Efficacy and Safety of Direct Antiviral Agents in Cirrhotic HCV-HIV Coinfected Patients

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Background

New direct antiviral agents (DAAs) have shown a great efficacy and safety in clinical trials and cohorts. However, the number of cirrhotic HCV/HIV coinfected patients included in most of these studies is small.

Methods and objectives

Multicenter prospective cohort analysis carried-out in 13 Spanish hospitals between January and December 2015. Inclusion criteria:

1) Adult patients (>18 years old)
2) Cirrhosis diagnosed by transient elastography (TE>14.6KPa) or by sonographic, endoscopic and/or clinical data.
3) HCV treatment based on DAAs according to drug availability and physician discretion.
4) HCV/HIV coinfection with stable ART and controlled HIV infection.

Primary endpoint: Overall efficacy (percentage of patients with undetectable HCV-RNA at week 12 after treatment - SVR12).

Secondary endpoints: Safety (percentage of withdrawal due to toxicity and/or hepatic decompensation) and efficacy according to regimen used and HCV genotype. Change in TE after HCV treatment was also evaluated.

Results

- 170 patients analyzed (Table 1). Mean TE 20.6kPa (IQR 16.1-33.7).
- Genotype distribution: Gt-1a, 68 (40%); Gt-1b, 21 (12.4%); Gt-4, 47 (27.6%), Gt-3, 26 (15.3%) y Gt-2, 1 (0.6%).
- Overall, 92.9% (158/170) SVR12 rate, without differences between genotypes (Table 2).
- Lower SVR12 rate in treatment-experienced patients (88.8% vs. 97.5%;p=0.026) driven by a poorer SVR12 among pretreated patients with Gt-1a (87.2% vs. 100%; p=0.045) (Figure 1).
- Causes of failure: 7 (4.1%) relapses, 2 (1.2%) lost to follow-up, 1 (0.6%) toxicity, 1 (0.6%) hepatic decompensation and 1 (0.6%) viral breakthrough.
- Patients with relapse after HCV treatment are summarized in table 3.
- Twenty (16.3%) patients treated with RBV needed dose modification, mainly due to anemia (n=17)
- On-treatment hepatic decompensation was observed in 4 (2.4%) patients (2 encephalopathy and 2 ascites).
- TE a week 12 after treatment finalization decreased a mean of 5.6 kPa (95%CI 1.8-9.2; p=0.004) as compared with baseline .

Conclusions

- In our cohort of HCV/HIV coinfected patients with compensated cirrhosis, treatment with DAAs-based combinations was highly safety and efficacious. Viral eradication was associated with a significant decrease in liver stiffness.
- Our data reinforces current recommendations to treat HCV/HIV coinfected patients with the same regimens as HCV monoinfected patients.

Table 1. Baseline charateristics

	Value
Sex, male	125 (73.5)
Age, years	51 (47-54)
Race, Caucasian	167 (98.2)
Risk factor for HCV	
ex-IDU	138 (81.2)
Heterosexual	18 (10.6)
MSM	8 (4.7)
Other	6 (3.5)
CD4+, cells/mm³	513 (320-697)
HIV-RNA <50 cop/mL	152 (89.4)
Current antiretroviral regimen	
2 NRTI + NNRTI	47 (27.6)
2 NRTI + INSTI	52 (30.6)
2 NRTI + PI	23 (13.5)
Other	46 (27.1)
Untreated	2 (1.2)
IL28B, non-CC	80 (62.9)
HCV-RNA log_{10}, IU/mL	6.1 (5.7-6.5)
Transient elastography, kPa	20.6 (16.1-33.7)
Child-Pugh class	
A	127 (74.7)
B	21 (12.4)
C	1 (0.6)
Not assessed	21 (12.3)
Prior hepatic decompensation, yes	28 (16.5)
Genotype	
1a	68 (40%)
1b	21 (12.4%)
2	1 (0.6%)
3	26 (15.3%)
4	47 (27.6%)
Other	7 (4.1%)
Previous HCV treatment	
Naive	81 (47.7)
pegIFN+RBV	65 (38.2)
pegIFN+RBV+TPV/BOC/SMV	23 (13.5)
SOF+SMV+RBV	1 (0.6)
Prior response to HCV treatment	
Null response	36 (40.4)
Partial response	12 (13.5)
Breakthrough	3 (3.4)
Relapse	15 (16.9)
Withdrawn	12 (13.5)
Unknown	11 (12.3)
DAA regimens used	
SOF/LDV	26 (15.3%)
SOF/LDV+RBV	43 (25.3%)
SOF+SMV	13 (7.6%)
SOF+SMV+RBV	34 (20%)
SOF+DCV	4 (2.4%)
SOF+DCV+RBV	25 (14.7%)
SOF+RBV	2 (1.2%)
SMV+DCV	1 (0.6%)
PR+SOF	9 (5.3%)
PrOD+RBV	7 (4.1%)
PrOD	3 (1.8%)
PrO+RBV	3 (1.8%)

