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Real life clinical outcomes in DAA-treated and untreated patients with HCV advanced liver disease. Interim one year data from the ongoing PITER cohort

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INTRODUCTION

Hepatitis C virus (HCV) chronic infection is an international public health concern, because it is one of the leading causes of cirrhosis, hepatocellular carcinoma (HCC) and liver transplantations worldwide. An estimated 71 million people have chronic hepatitis C infection and a significant number of those who are chronically infected will develop cirrhosis or liver cancer.
The recent development of direct-acting antiviral agents (DAAs) that specifically target the HCV represents a historical breakthrough, in that the second generation DAAs are capable of eradicating HCV and preventing chronic liver disease from developing into cirrhosis and HCC.
The real life impact on morbidity and mortality of DAAs is still unclear, in spite of high rate of HCV clearance.

Italy has the highest prevalence of HCV in Europe and the highest death rate from HCC and cirrhosis, however data on HCV disease profiles are scarce and do not represent the whole country reality.
In order to address the challenges and unanswered questions in the field of therapy of HCV and other coinfections, the Italian platform for the study of viral hepatitis therapies known as PITER (Piattaforma Italiana per lo studio della Terapia delle Epatiti viRali, www.progettopiter.it) was launched in 2012, as a structured network coordinated by the Istituto Superiore di Sanità, in collaboration with the Italian Society for the Study of the Liver (AISF) and the Italian Society for Infectious Diseases (SIMIT), and their affiliated clinical centers.

AIM

In the prospective real-life observational multicenter PITER cohort we aimed to evaluate the impact of DAA treatment on morbidity and mortality in HCV patients with advanced liver disease, as compared to patients awaiting treatment.

PATIENTS&METHODS

• Consecutive DAA treated patients enrolled in PITER, for whom follow-up data were available, were included in this analysis.

• Of 1457 DAA patients who completed treatment (median age 60: range 30-80 years; 627 classified as ≤F3 fibrosis by liver elastometry and 830 with cirrhosis by liver stiffness >12.5kPa and/or clinical cirrhosis), 1378 (95%) achieved SVR, 79 (5%) failed (25 were in F3 stage and 54 were cirrhotics).

• The morbidity and mortality were analyzed during a median follow-up of 12 months (range 1-16) in 811 treated patients with cirrhosis free of HCC at start of treatment. During the same follow-up period, 772 patients with cirrhosis, free of HCC, awaiting treatment were also enrolled in PITER and evaluated in this study.

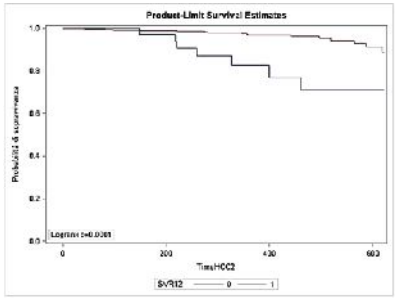
RESULTS

Compared to the 811 treated patients with cirrhosis, 772 patients with cirrhosis, free of HCC, awaiting treatment had similar **demographic characteristics** (age, gender) and **liver disease severity** (albumin, bilirubin and platelets levels) (p>0.05).

Clinical findings	Untreated Patients N=772	%	Treated Patients N=811	%
Mean Age	63 (SD±12)		61 (SD±10)	
Gender M/F	450	58	498	61
Previous IFN treated	445	57	446	55
Albumin levels < 3.5 mg/dl	249	32	289	36
Bilirubin levels >1.5 mg/dl	150	19	145	18
Platelets <150.000	201	26	187	23

• De novo HCC was detected overall in 4% of treated patients (median occurrence time: 12 months; range 1-16 months from the end of treatment) and in 2.6% of untreated patients (p=0.1).

• The HCC incidence in patients who failed *vs* those who achieved SVR was 13.2% (7/53) *vs* 3.4% (26/758) (p=0.001) respectively.



By Kaplan Meier analysis the one year HCC free survival was 97% *vs* 83% in patients who achieved SVR *vs* those who didn't (log rank test p=0.0001).

Predictors of HCC occurrence by Cox regression analysis in DAA treated patients (N= 811 patients)

Variables	Hazard ratios	Confidence Limits	
Age	1.09	1.04	1.13
Male gender	7.27	2.15	24.59
Albumin level <3.5mg/dl	0.61	0.27	1.41
Bilirubin level> 1.5 mg/dl	1.31	0.51	3.38
Platelets level <150,000	1.64	0.67	4.00
Non SVR12	6.99	2.78	17.58

In treated patients older age, male gender and failure event, were predictors of HCC occurrence by Cox regression analysis.

Predictors of HCC occurrence by Cox regression analysis in DAA untreated patients (N = 772 patients)

Variables	Hazard ratios	Confidence Limits	
Age	1.04	0.99	1.09
Male gender	1.48	0.57	3.85
Albumin level <3.5mg/dl	2.92	1.41	8.11
Bilirubin level> 1.5 mg/dl	1.25	0.43	1.66
Platelets level <150,000	1.48	0.52	4.16

In untreated patients albumin level was the only predictor of HCC occurrence by Cox regression analysis.

• Among treated patients who eradicated HCV and untreated patients, 11 (1.4%) *vs* 3 (0.4%) patients underwent OLT and 9 (1.1%) *vs* 19 (2.5%) patients died (p=0.05) respectively.
• In 6 (70%) of 9 treated *vs* 11 (60%) of 19 untreated patients who died, death was not liver related.

CONCLUSION

• These real life data confirm the high efficacy of DDAs treatment in achieving SVR in advanced liver disease patients.

• The short term HCC rate was similar in treated vs untreated patients, however, it was significantly higher in patients who failed vs those achieving SVR and vs the untreated comparable patients with cirrhosis.

• Death rate was lower in patients who achieved SVR vs untreated patients, being in the former mostly non liver-related.

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DISCLOSURES

Nothing to disclosure

AASLD AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES