REAL WORLD EFFECTIVENESS OF TREATMENT WITH OBV/PTV/R ± DSV IN HCV PATIENTS WITH CIRRHOSIS IN POLAND

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The analysis was conducted by **HTA Consulting**

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:

- ombitasvir / paritaprevir / ritonavir + dasabuvir (OBV/PTV/r + DSV),
- daklatasvir + 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/PTV/r ± DSV resulted with high rates of sustained virologic response (SVR) in patients with cirrhosis (91% of all starting treatment, 98% 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/PTV/r ± 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 entered the drug program B.71 between 1 Oct 2015 and 31 Jan 2016 and were treated with OBV/PTV/r ± 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 response, 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 margin due to reporting final visit date instead of end of treatment date by some investigators. All data on study participants were collected anonymously.

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.

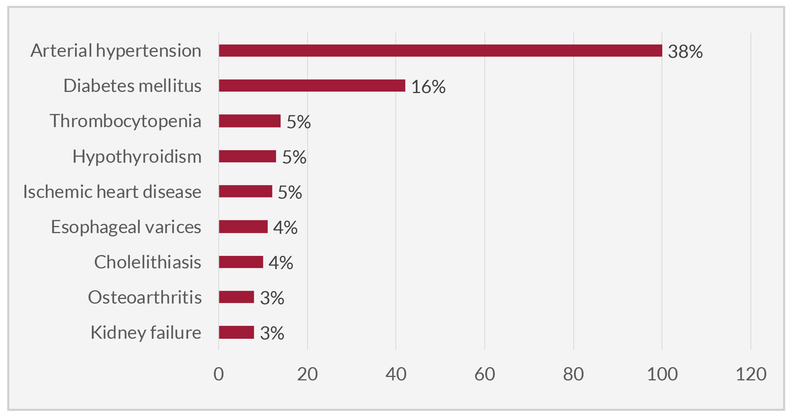
The average patient age at enrolment was 57 years, ranging from 24 to 90 years. Median HCV load was 618,000 IU/mL, 45 persons (17%) had viral load below 10^5 IU/mL and in 94 persons (35%) viral load was above 10^6 IU/mL. The dominant virus genotype, 1b, was observed in 95% of infections. Interleukin 28B genotype was determined for 61 persons, prevalent genotype was C/T (62%). 2 persons had HIV infection and 2 persons had HBV infection.

Table 1. Characteristics of patients on the day of drug program start

Patient characteristics	N=265	
Sex, n males %	133	50.2%
Age, mean SD	57	12
Log10 of HCV viral load, mean SD	5.68	0.75
Virus genotype, n %		
1a	4	1.5%
1b	251	94.7%
1 (subgenotyping not available)	3	1.1%
4	7	2.6%
Mixed	0	0.0%
Interleukin 28B genotype, n %	N=61	
C/C	13	21.3%
C/T	38	62.3%
T/T	10	16.4%
HIV, n %	2	0.8%
HBV, n %	2	0.8%
Other comorbidities, n %	178	67.2%

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

Figure 1. Number and frequency of most common comorbidities



144 patients (54%) had prior interferon-based therapy, the most frequent outcomes of IFN-based therapy were response with a subsequent relapse (n=56, 21%) and null response (n=47, 18%). The summary of prior IFN-based therapy outcomes is presented in Figure 2.

The most frequently used regimen was OBV/PTV/r + DSV complemented with RBV, prescribed to 209 patients (79%). 254 (96%) patients were offered 12-weeks treatment regimens. Detailed breakdown of treatment regimens is presented in Figure 3.

Figure 2. History of treatment with interferons (N=265)

