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Introduction: HIV/HCV co-infected patients have higher HCV loads and generally more rapid progression to fibrosis, end-stage liver disease and death. HIV and HCV viral infections are both characterized by systemic immune activation that plays an important role in disease progression. In the direct-acting antiviral (DAA) era, little is known about the immune-pathological response in HCV mono-infected and in HCV/HIV co-infected patients. The aim of the study was to analyze activation of T lymphocytes, DCs and Mo subsets in HCV and HCV/HIV patients under effective ART that receiving anti-HCV therapy.
Material and methods: In our study, we assessed 75 samples from 26 patients (13 HCV/HIV patients under effective ART and active HCV replication and 13 HCV patients) undergoing IFN-free regimens DAA based. Samples were collected before starting anti-HCV therapy (TO) and 12 weeks after the end of treatment when they obtained a sustained virologic response (SVR 12). Fourteen healthy donors (HD) were used as controls. We analyzed whole blood samples evaluating mDC, pDC, slanDC and typical, atypical and intermediate monocytes with a cytofluorimetric method based on seven fluorochromes. HLA-DR/CD38 CD4 and CD8 lymphocytes were also evaluated. Liver fibrosis was measured using FibroScan and FIB-4 score. ANOVA with Dunn's test, Mann–Whitney test, Wilcoxon test and Spearman correlation test were used for statistical analysis.
Results: All patients in both groups obtained SVR12. Activation of CD8 T cells was significantly higher in HIV/HCV and HCV patients than control ($p = 0.0002$ and $p = 0.0041$, respectively). Interestingly, a decrease in both groups was found (comparing SVR12 in HIV/HCV and HCV patients to HD, $p = 0.0186$ and $p = 0.0479$, respectively) up to a normalization after anti-HCV therapy. HLA-DR/CD38 CD4 levels were elevated only in co-infected patients ($p = 0.0003$) without modification during therapy (comparing SVR to control $p = 0.0385$). Intermediate Mo were increased in patients with HCV infection compared to HD ($p = 0.0654$) and normalized after therapy. Considering the sub-population of DCs, Mdc and pDC were reduced only in HIV/HCV patients ($p < 0.001$ and $p < 0.01$, respectively), and normalize after therapy, while MDC8 were decreased both in HIV/HCV and HCV patients compared to HD ($p < 0.001$ and $p < 0.01$, respectively); this decreases persist after therapy.
Conclusions: A different pattern of immune dysfunction was found in HIV/HCV co-infected and HCV mono-infected subjects. IFN-free treatments seem to reverse some of these alterations that should be monitored with a longer follow-up.

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Real-life renal impact of ledipasvir/sofosbuvir on a cohort of HIV-infected patients treated with tenofovir combined with a boosted protease inhibitor

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Introduction: Regarding the treatment of HIV/HCV co-infected patients, we still have some concerns about the renal safety of the interaction between ledipasvir (LDV)/sofosbuvir (SOF) and an ARV regimen including tenofovir and a boosted protease inhibitor (PI). Data are lacking from clinical trials to support this co-administration, since these patients were excluded from the main studies in co-infected patients. Increased levels of tenofovir and risk of renal impairment might prompt preventive ARV therapy switch recommendations, not possible in all patients due to their history of previous ARV regimens.
Methods: An observational study was conducted among the co-infected on an ARV regimen including tenofovir and boosted PI, who started HCV treatment with DAAs, between 1 January 2015 and 20 May 2016. Data on demographic, clinical and virological features were collected by analysis of clinical files.
Results: A total of 149 patients were treated with tenofovir/emtricitabine, from which 68 with SOF/LDV and an antiretroviral regimen that included a boosted PI: 30 on DRV/r, 22 on LPV/r, 14 on ATV/r, 1 on SQV/r and 1 on FPV/r. Mean age was 47 years, 72% males. Regarding HIV infection, 85% of the patients had undetectable viral load (<20 copies/mL), ranging below 100 copies/mL in the remaining, with a median of 582 T CD4+ cells/μL (141–1570). Treatment was planned for 24 weeks in 35% (24) of patients, according to liver fibrosis stage. At baseline, four patients had CKD stage IIi (Mean EgFR 54 mL/min) and by week 8 three of them had their FTC/TDF regimen switched (Mean EgFR 44 mL/min). By the end of treatment, these three patients had egfR >60 mL/min. Only one of the remaining 64 patients presented with an egfR <60 mL/min during treatment, requiring no switch on ARV regimen. From the 48 patients with available data at week 12 post-treatment, all but one had sustained virological response.
Conclusion: In our study, SOF/LDV did not have a major negative impact in patients on TDF and a boosted PI. In this population, renal function must be carefully monitored, mainly in patients with other risk factors for renal impairment.

