Triple Therapy under Real Life Conditions: Telaprevir (TVR) and Boceprevir (BOC) in Combination with Peginterferon alfa-2a plus Ribavirin (P/R) in Treatment Experienced 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 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.
- Under conditions of clinical trials the addition of TVR to PegIFN alfa-2a/RBV resulted in significantly high rates of week 4 and 12 responses in previously treated patients with chronic HCV genotype 1 infection[1]. Is this reproducible in real life?

OBJECTIVE

- In this interim analysis after 12 weeks of treatment with TVR, PegIFN alfa-2a 180 µg and RBV HCV treatment experienced 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 experienced patients receiving TVR plus PegIFN alfa-2a/RBV who had, or had the potential to, complete 12 weeks of treatment and who started TVR at the same day as PegIFN alfa-2a/RBV or at most 7 days after.
- 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.
- Precision of measuring HCV RNA at week 4 or 8 was set to ±3 days.
- Extended rapid virologic response (eRVR) was calculated for patients with data for both week 4 and 12 (n=312).

RESULTS

Patients

- Between October 2011 and August 2012, 537 genotype 1 patients treated with TVR containing triple therapy and data up to week 12 were included (see Figure 1).
- 290 (54.0%) patients were prior relapsers, 231 (43.0%) non responders, 74 (13.8%) were classified as prior partial responders and 46 (8.6%) as prior null responders (multiple responses possible). The remaining patients discontinued prior therapy due to intolerability or personal reasons.

Baseline Data

- 63.3% of the patients were male.
- The mean age of the patients was 51.4 ± 10.7 years.
- The mean BMI was 26.7 ± 4.3 kg/m².

Table 1: Baseline data

		Parameter
Patients, n		537
Age >40 years, n (%)		457 (85.1%)
Male, n (%)		340 (63.3%)
Caucasian race, n (%)		526 (98.0%)
Body mass index (kg/m²), mean ± SD		26.7 ± 4.3
Diagnosis of cirrhosis*, n (%)		113 (21.0%)
Platelets (x10⁹/L), mean ± SD		197 ± 72
ALT (>3x ULN**), n (%)		107 (21.5%)
HCV RNA (log_{10} IU/mL), mean ± SD		6.0 ± 0.8
HCV RNA (>400,000 IU/mL), n (%)		389/511 (76.1%)
Genotype, n (%)	1a	132 (24.6%)
	1b	287 (53.4%)
Genotype 1 subtype:	other/unknown	118 (22.0%)
IL28B genotype	CC	23 (4.3%)
	CT	74 (13.8%)
	TT	27 (5.0%)
	Unknown	413 (76.9%)

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

- The mean ALT was 97.2 ± 86.5 IU/L.
- 76.1% of the patients had high viral load (>400,000 IU/mL).
- 19.7% of the patients had platelets <140x10⁹/L and 21.0% liver cirrhosis (at least one result of sonography, biopsy, elastography or clinical appearance).
- 132 (24.6%) and 287 (53.4%) of patients were infected with HCV G1a and G1b, respectively (3, 0.6% other genotype; 115, 21.4% unknown).
- Baseline data are shown in Table 1.

Viral Response

- Since 25.0% and 13.0% of patients did not have an evaluable HCV RNA at week 4 and 12, respectively, the following results show adjusted data of virological responses. Each virological response is given as LLOD (<10 IU/mL).
- **Rapid viral response** (**RVR**; HCV RNA <10 IU/ml 4 weeks after start of antiviral therapy) was observed in 61.6% of the patients (see Figure 2).
- At week 12 of therapy a **complete early viral response (cEVR**; HCV RNA <10 IU/ml or undetectable 12 weeks after the start of antiviral therapy) was observed in 78.5% of the patients (see Figure 3).
- At week 12 of therapy an **extended rapid viral response (eRVR**; HCV RNA <10 IU/ml or undetectable 4 and 12 weeks after the start of antiviral therapy) was observed in 61.5% of the patients (see Figure 4).