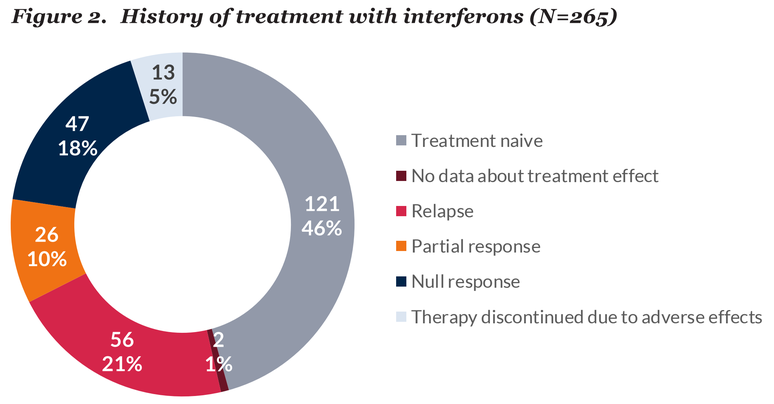
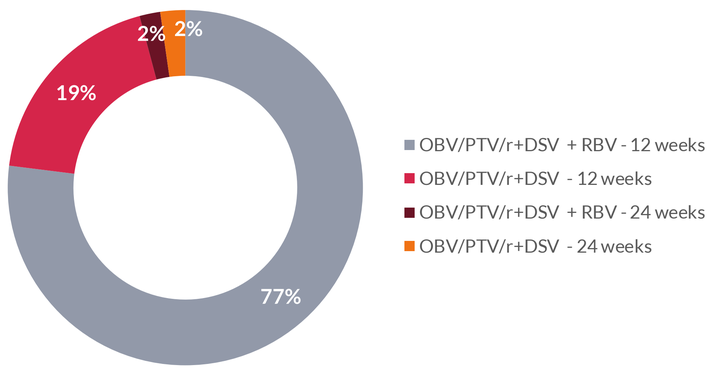


Figure 3. Treatment regimens prescribed to patients (N=265)



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

Treatment effectiveness

263 patients completed antiviral treatment and were assessed for end of treatment response, 259 (98% of the whole sample) had ETR, 4 persons (2%) were still HCV RNA positive after OBV/PTV/r ± DSV therapy. 256 patients had virologic outcome evaluated 24 weeks after therapy. 250 persons (94% of all treated patients, 98% of patients who had SVR24 assessed) showed SVR24.

Among 7 persons whose SVR24 assessment was not possible, 4 were lost to follow-up and 3 died after they completed treatment but before 24 weeks post-treatment assessment. For 2 persons the reason for death was reported, 1 liver failure and 1 hepatocellular carcinoma.

In comparison, out of 238 noncirrhotic (liver fibrosis stages F1-F3) patients from the same study, SVR24 was assessed in 225 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 2 presents the summary of response to antiviral therapy, loss to follow-up, and the number of deaths 24 weeks after completing treatment, broken down by HCV genotype and the history of interferon treatment. Patients for whom no information was available about the outcome of IFN-based therapy were excluded. Results for subgroups with small number of patients should be treated with caution.

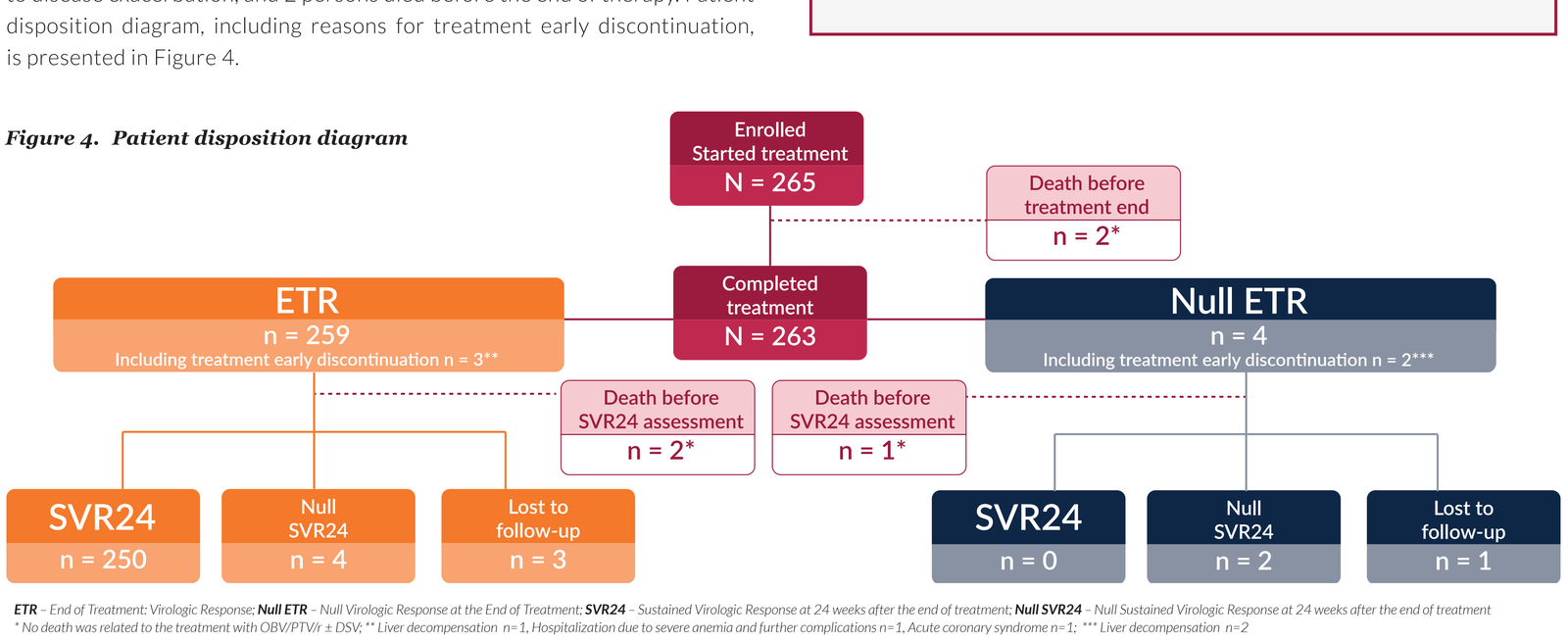
Table 2. SVR24 in subgroups by genotype and history of interferon therapy

