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IFN-FREE THERAPY IS EFFECTIVE AND SAFE FOR HCV RECURRENCE IN LT HCV/HIV CO-INFECTION

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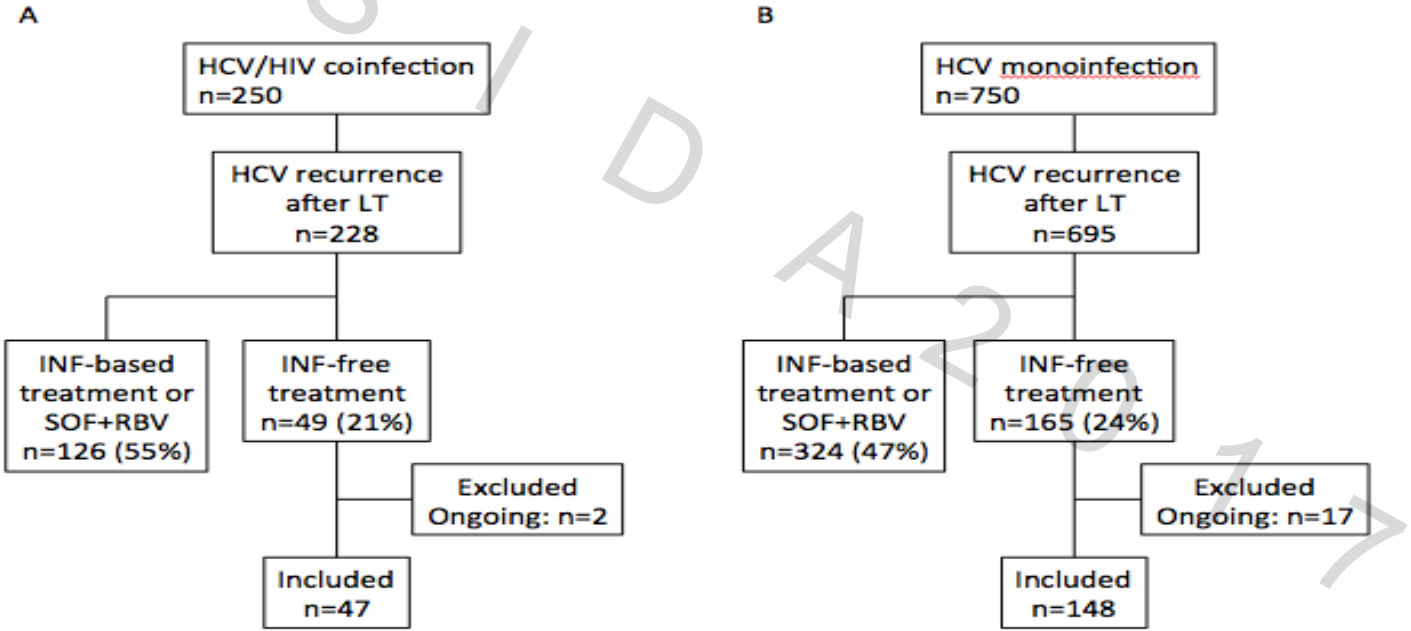
Background

- Survival in HCV/HIV-coinfected people who undergo liver transplant (LT) is lower compared with HCV mono-infected recipients.
- However, HIV/HCV patients cured from HCV recurrence achieve 5-year survival rates similar to the HCV mono-infected population.
- In the Interferon era, therapy against hepatitis C virus (HCV) recurrence after (LT) had poor effectiveness and tolerability both in HCV-mono-infected (≈30% of sustained virological response [SVR]) and HIV-HCV co-infected LT recipients (≈20% of SVR).
- Only small case series have reported on the use of direct antiviral agents (DAAs) in LT HCV/HIV co-infected recipients.

Aim & Methods

- This study aims to determine the effectiveness and safety of IFN-free regimens in a nationwide cohort of HIV-HCV co-infected individuals having undergone LT.
- 272 consecutive HIV-infected patients who underwent LT between 2002 and 2012 and who were followed until December 2016 were matched with 813 LT recipients without HIV infection in 22 Spanish institutions.
- Matching criteria were: same site, age (±12 years), gender, calendar year, and LT indication. Those patients who received IFN-free therapy for HCV recurrence were included.

