SA1051

Boceprevir Based Triple Therapy in Combination with Peginterferon alfa-2a plus Ribavirin (P/R) under Real Life Conditions in Treatment Naïve Patients Infected with Chronic Hepatitis C, Genotype 1: An Interim Analysis at Week 12 after Start of Treatment

Moog G[1], Mauss S[2], Hueppe D[3], Spengler U[4], Schott E[5], Eisenbach C[6], Schober A[7], Heyne R[8], Jung M-C[9], Teuber G[10], Frank Doss M[11], Rössle M[12], Pape S[13], Schuchmann M[14], Alshuth U[15], Buggisch P[16] and the bng study group

[1] Center of Gastroenterology, Kassel; [2] Center for HIV and Hepatogastroenterology, Duesseldorf; [3] Center of Gastroenterology, Herne; [4] Dept. of Internal Medicine I, University Hospital Bonn, Bonn; [5] Dept. of Gastroenterology, Hepatology, Charité, Campus Virchow Klinikum, Berlin; [6] Dept. of Gastroenterology, University of Heidelberg, Heidelberg; [7] Center of Gastroenterology, Goettingen; [8] Center of Gastroenterology and Liver Center, Berlin; [9] Liver Center, Munich; [10] IFS, Interdisziplinaeres Facharztzentrum Sachsenhausen, Frankfurt/M; [11] Center of Gastroenterology, Marburg; [12] Gastrointestinal and Endocrinological Center, Freiburg; [13] Center of Gastroenterology, Paderborn; [14] Dept Med 1, Gastroenterology and Hepatology, Johannes Gutenberg University Mainz, Mainz; [15] Virology, Roche Pharma AG, Grenzach-Wyhlen; [16] ifi-Institute for Interdisciplinary Medicine, Hamburg; all Germany

INTRODUCTION

- Boceprevir (BOC) is approved in Germany in combination with peginterferon alfa-2a or alfa-2b plus ribavirin in chronic hepatitis C (CHC) patients infected with HCV genotype 1. The efficacy and safety of BOC is well characterized in randomized clinical trials but real world experience is currently limited.
- Since 2003 the Association of German Gastroenterologists in Private Practice (bng, Berufsverband Niedergelassener Gastroenterologen Deutschlands e.V.) in cooperation with Roche, Germany, has been conducting real-world nationwide observational studies to determine the quality of treatment for CHC in routine clinical practice.
- Since 2011 the bng has been conducting a new German-wide, non-interventional study (PAN) in cooperation with Roche. Within this observational study HCV triple therapy including BOC or telaprevir (TVR), peginterferon alfa-2a 180 µg (PegIFN alfa-2a) and ribavirin (RBV) is being investigated.

OBJECTIVE

- In this interim analysis after 12 weeks of treatment with BOC, PegIFN alfa-2a 180 µg and RBV HCV genotype 1-patients were evaluated for efficacy and safety parameters.

METHODS

- This evaluation is part of a large ongoing German multicentre, open-label observational study including adults with detectable HCV RNA. The study allowed the choice of either of the two currently approved protease inhibitors with the dose and duration of HCV treatments including PegIFN alfa-2a (40KD) and RBV at the discretion of the physician. Patients were eligible if they were prescribed TVR or BOC plus PegIFN alfa-2a/RBV.
- The screening data include patient age, sex, weight, height, duration of and risk factors for infection, prior antiviral treatment, clinical symptoms, histology, genotype, viral load, concomitant diseases and social status.
- Here we restrict the analysis to treatment naive patients receiving BOC plus PegIFN alfa-2a/RBV who had, or had the potential to, complete 12 weeks of treatment including a 4 week lead-in phase with PegIFN alfa-2a/RBV. Patients who initiated BOC <21 days or >30 days after starting PegIFN alfa-2a/RBV were excluded from the analysis.
- The data collection was performed online via the internet.
- The data collected should reflect the routine clinical practice of the participating physicians and only descriptive statistics were reported.
- Due to the ongoing nature of the study, the status of data was frozen on August 15th, 2012.

RESULTS

Patients

- Between October 2011 and August 2012 129 treatment-naive patients with BOC containing triple therapy and data up to week 12 were included (see Figure 1).
- In 68 of these patients, BOC was started between day 21 and 30 after the initiation of PegIFN alfa-2a/RBV. 9 patients were excluded because they started BOC <21 days after starting PegIFN alfa-2a/RBV and 52 were excluded because they started BOC >30 days after starting PegIFN alfa-2a/RBV.

Table 1: Baseline data

		Parameter
Patients, n		68
Age >40 years, n (%)		52 (76.5%)
Male, n (%)		36 (52.9%)
Caucasian race, n (%)		68 (100%)
Body mass index (kg/m^2), mean ± SD		27.0 ± 5.2
Diagnosis of cirrhosis*, n (%)		8 (11.8%)
Platelets (x10^9/L), mean ± SD		220 ± 74
ALT (>3x ULN**), n (%)		12 (20.0%)
HCV RNA (log$_{10}$ IU/mL), mean ± SD		6.0 ± 0.9
HCV RNA (>400,000 IU/mL), n (%)		46/64 (71.9%)
Genotype, n (%)	1a	21 (30.9%)
	1b	32 (47.1%)
Genotype 1 subtype:	other/unknown	15 (22.1%)
IL28B genotype	CC	9 (13.2%)
	CT	9 (13.2%)
	TT	2 (2.9%)
	Unknown	48 (70.6%)

* ≥1 result concluding cirhosis: biopsy, clinical appearance, sonography, elastography
** ULN = upper limit of normal

Baseline Data

- 52.9% of the patients were male.
- The mean age of the patients was 47.8 ± 10.1 years.
- The mean BMI was 27.0 ± 5.2 kg/m^2.
- 71.9% of the patients had high viral load (>400,000 IU/mL).
- Suspected mode of infection was transfusion in 11.8%, IDU in 25.0% and other in 16.2% (unknown in 47.1%).
- Baseline data are shown in Table 1.

