypes. In contrast, HCV-2 and HCV-4 isolates seem to be more closely related across the Spanish population, and also to isolates from other geographical areas.

P-45 Prevalence of the hepatitis C virus (HCV) polymorphism Q80K in HCV infected patients with genotype 1a in Spain

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Background & Aims: The Q80K polymorphism is a naturally occurring variation in the NS3 protease of hepatitis C virus (HCV) which substantially reduces the efficacy of triple therapy with simeprevir, interferon alpha, and ribavirin. The prevalence of Q80K polymorphism varies among different regions or countries. The aim of this study was to evaluate the prevalence of Q80K polymorphism in HCV infected patients with genotype 1a in Spain.

Methods: We evaluated the sequence of HCV NS3 protease gene in 2260 samples collected from HCV infected patients with genotype 1a in 113 hospitals distributed geographically across Spain (46 provinces), between October 2014 and June 2015. HCV-RNA was extracted from plasma by using the QIAamp MinElute Virus Spin Kit (QIAGEN). NS3 gene amplification was carried out by reverse transcription PCR (QIAGEN) and nested PCR (Roche). Next, NS3 gene was sequenced by Sanger-based technology. Besides, clade information for genotype 1a was obtained by using the software geno2pheno (<http://hcv.geno2pheno.org/>).

Results: In total, 742 out of 2260 samples analyzed corresponded to HIV/HCV co-infected patients. Overall, 241 samples had Q80K polymorphism (10.59%), 533 correspond to clade I (23.6%) and 1727 to clade II (76.4%). When Q80K polymorphism and clade I were analyzed according to HIV status, we found HIV/HCV coinfecting patients had the greatest frequency of Q80K polymorphism (13.2% vs. 9.5%; p = 0.009) and clade I (28.3% vs. 21.1%; p < 0.001). Moreover, the frequency of Q80K polymorphism was higher in patients infected with HCV genotype 1a clade I than patients infected with clade II (42.0% vs. 1.8%; p < 0.001). The higher prevalence of Q80K polymorphism was found in the regions of Ceuta (25%), Madrid (21.9%), Canary Islands (20.22%), and Aragon (17.6%). The Autonomous Communities with the lowest prevalence were Castilla La Mancha (0%), Valencia (7.1%), Cantabria (8.26%), La Rioja (8.3%), and Andalusia (8.5%).

Conclusions: The global prevalence of Q80K polymorphism was similar to that found in other European countries (France, Italy, Germany), but the distribution of Q80K

polymorphism in Spain was not homogenous. Moreover, HIV/HCV coinfecting patients had higher frequencies of Q80K polymorphism and clade I.

P-46 Prevalence of Q80K Polymorphism in HCV patients with genotype 1a and his clinical significance

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Background: Despite nowadays determination of polymorphism Q80K doesn't have a clinical repercussion in patients HCV receiving treatment with direct-acting antiviral (DAA) who are Interferon (IF) free, even though, this determination if have been very important to optimize triple treatment with Peg interferon + Ribavirin + Simeprevir (PR + SMP), and to refer them to IF free treatment in HCV genotype (GT) 1a. This study evaluates, in our cohort, the prevalence of polymorphism Q80K and analyze the effectiveness, both, global triple PR + SMP (complete data on another poster) and DAA IF free treatment in positive Q80K patients, reading preliminaries viral data at the end of treatment (week 24^a with PR + SMP and week 12^a with DAA IF free).

Methods: Retrospective analysis of Q80K through protease NS3A4 sequencing, in HCV GT 1a patients mono-infected and co-infected with HIV. We described prevalence of polymorphism and preliminary data of effectiveness on patients receiving triple treatment PR + SMP dismissing GT1a Q80K positive, and in last, treatment DAA IF free in HCV GT1a Q80K positive.

Results: Since September 2014 at March 2015 we have determined Q80K polymorphism in a total of 27 patients (8/19 Mono/Coinfected), 5 of them (18%) with a positive determination (1/4 Mono/Coinfected). The global response, undetectable HCV viral load (UI/ml) on intention to treatment at the end of triple regimen PR + SMP (24 weeks) it has been 78%. 3 of the 5 Q80K positive patients if have received Sofosbuvir (SOF)/SMP/R, SOF/Daclatasvir (DCV)/R and Paritaprevir/Ombitasvir-Dasavubir (3D)/R, have also been an undetectable HCV viral load (UI/ml) at the end of treatment (12 weeks), while two of the other patients are still waiting for treatment, because they are have a low range fibrosis (F0-1 Metavir).

Conclusions: In our patient's cohort with HCV GT1a, polymorphism Q80K have a prevalence of 18%, above other average groups. The determination of Q80K it has become possible an effectiveness of 78% at the end of

triple treatment PR + SMP. Patients Q80K positive have been derived to DAA IF free treatment, with excellent effectiveness and tolerance.

P-47 Prevalence of natural resistance mutations to hepatitis C virus polymerase inhibitors in Navarra naïve patients

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Background & Aims: The aim of this work was to investigate the prevalence of dominant resistance mutations against DAAs in our population.

Methods: We analyzed NS5B partial gene sequences from 155 treatment-naïve patients infected with different HCV genotypes (1a = 41 sequences; 1b = 80 sequences; 3a = 21 sequences; 4d = 6 sequences; and other less frequent genosubtypes).

HCV RNA detection was performed following protocol previously described (Chen&Weck, 2002), which amplified NS5B region between 227 and 335 aa positions. Sequence analysis was carried out using geno2pheno (<http://hcv.geno2pheno.org/index.php>) and ClustalW2 and MEGA6.0 softwares, to recognize aa changes in RNA polymerase previously associated with resistance.

Results: Several mutations related to polymerase resistance were found among these HCV sequences. In addition, other frequent polymorphisms were observed in some particular genotypes as shown in the table 7.

Mutation at S282T is the main position associated with resistance to nucleos (t)ide analogues (NA) such as sofosbuvir and mericitabine, which are very robust drugs. We found this position altered in one subtype 1a clade I strain and some 3a sequences corresponding to silent mutations. Of particular interest is this mutated position in both subtypes 4a studied.

Mutations at positions 316 and 320 have been described as other critical amino acids of the polymerase, conferring resistance to some non-nucleos (t)ide analogues (NNA) such as tegobuvir, setrobuvir or TMC647055. Genotype 1b in our patients displayed very frequently C316N mutation which could impair activity of tegobuvir against these HCV strains. Additionally, L320F mutation was displayed by 5% of genotype 1b sequences, which could affect activity of other drugs.

Table 7. RNA-dependent RNA polymerase mutations

Genotype	n	282	314	316	320	321	Other mutations (> 20%)
1a	41	1 (S282N)	0	0	0	0	R300Q, Q309R, A327Q, Q330E/P
1b	80	0	0	35 (C316N)	4 (L320F)	1 (V320I)	N231S, A252V, T300S/A, Q309R
3a	21	0 (3 AGC silent mutations)	0	0	0	0	N307G, D330N, A335T/I/S
4d	6	0	0	0	0	0	K231R, I276T
Others	7	2	0	0	0	0	T282S (subtype 4a)
TOTAL	155						

Future works should be addressed in order to know whether other polymorphisms found among these sequences could have any effect on the activity of DAAs. Additional mutations located between positions 414 and 556 should be also studied in order to get to know about the presence of natural mutations related to other NNA drugs.

Conclusions: The presence of natural polymorphisms in HCV genotypes affecting susceptibility to new direct-acting antivirals is low. Tegobuvir activity against genotype 1b can be particularly impaired by C316N natural mutation.

P-48 Utility of HCV core antigen quantification in the management of new therapies against HCV. (Proyecto GEHEP-06)

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Background & Aims: Current clinical guidelines have recommended that patients receiving new direct action antivirals (DAA) against hepatitis C virus should be monitored with PCR techniques which RNA detection limit is below 15IU/ml. Usually, the advise is to test for RNA level at baseline, 4, 12, 24 weeks of treatment and after treatment at 12 and 24 weeks. The aim of this study was to determine the correlation and the usefulness of quantitative HCV core antigen versus RNA quantification in patients treated with new DAA attended in the North Cadiz Health Area.

Methods: Samples from 86 patients treated with DAA were studied (52 monoinfected and 34 HIV-coinfected), the predominant genotype in monoinfected was 1b, and in coinfecting 1a. Routine use of these drugs started in our center on February, and more than half of the patients

remain in treatment right now. Sofosbuvir was included in 82% of patients; the second most common drug was Daclatasvir (35%) followed by Simeprevir (32.5%), Peginterferon (9%) and Ledipasvir, (6%); 52% of the patients added Ribavirin in their regimens. Quantitation of viral RNA was made by Cobas TaqMan® Amliprep (Roche) and the core antigen by Architect® HCV Ag Reagent Kit (Abbott Diagnostics) whose detection threshold is 3 fmol/l equivalents to approximately 1000 IU/ml of RNA. Viral and antigen quantification was monitored before treatment had started and also in weeks 1, 4 and 12 of treatment.

Results: RNA baseline level was 6.10log IU/ml (SD \pm 0.56, range 4.30 to 7.171) and 3.37log antigen fmol/l (SD \pm 0.59; range 1.51-4.44). The RNA/Ag correlation was determined in baseline samples showing high values (R = 0.75) similar to those described in the literature. RNA levels dropped dramatically from the first week (RNA 2.31 \pm 0.8, AgVHC 0.43 \pm 0.9). In the fourth week all samples except two showed RNA levels below 100 IU/ml. Only one sample had HCVAg levels higher than 10fmol/l. 30 patients have already reached 12 weeks of treatment, and only one has a detectable viral load below detection level and another had an antigen higher than 3fmol/l.

Conclusions: HCV RNA and antigen baseline levels are highly correlated and its kinetics was similar. There has not been any treatment failure, although the size of our series is an important limitation.

P-49 Trends in prevalence HCV genotypes in chronic infected patients in Santiago de Compostela District (Northwest Spain)

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Table 8. Cases and proportions in each age group

Genotype	≥ 70 years old	50-69 years old	≤ 49 years old	p-value
1	195 (85.5%)	432 (57%)	496 (62.2%)	< 0.001
1a	17 (7.5%)	167 (22%)	297 (37.3%)	< 0.001
1b	176 (77.2%)	260 (34.3%)	194 (24.3%)	< 0.001
1a/1b	2 (0.9%)	5 (0.7%)	5 (0.6%)	
2	16 (7%)	26 (3.4%)	16 (2%)	0.001
3	13 (5.7%)	173 (22.8%)	159 (19.9%)	< 0.001
4	3 (1.3%)	127 (16.8%)	125 (15.7%)	< 0.001
5	1 (0.4%)	0 (0%)	1 (0.1%)	
Cases	228	758	797	

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Background: Phylogenetic analysis has led to the classification of hepatitis C virus (HCV) into 1-7 major genotypes. HCV genotypes have different biological properties, clinical outcome and response to antiviral treatment and provide important clues for studying the epidemiology, transmission and pathogenesis.

Distribution of HCV genotypes may be changed over time. Epidemiological studies on distribution patterns of HCV genotypes in Galician population might assist for better treatment options and preventive strategies.

Methods: The genotype and subtype of the HCV were studied by line probe assay (INNO-LIPA HCV II, Siemens Healthcare Diagnostics Inc., Germany) in 1783 patients positives for HCV RNA. There were 1295 males and 488 females with a mean age of 52.8 years (range 26-94). Frequency of different genotypes among patients was assessed according to gender and age at the time of sampling. The age distribution was made according to the recommendations of the CDC.

Results: Table 8.

Conclusions: While HCV genotype 1b continues to be the most prevalent, specially among older groups, unexpected differences were found in genotype 1a in younger groups, changes in the relative frequency of genotypes 1, 2, 3 and 4 have been observed. This may have important implications for the control and prevention of the infection. Our results are consistent with recent studies that have reported more variation in the extent and diversity of HCV genotypes, and have shown associations between HCV genotypes, risk exposure, age and clinical groups. The introduction of new genotypes in a high risk group may rapidly impact on lower risk groups.

