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Effectiveness of DAAs In HIV/HCV-coinfected Patients with Decompensated Cirrhosis

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Background and Aim

- Clinical trials and real-life studies show high rates of success after all-oral therapy (Rx) with direct-acting antivirals (DAA) in HCV-monoinfected patients with decompensated cirrhosis.
- In addition, eradication of HCV with all oral DAAs has been associated with short-term improvement in clinical and biochemical indicators of liver disease between baseline and post-treatment week 12 including patients with Child-Turcotte-Pugh (CTP) class C cirrhosis.
- In this study, we assessed real-life outcomes of all-oral DAA Rx in HIV/HCV-coinfected patients with decompensated cirrhosis; an area of which little is known.

Madrid-CoRe

Madrid-CoRe (Madrid Coinfection Registry)
- Prospective registry of HIV/HCV-coinfected adults (≥18 years) undergoing therapy with DAAs for HCV infection in the region of Madrid
- Compulsory for all hospitals from the Madrid Regional Health Service (SERMAS)

Patients registered in MADRID-CoRe
- 2,402 patients registered between Nov 2014 and May 2016

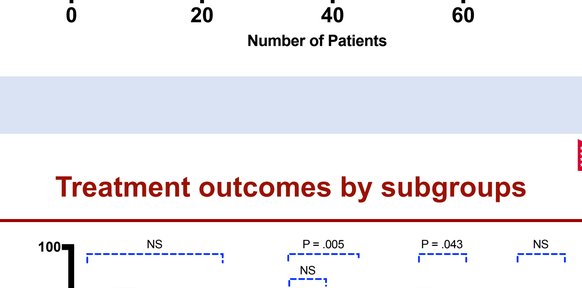
Eligibility criteria and study design

Key inclusion criteria
- HIV/HCV coinfection
- Treatment with DAAs for HCV
- Decompensated cirrhosis defined as current/prior CTP B/C or liver decompensation or hepatocellular carcinoma (HCC).
- Scheduled to finish treatment on May 31, 2016

Primary endpoint
- Wk. 12 sustained viral response (SVR_{12}) by ITT analysis

Secondary endpoints
- Viral relapse and viral breakthrough
- Rx discontinuation (D/C) due to adverse events (AEs) or other reasons

Flow chart

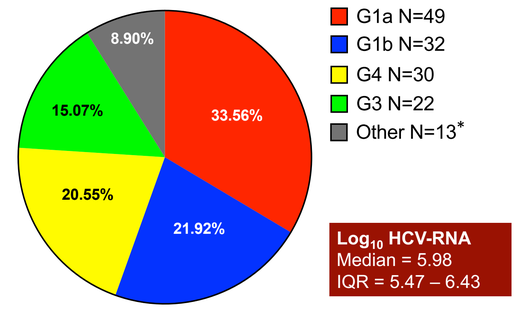


Patient characteristics

Variable	N = 146
Age years – median (IQR)	51 (48 – 54)
Male – n (%)	102 (69.9)
Prior IDU – n (%)*	85/97 (87.6)
CDC category C – n (%)*	33/97 (34.0)
CD4+ T cells/µL – median (IQR)*	474 (247 – 687)
cART – n (%)	125 (85.6)
Child-Pugh-Turcotte score – n (%)	
CPT A	75 (51.4)
CPT B	62 (42.5)
CPT C	9 (6.2)
MELD score – median (IQR)	10 (8 – 12)
History of hepatocellular carcinoma – n (%)	15 (10.3)
Liver transplantation – n (%)	1 (0.7)
Liver transplantation waiting list – n (%)	7 (4.8)
Anti-HCV – naïve – n (%)	88 (60.3)

*Based on 97 patients with available data

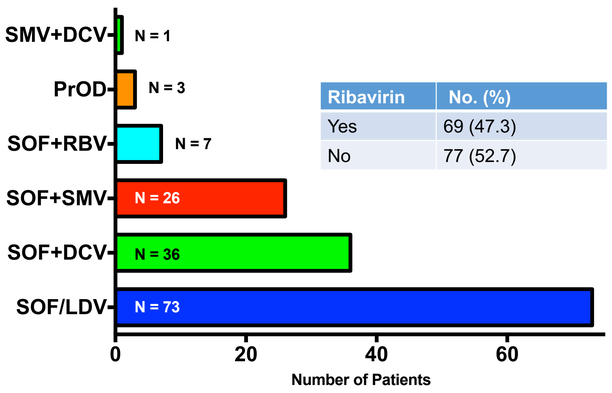
Genotypes and HCV-RNA



Total=146

* Non-subtyped G1, G2, mixed, undetermined

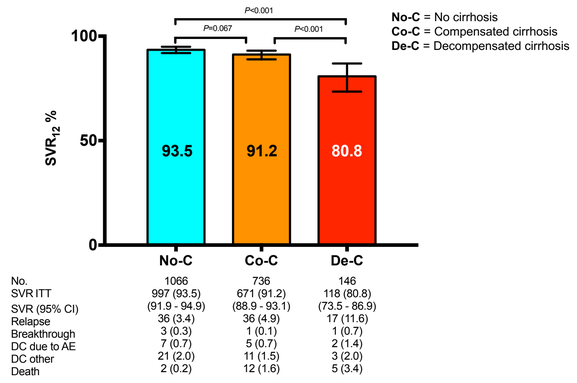
DAA-based regimens



Ribavirin	No. (%)
Yes	69 (47.3)
No	77 (52.7)

