SA1052

Triple Therapy under Real Life Conditions: Telaprevir (TVR) in Combination with Peginterferon alfa-2a plus Ribavirin (P/R) in Naïve Patients Infected with Chronic Hepatitis C, Genotype 1. The PAN Study

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INTRODUCTION

- Until recently experience with telaprevir (TVR) was based almost exclusively on the results of controlled randomized clinical trials in highly selected patients. In October 2011 TVR was 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.
- 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 boceprevir (BOC) or 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 TVR, PegIFN alfa-2a 180 µg and RBV HCV treatment naive, 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 TVR plus PegIFN alfa-2a/RBV who had, or had the potential to, complete 12 weeks of treatment.
- 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 239 patients with TVR containing triple therapy and data up to week 12 were included (see Figure 1).
- In 24 of these patients (10.0%) cirrhosis was diagnosed.

Baseline Data

- 57.3% of the patients were male.
- The mean age of the patients was 46.7 ± 12.2 years.
- The mean BMI was 25.6 ± 4.0 kg/m^2.

Table 1: Baseline data

		Parameter
Patients, n		239
Age >40 years, n (%)		163 (68.2%)
Male, n (%)		137 (57.3%)
Caucasian race, n (%)		234 (97.9%)
Body mass index (kg/m^2), mean ± SD		25.6 ± 4.0
Diagnosis of cirrhosis*, n (%)		24 (10.0%)
Platelets (x10^9/L), mean ± SD		211 ± 73
ALT (>3x ULN**), n (%)		50 (23.1%)
HCV RNA (log_{10} IU/mL), mean ± SD		6.0 ± 0.9
HCV RNA (>400,000 IU/mL), n (%)		174/230 (75.7%)
Genotype, n (%)	1a	63 (26.4%)
	1b	131 (54.8%)
Genotype 1 subtype:	other/unknown	45 (18.8%)
IL28B genotype	CC	15 (6.3%)
	CT	36 (15.1%)
	TT	14 (5.9%)
	Unknown	174 (72.8%)

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

- 75.7% of the patients had high viral load (>400,000 IU/mL).
- Suspected mode of infection was transfusion in 20.9%, IDU in 20.1% and other in 15.1% (unknown in 43.9%).
- 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 and 12 was 100/155 (64.5%) and 135/166 (81.3%), respectively (see Figure 2).
- A subset of 84 (35.1%) and 73 (30.5%) of patients did not have an evaluable week 4 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 < 1,000 IU/mL (futility threshold) was 94.3% (82/87) (see Figure 4).
- Among the 124 patients with adequate data to determine eRVR status (undetectable HCV RNA at week 4 and 12) 82 (66.1%) achieved an eRVR and would therefore be potentially eligible for shortened treatment duration.

Dosing of PegIFN alfa-2a and RBV

- Over the first 12 weeks 15.7% and 5.0% of patients dose modified RBV or PegIFN alfa-2a, respectively.

Haemoglobin

- Up to week 12, a total of 21 (8.9%) and 62 (26.3%) 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% included fatigue (49.8%), skin disorder (31.0%), pruritus (25.1%), nausea (24.7%), anaemia (23.0%) and headache (15.9%) (see Figure 6).

CONCLUSIONS

- Real world experience with telaprevir plus PegIFN alfa-2a/RBV is generally consistent with the results of the published phase 3 trials.
- Of concern a high proportion of patients did not have a week 12 value which is essential to determine treatment duration.

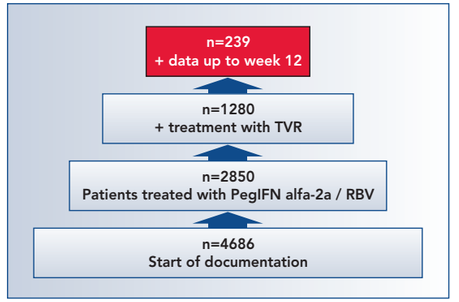

Fig 1. Study patients

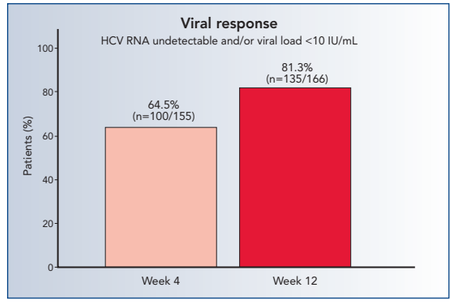

Fig 2. Viral Response

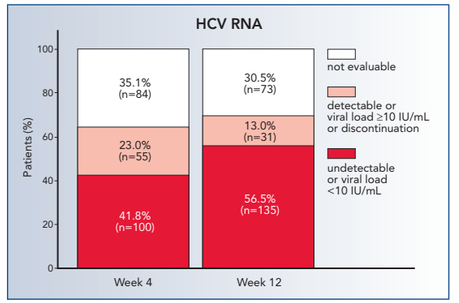

Fig 3. HCV RNA at week 4 and week 12

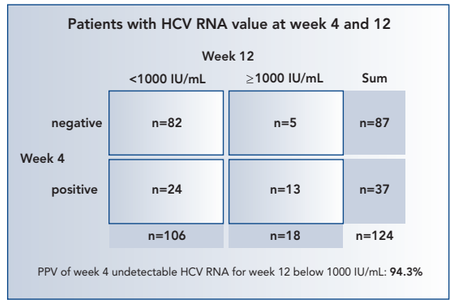

Fig 4. Patients with HCV RNA value at week 4 and 12

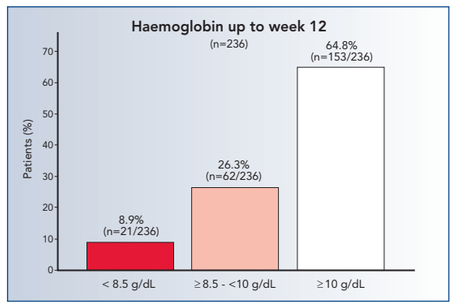

Fig 5. Haemoglobin up to week 12

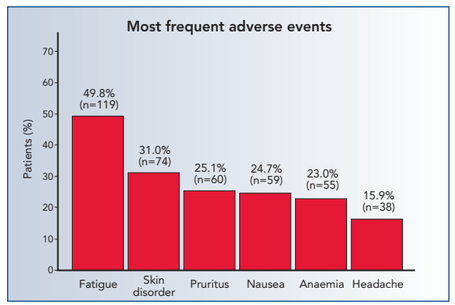

Fig 6. Adverse events

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