P-50 **Distribution of hepatitis C virus genotypes in the area of influence of the General University Hospital of Valencia**

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Background: Currently the genotype (Gt) of the hepatitis C virus (HCV) is essential for the treatment with the new direct-acting antiviral drugs.

Objective: To determine the prevalence and evolution of HCV Gt in our health area (including penal institution's population) in the last seven years and study their distribution according to their origin.

Methods: Retrospective and descriptive study of the results of HCV Gt available at our center from January 2008 to June 2015 inclusive. The variables studied were: Gt, year genotyping, HCV-HIV coinfection, origin, year of birth and gender. Genotyping was performed using both techniques, reverse hybridization on nitrocellulose strip (VERSANT HCV Genotype 2.0 (LiPA), Siemens®) or Real-Time PCR (HCV Genotype II assay, Abbott®).

Results: 2574 genotype patients were analyzed. The predominant was the Gt1 with 68.2% (33.4% Gt1a and 30.4% Gt1b); Gt3 and 4 were 16.9% and 11.7%; and Gt2 and 5 were 1.7% and 0.4%. Co-infections with different genotypes were observed in 0.9% and reinfection in 6 cases, with Gt1a in 5 of them. Looking at the evolution over time, a decrease in the frequency of Gt1a (from 35-36% in 2009-2011, to 32% in 2013-2014 and 26% in the first half

of 2015) can be seen, Gt1b to rise, striking in 2015 (42.9%). Separating the area's population without the penal institution's population (24%), the prevalence of Gt1b in the non-prison population is 36.9% compared to a 9.8% of convicts; while the Gt1a convicts dominates with 44.8% versus to 29.7% from the rest. When we divide the population in HCV monoinfected and HCV-HIV coinfecting (28.5%), very similar values to the prison population are observed. Therefore, we compared the population of the area (56.8%) separating the convicts and HCV-HIV coinfecting (43.2%); and Gt1b increases to 44.3% in the population with fewer risk factors. Taking in notice the patient's year of birth, a clear predominance of Gt1b is observed in patients older than 60 years (55-65%), while in the under 60 predominates Gt1a (34-40%), the 40-60 years patients are the 63.3% of the studied population. Finally, when analyzing the gender shows that women account for 29.5% with clear predominance of Gt1b (48%), and men are 70.5% with most Gt1a (37.9%).

Conclusions: Almost half of our studied population comes from the penal institution or are HCV-HIV coinfecting (men 40-60 years). In this specific population, Gt1a is more common while Gt1b predominates in the rest.

P-51 Prevalence of hepatitis C virus genotypes in chronic infected patients in Santiago de Compostela District (Northwest Spain)

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Background: Hepatitis C virus (HCV) has been classified into at least seven major genotypes and a series of subtypes, based on the nucleotide sequence variation. HCV genotype is a crucial predictive factor of response to treatment in chronic hepatitis C. On the other hand, HCV genotypes is not uniformly distributed in the world, there are differences between geographical regions, sometimes related to epidemiological factors such as the predominant transmission route, like this, different studies suggested that genotypes 1a, 3 and 4 are closely associated with intravenous drug use.

Methods: The genotype and subtype of the HCV were studied by line probe assay (INNO-LIPA HCV II, Siemens Healthcare Diagnostics Inc., Germany) in 1564 patients positives for HCV RNA. There were 1133 males and 431 females with a mean age of 52.21 years (range 26-94). Frequency of different genotypes among patients was assessed according to gender, age, risk factors at the time of sampling.

Results: HCV genotypes distribution was observed in 1564 chronically HCV infected individuals in the following pattern: 970 (62%) cases of genotype 1; 49 (3.1%) cases of genotype 2; 313 (20%) cases of genotype 3; 230 (14.7%) cases of genotype 4, and 2 (0.1%) cases of genotype 5. Among the genotype 1 infections, 43.3% cases were genotype 1a and 56.7% cases were genotype 1b, this distribution is influenced by the main risk factors: 874 (55.9%) cases associated with IDU whose mean age was 48 years, and 460 (29.4%) cases associated with unsafe medical procedures whose mean age was 61 years.

Conclusions: Genotype 1b, is the most prevalent genotype in our area. Compared to other studies in our country, we found a lower prevalence in genotypes 1a, 2 and 3. However we found a greater prevalence in genotype 4. We found significant differences in the association of risk factors and genotypes with age.

P-52 Prevalence of hepatitis C virus genotypes in chronic infected patients in different areas of Santiago de Compostela District (Northwest Spain)

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Background: Phylogenetic analysis has led to the classification of hepatitis C virus (HCV) into 1-7 major genotypes. HCV genotypes have different biological properties, clinical outcome and response to antiviral treatment and provide important clues for studying the epidemiology, transmission and pathogenesis. HCV exhibits high genetic diversity, characterized by regional variations in genotype prevalence. We also generate regional genotype prevalence estimates, inferring data for district.

Methods: The genotype and subtype of the HCV were studied by line probe assay (INNO-LIPA HCV II, Siemens Healthcare Diagnostics Inc., Germany) in 1564 patients positives for HCV RNA. There were 1133 males and 431 females with a mean age of 52.21 years (range 26-94). Frequency of different genotypes among patients was assessed according to gender, age and risk factors in different geographical areas in the Santiago de Compostela District (metropolitan, coastal and rural).

Results: In metropolitan area HCV genotypes distribution was observed in 697 chronically HCV infected individuals in the following pattern: genotype 1 (62.1%); 2 (3.6%); 3 (19.9%); 4 (14.2%), and 5 (0.1%), this distribution is influenced by the main risk factors in this area 54.9% cases associated with IDU and 29.6% cases associated

with unsafe medical procedures. Among the genotype 1 infections, 47.5% were genotype 1a and 52.5% were genotype 1b. In coastal area HCV genotypes distribution was observed in 560 chronically HCV infected individuals in the following pattern: genotype 1; 2 (2.1%); 3 (23.8%); 4 (16.2%). Among the genotype 1 infections 54% were genotype 1a and 46% were genotype 1b, this distribution is influenced by the main risk factors in this area 68.2% cases associated with IDU and 19.6% cases associated with unsafe medical procedures. In rural area HCV genotypes distribution was observed in 307 chronically HCV infected individuals in the following pattern: genotype 1 (69.4%); 2 (3.9%); 3 (13.4%); 4 (13%), and 5 (0.3%). Among the genotype 1 infections, 31.8% cases were genotype 1a and 68.2% cases were genotype 1b, this distribution is influenced by the main risk factors in this area 35.5% cases associated with IDU and 46.9% cases associated with unsafe medical procedures.

Conclusions: Genotype 1b was the most prevalent genotype in metropolitan and rural area, however genotype 1a was the most prevalent in coastal area. Significant differences were found in the distribution of genotypes and risk factors. HCV genotype distribution is not only associated with the transmission route, but also associated with the geographic region.

P-53 **Contrasting prevalence of chronic infection by hepatitis C virus genotype 3 in Santiago de Compostela (Northwest Spain) in intravenous drug users with and without HIV infection**

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Background: Chronic hepatitis C (CHC) is common in HIV-infected patients mainly among those who acquired the infection parenterally, such as intravenous drug users (IVDUs). Hepatitis C virus (HCV) has been classified into at least seven major genotypes and a series of subtypes, based on the nucleotide sequence variation. HCV genotype is a crucial predictive factor of response to treatment in CHC. On the other hand, HCV genotypes are not uniformly distributed in the world, there are differences between geographical regions, sometimes related to epidemiological factors such as the predominant transmission route, like this different studies suggested that genotypes 1a, 3 and 4 are closely associated with intravenous drug use.

Objective: to determine the prevalence and heterogeneity of infection by HCV genotypes in Santiago de Compostela (Northwest Spain) IVDUs with and without HIV infection.

Methods: The genotype and subtype of the HCV were studied by line probe assay (INNO-LIPA HCV II, Siemens Healthcare Diagnostics Inc., Germany) in 960 patients IVDUs positives for HCV RNA and histological diagnosed of CHC. There were 795 males and 165 females with a mean age of 48 years (range 28-89), 298 of them were coinfecting with HIV.

Results: Infection by HCV genotype 1a, genotype 3 and genotype 4 was detected in 103 (34.6%), 63 (21.1%) and 74 (24.8%) patients with anti-HIV antibodies, and in 236 (35.6%), 194 (29.3%) and 138 (20.8%) patients HIV negative. When prevalences of HCV genotypes were compared, only in genotype 3 unexpected differences were found between IVDUs with and without HIV infection. No significant effect of age, sex, CHC status and HCV viral load was observed between HCV genotypes in patients with and without HIV infection.

Conclusions: In contrast to previous reports, this study showed significant differences in the distribution of genotype 3 in Galician IVDUs with HIV infection. This study also confirm that in many European countries, genotype distributions vary within geographic areas and epidemiological groups.

P-54 **Current liver toxicity of antiretroviral regimens in patients with chronic viral hepatitis in a real-life setting: The HEPVIR SEG-HEP Cohort**

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Background & Aims: Little real-life data on the current frequency of antiretroviral therapy (ART)-induced liver toxicity is available. The objective of this study was to assess the frequency of grade 3-4 transaminase elevations (TE) and grade 4 total bilirubin elevations (TBE) in HIV-infected

patients with chronic hepatitis B and/or C, who started a new regimen of ART.

Methods: A total of 192 pre-treated or treatment-naïve HIV/hepatitis B virus and/or hepatitis C virus-coinfected patients who started ART in eight Southern Spanish centers between July 2011 and December 2013, were included in this prospective study. Patients were followed for 12 months.

Results: Forty-one (21.4%) subjects had been naïve to ART. The most frequently initiated nucleoside-analogue reverse transcriptase inhibitors (NRTI) were tenofovir/emtricitabine [49 patients (25.5%)], 89 (46.4%) patients started a ritonavir-boosted protease inhibitor and 77 (40.1%) a non-NRTI. Raltegravir and maraviroc were initiated in 24 (12.5%) and 9 (4.7%) individuals. Ten [5.21%; 95% confidence interval (CI): 2.53%-9.37%] patients presented grade 3 TE and 8 (4.17%; 95%CI: 1.82%-8.04) subjects showed grade 4 TBE. No episode of grade 4 TE and no ART discontinuation due to hepatotoxic events were observed. There was no factor independently associated with grade 3-4 TE. In a multivariate analysis adjusted for age, sex and baseline HIV-RNA levels, the use of ritonavir-boosted atazanavir was the only independent predictor for grade 4 TBE [adjusted odds ratio: 9.896 (95%CI: 2.099-46.66); $p = 0.004$].

Conclusions: The current frequency of severe TE and TBE associated with ART under real-life conditions in patients with chronic viral hepatitis is similar to what has been reported previously. However, episodes of grade 4 TE are less frequent, severe TE are well managed and do not lead to treatment discontinuation.

P-55 **Hepatic safety of RPV/FTC/TDF single tablet regimen in HIV/HCV-coinfected patients. The hEPAtic Study**

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Background & Aims: Data on hepatic safety of the new single tablet regimen including RPV/FTC/TDF (EPA) is

mainly derived from clinical trials that include a low number of patients with hepatitis C virus (HCV) coinfection. The aim of this study was to evaluate the incidence of transaminase elevations (TE) and total bilirubin elevations (TBE) during the first 48 weeks of therapy with EPA in a large population of HIV/HCV-coinfected subjects in clinical practice.

Methods: This is a retrospective analysis of HIV/HCV-coinfected subjects who started EPA at the infectious diseases units of 17 centres throughout Spain, included as cases. Subjects who started an antiretroviral therapy (ART) different to EPA during the study period at the same hospitals were randomly selected as controls. The primary outcome variables were grade 3-4 TE and grade 4 TBE. Patients were included if clinical visits were available at baseline and, at least, after 12, 24 and 48 weeks thereafter.