Treatment outcomes by severity of liver-disease

Patients w & w/o cirrhosis in Madrid-CoRe scheduled to finish treatment on May 31, 2016

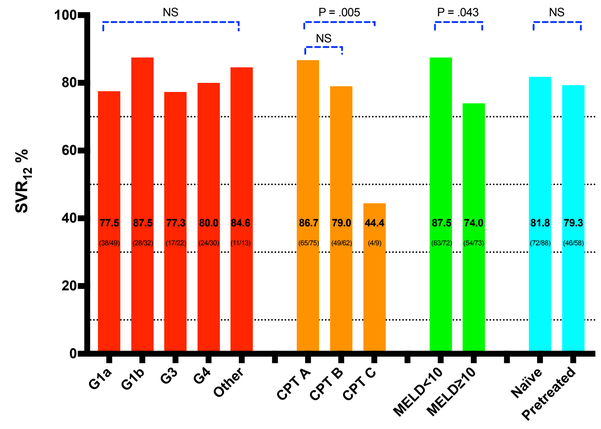


	No-C	Co-C	De-C
No.	1066	736	146
SVR ITT	997 (93.5)	671 (91.2)	118 (80.8)
SVR (95% CI)	(91.9 - 94.9)	(88.9 - 93.1)	(73.5 - 86.9)
Relapse	36 (3.4)	36 (4.9)	17 (11.6)
Breakthrough	3 (0.3)	1 (0.1)	1 (0.7)
DC due to AE	7 (0.7)	5 (0.7)	2 (1.4)
DC other	21 (2.0)	11 (1.5)	3 (2.0)
Death	2 (0.2)	12 (1.6)	5 (3.4)

SVR_{12} by DAA regimens and by HCV genotype

Regimen	G1a		G1b		G3		G4		Other		All	
	No.	SVR	No.	SVR	No.	SVR	No.	SVR	No.	SVR	No.	SVR
SOF/LDV	25	19 (76.0)	16	15 (93.7)	9	7 (77.8)	18	14 (77.8)	5	5 (100.0)	73	60 (82.2)
SOF+DCV	9	9 (100.0)	6	4 (66.7)	10	8 (80.0)	7	7 (100)	4	3 (75.0)	36	31 (86.1)
SOF+SMV	10	6 (60.0)	9	8 (88.9)	0	-	5	3 (60.0)	2	2 (100.0)	26	19 (73.1)
SOF+RBV	1	1 (100.0)	1	1 (100.0)	3	2 (66.7)	0	-	2	1 (50.0)	7	5 (71.4)
PrOD	3	3 (100.0)	0	-	0	-	0	-	0	-	3	3 (100)
SMV+DCV	1	0 (0)	0	-	0	-	0	-	0	-	1	0 (0)
All	49	38 (77.5)	32	28 (87.5)	22	17 (77.3)	30	24 (80.0)	13	11 (84.6)	146	118 (80.8)

Treatment outcomes by subgroups



Factors associated with treatment failure by logistic regression analysis

Covariate	Odds Ratio	95% CI	*P*
Sex			
- Male	1		
- Female	0.291	0.090 – 0.947	0.040
Child-Turcotte-Pugh score			
- CTP A	1		
- CTP B	1.723	0.689 – 4.312	0.245
- CTP C	9.425	2.011 – 44.167	0.004

Univariate logistic regression analysis was performed to assess the de association of the following baseline variables with treatment failure: age, sex, prior IDU, CDC category, CD4+ cells, concurrent ART, HCV genotype, HCV-RNA, CTP score, MELD score, history of HCC, liver transplantation (LT), LT waiting list, prior anti-HCV therapy, DAA regimen, and RBV use.

The final multivariate logistic regression model included baseline variables with a *P* value < 0.1 in the univariate analysis (sex and Child-Turcotte-Pugh score)

Conclusions

- The SVR12 rate with all-oral DAAs in coinfected patients with decompensated cirrhosis was 80.8%; significantly lower than in patients without cirrhosis and than in patients with compensated cirrhosis
- Male sex and Child-Turcotte-Pugh stage C were the only variables associated with treatment failure patients with decompensated cirrhosis
- The long-term impact of all-oral DAA therapy in HIV/HCV-coinfected patients with decompensated cirrhosis remains to be determined.

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