Survival Of HIV-HCV Co-infected Patients With Compensated Liver Cirrhosis: Impact Of Hepatitis C Therapy

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BACKGROUND

- Liver cirrhosis is an important cause of morbidity and mortality in HIV-infected patients.
- Chronic hepatitis C is the cause of more than 90% of the cases of liver cirrhosis in HIV-infected patients.
- There is limited data about the benefit of hepatitis C therapy in HIV/HCV coinfected patients with compensated liver cirrhosis.

OBJECTIVE

- To evaluate the effect of therapy for chronic hepatitis C in HIV-HCV coinfected patients with compensated liver cirrhosis on:
  - Survival
  - The incidence of first hepatic decompensation

STUDY DESIGN (1)

- Multicenter national prospective cohort
- Compensated Cirrhosis Diagnosis:
  - **Biopsy**-proven cirrhosis or advanced bridging fibrosis.
  - **Bonacini Score*** $\geq$ 8: Sensitivity: 46%, Specificity 98% (HIV-negative).
  - Lack or history of prior hepatic decompensation (gastrointestinal bleeding, ascites, encephalopathy, SBP hepatorenal syndrome.

*Bonacini et al. Am J Gastroenterol 1997;92:1302. .

STUDY DESIGN (2)

- Total planned follow-up: 60 months.
- Visits: baseline and then every 6 months.
  - Each visit:
    - Personal interview.
    - Hematology, Biochemistry, Inmmunology, Virology, alfa-fetoprotein.
    - Abdominal ultrasound.
  - Each year:
    - Endoscopy to detect esophageal varices (according to Schepis criteria*).

Schepis et al. Hepatology 2001; 33:471-2.

STUDY DESIGN (3)

- **SURVIVAL**: time from the date of entry until the first endpoint occurred: death, hepatocarcinoma or liver transplant.
- **TIME TO FIRST HEPATIC DECOMPENSATION**: time from the date of entry until the first episode of gastrointestinal bleeding, ascites, encephalopathy, SBP or hepatorenal syndrome.
- **STATISTICAL ANALYSIS**: Time-to-event analyses were performed using Kaplan-Meier survival curves, the long rank test, and Cox proportional hazards regression.

BASELINE CHARACTERISITICS (1)

	All	HCV Treated	HCV Non Treated	P
N	248	184	64	
Mean age (years)	42	42	42	0.54
Female n (%)	55 (22,2)	40 (21,7)	15 (23,4%)	0.86
Cirrhosis diagnosis (%)				
- Biopsy	213 (85,9)	172 (94)	40 (62.5)	< 0.001
- Bonacini Score ≥8	35 (14,1)	11 (6)	24 (37.5)	< 0.001
Cirrhosis causes (%)				
- Hepatitis C	248 (100)	184 (100)	64 (100)	
-Genotypes 2,3	59 (23,8)	50 (27.2)	9 (14)	0.04
- Hepatitis B	9 (4,3)	6 (3,8)	3 (6.1)	0.48
- Prior alcohol abuse	68 (27,4)	46 (25)	22 (34.4)	0.19
Child Pugh score				
-A	224 (90.3%)	171 (93%)	52 (82.5%)	0.02
-B,C	24 (9.7%)	13 (7%)	11 (17.5%)	

BASELINE CHARACTERISITICS (2)

	All	HCV Treated	HCV Non Treated	P
Median duration HIV infection (years), (IQR)	13 (9-17)	12 (8-16)	13(9-17)	0.18
Median duration HCV infection (years)	23	23	23	0.77
Transmission route IVDU (%)	213 (85.9)	158 (86)	55 (86)	1
CDC stage C (%)	79 (32)	58 (31.5)	21 (33.3)	0.96
Receiving HAART at baseline (%)	218 (88.3)	166 (90.2)	52 (82.5)	0.11
-HIV-RNA *Below limit of quantification (50-200) c/ml.				
- Baseline (median, IQR)	50 (49-199)	50 (49-199)	50 (50-1765)	0.001
- % HIV RNA BLQ*	60.4	66.5	51.7	0.04
Baseline CD4 cell count (median, IQR)	437 (284-646)	441 (293-644)	424 (212-648)	0.71
Nadir CD4 cell count (median IQR)	179 (83 - 272)	180 (91-261)	160 (72-333)	0.25
HCV treatment received (%)	184 (74,2)	184	-	-
–Sustained virological response (%)		44 (24)	-	-
–Still receiving HCV treatment (%)		3 (1.6%)	-	-
–Non responders or relapsers (%)		137 (74.4)	-	-