Results: Of the 519 patients included, 173 individuals started EPA and the remaining ones were controls. Nine (5.2%) subjects of the EPA group and 49 (14.2%) controls were naïve to ART. The median (Q1-Q3) follow-up was 11.2 (9.7-3.9) months. TE was observed in 2 [1.2%; 95% confidence interval (CI): 0.14%-4.1%] individuals receiving EPA and 11 (3.2%; 95%CI: 1.6%-5.6%; $p = 0.136$) controls ($p = 0.136$). All TE were grade 3 and no patient discontinued ART due to TE. One (0.6%; 95%CI: 0.01%-3.1%) patients on EPA and 9 (2.6%; 95%CI: 1.2%-4.9%) subjects of the control group developed TBE ($p = 0.102$), none of these patients developed a hepatic decompensation during follow-up. A total of 3 (2.3%) subjects with cirrhosis versus 10 (3.1%) without cirrhosis showed grade 3 or 4 TE ($p = 0.451$).

Conclusions: The frequency of severe liver toxicity in HIV/HCV-coinfected patients receiving EPA under real life conditions is very low. TE episodes in patients who are given EPA are mild and usually do not lead to drug discontinuation. All these data confirm EPA is safe in this particular subpopulation.

P-56 **Sustained virological response rates with DAAs-based triple-therapy in HCV genotype-1 mono and co-infected patients in a real-world setting**

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Background & Aims: We evaluate the rates of sustained virological response (SVR) achieved with DAAs after two years of triple-therapy regimes in our Area and the analytical properties of those who had no success.

Methods: Observational, retrospective study. Medical records and analytical data of all patients who started triple therapy in our Healthcare Area were reviewed: gender, viral genotype, liver stiffness by fibroScan® (advanced fibrosis considered when > 9.5kPa, and F4 grade when > 14.6kPa), IL-28 polymorphism, patient classification based on previous treatment with peginterferon (PegIFN) and ribavirin (RBV) (naïve, relapser, partial-responder, null-responder or unknown previous response), HCV RNA quantification at weeks 4, 12, 24 and 12 after treatment completion. Patients who had not available data of HCV RNA at 12 weeks after treatment completion were excluded. Data was analysed using SPSS statistical package.

Results: A total of 31 patients (32% female) were included. Depending on fibrosis stage, 18 (58%) were cirrhotic, 11 (35.5%) were F3 and 2 (6.5%) were F2. 14 patients (45.16%) were naïve, 11 (35.48%) were relapsers, 6 (19.35%) cases were partial responders and one case (5.3%) null responder.

SVR was achieved in 20 (64.52%) patients. Two patients (6.45%) discontinued treatment due to adverse effects.

In our series, 100% (6) of patients not achieving response at week 12 did not obtain SVR. Two patients who obtained viral response at week 4 and week 12 did not achieve SVR and three patients were finally relapsers.

66.7% of partial responders to previous bi-therapy did not achieve SVR, while 71.4% and 81.8% of naïve and relapsers respectively did it, resulting this difference statistically significant ($p = 0.009636$).

Conclusions: The proportion of patients who achieved SVR in our series was slightly lower than other studies in a real world setting. Despite having a high percentage of cirrhotic patients, triple therapy was well tolerated, with low discontinuation rates. Based in our results, not achieving viral response at week 12 and being partial responder to previous PegIFN-RBV treatment were found to be negative predictors of efficacy.

P-57 Sustained virological response at week 4 in mono and coinfecting patients starting Sofosbuvir + Daclatasvir regimen

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Background & Aims: Sofosbuvir + Daclatasvir combination with or without ribavirin is considered gold standard in the treatment of patients with chronic hepatitis genotypes 1, 3 and 4. The aim was to determine virus load at

week 4 on the first batch of 16 patients mono or coinfecting, under Sofosbuvir + Daclatasvir 12 or 24 weeks regimen with or without ribavirin.

Patients and methods: 16 patients on SOF/DCV after the first 4 weeks of treatment were reviewed. The following items were studied: age, gender, genotype, initial HCV load, fibrosis stage, use of ribavirin, GFR and ART on HIV coinfecting. The determination of the virus load was based on COBAS Ampliprep/COBAS Tagman HCV Quantitative Test, v2.0 methodology.

Results: 11 men and 5 women, mean age 49.9 years, Genotype 3 (10/16); Genotype 1 (4/16) and Genotype 4 (2/16). Fibrosis stage: F1-F2 (2/16), F3 (5/16), F4 (9/16). On Ribavirin regimen (9/16). Mono-infected (5/16), coinfecting HCV/HIV (11/16) of which 10 followed ART including as third drug: PIs (6/10). Three of them were on TDF + FTC), Raltegravir (2/10), Dolutegravir (1/10) and Rilpivirin (1/10). The HCV viral load exceeded 2.000.000 IU/mL (9/16). Previous treatment attempts yielded the following data: no response (7/16), relapse (1/16), unknown situation (2/16). 50% of the patients studied had Ribavirin in their treatments. 6/16 were naïve patients.

The glomerular filtration rate remained unchanged at week 4 of treatment when compared to previous GFR data from the patients. Negative HCV viral load was attained (undetectable below the threshold < 15 IU/mL (11/16), detectable yet under the < 15 mark (3/16) and detectable above the threshold (2/16). 63% of the patients with negative viral load had Ribavirin on their regimens.

Conclusions: Good initial response to the treatment Sofosbuvir + Daclatasvir, with great tolerance. None of the subjects on Ribavirin regimen had their doses adjusted.

P-58 The addition of Nitazoxanide does not increase the efficacy of pegylated interferon and ribavirin for HCV genotype 4/HIV-coinfecting Patients

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Background: Nitazoxanide (NTZ) plus pegylated interferon and ribavirin (Peg-IFN/RBV) improved the sustained virological response (SVR) rates achieved with Peg-IFN/RBV in hepatitis C virus genotype 4 (HCV-4)-mono-infected patients. There is no data currently on the efficacy of Peg-IFN/RBV plus NTZ for human immunodeficiency virus (HIV)/HCV-4 coinfection. Therefore, the objectives of this clinical trial were to assess the efficacy and to evaluate the safety of Peg-IFN/RBV plus NTZ in HIV/HCV-4-coinfected patients.

Methods: This was an open-label, single arm, multi-center phase II pilot clinical trial (NCT01529073) enrolling HIV-infected individuals with HCV-4 chronic infection, naïve to HCV therapy. Patients were treated with NTZ 500 mg bid for 4 weeks, followed by NTZ 500 mg bid plus Peg-IFN alpha-2b 1.5 mcg/Kg/week plus weight-adjusted RBV during 48 weeks. Analyses were done by intention-to-treat (ITT, missing = failure). A historical cohort of HIV/HCV-4-infected patients treated with Peg-IFN alpha-2b and RBV at the same area was used as control.

Results: Two (9.5%) of 21 patients included in the trial compared with 5 (21.7%) of 23 patients included in the historical cohort achieved SVR (difference between SVR rates, -12.2%; 95% confidence interval, -33.2% to 8.8%; $p = 0.416$). Virological failure was due to lack of response in 13 (62%) individuals recruited in the trial. Two (9.5%) patients included in the trial and two (9.5%) individuals from the historical cohort discontinued permanently due to adverse events.

Conclusions: No increase in SVR was observed among HIV/HCV-4-coinfected patients receiving Peg-IFN/RBV plus NTZ compared with a historical cohort treated with Peg-IFN/RBV. The rates of interruption due to adverse events of Peg-IFN/RBV plus NTZ were similar to those with dual therapy.

P-59 **Adverse events analysis of the new all-oral HCV regimes in daily clinical practice**

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Background & Aims: New direct-acting antivirals (DAA) have supposed an improvement in efficacy and safety of HCV treatment regimes, but lack of information is still a concern with these agents considering that safety data available to date is derived from clinical trials, and may not reflect the day-to-day practice. We analyze the type and frequency of adverse events (AE) of mono and

co-infected patients who start HCV therapy with DAAs in our HealthCare Area as well as drop-out rates and changes in treatment due to these events.

Methods: Retrospective observational study. Medical records (gender, viral genotype, presence/absence of cirrhosis, DAA regimen with/without RBV, treatment duration, type and grade of AE ("Common-Terminology-Criteria-for-AE v4.0", From Grade-1: Mild to Grade-5: Death due to AE), change/discontinuation due to AE and supportive care if necessary) and analytical data of all mono and co-infected patients who started therapy with new DAA agents (simeprevir, sofosbuvir, ledipasvir, daclatasvir, ombitasvir/paritaprevir/ritonavir, dasabuvir) and patient's interviews were recorded on the Outpatients Pharmacy's Database and analysed using SPSS statistical package.

Results: 47 patients (17% female) were finally reviewed, with a median follow-up of 7 weeks. 89.4% were HIV/HCV-coinfected and 70.2% cirrhotics. According to genotype, they were mainly G1 (59.6%), followed by G3 (21.3%), G4 (17%) and G2 (2.1%). 37 patients (78.7%) had RBV in their HCV regimen.

20 patients (42.6%) experienced at least one AE, being headache (14.9%) the most frequent, followed by fatigue (12.77%), insomnia (6.38%), skin rash (6.38%), arthralgia (4.26%), and cold sores, generalized malaise, dizziness, stomach heaviness and muscle spasms in right arm (2.1% each). 85.2% of AE were classified as grade I-II (Mild-Moderate).

Between patients with RBV (43%) and no RBV (40%) AE frequency did not differ, but types were different: insomnia and fatigue were felt exclusively in RBV patients and Hb fell below 10 g/dL in 7 (18.92%) RBV patients, but none required neither RBV-dose reduction nor supportive care.

AE motivated one treatment change (skin rash/cold sores grade III) and one voluntary dropout (headache/arthralgia grade IV).

Conclusions: Following our results, AE of DAAs regimens in real-life conditions are similar to those published in clinical trials, with generally well tolerated AE and low discontinuation rates. Regimens with RBV varied in AE type but not in frequency of AE.

P-60 **Changes in the profile of HIV/HCV coinfecting patients who are potential candidates for HCV therapy**

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Background & Aims: The spread of HCV treatment in HIV/HCV coinfecting patients (pts) may be changing the

Table 9.

Characteristic	2006-2007	2014	Signification (p)
HCV-PCR positive, n (%)	144 (57.4)	120 (58.2)	0.8494
Mean age, year \pm SD)	40.6 \pm 5.4	45.9 \pm 5.8	< 0.0001
Sex, n (%) of males	114 (79.2)	94 (78.3)	0.8690
On HIV therapy, n (%)	122 (84.7)	115 (95.8)	0.0030
HIV-1 viral load < 50 copies/mL, n (%)	91 (63.2)	83 (69.2)	0.3080
HCV Genotype, n (%)			
G-1a	55 (38.2)	50 (41.7)	0.5659
G-1b	23 (16)	14 (11.7)	0.3157
G-1 other	7 (4.9)	7 (5.8)	0.7256
G-2	1 (0.7)	1 (0.8)	0.8969
G-3	23 (16.0)	17 (14.1)	0.6837
G-4	31 (21.5)	27 (22.5)	0.8493
Polygenic	2 (1.3)	1 (0.8)	0.6715
Liver fibrosis degree, n (%)			
Not performed	72 (50.0)	19 (15.8)	< 0.0001
Fibrosis 0*	17 (23.6)	19 (18.8)	0.4434
Fibrosis 1*	33 (45.8)	25 (24.7)	0.0038
Fibrosis 2*	13 (26.6)	13 (12.9)	0.3469
Fibrosis 3*	3 (18.0)	16 (15.8)	0.0155
Fibrosis 4*	6 (8.3)	28 (27.7)	0.0016
Naïve for HCV therapy, n (%)	100 (69.4)	76 (63.3)	0.2943

*Percentage calculated among those who had an available liver biopsy or liver elastometry.

profile of those with HCV viremia. Moreover, the recent marketing of second generation direct-acting antivirals has raised the interest to know the epidemiological situation of pts infected with HCV to anticipate future drug needs. The aim of this study is to analyze the changes in the profile of viraemic pts in recent years.

