# HEPATITIS C
## REAL WORLD EFFECTIVENESS OF HCV TREATMENT IN POLAND

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The study was designed and conducted by **HTA Consulting**

# Introduction

**A new drug program for chronic hepatitis with interferon-free therapy (B.71)** was introduced in Poland in July 2015. Since November 2015 the program is offering four innovative regimens, whose clinical trials outcomes had very promising results: ombitasvir / paritaprevir / ritonavir + dasabuvir (OBV/PTV/r+DSV), daklatasvir + asunaprevir, sofosbuvir and sofosbuvir/ledipasvir. The treatment with OBV/PTV/r was offered to adults with chronic HCV of genotype 1 or 4 (and with liver fibrosis). It can be administered in monotherapy or co-administered with DSV and/or ribavirin (RBV) for 12 or 24 weeks. According to Polish Ministry of Health (MH) reports, the number of patients treated within B.71 program amounted 3798 in the first semester of 2016, 67% of them were assigned to OBV/PTV/r±DSV±RBV treatment.

The objective of the study was to evaluate response of patients with chronic hepatitis C to OBV/PTV/r±DSV treatment in real-life settings, as is the national drug program.

# Methods

Data were collected on patients treated with OBV/PTV/r±DSV±RBV enrolled to drug program B.71. The study was carried out in two stages. In June 2016 basic characteristics, previous treatment and end of treatment response (ETR), including reasons for early treatment termination were collected retrospectively. In the second stage (September - October 2016) the sustained virologic response after 12 weeks (SVR12) and after 24 weeks (SVR24) since the end of treatment were added.

The study sample comprised all persons enrolled in the drug program between 1st October 2015 and 31st January 2016 in 7 non-randomly selected medical centers. The centers of different size, located across the country had also different number of patients enrolled in the program. SVR12 assessment was performed by default only in one center, and only those SVR12 results were included in the study. In case of one center, data for only a part of the sample (113 out of 143) was collected at the time of the database lock. Some observations lack SVR24, as in some cases (e.g. 24-week therapy) the results of the HCV RNA tests were not available on the day of the database lock. Complete results will be presented in the final report. Data of study participants were collected and analyzed anonymously and presented only in aggregated form. The study did not include any intervention in the patient treatment or visit schedule.

# Results

## Patient characteristics

A total of 477 participants of B.71 drug program was enrolled in the study. Basic characteristics of patients included in the survey are presented in Table 1.

***Table 1. Characteristics of patients enrolled in the study***

| Patient characteristics | N=477 | |
|---|---|---|
| Sex, n males % | 241 | 51% |
| Age, mean SD | 54 | 13 |
| Log10 of HCV viral load, mean SD | 5.69 | 0.75 |
| Virus genotype, n % | | |
| 1a | 23 | 5% |
| 1b | 430 | 90% |
| 1 (subgenotyping not available) | 7 | 1% |
| 4 | 15 | 3% |
| Mixed | 9 | 2% |
| Interleukin 28B genotype, n % | N=135 | |
| C/C | 38 | 28% |
| C/T | 79 | 59% |
| T/T | 18 | 13% |
| Liver fibrosis score (METAVIR scoring system), n % | | |
| F1 | 39 | 8% |
| F2 | 83 | 17% |
| F3 | 110 | 23% |
| F4 | 245 | 51% |
| HIV, n % | 3 | 1% |
| HBV, n % | 6 | 1% |
| Other comorbidities, n % | 268 | 56% |

The average age of patients at baseline (day of recruitment to the drug program) was 54, ranging from 21 to 90. The average log10 HCV load was 5.69 and was distributed normally (**Figure 1**), most patients (51%) had cirrhosis (F4 on the METAVIR scale). Genotype 1b was observed in 90% of the sample. The most frequent interleukin 28B genotype among patients who performed the genotyping was C/T (n=79, 59%). 56% of patient sample (n= 268) reported comorbidities, the most frequent being hypertension (31%) and diabetes (12%). The list of most frequently occurring comorbidities is presented in **Table 2**.