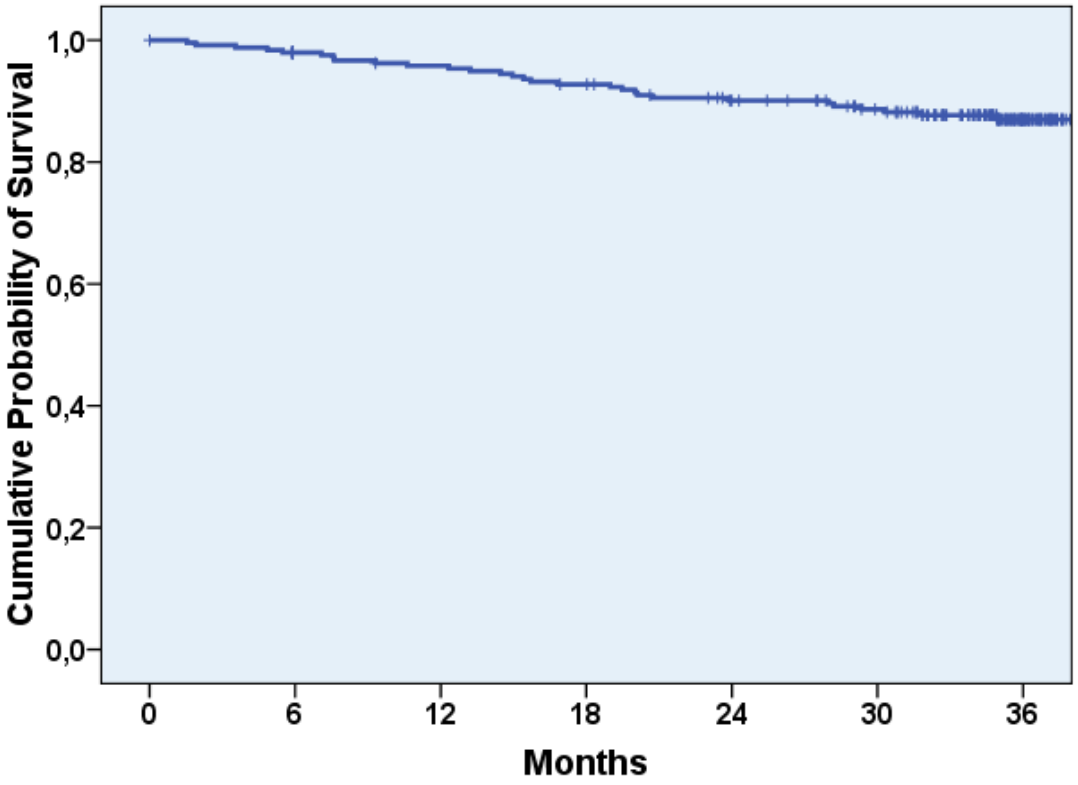
RESULTS (1)

	All Patients	HCV Treated	HCV Non Treated
Follow-up (median, IQR) months	34 (17-38)	35 (32-36)	31 (9-36)
Lost to follow-up (%)	27 (10,9)	12 (6,5)	15 (23,4)
Endpoints, n (%)			
Any	30 (12)	16 (8.7)	14 (21.9)
Death	25 (10)	12 (6.5)	13 (20.3)
Hepatocarcinoma	2 (0.8)	2 (1.1)	0
Transplant	5 (2)	4 (2.2)	1 (1.6)
Deaths, n (%)			
Hepatic causes	18 (72)	7 (58.3)	11 (84.6)
Other	7 (28)	5 (41.7)	2 (15.4)
Unknown	–	–	–