Methods: Serial cross-sectional study conducted in a single center. All HIV-infected pts who attended the outpatient clinic between October 2006 and Mars 2007, and between January and June 2014 were included. Epidemiological data focused on HIV and HCV infection were collected.

Results: In each reporting period 417 and 415 pts were included, 251 (60.2%) and 206 (49.6%) of them had respectively a positive serology for HCV ($p = 0.002$). In the first period, 32 (12.7%) pts had obtained a sustained viral response vs 48 (23.3%) in the second one. Differences between patients with detectable viraemia are shown in the following table 9.

Conclusions: The prevalence of HIV/HCV coinfection has decreased significantly. In the second analyzed period, viraemic patients are older, and have a better control of their HIV infection. A mild trend to a decline in HCV genotypes with a better treatment response was observed, with no major global changes. However, the prevalence of liver cirrhosis is considerably higher.

P-61 Impact in the levels of hemoglobin with the new direct-acting antiviral drugs, associated or not with ribavirin

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Background & Aims: Study of variations in the hemoglobin (Hb) in patients treated with the new direct-acting antivirals (DAA).

Methods: It has been analyzed HCV-infected patients treated with the new DAA in the Hospital Universitario Araba from November 2014 to June 2015, using both database from our hospital and each patient's clinical history. Variations in hemoglobin values, determined before treatment, during and after finishing it, have been compared in the different therapeutic regimens depending on whether Ribavirin (RBV) was administered or not.

Results: According to genotype, treatment received previously and interactions, 57 patients, (77.19% male, with an age range of 34-63 years), were treated with different therapeutic options classified in three groups: i) direct-acting antivirals without Ribavirin; ii) direct-acting antivirals

Table 10

Treatment	With RBV	Without RBV
Percentage of cases with Hb decrease	85%	71.4%
Maximum Hb decrease	6.4 g/dl	2.4 g/dl
Hb decrease average	2.89 g/dl	1.06 g/dl

Analyzing by therapeutic groups:

Treatment	Percentage of cases with Hb decrease	Maximum Hb decrease	Hb decrease average	Hb decrease greater than 2 g/dl
DAA + RBV	90.9%	4.1 g/dl	2.83 g/dl	63.6%
Peg-Inf + DAA + RBV	77.8%	6.4 g/dl	2.97 g/dl	44.4%
DAA	64.3%	2.4 g/dl	1.02 g/dl	7.1%

Hemoglobin after receiving treatment:

	Percentage of cases	Treatment received		
		DAA + Peg-Inf + RBV	DAA + RBV	DAA
Hb 8-10 g/dl	2.9%	100%	–	–
Hb 10-12 g/dl	11.8%	–	50%	50%
Hb 12-14 g/dl	35.3%	41.7%	33.3%	25%
Hb > 14 g/dl	50%	17.6%	29.4%	52.9%

with Ribavirin; iii) direct-acting antivirals with Peg-Interferon and Ribavirin. 34 patients finished the treatment, of whom 58.9% received it combined with Ribavirin (32.4% associated with DAA and 26.5% associated with DAA + Peg-Interferon). A decrease in hemoglobin was found in 82.35% cases, with an average of 1.99 g/dl. Decreases greater than 2 g/dl occurred in 35.2%, and all these patients had a baseline hemoglobin over 15.5 g/dl except two, whose hemoglobin was greater than 13 g/dl (Table 10).

Conclusions: The antiviral treatment results in a decrease of hemoglobin in 2 g/dl in nearly 8/10 patients.

When Ribavirin is administered, the decline is 14% more frequent, almost three times more pronounced and it is more severe, of about 2.9 g/dl against 1 g/dl in the group without Ribavirin. The group DAA + Peg-Inf + RBV has an average drop slightly higher (0.15%) than group DAA + RBV, and it registered the greatest fall (6.4 g/dl). However, none of the analyzed patients required blood transfusion or erythropoietin.

In conclusion, it is advisable to perform blood count monitoring once the treatment is started, especially in those requiring Ribavirin.

P-62 Final answer of chronic hepatitis C patient treated with Simeprevir, interferon and ribavirin

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Background & Aims: Simeprevir is a second generation of a protease inhibitor of HCV, recommended for patients with genotype 1 and 4 of chronic hepatitis C (HCV), available in Spain since the first of August 2014. There are few published data patients with this treatment in coinfecting HIV/HCV real-life. The aim was to assess the security and effectiveness of the treatment with SMP + INF + RBV in real-life co-infected patients.

Methods: We have data of 9 co-infected patients that were treated for 12 weeks with Simeprevir, interferon and ribavirin then treated for 12 more weeks, for maintenance, with interferon and ribavirin. The HCV-viral load were measured using COBAS Ampliprep/COBAS Taqman HCV Quantitative Test, v2.0.

Results: Medium Age: 52.22; Male/Female relationship: 5/4. The distribution of genotypes were 8/9 genotype 1 (6 GEN-1b; un G-1a (without Q80K) and a G1 not subtyping) and one genotype 4. The interleukin 28 B were CT in all the patients except in one patient, that were CC, and in the one that were genotype 4 that was not measure. The hepatic fibrosis were measure by FibroScan®: 2 patients F1; 2 F2; 4 F3 y one F4. Regard treatment history: 5 patients were naives and the other 4 pre-treatment (3 null response and one partial response). The HCV viral load basal were less that 2 million IU in 3/9 patients and higher of 2 million IU in 6/9. Two naives patients abandoned because of the intolerance to interferon, then with undetectable viral load.

Conclusions: Viral response was achieved at the end the treatment in 77% of co-infected patients treated with SMP + INF + RBV. Two patients discontinued treatment because of intolerance to interferon + Ribavirin, being the viral load undetected at that moment. There was no differences in response between naives and pretreatment patients.

P-63 **Predictors of SVR in cirrhotic patients with hepatitis C virus**

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Background & Aims: To develop a predictive model of SVR in cirrhotic patients treated with protease inhibitors (PIs).

Methods: Retrospective observational study performed at a tertiary hospital, with a health area of 440,000 inhabitants. All patients treated with IPs from September 2012 to February 2015 were included. Demographics data, disease characteristics, treatment received and response obtained were collected. Data were analyzed by intention to treat. The different variables were analyzed with chi-square test for qualitative variables and bivariate correlation for quantitative variables. The variables that reached statistical significance were introduced into a binary logistic regression model to confirm this result.

Results: 116 patients were included, 21 of them coinfected with HIV, 81.9% male, mean age 52.8 ± 9.2 years. 26 patients received boceprevir (BOC), 57 telaprevir (TVR) and 33 simeprevir (SMV). 82 patients were previously treated, of which, 15.8% were null responders, and 29.3% partial responders. 65.4% had no CC IL28B polymorphism, 67.3% viral load (VL) basal > 800.000IU/mL and 53.8% cirrhosis. SVR rates were 60% for TVR, 50.4% for BOC and 67.2% for SMV ($p = 0.044$). A statistically

significant relationship between SVR rates and genotype, baseline VL IL28B polymorphisms, rapid virologic response (RVR), early virologic response (EVT) and response to previous treatment received was found. The SVR rate was significantly higher in patients with genotype 1b vs 1a (78% vs. 51.1%, $p = 0.003$), patients with basal VL < 800,000 IU/mL (84.6% vs 55.2%, $p = 0.002$), patients with CC IL28B polymorphism vs TT and CT (84.4%, 69.9% and 56.3%, $p = 0.017$), patients who achieved RVR (84, 4% vs 52.5%, $p < 0.001$) and EVR (87.9% vs 39.6%, $p < 0.001$). Also, SVR rates were higher in relapsers against partial and null responders (78.1% vs 47.1% vs 11.1%, $p = 0.001$). Multivariate analysis confirmed these results, showing a model composed of four variables: PI used, genotype, having achieved RVR and response to previous treatment, which can explain the 59.6% of cases of SVR obtained in our population.

Conclusions: The combination of the PI used, viral genotype, RVR and response to prior treatment in cirrhotic patients with HCV predicts SVR in a high percentage of patients. Our results support the desirability of a response prognostic criteria allowing a useful element on which to base decision-clinical and therapeutic decisions.

P-64 **Preliminary analysis of the effectiveness of the new all-oral HCV regimes in a real-world setting**

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Background & Aims: The possibility of prescribing the new direct acting antiviral (DAA) agents for the treatment of HCV in interferon-free regimens, with high-cure and low-discontinuation rates described in Clinical Trials, represents an opportunity to eradicate HCV in our patients. In this study we analyze the preliminary data of efficacy of these regimens against HCV in the everyday practice of an Infectious Disease Outpatient clinic.

Methods: Observational retrospective study. Baseline characteristics and HCV-RNA quantification at weeks 1, 2, 4, 12/24 (end of treatment) and weeks 4 & 12 post-treatment were collected and analyzed of every mono- and HIV/HCVcoinfected patient who started HCV-therapy between 15-March and 15-June 2015. The regimens prescribed (SOF + SMP ± RBV, SOF/LDV ± RBV, 3D/2D ± RBV, PR + SOF, SOF + DCV + RBV) were in line with current guidelines and approved drugs at every time. Data was analysed using SPSS statistical package.

Results: A total of 46 patients (82.6% male) were included, 41 (89.1%) were HIV/HCV coinfecting, with a median CD4 value of 498 (356-760) and HIV-RNA undetectable in 32 (78.04%) cases. 39 patients (84.8%) were ex-injecting drug users.

According to Genotype, 28 (60.9%) patients were G1 (of which, 6 were 1a, 5 1b and 17 not-known subtype), 1 (2.2%) G2, 9 (19.6%) G3 and 8 (17.4%) G4. 32 (69.6%) patients were cirrhotic, of which 19 (59.4%) were G1, 8 (25%) G3 and 5 (15.6%) G4; 7 (15.2%) patients had previous decompensation episodes (5 edemato-ascitic and 2 hepatocellular-carcinoma). Regarding treatment, 26 (56.5%) were naïve, and the expected duration was 12 weeks in 37 (80.4%) patients.

HCV-RNA was undetectable at week-1 in only 4 (8.7%) patients, at week-2 in 21 (45.7%) and at week-4 (RVR) in 40 (87%) patients. 100% of 14 patients who completed treatment achieved end-of-treatment response (ETR) and the 4 of them (100%) with quantification at week 4 post-treatment have undetectable HCV-RNA.

The 6 patients who did not achieve RVR had HCV-RNA between 20-119 U/L. 3 were G1 cirrhotics (2 patients with 3D + RBV, 1 with SOF + SMP + RBV), 2 were G3 cirrhotics (SOF/LDV + RBV, SOF + DCV + RBV) and 1 G4 non-cirrhotic (SOF + SMP).

Conclusions: In our series, there is a low proportion of patients achieving undetectable HCV-RNA at weeks 1 and 2 with the new DAA agents, and RVR is slightly lower than those reported previously. Despite this, and even considering that are preliminary data and a significant proportion of patients has not yet finished the treatment, 100% who have done so have achieved ETR and SVR at week 4.

P-65 **Simeprevir and sofosbuvir in patients with chronic hepatitis genotypes 1 and 4. Response to treatment in the real life**

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Background & Aims: Simeprevir/sofosbuvir combination has proven effective to treat HIV/HCV mono and coinfecting patients with chronic hepatitis C genotypes 1 and 4, naïves or previous non-responders to treatment with interferon plus ribavirin. The aim of this study was to assess our experience in real life, for the treatment of patients with chronic hepatitis C genotype 1 or 4 in mono and HIV/HCV coinfecting patients.

Methods: 46 patients were treated with sofosbuvir and simeprevir, with or without ribavirin for 12 weeks. The

virological response was determined at week 4, 8 and end of treatment (12 week), and sustained viral response by the fourth week post treatment. The HCV viral load was measured using COBAS Ampliprep / COBAS Taqman Quantitative HCV Test, v2.0.

