

## 1.0 Abstract

### Title

Drug use-results survey of paritaprevir/ritonavir/ombitasvir in patients infected with hepatitis C virus genotype 1 in Japan

### Keywords

HCV, DAA, paritaprevir/ritonavir/ombitasvir, real world, Japan

### Rationale and Background

[Background]

AbbVie regimen of paritaprevir/ritonavir/ombitasvir was approved for treatment of HCV genotype 1 (GT1) in September 2015 and launched to the market in November 2015 in Japan as the third IFN-free regimen. In general, the Pharmaceuticals and Medical Devices Agency (PMDA) requests pharmaceutical companies to collect data on the safety and effectiveness of new drugs in routine daily practice.

[Rationale]

Clinical studies of Phase 2 and 3 have been conducted in Japan for patients infected with HCV genotype 1b. To collect data on the safety and effectiveness of paritaprevir/ritonavir/ombitasvir in routine daily practice, further follow-up studies were needed. Moreover, this study addressed evaluating appropriate use of this regimen as described in the J-RMP.

### Research Question and Objectives

The objective of this study was to evaluate the safety and effectiveness of paritaprevir/ritonavir/ombitasvir used for patients infected with HCV genotype 1 in daily practice in Japan.

## **Study Design**

This is a prospective, multi-center, post-marketing observational study (PMOS).

## **Setting**

453 investigative sites were contracted with AbbVie GK to conduct this study, and 387 of these sites enrolled patients into the study. Recruitment period was from December 2015 to May 2017. AbbVie did not provide any study medication. Paritaprevir/ritonavir/ombitasvir was only be prescribed to patients as per Japan label by a physician with sufficient knowledge and experience in the treatment of hepatic viral disease. The recommended dose in adults is two tablets oral once daily with food or immediately after food for a duration of 12 weeks. The observational period consisted of treatment period (12 weeks) and follow-up period (24 weeks). The data gathered in daily practice was collected in this study.

## **Patients and Study Size, Including Dropouts**

[Patients]

- Inclusion Criteria  
HCV genotype 1 patients treated with paritaprevir/ritonavir/ombitasvir in daily practice
- Exclusion Criteria  
Patients who have been previously treated with paritaprevir/ritonavir/ombitasvir

[Study Size]

3,000 patients

## **Variables and Data Sources**

[Variables]

- Safety
  - Adverse drug reactions (ADRs), serious adverse events (SAEs)
  - ADRs of special interest;  
“Fluid retention”, “Hepatic disorder, Hepatic failure” and “Acute renal failure”
  - Clinical laboratory tests ;  
Hematology; WBC, RBC, Hemoglobin, PLT, PT-INR  
Blood chemistry; ALT, AST, ALP, Albumin, total/direct-Bilirubin, Creatinine,  
BUN  
Other; Alpha Fetoprotein
- Effectiveness
  - Primary variable; SVR12

[Data Source]

Data source in this study was from institute’s medical chart. Participating physicians in this study transcribed the data from medical chart to Case Report Form (CRF) which AbbVie prepared. If the event fulfilled the serious criterion (Serious Adverse Event), the "Serious Adverse Event Report" form was completed additionally.

**Results**

The number of contract sites was 453, and the number of registered patients was 3042. The safety analysis set included 2954 patients and the effectiveness analysis set included 2666 patients.

[Safety]

The rates of related adverse event, adverse drug reactions (ADRs) was 16.22% (479/2954 patients), and the rates of SAEs was 3.86% (114/2954 patients). The rates of ADRs in the clinical trial conducted in Japan was 22.87% (83/363 patients). The rates of ADRs in this study was not higher than that in the clinical trial conducted in Japan. The rates of ADRs as special interest in this study were 0.98% (29/2954

patients) for "Fluid retention", 6.50% (192/2954 patients) for "Hepatic function disorder/hepatic failure", and 2.03% (60/2954 patients) for "Acute renal failure". There was no new safety concern regarding clinical laboratory tests.

[Effectiveness]

SVR12 rate, the primary effectiveness variable, was 97.94% (2611/2666 patients, 95% CI: 97.32 -98.44). This rate was slightly higher than the efficacy rate in noncirrhotic patients of 94.9% (204/215 patients, 95% CI: 91.1 -97.1) and in cirrhotic patients of 90.5% (38/42 patients, 95% CI: 77.9 -96.2) in the phase III clinical trial conducted in Japan. The most common type of virologic treatment failure was "Relapse" in 0.90% (24/2666 patients).

### **Discussion**

The results of this observational study support the safety and effectiveness of paritaprevir/ritonavir/ombitasvir used for patients infected with HCV genotype 1 in routine daily practice in Japan. The safety results of this study were consistent to the currently documented safety profile of the product, as described in the label and periodic safety update reports.

### **Marketing Authorisation Holder(s)**

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