RESULTS (2)

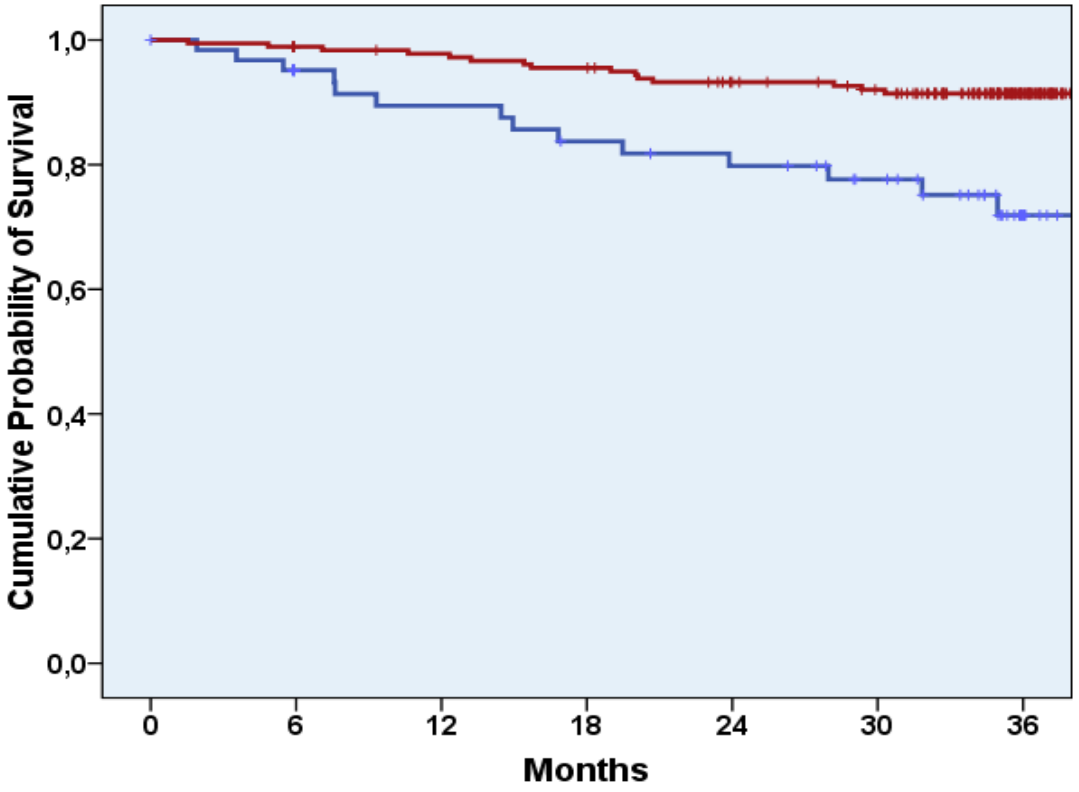
	All Patients	HCV Treated	HCV Non Treated
Decompensations n (%)	28 (11)	17 (9.2)	11 (17.2)
Type of Decompensation n (%)			
Ascites	23 (82)	14 (82.4)	9 (81.8)
GI bleeding	4 (14.3)	3 (17.6)	1 (9.1)
Encephalopathy	15 (53.6)	7 (41.2)	8 (72.7)
HRS	3 (10.7)	2 (11.8)	1 (9.1)
SBP	2 (7.1)	1 (5.9)	1 (9.1)
Unknown	–	–	–