Results: Patients 46; 28/46 were men; medium age 54.7 years. Twenty-six (26/46) had HIV/HCV coinfection, the rest were monoinfected 20/46. The distribution of genotypes was: G-1a 19/46; G-1b 15/46; G-1 not subtyping 7/46 and G 5 was 5/46 patients. Fibrosis stage: 2 patient F1; 2 F2; F3 11 and 31. The treatment naïves were 23/46 (50%), and the rest 13 pre-treated relapser; and 10 patients partial or null response. Ten patients had experience with the first generation of protease inhibitors. Viral response to treatment was 100% (46/46). Week 4 post-treatment were reached in 26 patients. From them; 24 had undetectable viral load and two relapsed

Conclusions: High efficiency in week four post-treatment therapy with sofosbuvir and simeprevir both in mono and coinfecting patients.

P-66 **Descriptive study of patients treated with the new direct-acting antiviral drugs of chronic hepatitis C infection in a prison**

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Background & Aims: Analyse the characteristics of chronic hepatitis C patients treated with the new direct-acting antiviral (DAA) drugs in the correctional center Araba.

Methods: Review of patient's clinical history who have received or are receiving treatment with new DAA in our prison and analysis of virologic response obtained in the first and third month of treatment depending on the degree of fibrosis and the type of treatment received.

Results: We have treated or are treating 15 patients, all of them males. The most common comorbidity was HIV coinfection (60%) and there were 2 cases of coinfection with hepatitis B-D. 3.33% of our patients presented a genotype 1 infection, 26.67% genotype 3 and 40% genotype 4. The average baseline degree of fibrosis was 24.5 kPa (range 6-69.1). 47% (n = 7) of the patients had been treated previously, 86% (n = 6) with dual therapy and one with first generation protease inhibitors. 5 patients presenting 31.5 kPa average fibrosis were treated with

sofosbuvir (SOF) + simeprevir (SIM) ± ribavirin (RBV), four of them reached undetectable serum viral load (VL) in the first month. In the third month, there was a breakthrough in one of the patients, obtaining in other cases, including the one who had a VL detectable in the first month, a favourable response at the end of the treatment. 4 patients with 24 kPa fibrosis average were treated with pegylated interferon (PEG-IFN) + RBV + SOF, being the VL undetectable in 3 cases in the first month and one of them has not reached the first month. In the third month 2 patients had undetectable VL and in the other 2 the VL is pending. A patient presenting 6 kPa fibrosis was treated with PEG-IFN + RBV + SIM, with a VL undetectable since the first month of treatment and favourable response at the end of treatment. 5 patients with 21.5 kPa fibrosis average have started treatment with paritaprevir + ombitasvir + RBV ± dasabuvir. One patient has an undetectable VL in the first month of treatment, and we are expecting results for the remaining patients.

Conclusions: In this prison we have treated or are treating 100% of patients with advanced fibrosis (F4). Taking into account the patients of whom we have obtained VL results, we have achieved a 90% intra-treatment response rate in the first month and 87.5% in the third month, but it remains to determine the sustained virologic response awaiting the final results of our prison population.

P-67 Experience with new direct-acting antivirals (DAA) against HCV in patients with advanced liver fibrosis

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Background & Aims: A retrospective study to analyze our experience with DAA against HCV chronic infection in patients with advanced fibrosis.

Methods: A systematic review of our databases and patients clinical histories to determine the virologic response (VR) obtained during DAA therapy. We measured HCV RNA titers at baseline, 4th and 12th treatment week. The VR obtained after first and third month were analyzed according to treatment regimens and liver fibrosis by FibroScan®.

Results: A total of 57 patients were included, 45 male (77%) and 12 female with an age range from 34 to 63 years. 64% of them were infected by genotype 1, 15% by genotype 3 and 21% by genotype 4. 61% had already been treated; 56% with dual therapy and 5% with first generation IP. The average liver fibrosis at baseline was 26.8 kPa. Most common comorbid conditions were HIV

coinfection in 60%, alcohol abuse in 30% and HBV coinfection in 5%. 2 patients were waiting for liver transplantation for hepatocellular carcinoma. The most frequent extrahepatic manifestations were cryoglobulins in 5 cases and porphyria cutanea tarda in 2.

Treatment regimens used were as follows:

- Sofosbuvir + Simeprevir ± RVB: 24 patients with 21 kPa average fibroscan. The VR after first month was 56%. We reported one case of viral breakthrough during treatment and the rest reached undetectable viral load after third month.
- Sofosbuvir + Peginterferon + RVB: 9 patients with 23 kPa medium fibrosis achieved 83% VR after first month and 100% after the third.
- Simeprevir + Peginterferon + RBV: 5 patients with 14.2 kPa fibrosis. All of them got undetectable viral load after first month and reached end of treatment response.
- Sofosbuvir + Daclatasvir + RBV: 2 patients with 27 kPa fibroscan got 100% undetectable viral load at 1st and 3rd month
- Paritaprevir/r-Ombitasvir + Dasabuvir (3D)/Paritaprevir/r-Ombitasvir (2D): 15 patients with a middle fibrosis of 23.6 kPa. 66% of them got VR after 4th week but they are still on treatment now so we don't have 3rd month datas.
- Sofosbuvir/Ledipasvir ± RBV: 2 patients with 75 and 27.7 fibroscan, both got VR after 1st month and still waiting for 3rd month results

Conclusions: A high rate of on-treatment VR was reached in our series of advanced liver damage; 71% after first month and 97% after third. Final results to determine the sustained virologic response in our patients will be available soon.

P-68 Preliminary results of hepatitis C treatment with direct-acting antivirals (DAA) in HIV-HCV coinfecting patients

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Background & Aims: The hepatitis C treatment has undergone a revolution since the emergence of DAA. It has achieved success rates greater than achieved with previous treatment regimens. The primary endpoint is to describe the characteristics of patients that have started a treatment with a DAA regimen, and the preliminary results.

Methods: Observational and retrospective study. Sample of 38 patients who have started a hepatitis C treatment with a DAA regimen in La Princesa Hospital (Madrid)

between February and July of 2015. The same data have been collected for all patients, basal characteristics, parameters of liver disease and HIV&HCV infection, and data about the treatment and first results. Statistic analysis with SPSS22.

Results: 38 coinfecting patients, mean age of 50.8 years old (SD6.7), 73.7% (28) were men. 60.5% (23) met the criteria of pluripathology, and 73.7% (28) of polypharmacy. 79% (30) had advanced stages of liver fibrosis (F3-F4 by FibroScan®); 15.8% (6) had had previous liver decompensation (ascites, encephalopathy, bleeding esophageal varices or SBP), the mean MELD value was 7.34 (SD1.8). 39.5% had genotype 1a infection, followed by genotype 4 infection (23.7%). 60.5% had HCV-VL > 800.000cp/ml. 86.8% (33) had undetectable HIV-VL, with a mean CD4 of 660cel/mm³ (SD421). 63% had received hepatitis C treatment previously, all of them with IFN monotherapy or IFN + RBV, and 5 patients also with a first generation protease inhibitor triple regimen. None had been previously treated with DAA. The treatment used were Sofosbuvir + Ledipasvir ± RBV (42.1%, 16), Dasabuvir + Ombitasvir Paritaprevir ± RBV (23.7%, 9), Sofosbuvir + Simeprevir ± RBV (13.2% 5), Simeprevir + PegIFN + RBV (7.69%, 3), Sofosbuvir + Daclatasvir ± RBV (7.9%, 3), Ombitasvir + Paritaprevir + RBV (5.3%, 2). Two patients have finished the treatment, achieving end of treatment response. 22 patients have reached the first month of treatment, 77.3% (17) of them with undetectable HCV-VL (< 12 cp/mm³). 8 patients have reached 8 weeks of treatment, 100% of them with undetectable HCV-VL. 4 patients have reached 12 weeks of treatment, one of them has suffered a recurrence after discontinuing the treatment because of an adverse event. 31.6% (12) had adverse events, only one a serious adverse event that forced to discontinue the treatment. No death has been reported.

Conclusions: Patients who have started hepatitis C treatment with DAA have advanced age and a significant rate of pluripathology and polypharmacy. They had an advanced liver disease, with a good HIV infection control. Most of them had received a previous treatment. The preliminary results are good, only one patient had to discontinue treatment due to an adverse event.

P-69 Experience with the new DAAs in co-infected patients with HIV-HCV at the Hospital Universitario de Burgos (HUBU)

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Background & Aims: To know the characteristics of the infected patients with HCV-HIV who have initiated the treatment with the new directly acting antivirals (DAAs) in HUBU. Moreover, we are going to analyze its reaction and the possible appearance of side effects.

Methods: This is a retrospective descriptive study done in a third level hospital. The data about the patients treated with DAAs was obtained in the consultation register and the computer system. For the analysis, SPSS Statistics 20 was used.

Results: In our hospital there are 28 patients infected with DAAs, 20 men and 8 women. The average age is 50.3 (SD:7.2). 53.6% (15 patients) had previously received the treatment for HCV, 46.7% from them had completed it and 53.3% had not. The previous response was: 3 patients (20%) had null response, 3 (20%) had a partial response, 3 (20%) had a relapsed, 5 were suspended because of side effects (33.3%) and 1 abandoned it voluntarily (6.7%). The genotypes HCV were: 1 (15 patients-55.6%), 3 (9-33.3%), 4 (3-1.1%); and the genotypes IL28: CC (2-7.1%), CT (3-10.7%), TT (2-7.1%) and in the 75% was not determined. At the beginning of the treatment, the degree of fibrosis measured by FibroScan® was: F1: 2 patients (7.1%), F2: 1 (3.6%), F3: 9 (32.1%) and F4: 16 (57.1%) being the media of the obtained value: 20.64 (SD:14.38%). As regards the cirrhotic patients, the mean Child-Pugh score was 6 points (SD:1.68) and MELD 8.29 (SD:4.26).

3 (10.7%) patients have completed the treatment and 25 (89.3%) have not yet. There has not been any abandonment until now.

The marked treatments are the following: i) Simeprevir + Sofosbuvir (15 patients-53.6%); ii) Daclatasvir + Sofosbuvir (9-32.1%); iii) Ombitasvir-paritaprevir-ritonavir plus dasabuvir: (1-3.6%); iv) Ledipasvir-sofosbuvir (3-10.7%). One patient also took Ribavirin. 12 out of 20 patients have already reached the 4th week; they have a HCV viral load undetectable (mean: 34.5). In the 3 patients who have completed 12 weeks, it is also undetectable. Only 8 (28.6%) presented side effects: 6, grade 1 (somnolence, myalgia), and 2, grade 2 (sickness). There were neither cytopenia nor secondary kidney failure to the treatment. One patient suffered from a respiratory tract infection.

Conclusions: As previously reported, the new HCV treatments are very effective with barely side effects which we have also observed in our cohort of patients infected with HIV. It will be necessary a later evaluation with all the patients when the treatment will be finished.

P-70 Effectiveness of new direct-acting antivirals in a real-life cohort of difficult-to-treat HCV and HIV/HCV-coinfected patients

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Background & Aims: Chronic hepatitis C (CHC) is the leading cause of liver cirrhosis, hepatocarcinoma and liver transplantation. The development of new direct-acting antivirals (DAA) has marked a new therapeutic era.

Methods: From April 2013 to June 2015 we included all patients HCV infected who received DAA based treatment with available data about sustained virological response (SVR). We analyzed the data through an intention to treat (ITT) and on treatment (OT) statistical analysis using spss 20.0 version.

Results: A total of 362 anti HCV DAA based treatments were started. 81 of them with available data regarding SVR (19 received 12 weeks, 28 received 24 weeks, 33 other). 54 patients were HIV coinfecting. 42 patients were liver or kidney transplant. 65 were cirrhotic and 52 had received previous treatment (33.3% null responders, 25% partial responders, 4.2% with breakthrough, 16.7% relapsers and 20.8% finished because toxicity).

