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EFFICACY AND SAFETY OF BOCEPREVIR-BASED THERAPY IN HCVG1 TREATMENT-EXPERIENCED PATIENTS WITH ADVANCED FIBROSIS/CIRRHOSIS: THE ITALIAN AND SPANISH NPP EARLY ACCESS PROGRAM

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Background and Aims: To maximize cost/efficay of boceprevir-based triple therapy (BOC) in patients with HCV-related advanced fibrosis/cirrhosis.
Methods: ITT SVR12, safety and futility rules value were evaluated in the multicenter national Italian and Spanish early access Name-Patient-Program which includes treatment-experienced patients with HCVG1-related advanced fibrosis/cirrhosis (Metavir F3/4) treated with BOC in both countries.
Results: 402 patients (mean age 55 years; range 22–75), 316 (78.6%) G1b, 255 (63.4%) F4, 60 (30.9%) with oesophageal varices, 137 (34.1%) relapsers, 95 (23.6%) partial and 168 (41.8%) null responders were enrolled. Platelets count <100,000 and albumin levels <3.5 g/dl were present in 49 (12.2%) and 22 (6.3%) patients, respectively. 369 (91.8%) received at least 1 dose of BOC. Overall ITT SVR12 rates and according to prior response to P/R, fibrosis stage and TW8 HCV-RNA value to P/R/BOC are reported in the table.
At multivariate analysis, the strongest predictors of SVR12 were TW8 HCV-RNA undetectability (RR, 30.8; 95% CI, 8.7–108.7) and HCV-RNA detectable but <1000 IU/mL (RR, 9.1; 95% CI, 2.6–31.8) compared to those with HCV-RNA ≥1000 IU/mL.
Two patients (0.5%) died from multi-organ failure, 13 (3.2%) developed hepatic decompensation, 41 (10.2%) had severe anemia (<8.5 g/dl) and 31 (7.7%) required at least one blood transfusion.
Conclusions: In treatment-experienced patients with advanced fibrosis/cirrhosis, SVR12 attained by BOC was satisfactory. Mortality, life-threatening adverse events and severe anemia rates were similar to those reported in other real-practice studies. A TW8 futility rule enables a safely discontinuation of BOC in patients who are extremely unlikely to achieve SVR, thus optimizing the effectiveness of treatment in this difficult-to-cure population.

Table: SVR12 by at-entry characteristics and TW8 HCV-RNA

Strata	SVR12, N (%)	Number Needed to Treat (NNT)
All subjects	172/358 (48.0)	2.1
TW8 HCV-RNA undetectable	112/162 (69.1)	1.4
TW8 HCV-RNA detectable		
<1000 IU/ml	50/127 (39.4)	2.5
≥1000 IU/ml	3/43 (7.0)	14.3
Prior relapsers	74/125 (58.2)	1.7
Prior partial responders	41/84 (48.8)	2.0
Prior null responders	56/147 (38.1)	2.6
Metavir F3	73/133 (54.9)	1.8
Metavir F4	99/225 (44.0)	2.3

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SAFETY ASSESSMENT OF 12 WEEK INTERFERON-BASED REGIMEN IN HCV G1 CIRRHOTIC PATIENTS WITH POOR CLINICAL CHARACTERISTICS

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Background and Aims: Scanty data are available, so far, about the safety profile of a short-course of interferon-based therapy (IFN) in cirrhotic patients with severe clinical characteristics. Aim of this analysis was to retrospectively assess the rate of complications and death occurred during 12 week IFN in cirrhotic patients enrolled in the Eltrombopag Enable 1 and 2 cohorts, where only patients with PLT < 75,000 were included.
Methods: Patients infected by HCVG1 and albumin cut-off value below of 35 g/dl were considered.
Results: Among 1569 patients included in both studies, 414 (24%) subjects [281 males, median age 53 (range 27–70), 390 Child–Pugh A], had less than 35 g/dl. During the first 84 days period in the double-blind phase, 3 patients (0.7%) died (due to multi-organ failure in 2 patients and sepsis in 1 patient) and 44 (10.6%) developed decompensation or severe infection/sepsis. Post-hoc analysis of the pooled Enables-studied patients who completed the entire treatment duration highlights that treatment with eltrombopag compared to placebo leads to improved SVR even in this poorest sub-group of patients (SVR 11% vs 8%).

Table: Events in eltrombopag-treated patients

Event	Number of patients
Ascites	29
Oesophageal varices bleed	3
Sepsis	3
Encephalopathy	7
Bacterial peritonitis	2

Conclusions: These results suggest that, while waiting for all-oral regimens, 12 weeks IFN in combination with newer, safer DAAs, which was reported being associated with high (>80%) cure rates in HCVG1 patients with cirrhosis might be cautiously proposed as a life-saving therapy in patients with either low PLT counts or albumin value. Eltrombopag addition would be a useful platelet support to increase the number of patients to be treated and to optimize the on-treatment course dosing of therapy.