GLOBAL SURVIVAL



N	247	226	220	212	199	184	81

SURVIVAL AND TREATMENT OF HEPATITIS C



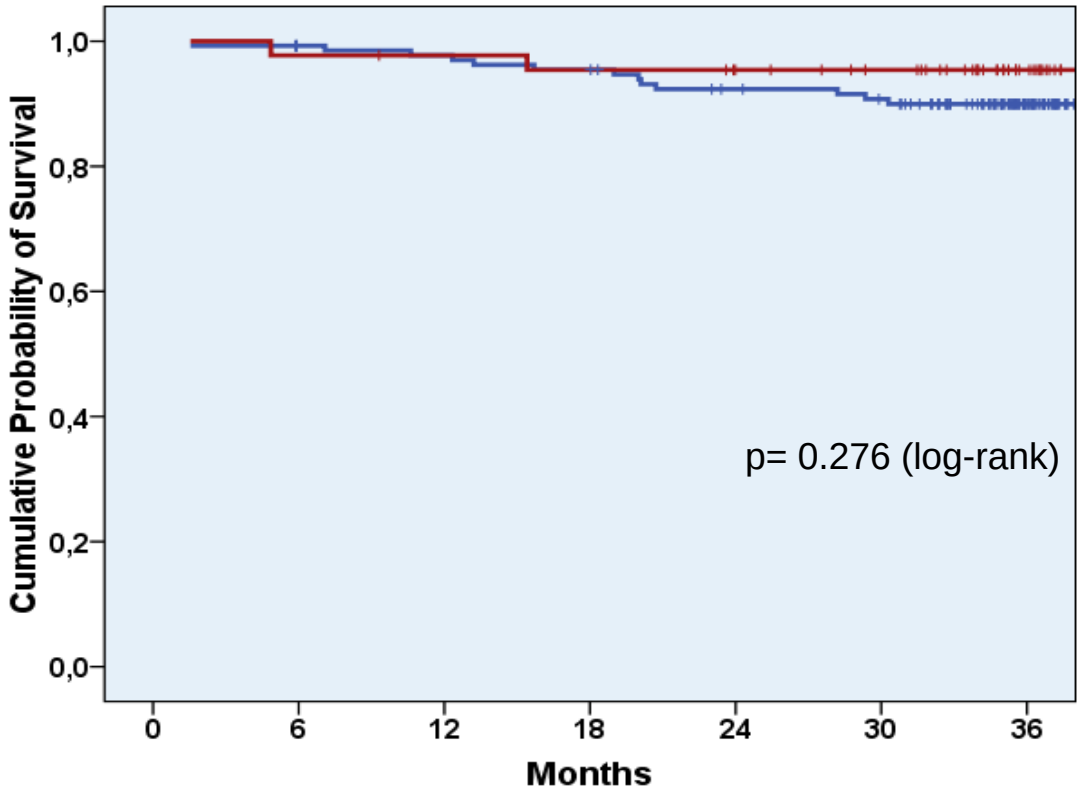
0.91 **HCV Treated**

0.71 **HCV Non Treated**

p= 0.001 (log-rank)

N	**63**	**50**	**47**	**43**	**40**	**34**	**12**	**HCV Non Treated**
	184	**176**	**173**	**169**	**159**	**150**	**69**	**HCV Treated**