Regarding to HCV 23 patients had genotype 1a, 34 had 1b, 8 had 3a and 16 had genotype 4. 28 patients received Daclatasvir/Sofosbuvir, 22 Daclatasvir/Simeprevir, 15 Sofosbuvir/Ribavirin, 13 Sofosbuvir/Simeprevir, 2 Sofosbuvir/Ledipasvir and 1 Ombitasvir/Paritaprevir/Ritonavir/Dasabuvir.

Regarding the 54 HIV coinfecting, 44 were under TARGA based on integrase inhibitors, 22 were C3 CDC. The overall median CD4 cell count was 364.

In the ITT analysis SVR rates were in SOF/RBV regimen 20% in genotypes 1a, 1b; 50% in genotype 3a and 33.3% in 4. Most of these patients were under expanded access and changed DAA regimen when it was possible. For DCV/SOF regimen SVR was 66.7% in genotypes 1a and 1b, and 100% in 3a and 4. With SMP/DCV 33.3% SVR in 1a, 40% in 4 and 78.6% in 1b. SMP/SOF 25% SVR in 4, 66.7% in 1a and 75% in 1b. The 2 patients under SOF/LDV died and were not treatment attributable.

54 patients were OT analyzed. SVR rates were SOF/RBV 100% in genotypes 1a, 3a and 4 and 25% in 1b. For DCV/SOF SVR 100% in genotypes 1b, 3a and 4 and 85.13% in 1a. With SMP/DCV 100% SVR in 1a and 4 and 90.9% in 1b. SMP/SOF 75% SVR in 1b and 4 and 66.7% in 1a.

Conclusions: In our real life population the new DAA for the treatment of chronic hepatitis C showed high SVR rates including coinfecting, cirrhotic and pretreated patients. The combinations SOF/RBV and SMP/SOF have a worse trend in HCV 1b and HCV 1a, 1b and 4 genotypes respectively. More data are needed.

P-71 **Effectiveness and safety of direct-acting antiviral agents in the treatment of chronic hepatitis C virus infection: preliminary results**

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Background & Aims: Direct-acting antiviral agents (DAAs) have become the standard of care for the treatment of chronic hepatitis C virus (HCV) infection but data regarding real practice are scarce.

The objective of this study is to assess treatment effectiveness and safety of DAAs in routine medical practice.

Methods: Descriptive, non-interventional study. Inclusion criteria: all HCV monoinfected patients who started treatment with DAAs after 1st of April 2015 and whose follow-up period was 8 weeks.

The following variables were collected prospectively from the digital medical record: demographic, degree of fibrosis, clinical data (decompensated cirrhosis, hepatocellular carcinoma, liver transplant), response to previous HCV-treatment and viral genotype. Viral load and analytical data were collected at baseline and at 4 and 8 week. Adverse events were collected through clinical interview at baseline and every 4 weeks-visits and were classified according to Common Terminology Criteria for Adverse Events v4.0.

Primary effectiveness endpoint was virologic response (undetectable virus load) 4-8 weeks after treatment begins. Secondary endpoint was normalization of serum transaminases.

Safety was evaluated by laboratory abnormalities and adverse events.

Results: 134 patients were included: 90 (67%) were male with an average age of 59 (SD 9.1). One hundred and seven (80%) patients were cirrhotic, 20 (15%) and 6 (5%) patients had F3 and had F2 degree of fibrosis respectively. There were 8 (14%) patients with decompensated cirrhosis, 4 (3%) with hepatocellular carcinoma and 7 (5%) had received a liver transplant. Fifty-two patients (39%) were treatment-naïve, 66 (49%) had failed to prior therapy with peg-interferon/ribavirin and 15 (12%) to protease inhibitor.

Distribution of virus genotypes were as follows: genotype 1a, 26 (19%) patients; genotype 1b 84 (63%); unknown subtype genotype 1.5 (4%); genotype 3 9 (6.7%); and genotype 4, 10 (7.3%).

The prescribed DAAs were: OTP/PTV/r + DSV 81 (60%), SOF/LDV 49 (37%), SOF + DCV 2 (1.4%), OTP/PTV/r 1 (0.8%), other 1 (0.8%). Ribavirin was present in 98 (73%)

of patient's treatment. The expected treatment duration was 12 weeks in 89 (66%) patients and 24 weeks in 45 (34%).

Virologic response was achieved in 98% of patients with data available (82%). Moreover, 90% of patients with available laboratory data (92%) had normalized serum transaminases.

The most frequent adverse event were: ribavirin-associated anemia 67 (68%), headache 12 (9%), asthenia 29 (21%), insomnia 13 (10%), irritability 15 (11%), pruritus 19 (14%), and dry skin 14 (10.5%). Only one patient had grade 3 anemia and three patients had grade 3 hyperbilirubinemia.

Conclusions: Preliminary data show a high percentage of virologic response in the first 8 weeks of treatment. Most of adverse events were mild and did not differ from those described in clinical trials.

P-72 Strategic initiative to tackle HCV in Spain

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Background & Aims: Hepatitis C (HCV) in Spain is a public health concern that requires urgent solution. There are currently 481.000 people with HCV: prevalence 8 times higher than HIV. Furthermore, HCV is underreported, as 70% of the patients remain undiagnosed, while the virus continues damaging their livers causing cirrhosis, liver cancer and even death. This way, 10-12 people die daily from HCV in Spain. Besides, forecasts show that HCV-associated liver complications will reach maximum levels by 2030, since most patients will reach more severe and costly stages of the disease in the next years.

Despite this data, access to treatment in Spain is still inadequate, as only 5-10% of the patients receive treatment and, there has not been a priority approach at a policy level proportionate to the magnitude of the problem yet.

Therefore, in the light of the alarming situation, the aim of the project is not only to promote the clinical cure of the patients with HCV, but also to control the disease at a population level in terms of public health.

Methods: Regular meetings of a multidisciplinary work group composed by different agents with the capacity to control HCV in Spain have been held (primary care physicians, hepatologists, infectious disease specialists, nursery, prison doctors, epidemiologists, researchers, preventive medicine and public health experts, hospital managers, patients associations and federations), with a working methodology and intervention framework to tackle HCV in the continuum of care (primary prevention, early detection, clinical management and follow-up).

Results: The result of this exercise is a comprehensive action plan composed by interventions from each of the phases of the continuum of care, supported by all the agents with the objective of controlling the disease. Likewise, after analyzing the main deficiencies in the disease management, the group of experts prioritized 3 specific interventions for implementation: screening, training and information (to general population, risk groups, patients and health professionals) and the implementation of a care pathway integrating the different levels of care.

Conclusions: With the emergence of new treatments there is the possibility not only of curing HCV, but also of controlling it in terms of public health if interventions are implemented in the whole continuum of care. Currently, this is entirely possible in the Spanish context if the different interventions identified are implemented.

To do this, the alignment among the different agents of the system is key: planners, health structures managers and social and health professionals.

P-73 Prevalence of hepatitis C infection in a cohort of HIV positive patients

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Objectives: This study was aimed at determining the prevalence of chronic hepatitis C infection in a cohort of HIV-patients.

Methods: HIV positive patients followed at the Dr. Negrin General Hospital were enrolled. Sex and age were collected as well as risk factors related to hepatitis C infection. All patients were screened for anti-HCV and if positive, CRP through COBAS amplicor V2.0 was subsequently used to determine the presence of viral RNA and genotype was determined using INNO Lipa.

Results: A total of 204 patients were included in the study. The average age was 44.8 ± 13.73 years and men comprised for (85.3%) of those surveyed. Fifty seven percent (116/204) of patients were either homosexual or

bisexuals; 21.6% (44/204) had previous antecedents of parenteral drugs consumption and 19.6% (40/204) stated to have risky sexual behavior. Infection transmission through blood transfusion was found in two cases and no risk factors were identified in other two cases. Serology screening tests came back positive in 48 patients (23.5%) and 9 (19.75%) out of them spontaneously cleared the infection. Infection evolved to chronicity in 39 (19.1%) of the patients requiring antiviral treatment with pegylated interferon and ribavirin 22, with a sustained virologic response (SVR) of 63.6% (14/22). Genotype 1 was the most frequently found accounting for 59% (23/39), followed by genotype 3 with 25.6% (10/39); genotype 4 in 10.25% (4/39) and genotype 2 in only one case 1 (2.5%). We were not able to identify the phenotype in one patient. In patients with genotype 1, the subtype 1a was identified in 12/23 (52.1%).

Prevalence of hepatitis C virus infection in our cohort was lower compared to those reported in similar studies. This result could be due to the fact that, men who had sex with men, was the most common way of transmission and not through parenteral drugs consumption. Among patients infected only with the hepatitis C virus in our hospital, the subtype 1b is the most prevalent one. In contrast to it, in co-infected ones as in our study, subtype 1a was the most prevalent one. This finding is of high interest regarding the new treatments with AAD

Conclusions: In our cohort, 23.5% of VIH patients also tested positive for hepatitis C virus infection. Prevalence of active chronic infection was 19.1% and genotype 1 the most frequent. The main risk factor identified in our cohort was sex among men.

P-74 Incidence of acute hepatitis C infection among HIV infected patients in a Southern Spanish hospital. Preliminary results

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Background & Aims: High incidences of acute hepatitis C virus (HCV) infection (AHCVI) have been observed in the HIV-infected man who had sex with men (MSM) in specific cities in developed countries, and outbreaks have been reported from Madrid and Barcelona. However, no data is available on the incidence of AHCVI in Southern Spain, where the prevalence of HIV/HCV coinfection is considerably high. The objective of this study was to

determine the incidence of a first episode of AHCVI, as well as the incidence of reinfections with HCV, in HIV-infected patients seen at a Southern Spanish hospital.

Methods: In a prospective cohort study, all HIV-infected patients who are followed in the Infectious Diseases Unit of an outpatient clinic in Seville and who had presented either negative HCV antibodies (Anti-HCV) or positive HCV antibody with undetectable plasma HCV-RNA in an epidemiologic analysis conducted between January and June 2013, were included. The patients were evaluated two years after their participation in the previous study. A first episode AHCVI was diagnosed upon the detection of Anti-HCV in previously seronegative patients, while reinfection was defined as reappearance of HCV-RNA in plasma in those patients who had presented positive Anti-HCV with undetectable HCV-RNA. The herein presented results represent a preliminary analysis of the data available to date.

Results: A total of 251 HIV infected patients fulfilled the inclusion criteria and they were evaluated so far. Of these, 190 (76%) subjects had been seronegative for Anti-HCV in 2013. A total of 4 (1.6%) patients showed AHCVI, 3 (75%) subjects were previous injecting drug users and the other one was a MSM. All had been seropositive for Anti-HCV previously with confirmed undetectable HCV-RNA, and were thus classified as likely reinfections until genotype analyses are available, accounting for a reinfection rate of 6.4% (4/61 patients). It confirmed that 2 (50%) patients continued with risk practices. The overall incidence of AHCVI was 0.9 cases per 100 person-years, while the incidence of reinfection was 3.7 cases per 100 person-years. Two patients who developed reinfection had been treated previously obtaining sustained virologic response and showed detectable HCV-RNA 16 and 82 months later. The remaining two patients experienced a spontaneous clearance and showed detectable HCV-RNA 10 and 2 months thereafter, respectively.

Conclusions: The incidence of primary AHCVI is very low in the Southern Spanish area. However, there is evidence for a considerable incidence of reinfections among patients with ongoing risk factors.

P-75 Hepatitis C virus (HCV) acute infection in HIV-infected MSM due to sexual transmission: description of fifteen cases

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Background & Aims: The transmission of HCV happens mostly across percutaneous exposure to blood. The role of sexual transmission has not been well defined. In the last years HCV cases due to sexual transmission in

HIV-infected MSM have been described in some parts of Europe, USA and Australia

Methods: Descriptive study of HIV-infected patients seen in our clinic, who showed HCV antibodies (ELISA) simultaneously with HCV-RNA-positive test (PCR) and that previously had a negative test for antibody, without reporting injection drug use. Period of study: August 2011 to June 2015.