Viral Response

- Among patients with evaluable data at each time point the proportion with undetectable HCV RNA at week 4, 8 and 12 was 6/53 (11.3%), 27/44 (61.4%) and 40/52 (76.9%), respectively (see Figure 2).
- A subset of 15 (22.1%), 24 (35.3%) and 16 (23.5%) of patients did not have an evaluable week 4, 8 and 12 HCV RNA value, respectively (see Figure 3).
- The positive predictive value (PPV) of week 4 undetectable HCV RNA for week 12 HCV RNA <100 IU/mL (futility threshold) was 100% (4/4), but the numbers of patients currently evaluable to determine the positive predictive value are few and therefore should be interpreted with caution (see Figure 4).

Dosing of PEG and RBV

- Over the first 12 weeks 11.9% and 5.9% of the patients required dose modifications of RBV and PegIFN alfa-2a, respectively.

Haemoglobin

- Up to week 12 a total of 2 (3.0%) and 17 (25.4%) of the patients had haemoglobin < 8.5 g/dL or ≥8.5 but < 10 g/dL, respectively (see Figure 5).

Adverse Events

- Adverse events reported at a rate of ≥15% of patients included fatigue (52.9%), nausea (26.5%), headache (25.0%), skin disorder (23.5%), dysgeusia (19.1%), pruritus (19.1%), myalgia (17.6%), anaemia (16.2%) and arthralgia (16.2%) (see Figure 6).

CONCLUSIONS

- Real world experience with BOC plus PegIFN alfa-2a/RBV in Germany show similar virological outcomes and side effects to the phase 3 trials.
- Week 8 HCV RNA values essential to determine suitability for reduced treatment duration were not collected in a significant proportion of patients.

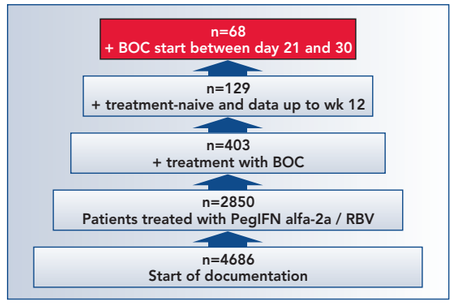

Fig 1. Study patients

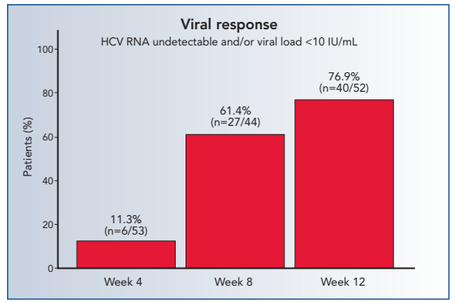

Fig 2. Viral response

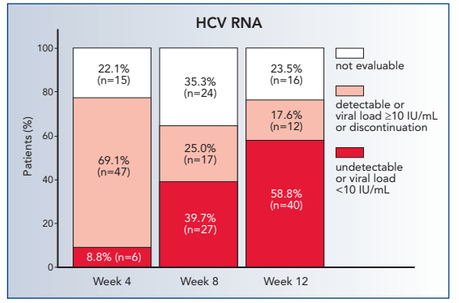

Fig 3. HCV RNA at week 4, 8 and 12

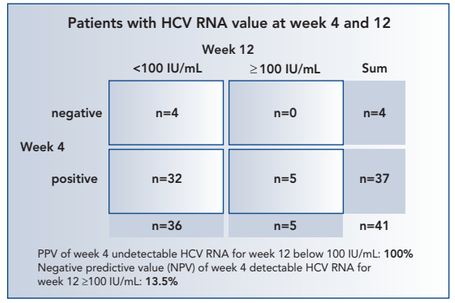

Fig 4. Patients with HCV RNA value at week 4 and 12

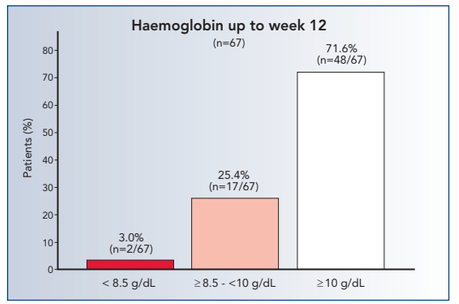

Fig 5. Haemoglobin up to week 12

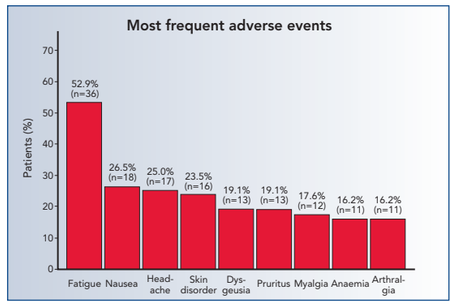

Fig 6. Adverse events

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