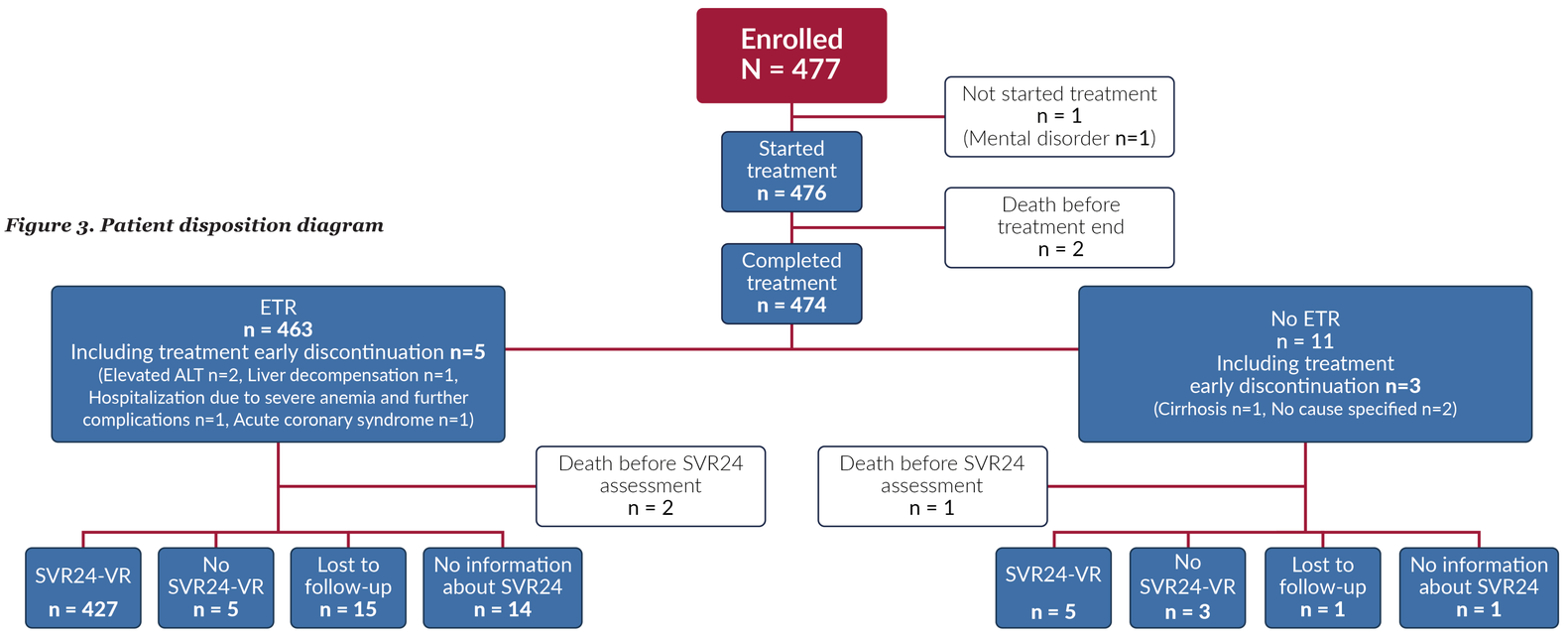
244 patients (51%) used interferon-based therapy prior to OBV/PTV/r±DSV treatment. The most frequent therapy outcome was response with a subsequent relapse (n=96, 20%) and no response (n=71, 15%). The summary of prior interferon therapy outcomes is presented in **Figure 2**.

## Treatment effectiveness

12-weeks regimens were dominant in the studied sample: 247 patients (52%) were prescribed OBV/PTV/r+DSV complemented with RBV, another 211 (44%) were to take OBV/PTV/r+DSV and 5 (1%) started on OBV/PTV/r + RBV. 24-weeks regimens were offered to 14 patients: 7 (1%) was prescribed OBV/PTV/r+RBV and 7 (1%) OBV/PTV/r+DSV +RBV.