Results: We have diagnosed fifteen cases. Age: 39 ± 6.30 y.o; length of HIV infection: 6 ± 5.46 yr. All reported that in the prior 6 months they had engaged in high-risk behaviors for sexual transmitted infections (STI). All were on ART and with HIV viral load ≤ 50 copies/ml. HBV-coinfection in three cases. Previous STI in the last two years 87%. Baseline CD4 count: 719 ± 231.9 cells/ μ L. Median ASAT 268 ± 143.7 IU/L; median ALAT: 454 ± 328.6 IU/L. Median HCV-RNA at presentation: 6.34 ± 0.69 log. HCV genotype: G4 (7/15), G1 (7/15), G3 (1/15). Polymorphism of IL28B: rs12979860 (6CC;6CT; 2TT) and rs8099917 (7 TG, 6TT, 1 GG) (1 result pending). FibroScan[®] at diagnosis: F0 (2/15), F1 (4/15), F2 (5/15), F3 (2/15), (2 results unknown yet). Three patients showed abdominal pain or coluria as clinical presentation. No patient presented decline ≥ 2 log of HCV-PCR at 1st month of the diagnosis, neither on the 3rd month spontaneous viral clearance. Eight patients received treatment with pegIFN + ribavirin for 48 weeks. Two had to stop the treatment because of adverse effect, other one because of non-response. Five patients finished the treatment (four of them showed early virological response). As well, all of them presented sustained viral response at 24 weeks after end of treatment. One patient started treatment with sofosbuvir/ledipasvir and one with pegIFN + ribavirin + simeprevir, both of them with early virological response. One patient could not start treatment because of an intercurrent infection, one abandoned the study because of changing to other hospital and the other three patients did not start treatment yet.

Conclusions: This report suggests that hepatitis C is an emergent STI in HIV-infected MSM population, and it should be a part of the annual screening, especially in those with high risk behavior for STI. It should also be considered in case of sudden increase of transaminases, even without symptoms.

P-76 Spontaneous viral clearance of chronic hepatitis C infection in HIV patients after HAART initiation

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Background & Aims: The expected benefits of initiating HAART early in HIV/HCV co-infected patients go beyond that of just HIV infection control. It is rare to observe the spontaneous resolution of chronic HCV infection in HIV/HCV co-infected patients on HAART. Here we evaluate a series of spontaneous resolutions of chronic HCV infection in HIV infected patients after HAART initiation.

Methods: HIV-infected patients chronically co-infected with HCV in follow-up at two reference hospitals in southern Spain were included in the study. Patients were included in the analysis if they fulfilled the inclusion criteria: i) chronic HCV infection, defined as two consecutive positive HCV RNA results for at least 6 months; ii) naïve to HAART at the diagnosis of chronic HCV infection; iii) having an HCV RNA measurement after HAART initiation. The outcome variable was chronic HCV viral clearance, defined as spontaneous resolution of HCV chronic infection after HAART initiation. A descriptive analysis of clinical and genetic variables was performed.

Results: A total of 509 chronically infected HCV patients were evaluated. Eight patients were identified with spontaneous clearance of chronic HCV. The rate of spontaneous viral clearance for chronic HCV in our cohort was 1.5% (95% CI: 0.07%-2.96%). Six patients were male (75%), four had AIDS-defining criteria in the past (50%), all were injecting drug users (100%) and six patients were IL28B CC (75%). The distribution of HCV genotypes was: 4 genotype 1 (50%), 2 genotype 4 (25%) and 2 genotype 3 (25%). The median time not receiving HAART was 52 months (IQR: 11-77). At spontaneous viral clearance of chronic HCV, two patients had liver cirrhosis; after spontaneous viral clearance, the liver stiffness values of both cirrhotic patients were less than 14.6 kPa.

Conclusions: Chronic HCV viral clearance was a rare event in our cohort. Our results argue in favor of start HAART prior to HCV treatment in HIV/HCV co-infected patients, especially those carrying the favorable IL28B genotype. Furthermore, liver damage was reversed in both cirrhotic patients with viral clearance.

P-77 Analysis of cases of HCV in newly diagnosed HIV persons

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Background & Aims: It is estimated that the prevalence of HCV infection among HIV-infected patients in the

United States and Europe is around 33%, and even higher in the Mediterranean countries. The aim of this study is to analyze the prevalence of HCV, and their characteristics in new HIV diagnoses in our health area.

Methods: Retrospective observational study carried out in a tertiary hospital with a health area that comprises a population of 440,000. All new cases of HIV infection diagnosed between 2009 and 2014 with HCV infection were selected. Demographic data, route of transmission and disease characteristics were collected.

Results: Of the 116 new cases of HIV infection, a percentage of 18.1% presented HIV-HCV coinfection, coexisting HBV infection in 9.5% of cases. The HCV diagnosis was later than HIV diagnosis in 83.4% of cases. 76.2% were male; mean age 44.76 ± 8.3 years, and just 16.1% of them are foreigners. The main mechanism of transmission was sexual contact (58.1%), being gay majority (67.4%), followed by parenteral route (41.9%). 84.2% of patients admitted not use condoms, 75% have no steady partner and 70% admitted sexual promiscuity. Of all HCV patients, 41.2% had genotype 1a, 29.4% 1b, and 23.5% genotype 4, one patient presenting a mixed genotype 1b + 4. 61.9% of patients had CT IL28B polymorphism and only 9.5% of patients were cirrhotic.

Conclusions: The prevalence of co-infected patients among new HIV diagnoses in our health area is much lower than that reported in the literature for total HIV patients. HCV diagnosis often be after HIV diagnosis. In most new HIV diagnosis, the route of transmission of HCV infection were sexual, in patients who openly admit to not using prevention methods.

P-78 Burden of hepatitis C infection in Bilbao healthcare area

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Background & Aims: Treatment of hepatitis C virus (HCV) infection has suffered a great development in the last few years and now the majority of patients can recover, but treatment is very expensive in Spain.

We want to know the load of people who are susceptible to these treatments in our healthcare area.

Methods: This study was completed over a period of 15 years (2001-2014) in the Bilbao healthcare area. We made a retrospective study of those persons who had serology or/and viral load or/and genotype of HCV. We have eliminated maternal transmission studies. We evaluated the following determinations: HCV antibodies (Access, Beckman Coulter, Izasa and Centauro, Siemens), positive results were confirm by LIA (Line Immuno Assay,

Table 11

Group	Determinations	n	Positives (%)
1	Antibodies	126,124	1.62
2	Virus load	2,760	20.37
3	Antibodies + virus load	1,041	10.95
4	Genotype	5,355	

Innogenetics), virus load (Roche) and genotype by LiPA (line probe assay, Innogenetics and Siemens). Not all patients had all the determinations (anti-HCV antibodies, virus load and genotype) made.

Results: We studied 229,986 samples from 135,280 patients. They had between one sample (89,931 patients) and 51 samples (1 patient). They were between 1 and 99 years old and 46.36% were men. We were asked for the determination of anti-HCV antibodies in 127,890 patients (2,978 positives), viral loads in 7,786 patients (834 positives) and genotypes in 6,246 patients but, in 891 patients, there was not enough viral load to determine genotype. We divided patients in four groups depending on the determinations made (table 11).

Besides, in group 3 there were 643 patients negatives, 240 patients only with antibodies and 11 patients only with virus load. These last 11 patients corresponded with acute HCV infection. In group 4, distribution of genotypes was: 1b, 32.90%; 1a, 23.44%, 3a, 20.99%; 4a/4c/4d, 10.16%; 1, 4.31%; 4, 3.81%; other mono-infections, 2.69% and; coinfections, 1.70% (the most frequent was: 1a + 1b, 42 patients). More than 2% of people born between 1953 and 1972 had antibodies and they represented the 67.40% of our patients with positive viral load.

Conclusions: 2.41% of our patients had anti-HCV antibodies. Of them, 28% had positive HCV viral load and the majority of genotypes are 1a and 1b (56.34%). Coinfection with 2 or more genotypes is not very frequent. In order to study population susceptible of having HCV infection we should start for people born between 1953 and 1972.

P-79 Increases in liver steatosis in HIV-infected patients are strongly associated with body mass index elevation

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Background & Aims: There is scant data on the progression of hepatic steatosis in HIV infection. Because of this, we evaluated the changes in HS determined by the controlled attenuation parameter (CAP) over time in HIV-infected patients.

Methods: A prospective cohort of 326 HIV-infected patients was included in this study. All patients underwent a CAP measurement. Changes in steatosis were evaluated calculating the median (Q1-Q3) difference between baseline and 12 month CAP values (DCAP).

Results: The median (Q1-Q3) CAP was 221 (196-252) dB/m at baseline and 224 (198-257) dB/m at the 12-month visit ($p = 0.617$). Significant steatosis, i.e. $CAP \geq 238$ dB/m, was observed in 76 (37%) individuals at baseline and in 80 (39%) at the 12-month visit ($p = 0.683$). The following variables were associated with DCAP: plasma HIV RNA, < 50 vs. ≥ 50 , 4 (-21, 27) vs. -21 (-49, 4) dB/m, $p = 0.024$; body mass index (BMI) increase, no vs. yes, -13 (-40, 4) vs. 14 (-6, 32) dB/m, $p < 0.001$; triglycerides increase, no vs. yes, -1 (-30, 22) vs. 15 (-3, 40) dB/m, $p = 0.001$; impaired fasting plasma glucose, no vs. yes, -4 (-31, 16) vs. 30 (15, 49) dB/m, $p < 0.001$; raltegravir, no vs. yes, 5 (-20, 29) vs. -11 (-37.5, 15) dB/m, $p = 0.018$. The only factor independently associated with DCAP was BMI [B (SE): 9.03 (1.9); $p < 0.001$].

Conclusions: Increases in CAP values over a period of 12 months among HIV-infected patients are strongly associated with elevations in BMI. On the other side, other metabolic factors and antiretroviral drugs were not predictors of CAP changes independent of BMI.

P-80 **Impact of HCV infection in a HIV cohort followed over 18 years: past and present**

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Background: This study evaluates the impact of HCV infection in a cohort of HIV infected patients followed over 16 years and trends in hospitalizations and mortality.

Methods: A cohort of HIV-infected patients was followed at our institution between 1996-2013. Epidemiological, clinical and main data related with hospitalizations and mortality was recorded. Data has been analyzed considering HIV-mono and HIV/HCV populations and two periods of nine years each.

Results: A total of 2257 HIV infected patients (857 HIV/HCV co-infected) were retrospectively examined over 16 years. Overall, 76% were men, median age of 31 (25-37) years and 57% have an AIDS event during the follow-up. Patients under antiretroviral therapy (ART) was similar in HIV/HCV and HIV-mono in both periods ($> 87\%$). Main results are depicted in the table.

Overall, HIV/HCV co-infected population have significant lower CD4 counts (cell/mm³) in both periods (505 vs 312 and 542 vs 322; $p < 0.001$, respectively). A lower rate of patients achieved HIV-RNA < 50 cop/mL in the second period compared with HIV-mono (59.2 vs 56.4 and 75.3 vs 67.2; $p = 0.03$, respectively). In this population, a low rate of patients received HCV treatment although was higher in the second period (6.9% vs 11.5%, $p = 0.01$). Consequently, a higher proportion of patients achieved sustained virological response (SVR) in the second period (61% vs 70%, $p = 0.03$). The rate of liver-related mortality was significantly higher in HIV/HCV compared with HIV-monoinfected with an increase in the second period ($p = 0.02$). Moreover, hospitalizations related with liver-disease were higher in HIV/HCV and were higher in the second period ($p = 0.04$). Among patients achieving SVR, only 3.2% and 3.6% in both periods, respectively, had a liver-related hospitalization and none died.

Conclusions: HCV infection has a negative impact on HIV outcome related with lower CD4 recovery and lower rates of virological success in HIV/HCV patients under ART. However, HCV infection does not impact on the mortality related with infectious, tumoral or cardiovascular diseases and only increase the rate of liver-related mortality in HIV/HCV patients compared with HIV-monoinfected. Moreover, HCV infection significantly increased liver-related hospitalizations and mortality on the long-term. Considering the low rate of patients receiving HCV treatment in this cohort, these data confirm the harmful contribution of uncontrolled HCV infection in HIV/HCV infected population.