	Virologic response	Virologic failure	Lost to follow-up	Death
Genotype (N=265)				
1a (n=4)	4 (100%)	0 (0%)	–	–
1b (n=251)	239 (95%)	6 (2%)	1 (0%)	5 (2%)
4 (n=7)	6 (86%)	0 (0%)	1 (14%)	–
Other (n=3)	1 (33%)	0 (0%)	2 (67%)	–
History of interferon therapy (N=263)				
Treatment naive (n=121)	116 (96%)	2 (2%)	1 (1%)	2 (2%)
Null response (n=47)	41 (87%)	3 (6%)	1 (2%)	2 (4%)
Partial response (n=26)	26 (100%)	0 (0%)	–	–
Relapse (n=56)	53 (95%)	0 (0%)	2 (4%)	1 (2%)
Intolerance to IFN (n=13)	12 (92%)	1 (8%)	–	–

Conclusions

Presented real-world data from Poland regarding OBV/PTV/r ± DSV therapy of HCV infected patients with cirrhosis confirms the high effectiveness of this regimen, even if slightly lower than for milder fibrosis stages (94% vs 93% of all starting treatment, 98% vs 99% of those who had SVR24 assessed). Shown results are further reinforced by RWE study performed by Flisiak 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.

Figure 4. Patient disposition diagram



***ETR** – End of Treatment: Virologic Response; **Null ETR** – Null Virologic Response at the End of Treatment; **SVR24** – Sustained Virologic Response at 24 weeks after the end of treatment; **Null SVR24** – Null Sustained Virologic Response at 24 weeks after the end of treatment*
** No death was related to the treatment with OBV/PTV/r ± DSV; ** Liver decompensation n=1, Hospitalization due to severe anemia and further complications n=1, Acute coronary syndrome n=1; *** Liver decompensation n=2*

Sources

[1] R. Plisko et al., „Hepatitis C – Real World Effectiveness of HCV Treatment in Poland", Value in Health, (19) 7, p. A408, November 2016. Poster presented at ISPOR 19th Annual European Congress Vienna, Austria – 29 October-2 November 2016, available at: https://www.ispor.org/ScientificPresentationsDatabase/Presentation/69702?pdfid=48518.

[2] R. Flisiak et al., „Real World Evidence of the Effectiveness of Paritaprevir/r + Ombitasvir, ± Dasabuvir, ± Ribavirin in Patients with Chronic Hepatitis C – An Observational Study in Poland (interim report)". Poster presented at XIX Conference of the Polish Association for the Study of the Liver, Mikołajki, July 2017.