One person did not start therapy after being qualified for it on account of mental disorder (this case was excluded from the further analysis). Among treated patients 2 died before the end of therapy and 9 (2%) ended therapy earlier than planned due to adverse event or disease exacerbation. The reasons for early treatment termination have been presented on **Figure 3**.

***Figure 3. Patient disposition diagram***




ETR – End of Treatment: Virologic Response ; no ETR – End of Treatment: no Virologic Response;
SVR24 – Sustained Virologic Response at 24 weeks after the end of treatment; SVR24-VR – SVR24: Virologic Response; no SVR24-VR – SVR24: no Virologic Response

The average initial dose of Moderiba was 1045 mg (n=265), with 124 patients (47%) taking 1000 mg per day, 104 (39%) using 1200 mg and 32 (12%) using 800 mg. During treatment Moderiba was stopped in 3 patients, and Moderiba dose was reduced in another 29 cases (average dose reduction of 276 mg). 7 patients had Moderiba dose increased (on average by 257 mg) throughout the treatment within the drug program.

***Figure 1. Histogram of HCV viral load***

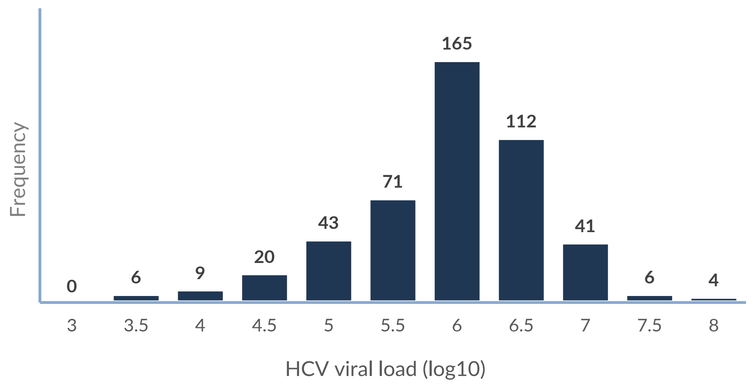
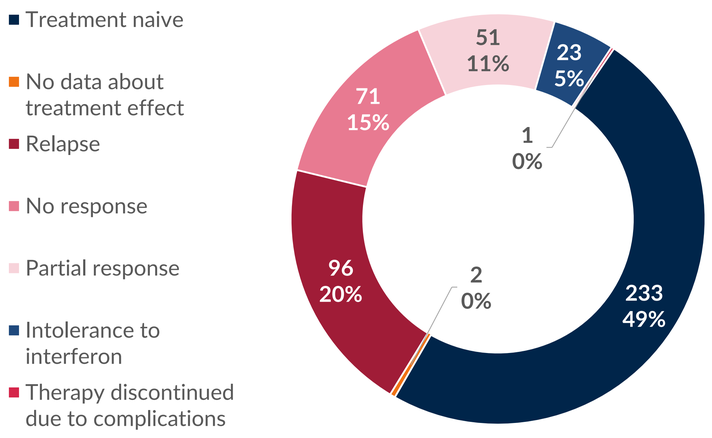



***Table 2. Most frequent comorbidities***

| Most frequent comorbidities | N=477 |
|---|---|
| Arterial hypertension | 147 (31%) |
| Diabetes mellitus | 55 (12%) |
| Cholelithiasis | 19 (4%) |
| Hypothyroidism | 18 (4%) |
| Ischemic heart disease | 17 (4%) |
| Thrombocytopenia | 15 (3%) |
| Osteoarthritis | 15 (3%) |
| Esophageal varices | 14 (3%) |
| Depression | 11 (2%) |
| Kidney failure | 9 (2%) |