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Changes in lipid profile during and after hepatitis C virus (HCV) treatment with direct-acting antiviral (DAA), interferon-free regimens in patients co-infected with HIV

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Introduction: HCV infection is associated with lower lipid levels in HIV co-infected patients treated or not with ART [1]. This has been related both to the HCV infection and to the impairment of the liver function. Some studies have reported increased lipid values after sustained virological response (SVR) with therapy based on interferon (INF) [2]. We aim to evaluate lipid changes in HIV/HCV co-infected patients receiving all-oral HCV therapy.
Methods: Retrospective longitudinal study in a cohort of HIV/HCV co-infected patients treated with direct-acting antiviral (DAA) and INF-free therapy. All patients whose treatment finished on 30 December 2015 or before, and whose 24-week post-treatment evaluation was on or before 15 June 2016, were included. The values of triglycerides (TG), total cholesterol (TC), high-density lipoprotein (HDL) cholesterol (HDL-c) and low-density lipoprotein (LDL) cholesterol (LDL-c) were collected at three time points: (1) 12 weeks before starting DAAs (pre-treatment); (2) between week 4 and the final day of treatment (on-treatment); (3) weeks 12 to 24 after the end of HCV therapy (post-treatment). Means were compared with the repeated measures ANOVA test. Results have been adjusted by a general linear regression which includes the following variables: age, gender, basal HCV RNA, presence of a protease inhibitor (PI) drug in the DAA regimen, presence of a PI drug in the ART regimen and estimated liver fibrosis (cirrhosis has been considered when liver stiffness ≥ 14.6 kPa).
Results: Two hundred and fifty patients had reached week 24 post-treatment on 15 June 2016. Only 130 patients had available lipid data

Table 1. Baseline characteristics

Age, mean (SD)	50.9 (5.5)
Gender: male/female, n (%)	93 (71.5)/37 (28.5)
Risk group: PWID/heterosexual/MSM, n (%)	113 (86.9)/13 (10.0)/4 (3.1)
CDC (93) classification system's C stage, n (%)	48 (36.9)
Basal HCV RNA, medIAn (UI/mL) (IQR)	2,047,181.5 (3,879,143.0)
Prior INF-based therapy: none/failure/relapse/intolerance, n (%)	79 (60.8)/35 (26.9)/8 (6.2)/8 (6.2)
Liver fibrosis assessed by transient elastography: F0–1, F2, F3, F4, n (%)	1 (0.8)/54 (41.5)/14 (10.8)/61 (46.9)

MSM, men who have sex with men; PWID, people who inject drugs.

before, during and after HCV therapy. Table 1 shows baseline characteristics. SVR was achieved in 127 patients (97.7%). TC and LDL-c values statistically increased on and after treatment ($p < 0.001$) versus pre-treatment. There were no significant changes when comparing TC and LDL-c values on versus after-treatment, nor between TG and HDL-c values pre-treatment versus on-treatment or post-treatment (Table 2). Changes in TC and LDL-c values are not influenced by gender ($p = 0.55$ and $p = 0.86$, respectively), age ($p = 0.07$ and $p = 0.06$), basal HCV RNA ($p = 0.21$ and $p = 0.1$), presence of PI in the ART regimen ($p = 0.50$ and $p = 0.46$) nor cirrhosis ($p = 0.41$ and $p = 0.19$). Moreover, changes between LDL-c values are not influenced by the presence of PI in the DAA regimen ($p = 0.18$), but DAA regimens including a PI were associated with increased TC values ($p = 0.005$).

