# 1.0 Abstract

**Title**

Real World Evidence Study of the Effectiveness of Paritaprevir/r – Ombitasvir, + Dasabuvir without Ribavirin in Patients with Chronic HCV Gt1b infection and Compensated Liver Cirrhosis in the RussIan FederaTion- An ObseRvational, MultI-CeNter Study (CITRIN)

**Keywords**

Paritaprevir/r – Ombitasvir, + Dasabuvir, Chronic HCV Gt1b infection, Compensated Liver Cirrhosis, Russia

**Rationale and Background**

According to the recently published results of TURQUOISE III study Gt1b patients with cirrhosis can be successfully treated with Paritaprevir/r – Ombitasvir, + Dasabuvir (3D) regimen without ribavirin (RBV).

Current study was developed in order to assess RW effectiveness and safety of 3D regimen without RBV in Gt1b patients with compensated cirrhosis in Russia.

**Research Question and Objectives**

*The Research Question:*

- What is the effectiveness of the interferon-free 3D regimen without RBV in patients with HCV Gt1b infection and compensated liver cirrhosis in a real life setting?

*Primary Objective*

- To describe the effectiveness of the interferon-free 3D regimen without RBV in patients with HCV Gt1b infection and compensated liver cirrhosis as evidenced

by sustained virological response at 12 weeks after the end of treatment in routine clinical practice.

*Secondary Objectives*

- To describe the end-of-treatment (EoT) response rate
- To assess the rate of relapse (timeframe for assessing relapse - between EoT and SVR 12)
- To describe baseline characteristics of patients with HCV Gt1b and compensated cirrhosis treated with 3D regimen.
- To collect information on co-morbidities and concomitant medications in cirrhotic patients in the Russian population
- To describe the tolerability of the 3D regimen

**Study Design**

This was a prospective, multi-center observational study in patients receiving the interferon-free 3D regimen without RBV. The prescription of a treatment regimen was at the discretion of the physician in accordance with local clinical practice and label.

**Setting**

Approximately 5-7 national and regional hospitals/outpatient services were planned to be included in the program.

**Subjects and Study Size, Including Dropouts**

The main criteria for inclusion were the following: treatment-naïve or IFN/RBV-experienced male or female patients aged 18 and older with confirmed CHC Gt1b and compensated liver cirrhosis, receiving therapy with the interferon-free 3D regimen without co-administration of RBV.

60 patients were planned to be included in this descriptive study without any priory sample size calculation.

**Variables and Data Sources**

Data for the study were collected within clinical interview with the patient and source document at the center. Source documents were original documents, data and records.
*Primary Variable*

- The percentage of patients achieving SVR12 (undetectable viral load at 12 week after the last actual dose of the 3D regimen)

***Secondary Variables***

- Baseline characteristics of patients with HCV Gt1b and compensated cirrhosis treated with 3D regimen
- Co-morbidities and concomitant medication
- Serious and non-serious adverse events

**Results**

Overall, 60 subjects were enrolled into the study. One subject was excluded from the Core Population (CP) because of prematurely therapy discontinuation after 40 days of treatment. The CP included 59 subjects (98.3%). The median age of subjects was 52.0 years; approximately half of the subjects were females. All patients were white, Caucasian in race.

The median duration of HCV infection diagnosis was 7.0 years. The IL28B gene polymorphisms rs12979860 and rs8099917 were unknown for the 63% and 68% of subjects, respectively. The prevalence of rs12979860 CC, CT, and TT variants were 12%, 17% and 9%, respectively; rs8099917 GG, TG, and TT - 2%, 10% and 20%, respectively.

48% of subjects reported esophageal varices in anamnesis.

10% of subjects reported liver and/or CHC related co-morbidities including cryoglobulinaemia and non-alcoholic fatty liver; 80% reported any other co-morbidities. The most frequently reported other co-morbidities were hypertension (34%), chronic pancreatitis (27%), chronic cholecystitis (15%) and chronic gastritis (12%).

A total of 29% patients were treatment-experienced. Previous treatment included peginterferon alfa or interferon alfa with RBV.

Overall, 32% patients received concurrent medications during the program. The most frequent pharmacological subgroups were: ACE inhibitors (plain), angiotensin II antagonists and diuretics fixed dose combinations (FDC), beta blocking agents (selective), insulins and insulin analogues for injection (fast-acting).

The sustained virological response at 12 weeks after the end of treatment (SVR12) was achieved in 98.3% (95% CI, 90.91 - 99.96%) of subjects in the CP. The end-of-treatment (EoT) was 100.0% (95% CI, 93.94 - 100.00%) and response rate and SVR12 non-response rate was 1.7% (95% CI, 0.04 - 9.09%) due to one subject (or 1.7%) with missing SVR12 data. The rate of relapse was 0.0% (95% CI, 0.00 - 6.06%); there were no subjects with breakthrough, on-treatment virological failure, or subjects who premature discontinued study drug because of any reason except virological failure.

Overall, 2 subjects (3%) experienced adverse events during the program. There were only 2 reported events in the study: ascariasis and hyperbilirubinemia. One of the reported events (hyperbilirubinemia) was reported as serious adverse event and considered to have reasonable possibility of a causal relationship to the study drug. This event was severe.

**Discussion**

The interferon-free 3D regimen without RBV was highly effective and well-tolerated in patients with HCV Gt1b infection and compensated liver cirrhosis in a real life

setting as was evidenced by SVR12 achieved in 98.3% (95% CI, 90.91 - 99.96%) of subjects.

**Marketing Authorisation Holder(s)**

[redacted]

**Names and Affiliations of Principal Investigators**

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