P-81 **Real-life data in a cohort of HIV/HCV coinfecting patients. Variables associated to liver fibrosis**

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Background & Aims: Analysis of real-life data and variables associated to liver fibrosis in a cohort of HIV/HCV coinfecting patients.

Methods: Epidemiological and clinical data of HIV/HCV coinfecting patients were prospectively recorded in a database during year 2014. Quantitative variables were compared among groups using t-student test. For the qualitative variables, chi-square test was used. A logistic regression analysis was used to assess variables associated to high liver fibrosis (\geq F3).

Results: A total of 469 patients infected with HIV, were included. Of all, 109 were coinfecting with HCV. Complete data were available in 84. Median age was 49 years (IQR 46-53), 65 (77.38%) were male. The most prevalent route of transmission was IDU (80.95%). Alcohol consumption was $>$ 30g per day in 7.14%.

Distribution by CDC stages was: A 36 (42.86%), B 15 (17.86%) and C 33 (39.28%). CD4 cell count was $>$ 200/ μ l in 92.86%. 81 patients (96.43%) were on antiretroviral therapy (ART), 90.12% had HIV-RNA viral load \leq 50 cp/ml. Median of years since HCV diagnosis was 18 (IQR 11-21.75).

The distribution of HCV genotypes (GT) was: 47 (55.95%) GT1 (30, 1a; 17, 1b), 16 (19.05%) GT3 and 21 (25%) GT4. IL28B genotype was: CC in 35 patients (41.67%), CT 37 (44.05%), TT 11 (13.09%) and unknown 1 (1.19%). HCV-RNA viral load was $>$ 6000000IU/ml in 16 (19.05%) patients. Liver fibrosis was measured by transient elastography (FibroScan[®]): F4 in 24 patients (28.57%), F3 in 11 (13.09%), F2 in 12 (14.29%), F0-F1 in 37 (44.05%).

42 (50%) patients had failed on a previous treatment based on pegIFN and ribavirin. IL28B genotype in this subgroup was: CC in 13 and CT/TT in 29 (31% vs 69%, $p = 0.047$).

The univariate analysis showed a trend to higher fibrosis (\geq F3) associated to: increasing age (50.37 ± 6.04 vs 47.9 ± 5.53 years, $p = 0.057$), B-C CDC stage (71.4% B-C vs 44.9% A, $p = 0.025$), GT1 (71.4% GT1 vs 44.9% GT3-4, $p = 0.026$), IL28B genotype CC (58.8% CC vs 30.6% CT/TT $p = 0.013$) and lower CD4 cells (517.6 ± 333.1 vs 727.8 ± 349.33 , $p = 0.007$). A logistic regression analysis showed higher fibrosis (\geq F3) associated to: GT1 (OR 3.94; 95% CI 1.19-13.04), IL28B genotype CC (OR 4.19; 95% CI 1.21-14.51) and lower CD4 cells (OR 0.997; 95% CI 0.995-0.999).

Conclusions: Most of our patients was on ART and had suppressed HIV-RNA viral load. Variables associated to higher liver fibrosis in HIV/HCV coinfecting patients were: GT1, IL28B genotype CC and lower CD4 cells.

P-82 Impact of ART including coreceptor inhibitor (maraviroc) on liver stiffness in cirrhotic coinfecting HIV / HCV patients. HEFICO sub-study

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Background & Aims: The fibrogenesis analysis in quimeric CCR1 and CCR5 mice revealed that CCR5 mediates its pro-fibrogenic effects in hepatic cells and promoting stellate cells. The blockage of co-receptors could preserve the progression of hepatic fibrosis in HIV/HCV co-infected patients. The aim of the study was to assess the impact of ART including a CCR5 antagonist (maraviroc) in cirrhotic patients HIV/HCV co-infected, HEFICO sub-study.

Methods: We evaluated 20 cirrhotic patients, which were available data determining liver stiffness at the beginning and end of the track. We analyzed the following parameters. The age, sex, baseline CD4, genotype, liver fibrosis (FibroScan[®]) with a melting point above or below 20 kilopascals (kPa), initial and final cut, Child-Pugh stage and average time tracing.

Results: The mean age was 47.35 years, and 16/20 were men. The mean follow-up was 27.05 months, 11/20 were followed $>$ 2 years. Child-Pugh Stadium was: 16/20 A stage, 2 B, and 2 C stage. The HCV genotypes distribution were: 9/20 G-1; 2/20 G-2; 4/20 G-4 and 5/20 G-5. The CD4 basal: 15/20 patients were below 500 c/mm and 4/14 below them 250c/mm. Regarding the baseline liver stiffness: 9/20 present liver stiffness higher to 20 kPa. During monitoring: 12/20 patients maintained their baseline levels of fibrosis, 8/20 patients experienced variations, one patient experienced fibrosis progression from 17 to 43 kPa, and one decreased from 38.5 to 12.8. Six (6/20) patients with F4 (Metavir) ($>$ 14.2 $<$ 20 kPa) reduced the fibrosis level: 3 patients to F2 and 3 patients to F3. In 5/20 patients with a higher follow-up of treatment (28 months) two alterations in liver stiffness was observed: 2 patients from F4 to F2 and one patient from F4 to F3.

Conclusions: ART including a CCR5 antagonist appears to have a beneficial effect in cirrhotic patients coinfecting with HCV and a CCR5 HIV tropism. The longer duration of treatment seems to be positive. The immunological improvement achieved with a powerful TAR including maraviroc may play a role central in this effect.

P-83 Characteristics of a chronically infected population with hepatitis B virus

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Background & Aims: Describe the characteristics of a chronically infected population with hepatitis B virus (HBV). Assess the prevalence of significant fibrosis and cirrhosis by transient elastography (TE) in a population with chronic hepatitis B. Analyze correlated variables with higher scores on TE.

Methods: All patients between 18 and 80 years with serum HBsAg for more than 6 months and follow-up in our hospital were included. We collected epidemiological, clinical, laboratory and ultrasound data, and we performed an TE with FibroScan®. We analyze data using SPSS. TE was considered optimal when there were ≥ 10 valid measurements, a success rate $> 60\%$ and interquartile range $< 30\%$. The following reference values were taken: no significant fibrosis ≤ 6 kPa, 6-9 kPa gray area, 9-12 kPa significant fibrosis and ≥ 12 kPa cirrhosis.

Results: 76 patients had a chronic hepatitis B infection: 30% had chronic hepatitis (56% of them HBeAg positive) and 70% were HBV inactive carriers. In 65 patients who were available TE valid data we performed statistical analysis. Mean age was 50 years (range 20-75), with 66% males. 26% reported regular consumption of alcohol, but only 1 patient > 2 daily units of alcohol. Mean BMI was 27 kg/m² (48% overweight and 19% obese). 32% of patients had at least one comorbidity, and 4 patients also had HIV infection. 17% of patients had thrombocytopenia. 33% of patients had undetectable HBV DNA, most under antiviral treatment. 67% had a normal ultrasound, 17% steatosis and 17% ultrasound findings suggestive of chronic liver disease.

The mean value of TE was 6.6 (range 3-32.8); 9% of patients had a value > 9 kPa, indicative of significant fibrosis or cirrhosis. Related factors with a value greater than 6 kPa in TE were sex (males), alcohol consumption, presence of HBeAg, lower platelet count, higher values of AST and ALT and the existence of ultrasound abnormalities.

In the multivariate analysis, factors associated with higher TE values were the highest values of AST and ALT (OR 20.06 IC95% 3.68-109.46, p 0.001) and alcohol consumption (OR 9.23 IC 95% 1.55-54.75 p 0.014) and the existence of ultrasound abnormalities (OR4.24 IC95% 1.14-15.67 p 0.03).

Conclusions: Most patients with chronic hepatitis B have low values of fibrosis assessed by ET. The elevation of liver enzymes, alcohol consumption and the existence of ultrasound abnormalities correlate with a higher estimation of fibrosis.

P-84 Association between HEV seroconversion and liver decompensation in cirrhotic patients

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Background & Aims: It has already been established that HEV infection in patients with advanced liver disease is associated with rapid deterioration in liver function, which can lead to rapid liver decompensation and death. Furthermore, in HIV-infected patients with active hepatotropic viral co-infections, such as hepatitis C or B (highly prevalent in HIV-infected patients), HEV infection could trigger accelerated progression to liver cirrhosis and end-stage liver disease. Here, we evaluate the clinical impact of HEV seroconversion on HIV-infected and cirrhotic patients.

Methods: In this prospective longitudinal study, the study population consisted of HIV-infected cirrhotic patients who were seronegative for HEV antibodies at the start of the study. All patients included were followed up every 3-6 months during the study period. ELISA for anti-HEV IgG and IgM was performed on all patients at every visit. Liver decompensation was defined as hepatocellular carcinoma (HCC), portal hypertensive gastrointestinal bleeding (PHGB), ascites, hepatorenal syndrome (HRS), spontaneous bacterial peritonitis (SBP), and hepatic encephalopathy (HE), diagnosed according to criteria stated elsewhere.

Results: 83 patients in the study population had liver cirrhosis at the time of inclusion; 60 (72.2%) presented with active chronic HCV infection, 18 (21.6%) with a successfully treated chronic HCV infection, and 5 (6.2%) with active HBV infection. Eight cirrhotic patients (9.6%) experienced HEV seroconversion during the study. The median follow-up was 12.1 months (IQR: 14.52-9.3 months). During study period, four cirrhotic patients (4.8%) suffered decompensated cirrhosis. During the study, four events were observed (3 ascites and 1 PHGB), all four in patients with active chronic HCV ($n = 3$) or HBV ($n = 1$) hepatitis. The presence of liver decompensation was more common in patients who experienced HEV seroconversion (2/8; 25%) than in those who did not (2/75; 2.6%) ($p = 0.023$).

Conclusions: In our study, HEV seroconversion in cirrhotic patients was associated with liver decompensation. Because of its clinical impact in a high-sensitivity group, preventive measures against risk factors associated with transmission must be considered.

P-85 Clinical manifestations and analytical alterations associated with acute hepatitis e virus in HIV-infected patients

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Background: The natural history of HEV infection in HIV-infected patients has not been established and may differ from that of HEV infection reported in the general population. HIV-infected patients may represent a population more prone to suffering clinical manifestations in the presence of a new infection. The aim of this study was to evaluate the clinical manifestations and analytical alterations of HEV seroconversion in HIV-infected patients.

Methods: A prospective longitudinal study whose study population included HIV-infected patients who seroconverted to HEV. A data collection protocol was used for patients with HEV seroconversion to identify associated clinical manifestations and laboratory abnormalities. An analytical alteration was defined as a transitory increase

or decrease in a laboratory parameter measured coincident with the time of seroconversion. For patients with elevated baseline transaminase, an increase two times higher than the baseline value was considered an alteration in the liver function test. Patients receiving Atazanavir-based antiretroviral treatment were excluded from consideration for jaundice or bilirubin increases. Neutropenia was defined as a total neutrophil count declining to below 1,500 cells/mL. A CD4+ cell decline of more than 20% of the baseline count or of more than 50 cells/mL was considered an alteration.

Results: Forty-one patients developed detectable anti-HEV antibodies. Among HEV-seroconverted patients, 32 (78.04%) presented symptoms and/or analytical alteration. 26 patients (63.4%) showed clinical manifestations: asthenia (51.2%), fever (39.2%), digestive manifestation (29.2%), diffuse abdominal pain (24.3%), jaundice (24.3%), myalgia (14.6%) and liver descompensation (4.8%). 20 patients (48.7%) showed analytical alterations: altered liver function test (48.7%), CD4+ cell decline (46.3%), neutropenia (43.9%), HIV blips (36.5%), CRP elevation (36.5%), AP elevation (21.9%).

Conclusions: In our study, HEV seroconversion was frequently symptomatic and, interestingly, also associated with HIV blips and CD4+ decline.



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