Treatment

- Over the first 12 weeks, 16.8% of patients dose modified ribavirin and 12.1% discontinued therapy.

Haemoglobin

- Up to week 12, 9.3% and 23.7% 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 ≥20% were fatigue, skin disorder/rash, pruritus, anemia and nausea (see Figure 6).

References

[1] Zeuzem et al., N Engl J Med 2011; 364: 2417-28.

CONCLUSIONS

- Although real life patients were not selected according to inclusion and exclusion criteria, virological efficacy of triple therapy with TVR plus PegIFN alfa-2a/RBV in treatment experienced patients until week 12 is very similar to the pivotal trial.

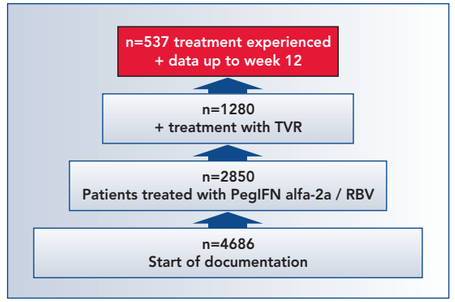

Fig 1. Study patients

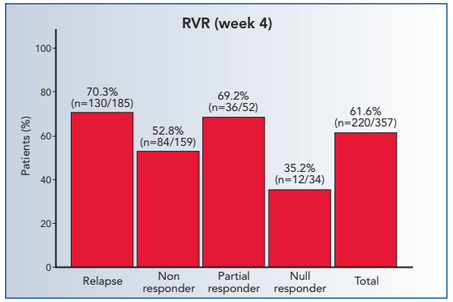

Fig 2. HCV RNA at week 4

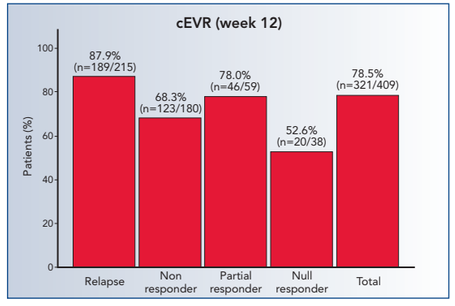

Fig 3. HCV RNA at week 12

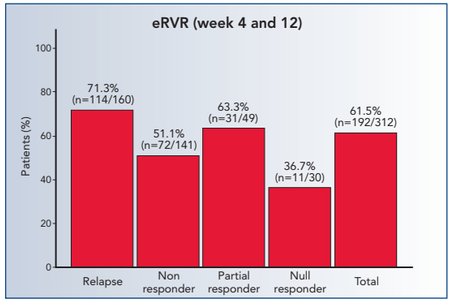

Fig 4. Patients with HCV RNA at weeks 4 and 12

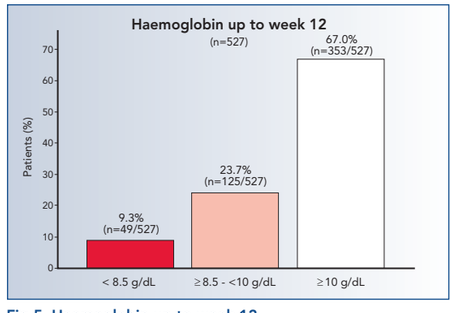

Fig 5. Haemoglobin up to week 12

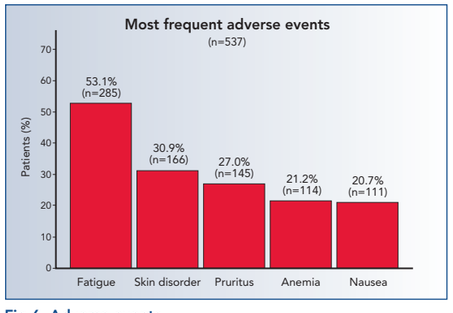

Fig 6. Adverse events

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