SURVIVAL AND TREATMENT OF HEPATITIS C RESPONSE

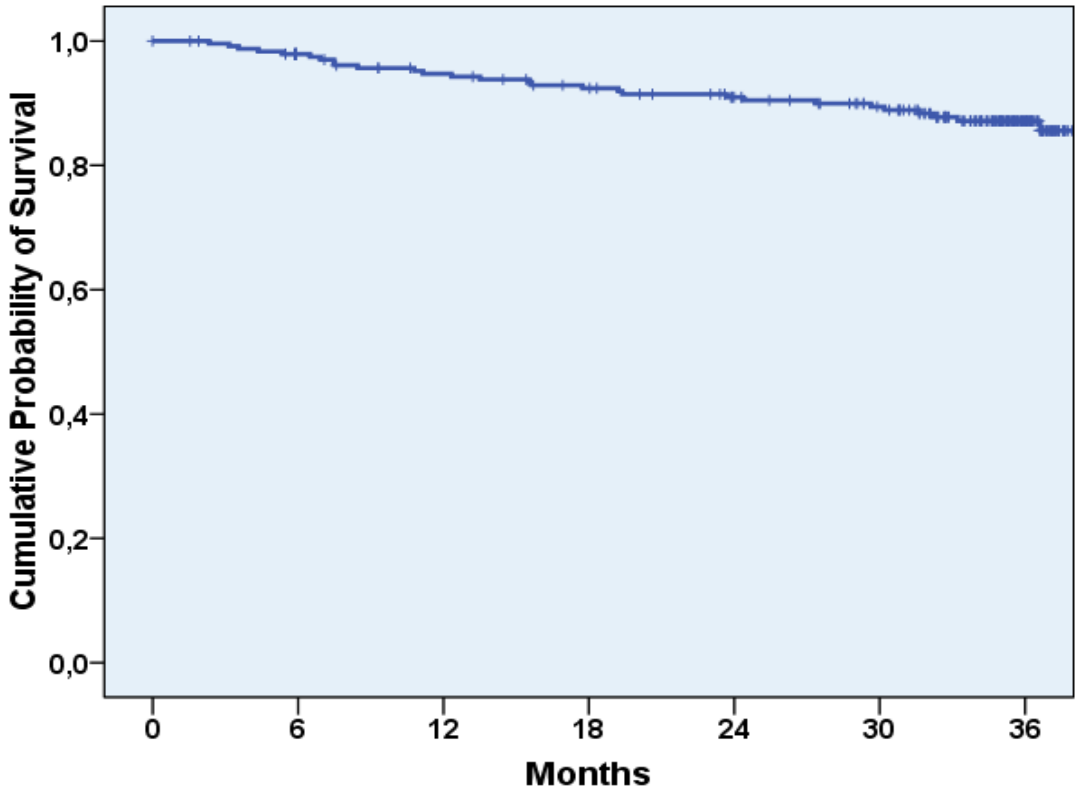


0.95 HCV responders

0.90 HCV non responders

N	**137**	**130**	**128**	**125**	**117**	**113**	**53**	**HCV responders**
	44	**43**	**42**	**41**	**39**	**34**	**15**	**HCV non responders**

