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Effectiveness of All-Oral DAAs for HCV Genotype 3 In HIV/HCV-Coinfected Patients

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Background and Aim

- Infection with HCV genotype 3 (GT3) is common among HIV/HCV-coinfected patients and has more frequently been associated with an increased risk of progression to cirrhosis and development of steatosis or hepatocellular carcinoma than other HCV genotypes.
- GT3 is currently the most difficult genotype to treat, with fewer therapeutic options based on all oral direct acting antivirals (DAAs) than other genotypes.
- Our aim was to evaluate treatment outcomes of DAA regimens for HIV/HCV-coinfected patients with GT3 and compensated liver disease.

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 analysis

Key inclusion criteria
- HIV/HCV coinfection.
- HCV Genotype 3.
- Scheduled to finish treatment on May 31, 2016.

Key exclusion criteria
- Current of previous decompensated liver disease defined as Child-Turcotte-Pugh (CTP) stage B or C, liver decompensation or hepatocellular carcinoma.

Primary endpoint
- Week 12 sustained viral response (SVR_{12}) by intention to treat analysis (ITT).

Secondary endpoints
- Viral relapse.
- Viral breakthrough.
- Treatment discontinuations (D/C)
- SVR_{12} by modified ITT (m-ITT) analysis, not including in the analysis patients with D/C due to reasons other than adverse events (AEs)

Patients and DAA-Regimens

- 273 coinfected individuals met the inclusion criteria.
- Daclatasvir + Sofosbuvir (DCV/SOF) 196 patients
  - 106 without RBV [8 wk, 1; **12 wk, 84**; 16 wk, 2; **24 wk, 19**].
  - 90 with RBV [**12 wk, 43**; 16 wk, 1; **24 wk, 46**].
- Ledipasvir/Sofosbuvir (LDV/SOF) 73 patients.
  - 62 with RBV [12 wk, 5; **24 wk, 57**].
  - 11 without RBV for 24 wk.
- Sofosbuvir/Ribavirin (SOF/RBV) 24 wk 4 patients

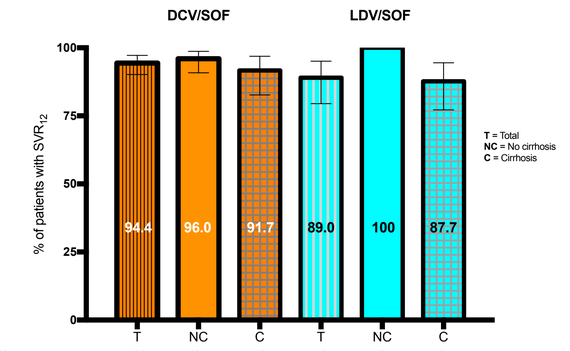
Patients treated with SOF/RBV
- 3 had liver cirrhosis (median TE value 20.8 kPa)
- 2 (50%) achieved SVR12
- 2 (50%) D/C Rx for reasons other than AEs

Characteristics of patients treated with DCV/SOF and LDV/SOF

	DCV/SOF			LDV/SOF		
Variable	**No-cirrhosis**	**Cirrhosis**	**Total**	**No-cirrhosis**	**Cirrhosis**	**Total**
No. of patients	124	72	196	8	65	73
Age**	51 (47-53)	52 (47-55)	51 (47-54)	50 (46-53)	51 (48-55)	51 (47-55)
Male*	95 (76.6)	63 (87.5)	158 (80.6)	6 (75.0)	52 (80.0)	58 (79.4)
Prior IDU*‡	65/77 (84.4)	44/50 (88.0)	109/127 (85.8)	2/4 (50.0)	44/49 (89.8)	46/53 (86.8)
CDC category C*‡	26/76 (34.2)	17/49 (34.7)	43/125 (34.4)	1/4 (25.0)	15/44 (34.1)	16/48 (33.3)
CD4+ cells/µL**‡	584 (409-781)	485 (310-678)	523 (379-781)	446 (315-627)	509 (331-781)	509 (331-730)
cART *	117 (94.3)	67 (93.1)	184 (93.9)	8 (100.0)	63 (96.9)	71 (97.3)
Log HCV-RNA **	6.2 (5.5-6.6)	6.1 (5.6-6.4)	6.1 (5.5-6.5)	5.9 (5.-6.6)	6.0 (5.6-6.6)	6.0 (5.5-6.6)
Liver stiffness**	9.1 (7.8-10.7)	21.3 (14.6-36.3)	10.9 (8.6-16.8)	11.1 (9.1-11.9)	20.5 (16.3-27.0)	18.5 (14.9-26.7)
HCV-naïve *	92 (74.2)	39 (54.2)	131 (66.8)	4 (50.0)	38 (58.5)	42 (57.5)

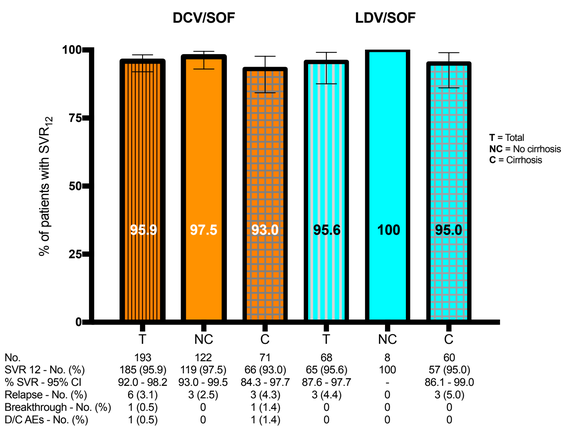
* No. (%), ** Median (IQR), ‡ Calculations based on the subset of patients with available information