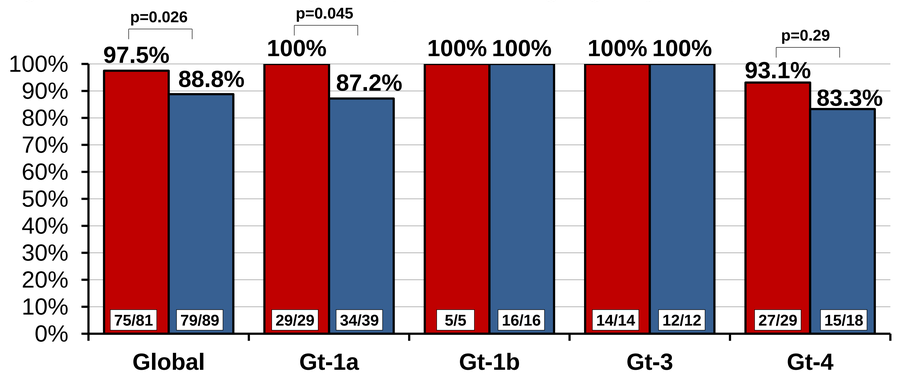
Table 2. SVR12 according to genotype and regimen

Genotype	Duration	Regimen	SVR12 Yes	SVR12 No
1	12w	3D	3(100%)	
		3D+RBV	2(100%)	
		PR+SOF	1(100%)	
		SOF/LDV	13(100%)	
		SOF/LDV+RBV	23(95.8%)	1(4.2%)
		SOF+DCV	1(100%)	
		SOF+DCV+RBV	5(100%)	
		SOF+SMV	5(62.5%)	3(37.5%)
		SOF+SMV+RBV	18(94.7%)	1(5.3%)
		Total	71(93.4%)	5(6.6%)
	24w	3D+RBV	5(100%)	
		SMV+DCV		1(100%)
		SOF/LDV	1(100%)	
		SOF/LDV+RBV	5(100%)	
		SOF+DCV+RBV	2(100%)	
		SOF+SMV	3(100%)	
		SOF+SMV+RBV	1(100%)	
		Total	17(94.4%)	1(5.6%)
2	12w	SOF+RBV		1(100%)
		Total		1(100%)

Table 2(cont.). SVR12 according to genotype and regimen

Genotype	Duration	Regimen	SVR12 Yes	SVR12 No
3	12w	PR+SOF	3(100%)	
		SOF/LDV	1(100%)	
		SOF+DCV+RBV	3(100%)	
		Total	7(100%)	
	24w	SOF/LDV	1(100%)	
		SOF+DCV	3(100%)	
		SOF+DCV+RBV	14(100%)	
		SOF+RBV	1(100%)	
		Total	19(100%)	
4	12w	PR+SOF	4(100%)	
		SOF/LDV	7(100%)	
		SOF/LDV+RBV	10(76.9%)	3(23.1%)
		SOF+SMV	2(100%)	
		SOF+SMV+RBV	13(92.9%)	1(7.1%)
		Total	36(90%)	4(10%)
	24w	2D+RBV	2(66.7%)	1(33.3%)
		SOF/LDV	3(100%)	
		SOF+DCV+RBV	1(100%)	
		Total	6(85.7%)	1(14.3%)
Mixed (1/4)	12w	SOF/LDV+RBV	1(100%)	
		Total	1(100%)	
Unknown	12w	PR+SOF	1(100%)	
		Total	1(100%)	

Figure 1. Sustained HCV virological response according to genotype and prior HCV-treatment status



Patients with genotype 1, not subtyped (n=4), genotype 2 (n=1), mixed genotype 1/4 (n=1) and 1a/1b (n=1) and unknown genotype (n=1) were excluded from the figure.

Table 3. Characteristics of patients relapsing after DAAs-based treatment.

Genotype	IL28B	Child-Pugh Class	Antiretroviral regimen	Previous HCV-treatment	Response to previous HCV-treatment	DAAs combination// duration	Baseline HCV-RNA (cop/mL)	HCV-RNA w4	HCV-RNA EoT
1a	CT	A	TDF,FTC,DTG	PR+PI	PR	SOF+SMV // 12w	1.400.000	BQL	BQL
1a	CT	B	TDF,ABC,ETR	PR	NR	SOF/LDV+RBV // 12w	47.480.000	183	BQL
1a	NA	A	TDF,FTC,RPV	PR+PI	Withdrawal	SOF+SMV+RBV // 12w	1.036.000	BQL	BQL
2	CC	NA	TDF,FTC,NVP	PR	Unknown	SOF+RBV // 12w	4.042.000	BQL	BQL
4	CT	A	DRV,RIT,MRV,RAL	PR	NR	SOF/LDV+RBV // 12w	5.302.000	50	BQL
4	CC	NA	TDF,FTC,RAL	PR	Unknown	SOF/LDV+RBV // 12w	116.500	BQL	BQL
4	CT	A	TDF,FTC,RPV	Naive		SOF+SMV+RBV // 12w	700.000	BQL	BQL

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