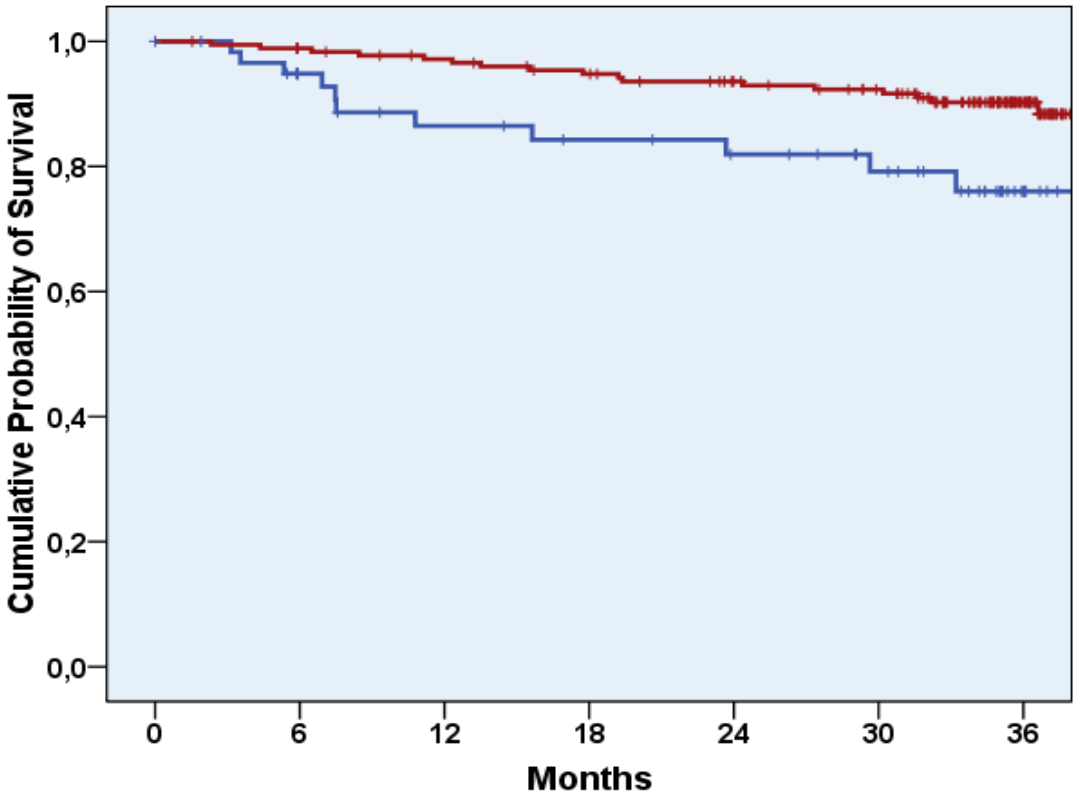
TIME TO FIRST DECOMPENSATION



0.87

N	241	218	206	196	184	169	77

TIME TO FIRST DECOMPENSATION AND TREATMENT OF HEPATITIS C



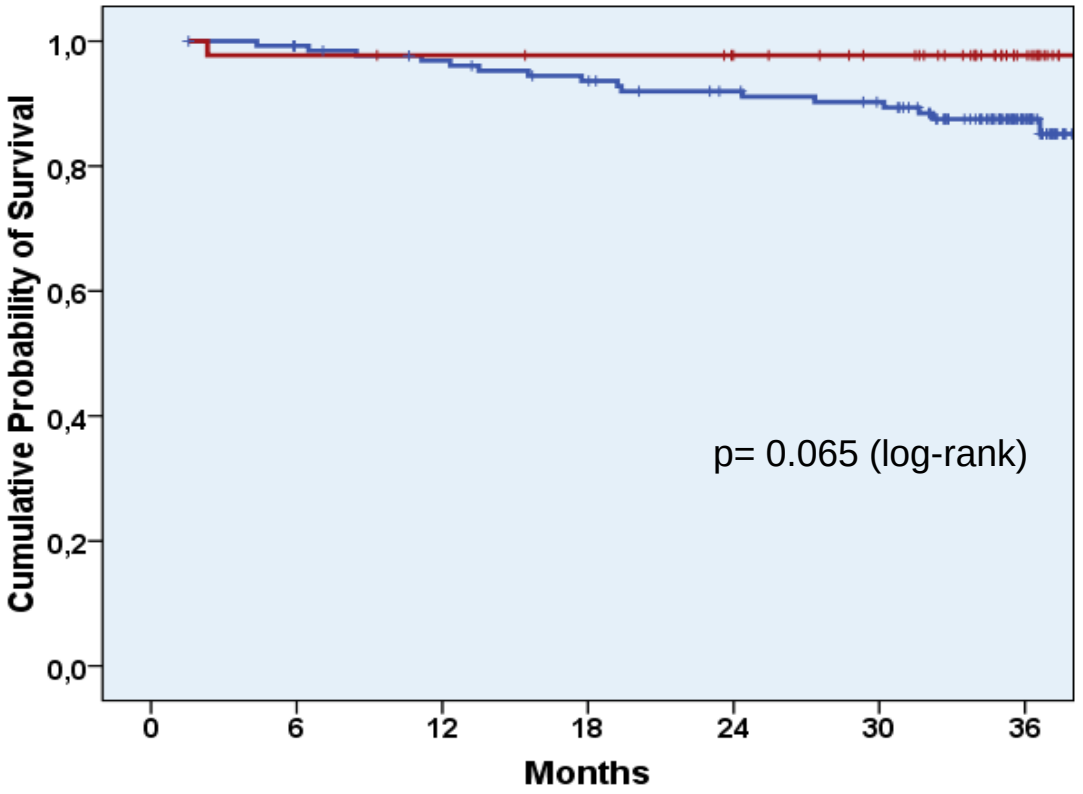
0.90 **HCV Treated**

0.75 **HCV Non Treated**

p= 0.01 (log-rank)