***Figure 2. History of treatment with interferons (N=477)***




Out of 474 patients who completed treatment 463 (97%) had ETR and 11 (2%) were HCV RNA positive. 91% of all treated patients showed SVR24. From 21 patients, whose virologic assessment was not possible, 16 persons were lost to follow-up and 3 persons have died after the treatment end but before the assessment. All persons who have died had liver fibrosis stage F4 at the time of enrollment, in 1 person reported reason for death was the liver failure and in 1 person - hepatocellular carcinoma. In 15 persons the assessment of SVR24 was not possible, as it passed less than 24 weeks since the last day of treatment and the test results were not available at the day of database lock. **For patients, whose virologic outcome was evaluated 24 weeks after treatment, 98% had virologic response**. The summary of virologic response to treatment is presented on **Figure 3**.

Among 113 patients from the center in which SVR12 was measured the virologic response was present in 91%. 4 persons (4%) failed to achieve response, 6 patients did not have the test, due to hospitalization (2) or non-medical reasons (2). **The effectiveness of OBV/PTV/r+DSV treatment among patients who were tested 12 weeks after treatment end was 96%.**

SVR24 in subgroups of patients divided according to HCV genotype, liver fibrosis score and interferon treatment history is presented in **Table 3**. Patients for whom information about HCV RNA test result was not available were excluded from the analysis. Results for subgroups with small number of patients should be treated with caution (e.g. in 'other genotype' category high percent of patients who did not attend the final visit influences strongly the result).

***Table 3. SVR24 in subgroups by genotype, liver fibrosis score and history of interferon therapy***

| | Virologic response | Virologic failure | Lost to follow-up | Death |
|---|---|---|---|---|
| Genotype (N=461) | | | | |
| 1a (n=21) | 17 (81%) | 1 (5%) | 3 (14%) | – |
| 1b (n=421) | 399 (95%) | 7 (2%) | 10 (2%) | 5 (1%) |
| 4 (n=11) | 11 (100%) | – | – | – |
| Other (n=8) | 5 (63%) | – | 3 (38%) | – |
| Liver fibrosis (N=461) | | | | |
| F1 (n=37) | 35 (95%) | – | 2 (5%) | – |
| F2 (n=81) | 76 (94%) | 1 (1%) | 4 (5%) | – |
| F3 (n=106) | 97 (92%) | 2 (2%) | 7 (7%) | – |
| F4 (n=237) | 224 (95%) | 5 (2%) | 3 (1%) | 5 (2%) |
| History of interferon therapy (N=459) | | | | |
| Treatment naive (n=226) | 210 (93%) | 3 (1%) | 11 (5%) | 2 (1%) |
| No response (n=68) | 64 (94%) | 2 (3%) | – | 2 (3%) |
| Partial response (n=49) | 48 (98%) | – | 1 (2%) | – |
| Relapse (n=93) | 88 (95%) | 1 (1%) | 3 (3%) | 1 (1%) |
| Intolerance to interferon (n=23) | 20 (87%) | 2 (9%) | 1 (4%) | – |

# Conclusions

Presented results of OBV/PTV/r ±DSV treatment in real-world settings show high effectiveness in all patients (91% for both SVR12 and SVR24) as well as in various subpopulations, including groups perceived as difficult to treat, such as patients with liver cirrhosis (95% SVR24), patients with no history of interferon treatment (93% SVR24) or patients with no response to interferons (94% SVR24). The results of the study are comparable to RCT results. For example, SVR24 for patients with no prior treatment and 1b genotype was achieved by 94% (196/208), while the MALACHITE I clinical trial reported 98% effectiveness in the same subpopulation.

## Sources

A Study to Evaluate the Efficacy and Safety of Three Experimental Drugs Compared With Telaprevir (a Licensed Product) in People With Hepatitis C Virus Infection Who Have Not Had Treatment Before (MALACHITE 1). [Cited 2016 Oct 18].
Available from: https://clinicaltrials.gov/ct2/show/results/NCT01854697?term=malachite+hepatitis&rank=1

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