TELPREVIR-BASED TRIPLE THERAPY IN PATIENTS WITH CHRONIC HEPATITIS C IN GERMANY – A 12 WEEK INTERIM ANALYSIS OF REAL LIFE DATA

Berg T.1, Buggisch P.2, Huerpe D.3, Mauss S.4, Wedemeyer H.5 and Decker-Burgard S.6

1) Universitätsklinik Leipzig, Germany 2) Ifi-Institut Hamburg, Germany 3) Gastroenterologische Gemeinschaftspraxis Herne, Germany 4) Praxis Duesseldorf, Germany 5) Medizinische Hochschule Hannover, Germany 6) Janssen-Cilag, Neuss, Germany

BACKGROUND AND OBJECTIVES

Hepatitis C is a liver disease affecting 170 million people worldwide, which corresponds to 3% of the total population according to the World Health Organization (WHO) [1]. Hepatitis C genotype 1 is the most prevalent genotype in Germany (approximately 60%) [2].

With the protease inhibitors new therapy options have become available in the treatment of chronic hepatitis C (HCV). They are characterized by significantly improved cure rates (sustained virological response, SVR) compared to dual therapy with pegylated interferon plus ribavirin, and a shorter duration of therapy [3]. Also patients without sufficient treatment success under dual therapy (relaps, partial responder, null-responder) show significantly higher cure rates when treated with telaprevir (TVR)-based triple therapy.

The aim of this interim analysis was to evaluate the implementation of futility rules, safety and efficacy of TVR-based therapy in daily practice in Germany.

METHODS

In this ongoing prospective, observational, non-interventional, multi-center study, TVR-based triple therapy in therapy-naive and pretreated patients with genotype 1 chronic HCV in Germany is investigated under real life conditions. Patients are treated with a combination of telaprevir, ribavirin and peg-interferon. The documentation period covers the entire treatment period and a 24 week post-treatment follow-up.

Sites were asked to document disease- and treatment-related information as well as HCV-related health resource consumption. Monitoring visits were performed to verify the data captured against source data. Additionally, electronic data checks on data completeness and consistency were conducted and resulting queries were resolved with the sites.

This interim analysis includes data from the first 100 patients (12.5% of the planned total) at 32 sites completing 12 weeks of treatment.

RESULTS

4 patients were co-infected with HIV. 32 patients were therapy-naive, 66 had received prior treatment against chronic HCV and for 2 patients, the previous treatment status was unknown. Demographic and anamnestic baseline data are presented in table 1.

36.4% of pretreated patients were prior relaper and 30.3% were prior null or partial responder.

The median HCV RNA level before initiation of TVR-based therapy was 795,000 IU/ml.

Response rates (i.e. HCV-RNA undetectable) during treatment course up to week 12 for patients with HCV-RNA measurements available are presented in figure 1.

Table 1: Demographic and anamnestic baseline data

<table>
<thead>
<tr>
<th>Population (N=100)</th>
<th>Total Population (N=100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years SD) at baseline</td>
<td>49.3 11.5</td>
</tr>
<tr>
<td>Males</td>
<td>65.0</td>
</tr>
<tr>
<td>BMI (kg/m2 SD)</td>
<td>25.8 4.3</td>
</tr>
<tr>
<td>Cirrhosis at baseline</td>
<td>11.0</td>
</tr>
<tr>
<td>HCV subtype</td>
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</tr>
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<td>1a</td>
<td>40.0</td>
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<tr>
<td>1b</td>
<td>50.0</td>
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<td>IL-28B genotype</td>
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<tr>
<td>CC</td>
<td>5.0</td>
</tr>
<tr>
<td>CT</td>
<td>25.0</td>
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<td>TT</td>
<td>8.0</td>
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<tr>
<td>IL-28B genotype unknown</td>
<td>62.0</td>
</tr>
</tbody>
</table>

HCV-RNA testing at week 2 was conducted for only 50% of all patients, increasing to 91% at week 4 and 93% at week 12.

At week 4, 67.0% of all patients with HCV-RNA measurements showed rapid virological response (RVR). RVR was higher in patients with pretreatment as compared to therapy-naive patients (71.0% vs. 57.1%). Similarly response rates after 12 weeks of treatment were slightly higher in pretreated patients (93.4% vs. 86.7%). 3 of the 4 patients with HIV co-infection had undetectable HCV-RNA at week 12.

The futility rule (i.e. treatment stop in case that the HCV-RNA level at week 4 exceeds 1000 IU/ml) was adhered to in all nine cases observed.

86.4% of the previous relaper were HCV-RNA negative both at week 4 and week 12, whereas this was the case for only 57.7% of therapy-naive patients. Only one patient achieving RVR at week 4 suffered a virological breakthrough at week 12.

Nearly all patients (99.0%) reported adverse events (AE) during the first 12 weeks of treatment. Serious adverse events were experienced by 8% of the patients up to week 12. Most AEs were of mild (63.0%) or moderate (34.6%) severity. About one third of all AEs were considered as likely or very likely related to TVR-based therapy. 32.0% of all AEs required treatment, mostly medication prescription.

Rash was rated as mild or moderate in 97.1% of the cases and required medical treatment in 68.6% of cases, mostly medication prescription (54.3% of all rash cases) or topical application of non-prescription creams (11.4%). Two of the rash cases were considered as serious AEs, one case required in-patient hospital treatment.

Anemia was reported as AE in 23.0% of all patients, but a decrease of Hb level below 12 g/dl (females) and 13 g/dl (males), respectively, during the first 12 weeks of treatment was observed in 87.0% of all patients. In the following, patients with an AE report of anemia or a decrease of Hb level below the above mentioned cut-offs are referred to as anemia cases.

Figure 2 shows the development of Hb levels over time.

The decrease in Hb levels was most pronounced in the first 4 weeks of treatment. Hb levels decreased below 10 g/dl in the first 12 weeks of treatment were observed in 44.0% of anemia cases. 11.0% of cases even showed Hb levels < 8.5 g/dl.

A reduction of the ribavirin dosage due to anemia was reported for 12.1% of the cases. 6.6% required transfusion of erythrocytes and one patient received erythropoietin treatment to compensate decreased Hb levels. Three cases of anemia were considered as serious AEs.

Likewise, thrombocyte levels clearly decreased from 198.1 g/dl at baseline to 122.4 g/dl at week 12. 79.0% of the patients reported thrombocyte levels below 150 g/dl at any time during the first 12 weeks of treatment; 9% even experienced thrombocyte level decreases below 50 g/dl (regarded as thrombocytopenia grade 3 and 4).

CONCLUSION

Results from this first interim analysis suggest that telaprevir-based triple therapy is efficient against genotype 1 chronic hepatitis C in a real life setting.

Adherence to futility rules was confirmed in all patients.

As observed in clinical trials, adverse events were reported frequently, including anemia and rash.

Results will be updated as more data become available.

LITERATURE


11th International Congress on Drug Therapy in HIV Infection, 11-15 November 2012, Glasgow, UK