N	**60**	**46**	**40**	**37**	**34**	**29**	**12**	**HCV Non Treated**
	181	**172**	**166**	**159**	**150**	**140**	**65**	**HCV Treated**

TIME TO FIRST DECOMPENSATION AND TREATMENT OF HEPATITIS C RESPONSE



0.98 HCV responders

0.87 HCV non responders

N	**134**	**126**	**121**	**115**	**108**	**103**	**49**	**HCV non responders**
	44	**43**	**42**	**41**	**39**	**34**	**15**	**HCV responders**

VARIABLES ASSOCIATED TO SURVIVAL

	Univariate analysis	P	Multivariate analysis	P
HCV therapy	0.3 (0.14-0.61)	0.001	0.75 (0.33-1.7)	ns
HCV sustained virological response	0.44 (0.1-1.9)	0.27		
Receiving HAART at baseline	0.55 (0.21-1.44)	0.22		
HIV RNA BLQ at baseline	0.62 (0.3-1.3)	0.19		
Non-Continuous HAART during follow up	5.7 (2.6-12.4)	0.000	3.94 (1.64-4.44)	0.002
CD4 <100 cel/µL at baseline	1.4 (0.2-10.3)	0.73		
CD4 nadir at baseline	0.99 (0.99-1)	0.45		
-Child Pugh score B at baseline	9.4 (4.4-20.6)	0.000	4.22 (1.84-9.7)	0.002
-Child Pugh score C at baseline	44 (9.7-201)	0.000	17.2 (2.83-104)	0.001
-Decompensation during follow up	10.71 (5.21-22)	0.000	5.1 (2.35-11.3)	0.001

VARIABLES ASSOCIATED TO FIRST HEPATIC DECOMPENSATION

	Univariate analysis	P	Multivariate analysis	P
HCV therapy	0.38 (0.18-0.82)	0.01	1.31 (0.35-4.8)	0.7
HCV sustained virological response	0.18 (0.02-1.38)	0.1		
Receiving HAART at baseline	1.4 (0.34-5.96)	0.63		
HIV RNA BLQ at baseline	0.96 (0.43-2.1)	0.92		
Non-Continuous HAART during follow up	3.5 (1.6-7.83)	0.002	2.5 (1.02-6.1)	0.046
CD4 <100 cel/µL at baseline	0.048 (0-1382)	0.56		
CD4 nadir at baseline	0.99 (0.99-1)	0.41		
-Child Pugh score B at baseline	8.2 (3.66-18.68)	0.000	5.8 (2.41-13.8)	0.001
-Child Pugh score C at baseline	60.5 (7.1-516.5)	0.000	62.2 (6.2-618)	0.001

CONCLUSIONS

- After 3 years of follow up, continuous HAART use and baseline CP scores were important prognostic factors.
- Anti-HCV treatment (regardless of response) was not predictive of survival or hepatic decompensation.
- HCV compensated cirrhotic patients who received HCV therapy had less advanced liver cirrhosis and better control of HIV infection.

DISCUSSION

- Our study does not rule out a possible survival benefit for coinfected patients with compensated liver cirrhosis who achieve SVR
  - Lack of power due to low number of patients achieving SVR.
  - Longer follow-up might be needed to show a benefit
- Our study emphasizes that despite the effort of clinicians to treat coinfected patients with compensated cirrhosis the success rate of anti-HCV therapy in this population remains low.
- Every effort should be made to avoid progression to cirrhosis in HIV-HCV coinfected patients.

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