Outcomes of advanced liver disease in patients with chronic hepatitis C with and without HIV coinfection following sustained virological response: a real life evaluation in the PITER cohort

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INTRODUCTION

Due to shared routes of transmission, HIV co-infection is common among patients with chronic HCV infection. In Italy, it is estimated that 40% of HIV-infected patients are also infected with HCV. It is well known that HIV accelerates the course of HCV-related chronic liver disease. Although DAA has revolutionized the treatment of HCV, including its treatment in patients with HIV co-infection, few data are available on liver disease progression following viral eradication due to DAA treatment in HIV/HCV-coinfected patients in real-life settings.

AIM

We aimed to assess the epidemiological, clinical and treatment aspects in a real-life cohort of patients with HIV/HCV coinfection compared to HCV monoinfected patients after successful DAA treatment. We evaluated differences in clinical evolution in terms of liver-related complications in patients with cirrhosis after SVR, according to HIV coinfection.

METHODS

Patients consecutively enrolled in the PITER cohort between April 2014 and June 2019, who have started DAA treatment and with at least 12 weeks follow-up after the end of DAA treatment (median follow-up 38.9 months, range 4.1-60.8), were analysed. Emergence of a liver complication (de novo HCC occurrence, hepatic decompensation, Child-pugh (C-P) class deterioration) was evaluated in patients with pre-treatment diagnosis of liver cirrhosis. Variables independently associated to development of a liver complication after achieving SVR12 were evaluated by Cox proportional hazard models. Analyses were carried out using the STATA/SE 15.1 statistical package.

RESULTS

We included 244 HIV/HCV coinfected patients (74.6% men, median age 52, range: 32-77) and 2870 HCV infected patients (54.1% men, median age 61, range: 20-86).

A total of 128 (52.2%) coinfected patients and 1445 (50.3%) monoinfected patients were classified in the F4/cirrhosis stage. **Table 1** describes main baseline characteristics of the cirrhotic patients. There were no significant differences between cirrhotic monoinfected and coinfected patients for baseline AST, platelet count, serum albumin, bilirubin and international normalized ratio (INR) value.

Compared to HCV infected patients, HCV/HIV coinfected patients had significant lower BMI (64.8% of coinfected patients are in the normal BMI group, while monoinfected patients are equally distributed between the normal (41.3%) and the overweight (44.5%) group (p<0.001). A significant different distribution of HCV genotypes in monoinfected compared to coinfected patients was observed. About half of the monoinfected patients (n=759, 52.5%) were infected by HCV genotype 1b, whereas genotype 1a and 3 were dominant in coinfected patients (n=39, 30.5% and n=41, 32%, respectively). Coinfected patients have significant younger age respect to monoinfected patients (p<0.001) and higher liver disease severity in terms of Child Pugh (C-P) class score (p<0.001). No differences were observed in the prevalence of HCC, history of decompensated cirrhosis and previous liver transplant, between monoinfected and coinfected patients.

Table 1. Baseline characteristics of cirrhotic patients

		HCV/HIV co-infected (N=128*)		HCV mono-infected (N=1445*)		
Quantitative variables		Median	Range	Median	Range	p†
Age		52	36 - 77	63	23 - 86	< 0.001
ALT		60.0	10.0 - 284.0	74.0	7.0 - 797.0	< 0.05
AST		60.0	16.0 - 371.0	70.0	12.0 - 652.0	> 0.05
Platelets		104000	29000 - 262000	117000	15000 - 590000	> 0.05
Albumin		3.9	2.5 - 5.1	3.9	1.9 - 7.3	> 0.05
Bilirubin		0.9	0.1 - 58.0	0.9	0.2 - 70.0	> 0.05
INR		1.1	0.9 - 1.5	1.1	0.5 - 5.0	> 0.05
Categorical variables		N.	%	N.	%	p‡
Sex	Male	105	82.0	865	59.9	< 0.001
	Female	23	18.0	580	40.1	
BMI	Underweight	5	3.9	16	1.1	< 0.001
	Normal	83	64.8	597	41.3	
	Overweight	30	23.4	643	44.5	
	Obese	10	7.8	188	13.0	
Alcohol use	Never	52	46.9	936	66.2	< 0.001
	Current	32	28.8	129	9.1	
	Past	27	24.3	349	24.7	
Genotype	nd	1	0.8	11	0.8	< 0.001
	1 (Non subtyped)	5	3.9	34	2.3	
	1a	39	30.5	190	13.1	
	1b	15	11.7	759	52.5	
	2	4	3.1	184	12.7	
	3	41	32.0	160	11.1	
	4	23	18.0	106	7.3	
	5	0	0.0	1	0.1	
Diabetes	Yes	17	13.3	303	21.0	< 0.05
	No	111	86.7	1142	79.0	
antiHBs and/or HBsAg	Yes	56	43.7	316	21.9	< 0.001
	No	72	56.2	1129	78.1	
Previous Interferon	Yes	35	27.3	484	33.5	> 0.05
	No	93	72.7	961	66.5	
HCC	Yes	3	2.3	95	6.6	> 0.05
	No	125	97.7	1350	93.4	
Decomp. cirrhosis	Yes	20	15.6	173	12.0	> 0.05
	No	108	84.4	1272	88.0	
Transplant	Yes	2	1.6	66	4.6	> 0.05
	No	126	98.4	1379	95.4	
Child-pugh score	A-5	45	51.7	859	67.0	< 0.001
	A-6	16	18.4	295	23.0	
	B-7	14	16.1	74	5.8	
	B-8	9	10.3	34	2.6	
	B-9	2	2.3	17	1.3	
	C-10	1	1.1	1	0.1	
	C-11	0	0.0	2	0.2	

* For some variables inconsistencies are due to missing values; † p value Mann–Whitney rank-sum test; ‡p value Chi-square test

Comparable rates of SVR12 were observed in coinfected and monoinfected patients (93.3% and 94%, respectively). HCC developed in 1 (0.9%) coinfected and in 3 (0.2%) monoinfected patients before the end of treatment (EOT). The incidence of HCC following EOT was 1.9% (n=2) and 4% (n=48) in coinfected and monoinfected patients, respectively (p>0.05). Factors independently associated to *de-novo* HCC occurrence were age, serum albumin and genotype 3 (**Table 2**).

