Background

Chronic hepatitis C virus infection is one of the leading causes of slowly progressive hepatic fibrosis, which, if untreated, leads to cirrhosis, hepatic failure, and increased risk of death. In HCV infected patients, compared to earlier stages of fibrosis, cirrhosis is associated with less effective IFN-based treatment and a higher risk of complications. Since 2015 an interferon free therapy drug program (B.71) is available in Poland for patients with chronic HCV, currently including five regimens: 

- ombrabavir / paritaprevir / ritonavir / dasabuvir (OBV/PTVr + DSV),
- daclatasvir / asunaprevir, 
- sofosbuvir, 
- sofosbuvir / ledipasvir, 
- grazoprevir / elbasvir.

Our previously presented evaluation of the program in 477 patients with liver fibrosis stages F1-F4 has shown that the new IFN-free direct acting antiviral therapy with OBV/PTVr ± DSV resulted with high rates of sustained virologic response (SVR) in patients with cirrhosis (93% of all starting treatment, 96% of those who had SVR24 assessed). Nonetheless, the rates were still lower than in patients without cirrhosis (90% of all starting treatment, 99% of those who had SVR24 assessed).[1] This report is an extension of the previous publication on the complete set of 504 participants of the observational study, but limited to the most vulnerable group, patients with compensated hepatic cirrhosis (F4).

Objective

The aim of this analysis was to assess the real world effectiveness of treatment with OBV/PTVr ± DSV in patients with HCV infection and compensated cirrhosis participating in Polish public drug program.

Methods

The analysis is based on all (N=265) participants of the abovementioned observational study with compensated hepatic cirrhosis, who enrolled the drug program B.71 between 1-Oct 2015 and 31 Jan 2016 and were treated with OBV/PTVr ± DSV under real life conditions in seven non-randomly selected hospitals located throughout Poland. First, in June 2016 data on genotype, comorbidities, past treatment, end of treatment assessment, and reason for early treatment cessation (including AE) was collected retrospectively. Then, the sustained virologic response after 24 weeks since the end of treatment (SVR24) was added. The duration of treatment was estimated with a ±2 weeks tolerance.

Results

Patient characteristics

A total of 265 participants of B.71 drug program with compensated hepatic cirrhosis were enrolled in the study. Baseline characteristics of the enrolled patients are presented in Table 1. The average patient age at enrolment was 57 years, ranging from 24 to 90 years. Median HCV load was 61,800,000 IU/mL, 45 persons (17%) had viral load below 10^4 IU/mL and in 94 persons (35%) viral load was above 10^7 IU/mL. The dominant virus genotype, 1a, was observed in 95% of infections. Interleukin-28B genotype was determined for 61 persons, prevalent genotype was C/T (62%). 2 persons had HIV infection and 2 persons had HBV infection.

The most frequently reported comorbidities were arterial hypertension (38%) and diabetes (16%). 33% persons did not report any comorbidity. The list of most frequently reported comorbidities is presented in Figure 1.

The most frequently used regimen was OBV/PTVr + DSV complemented with RBV, prescribed to 290 patients (79%). 254 (96%) patients were offered 12-weeks treatment regimes. Detailed breakdown of treatment regimes is presented in Figure 2.

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Among treated patients, 258 (97%) completed treatment according to schedule and 7 (3%) ended treatment earlier than planned: 4 due to adverse event, 1 due to disease exacerbation, and 2 persons died before the end of treatment. Patient disposition diagram, including reasons for treatment early discontinuation, is presented in Figure 4.

In comparison, out of 238 noncirrhotic (liver fibrosis stages F1-F3) patients from the same study, SVR24 was assessed in 222 patients, of which 222 achieved SVR24 (93% of all treated patients and 99% of patients whose virologic outcome was evaluated 24 weeks after treatment).

The summary of virologic response to treatment at the end of treatment and 24 weeks after therapy in persons with cirrhosis is presented in Figure 4.

Table 2a. SVR24 in subgroups by genotype and history of interferon therapy

<table>
<thead>
<tr>
<th>SVR24</th>
<th>Genotype</th>
<th>Interferon naive</th>
<th>Partial</th>
<th>Null</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a(n=4)</td>
<td>40 (100%)</td>
<td>0 (0%)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>1b(n=251)</td>
<td>239 (95%)</td>
<td>6 (2%)</td>
<td>1 (0%)</td>
<td>5 (2%)</td>
<td>-</td>
</tr>
<tr>
<td>4(n=7)</td>
<td>6 (86%)</td>
<td>0 (0%)</td>
<td>1 (34%)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Other(n=3)</td>
<td>0 (0%)</td>
<td>2 (67%)</td>
<td>0 (0%)</td>
<td>1 (33%)</td>
<td>-</td>
</tr>
</tbody>
</table>

Results for subgroups with small number of patients should be interpreted with caution.

Conclusions

Presented real-world data from Poland regarding OBV/PTV/r ± DSV therapy of HCV-infected patients with cirrhosis confirm the high effectiveness of this regimen even slightly lower than for milder fibrosis stages (74% vs. 95% of all starting treatment, 98% vs. 99% of those who had SVR24 assessed). Shown results are further reinforced by RME study performed by Fiháš et al. (2017), where 90 patients with cirrhosis reached SVR24 (72% of all starting treatment and 99% of patients who had SVR24 assessed). [2] The results indicate the effectiveness of Polish drug program in the cirrhotic patients subgroup.

References