Results: Patients' disposition



Results:Patients' characteristics

	HIV+	HIV-	P-Value
No. of cases	41	149	
Matching Variables			
Male	31 (75.6%)	121 (81.2%)	0.567
Age (year)	47.0 (6.48)	49.6 (5.97)	**0.041**
Data related to HIV infection (before OLT)			
HIV-1 risk factors: MSM	2 (5.00%)	--	--
Heterosexual relations	4 (10.0%)	--	--
Drugs use	28 (70.0%)	--	--
Hemophilia	3 (7.50%)	--	--
Other	3 (7.50%)	--	--
Plasma HIV-1 RNA <50 copies/ml	35 (85.4%)	--	--
CD4 T-cell count	367 [260;538]	--	--
Previous AIDS-definig events	7 (17.1%)	--	--
Duration of HCV infection (mo)	505 (419)	--	--
HCV infection characteristics			
HCV-RNA plasma levels(UI/mL)	1961627 [724200;4421294]	2410000 [893740;5167864]	0.351
Did receive previous HCV treatment	22 (53.7%)	84 (56.4%)	0.493
Months between LT and first anti-HCV treatment (months, median IQR)	40.8 [16.8;68.0]	45.3 [16.5;79.7]	0.152
Months between LT and DAA anti-HCV treatment (months, Median IQR)	72.8 [60.6;102]	78.2 [49.9;107]	0.238

	HIV+	HIV-	P-Value
Fibrosis Stage: F0-F1	11 (26.8%)	39 (38.2%)	0.363
F2	8 (19.5%)	10 (9.80%)	
F3	6 (14.6%)	23 (22.5%)	
F4	16 (39.0%)	30 (29.4%)	
Immunosupression before starting anti-HCV treatment:			
Cyclosporine Based	6 (15.4%)	15 (10.1%)	0.329
Tacrolimus-based	26 (66.7%)	109 (73.6%)	
Other regimens	7 (17.9%)	24 (16.2%)	
IFN-Free treatment characteristics			
Regimen: SOF + DCV	11 (26.8%)	14 (9.40%)	0.114
SOF + LDV	5 (12.2%)	13 (8.72%)	
SOF + SMV	0 (0.00%)	16 (10.7%)	
SMV + DCV	0 (0.00%)	3 (2.01%)	
SOF + DCV + RBV	3 (7.32%)	24 (16.1%)	
SOF + LDV + RBV	8 (19.5%)	37 (24.8%)	
SOF + SMV + RBV	11 (26.8%)	33 (22.1%)	
SMV + DCV + RBV	3 (7.32%)	4 (2.68%)	
3D	0 (0.00%)	5 (3.36%)	
Data at accomplishment of anti-HCV treatment			
Length of treatment with DAAs (weeks, median IQR)	12.1 [12.0;23.9]	12.4 [12.0;23.9]	0.999
SVR	38 (92.7%)	141 (94.6%)	0.239

Results:ARV

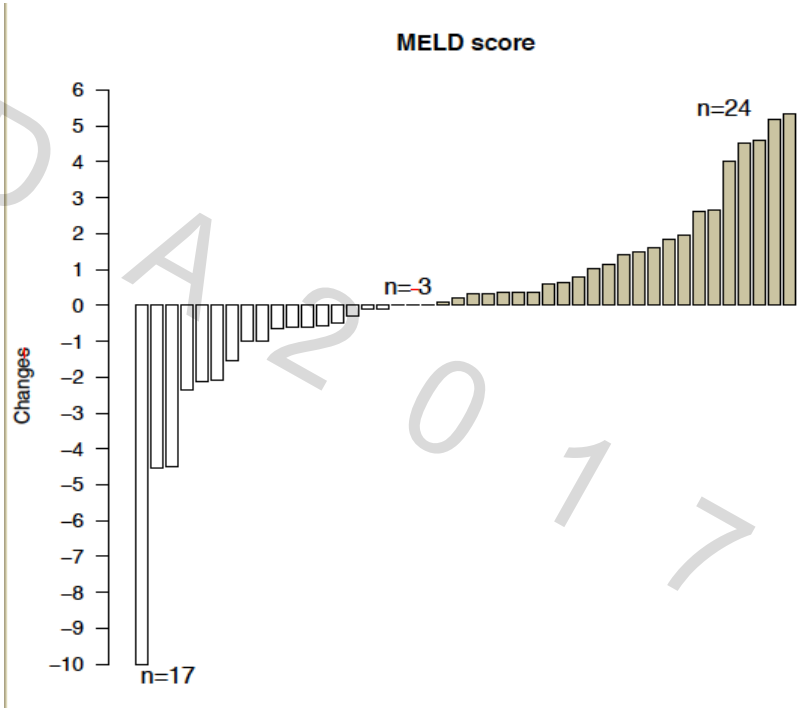
	N =47	%
2 NRTIs+ INSTI*	32	68,1
2 NRTIs+ NNRTI §	6	12,8
PI-based&	3	6,4
INSTI+NNRTI-based°	5	10,6
No treatment	1	2,1
NRTIs backbone		
TDF -based	28	59,6
plus either 3TC or FTC	27	57,4
TDF alone	1	2,1
Abacavir+ 3TC	16	34,0
NRTI-sparing	2	4,3