DCV/SOF and LDV/SOF for GT3 - SVR_{12} by ITT analysis



No.	196	124	72	73	8	65
SVR 12 - No. (%)	185 (94.4)	119 (96.0)	66 (91.7)	65 (89.0)	100	57 (87.7)
% SVR - 95% CI	90.2 - 97.2	90.8 - 98.7	82.7 - 96.9	79.5 - 95.1	-	77.2 - 94.5
Relapse - No. (%)	6 (3.1)	3 (2.4)	3 (4.2)	3 (4.1)	0	3 (4.6)
Breakthrough - No. (%)	1 (0.5)	0	1 (1.4)	0	0	0
D/C AEs - No. (%)	1 (0.5)	0	1 (1.4)	0	0	0
D/C other - No. (%)	3 (1.5)	2 (1.6)	1 (1.4)	5 (6.8)	0	5 (7.7)

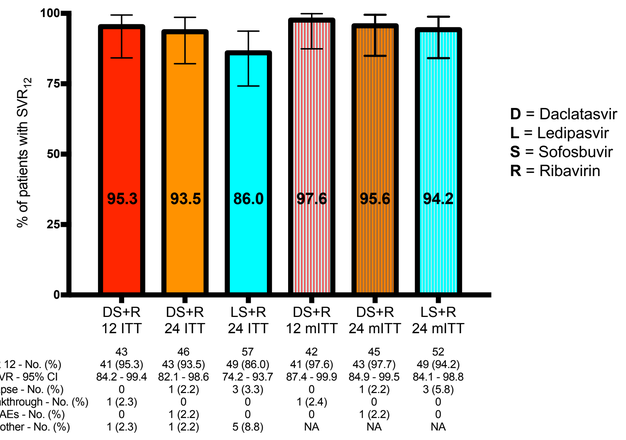
DCV/SOF and LDV/SOF for GT3 - SVR_{12} by m-ITT analysis



No.	193	122	71	68	8	60
SVR 12 - No. (%)	185 (95.9)	119 (97.5)	66 (93.0)	65 (95.6)	100	57 (95.0)
% SVR - 95% CI	92.0 - 98.2	93.0 - 99.5	84.3 - 97.7	87.6 - 97.7	-	86.1 - 99.0
Relapse - No. (%)	6 (3.1)	3 (2.5)	3 (4.3)	3 (4.4)	0	3 (5.0)
Breakthrough - No. (%)	1 (0.5)	0	1 (1.4)	0	0	0
D/C AEs - No. (%)	1 (0.5)	0	1 (1.4)	0	0	0

m-ITT: excluding patients with D/C other than AEs

DCV/SOF + RBV and LDV/SOF + RBV for 12 or 24 wks In patients with cirrhosis



No.	43	46	57	42	45	52
SVR 12 - No. (%)	41 (95.3)	43 (93.5)	49 (86.0)	41 (97.6)	43 (97.7)	49 (94.2)
% SVR - 95% CI	84.2 - 99.4	82.1 - 98.6	74.2 - 93.7	87.4 - 99.9	84.9 - 99.5	84.1 - 98.8
Relapse - No. (%)	0	1 (2.2)	3 (3.3)	0	1 (2.2)	3 (5.8)
Breakthrough - No. (%)	1 (2.3)	0	0	1 (2.4)	0	0
D/C AEs - No. (%)	0	1 (2.2)	0	0	1 (2.2)	0
D/C other - No. (%)	1 (2.3)	1 (2.2)	5 (8.8)	NA	NA	NA

m-ITT: excluding patients with D/C other than AEs

Factors associated with SVR_{12} Multivariate Logistic Regression Analysis

Covariate	Odds Ratio	95% CI	*P*
Cirrhosis			
- No	1		
- Yes	0.354	0.113 – 1.105	0.074
DAA regimen			
- DCV + SOF ± RBV	1		
- LDV + SOF ± RBV	0.767	0.271 – 2.174	0.618
- SOF + RBV	0.079	0.010 – 0.655	0.019

Univariate logistic regression analysis was performed to assess the de association of the following baseline variables with SVR_{12}: age, sex, prior IDU, CDC category, CD4+ cells, HCV-RNA, prior anti-HCV therapy, cirrhosis, liver stiffness, DAA regimen, treatment duration.

The final multivariate logistic regression model included baseline variables with a *P* value < 0.1 in the univariate analysis (cirrhosis and DAA regimen)

Conclusions

- We found DCV/SOF to be highly effective in HIV/HCV-coinfected patients with GT3 with or without cirrhosis, thus confirming the results of clinical trials.
- LDV/SOF was also highly effective in a difficult-to-treat population composed mainly of patients with liver cirrhosis and high liver stiffness values.
- Treatment with SOF/RBV was independently associated with treatment failure.
- A trend was found towards lower odds of SVR_{12} in patients with liver cirrhosis

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