Table 2. Variables independently associated to *de-novo* HCC occurrence

Baseline variables	Crude HR	95% CI	Adjusted HR	95% CI
HIV infection	0.45	0.11 - 1.86	0.56	0.06 - 4.77
Age (increasing years)	1.05	1.02 - 1.08	1.08	1.04 - 1.12
Sex (ref. female)	2.18	1.14 - 4.17	1.90	0.91 - 3.98
BMI: overweight/obese (ref. under-normalweight)	1.27	0.71 - 2.24	1.53	0.79 - 2.96
Current /past alcohol use (ref. never)	1.80	1.03 - 3.16	1.92	0.98 - 3.77
ALT (increasing U/L)	1.00	0.99 - 1.00	1.00	0.99 - 1.00
AST (increasing U/L)	1.00	0.99 - 1.01	1.01	0.99 - 1.02
Platelets (ref. >100.000 U/μL)	1.45	0.83 - 2.55	0.91	0.48 - 1.73
Albumin (decreasing g/dL)	3.54	1.98 - 6.34	3.03	1.46 - 6.30
Bilirubin (increasing mg/dL)	1.01	0.92 - 1.11	1.04	0.91 - 1.18
INR (increasing unit)	1.01	0.30 - 3.33	0.64	0.15 - 2.85
Genotype (3 vs others)	1.47	0.69 - 3.13	2.67	1.03 - 6.96
Diabetes	1.45	0.78 - 2.70	1.45	0.74 - 2.82
antiHBc and/or HBsAg	1.84	1.04 - 3.26	1.57	0.83 - 2.96
Previous Interferon	1.09	0.61 - 1.94	1.39	0.75 - 2.58
Previous decompensation event	1.12	0.48 - 2.64	0.90	0.35 - 2.34

Occurrence of hepatic decompensation was observed in 11 (9.9%) coinfected patients, of whom 4 (36.4%) are first decompensating event, and in 119 (9.1%) monoinfected patients, of whom 54 (45.4%) are first decompensating event. Factors independently associated with the appearance of a decompensating event (ascites, hepatic encephalopathy, portal hypertensive gastrointestinal bleeding) were low platelet count, serum albumin, pretreatment HCC and liver decompensation prior to treatment (**Table 3**).

C-P class worsened in 4 (6.8%) and in 89 (8.2%) of coinfected and monoinfected patients, respectively (p>0.05). Factors independently associated with C-P class deterioration, were low baseline platelet count (HR=1.79; 95% CI 1.13-2.82), high INR (HR=2.24; 95% CI 1.13-2.82) and pretreatment HCC (HR=2.00; 95% CI 1.03-3.88).

Table 3. Variables independently associated with the appearance of a decompensating event

Baseline variables	Crude HR	95% CI	Adjusted HR	95% CI
HIV infection	1.08	0.58 - 2.01	0.87	0.34 - 2.24
Age (increasing years)	1.01	0.99 - 1.02	1.01	0.99 - 1.04
Sex (ref. female)	1.41	0.98 - 2.03	1.23	0.78 - 1.93
Current /past alcohol use (ref. never)	1.13	0.79 - 1.63	0.96	0.61 - 1.50
ALT (increasing U/L)	0.99	0.99 - 0.99	1.00	0.99 - 1.01
AST (increasing U/L)	1.00	0.99 - 1.00	1.00	0.99 - 1.01
Platelets (ref. >100.000 U/μL)	2.70	1.89 - 3.86	2.01	1.29 - 3.12
Albumin (decreasing g/dL)	4.10	2.87 - 5.87	1.65	1.08 - 2.54
Bilirubin (increasing mg/dL)	1.01	0.95 - 1.08	0.80	0.61 - 1.05
INR (increasing unit)	2.13	1.53 - 2.95	1.40	0.72 - 2.76
Genotype (3 vs others)	1.42	0.87 - 2.31	1.10	0.55 - 2.19
Diabetes	1.53	1.05 - 2.23	0.94	0.59 - 1.50
antiHBc and/or HBsAg	0.75	0.49 - 1.15	0.74	0.45 - 1.22
Previous Interferon	0.79	0.54 - 1.15	0.74	0.48 - 1.16
HCC	2.42	1.45 - 4.03	1.83	1.02 - 3.26
Previous decompensation event	10.7	7.55 - 15.08	7.13	4.51 - 11.27

CONCLUSION

These real life data confirm the high effectiveness of DDA treatment in achieving SVR in advanced liver disease patients, independently by HIV coinfection. However, the effectiveness of DAA treatment in patients with advanced liver cirrhosis is not as high as its efficacy. HIV coinfection was not associated with a higher probability of developing liver complications in HCV-infected patients with advanced liver disease; an advanced pre-treatment liver disease (low platelet levels as surrogate of portal hypertension, low albumin levels, high INR and/or HCC), remained the main independent predictive factor for liver disease progression (C-P class deterioration, new events of liver decompensation and/or HCC development) following viral eradication.

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DISCLOSURES

Nothing to disclosure

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