*28 Raltegravir, 4 Dolutegravir; § 4 Efavirenz, 2 Nevirapine; & 2 DRV/r + RAL, DRV/r + MVC; ° 1 TDF/FTC+RAL+EFV, 1 ABC/3TC +RAL+ETV, 2 TDF/FTC/RPV+ DTG, 1 DTG +RPV+ MVC.

- Only 5 patients (11.1%) required a modification in cART before starting treatment with DAAs.
- All but 1 were switched to ART based on a non-boosted INSTI (raltegravir, 2 cases; dolutegravir, 2 cases).
- The other case was a multi-drug resistant virus previously treated with emtricitabine/tenofovir, lopinavir/ritonavir and raltegravir and was switched to emtricitabine/tenofovir/rilpivirine plus dolutegravir q.d, based on historic genotyping analysis.
- No dose adjustment of DAAs was needed in any cases.

Results:Safety

	At initiation, mean (SD)	At end, mean (SD)	p Value
ALT	71.2 (57.6)	21.3 (8.98)	**<0.001**
AST	68.6 (51.6)	25.4 (8.92)	**<0.001**
Gamma GT	189 (356)	78.8 (167)	**0.002**
AP	134 (76.1)	112 (55.4)	**0.005**
Albumin	4.03 (0.55)	4.14 (0.52)	0.067
INR	1.10 (0.20)	1.11 (0.19)	0.633
Creatinine	1.17 (0.36)	1.22 (0.37)	0.272
Total bilirubin	1.11 (1.08)	0.97 (0.72)	0.421
MELD	9.78 (3.29)	10.0 (3.07)	0.539



Results:Virological Failures

	1	2	3	4	5
Status	HIV+	HIV+	HIV+	HIV-	HIV-
HCV genotype	1b	4	4	1b	1b
Metavir Fibrosis Stage	F0-F1	F4	F0-F1	NA	F4
Descompensation HCV	No	Yes	Yes	Yes	No
Treatment	SOF + SMV + RBV	SMV + DCV + RBV	SMV + DCV + RBV	SMV + DCV + RBV	SMV + DCV + RBV
Treatment after virological failure	SOF + LDV + RBV	SOF + SMV +DCV + RBV	SOF + LDV + RBV	SOF + SMV + RBV	No
SVR after second IFN-free treatment	Yes	Yes	Yes	Yes	--

	6	7	8	9	10	11
Status	HIV-	HIV-	HIV-	HIV-	HIV-	HIV-
HCV genotype	1 (ns)	1b	4	1b	1b	1b
Fibrosis	F0-F1	F3	F3-F4	NA	F4	F4
Descompensation HVC	No	No	No	Yes	No	No
Treatment	SOF + LDV + RBV	SOF + DCV	SOF + SMV	SOF + DCV	SMV + DCV + RBV	SOF + LDV + RBV
Treatment after No SVR	SMV + DCV + RBV	No	No	No	SOF + LDV	SOF + DCV + RBV
SVR after No SVR	Ongoing	--	--	--	Yes	Ongoing

Conclusions

IFN-free regimens with DAAs for post-LT recurrence of HCV infection in HIV-infected individuals were highly effective and well tolerated, with results comparable to those of HCV-monoinfected patients.