Conclusion: TC and LDL-c values increase during the HCV treatment using DAA, INF-free regimens, and remain increased after stopping the HCV therapy.

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HIV/hepatitis C co-infection: successfully treating hepatitis C with direct-acting antivirals and managing those who do not access traditional care

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Introduction: In our HIV/hepatitis C virus (HCV) co-infected cohort, we are successfully treating HCV with direct-acting antivirals (DAAs) regardless of genotype, regimen, disease stage or prior treatment exposure. However, we recognize a proportion of patients for whom we are unable to provide treatment, because they do not engage in the traditional care setting. We report on the efficacy and safety of DAA therapy in our cohort of HIV/HCV co-infected individuals, the demographics of those not engaging in care and the strategies employed to tackle this population.

Methods: All patients co-infected with HIV and HCV in our cohort were included, and case notes were reviewed. Those who spontaneously cleared HCV infection, transferred care or died were excluded.

Results: At May 2016, the HIV/HCV co-infected cohort comprised 181 patients, of whom 89 (49%) had commenced HCV treatment. Thirty-three of these patients were treated successfully with interferon and ribavirin. Fifty-seven patients received ≥ 1 dose second-generation DAA, including 20 patients with cirrhosis, six in clinical trials. The majority were male (46/57) with a history of injecting drug use (35/57). The majority were HCV genotype 1 infected (48/57). Most were treatment naïve (43/57); six prior null responders; four relapsers after previous IFN/RBV; none were DAA experienced. Fifty-five of 57 were on a suppressive HIV antiretroviral regimen. At the time of writing, 52/57 patients had reached end of treatment. Forty-two had achieved SVR12 (42/42, 100%). Despite high success rates with those engaged in care, 92 (51%) patients remain untreated, of whom the majority are not attending scheduled hospital appointments, and many are currently struggling with addictions. Some are recently diagnosed as part of an ongoing outbreak of HIV and HCV amongst people who inject drugs. To target this population, we are implementing service change. New strategies will include local pharmacy ''directly observed therapy'' dispensing, specialist nurse-led service in the community and in addiction services. We show the area of residence of those who have over 50% non-attendance rates, in relation to the hospital where care is traditionally delivered to highlight the need for local services.

Conclusions: In those who access care, we observe excellent SVR rates in HIV-infected patients receiving DAAs for HCV. Serious adverse events with DAAs are rare and delivering treatment in the community to difficult-to-treat populations will increase engagement in HIV care and HCV cure rates. Poor engagement in care should be tackled by service redesign to reach out to these populations.

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Improving of glycaemic control associated with DAAs HCV treatment persists at SVR12

Abstract P271–Table 2. Means of the values in mg/dL with standard deviation

	Pre-treatment	On-treatment	After-treatment	p*	p†	p‡
TG	156.4 (79.7)	142.7 (68.1)	161.5 (85.2)	0.073	1.000	0.011
TC	176.0 (37.9)	199.5 (55.0)	196.1 (51.9)	<0.001	<0.001	1.000
HDL-c	49.3 (20.5)	52.0 (23.4)	49.9 (18.4)	0.100	1.000	0.751
LDL-c	97.6 (37.1)	121.1 (46.8)	114.2 (44.7)	<0.001	<0.001	0.107

Statistical significance p-value established in 0.05. Bonferroni correction has been done. *compares values pre-therapy versus on-treatment; †compares pre-therapy versus after-treatment; ‡compares on-treatment versus after-treatment.
TG, triglycerides; TC, total cholesterol; HDL-c, HDL cholesterol; LDL-c, LDL cholesterol.