Antiviral activity and safety of TMC435 combined with peginterferon α-2a and ribavirin in patients with genotype-1 hepatitis C infection who failed previous IFN-based therapy


Introduction

- A subpopulation of patients infected with hepatitis C virus (HCV) genotype 1 who are at risk of advanced liver disease are not suitable candidates for direct-acting antivirals either due to contraindications or a lack of interferon (IFN) responsiveness.

- The TMC435/PEGIFN combination offers a once-daily dosing regimen that may provide more sustained suppression of viral load and lead to improved outcomes.

- TMC435 is a potent, selective, oral inhibitor of HCV NS3/4A protease.

- TMC435 is in development as a component of a protease inhibitor (PI) and peginterferon (PEGIFN) regimen for the treatment of HCV genotype 1.

- The pharmacokinetic profile supported a once-daily dosing regimen.

- This study evaluated the safety and antiviral activity of TMC435 in combination with PEGIFN in treatment-naïve and treatment-experienced patients.

Methods

- The study design for OPERA-1 is shown in Figure 1. The study was conducted in Europe.

- All patients were randomized to receive either TMC435 75 mg QD, 150 mg QD, 200 mg QD or placebo as part of a triple therapy regimen, in combination with peginterferon (PEGIFN) and ribavirin (RBV).

- Male and female patients with chronic HCV infection and evidence of liver disease were included.

- Patients were excluded if they had evidence of active alcohol use, cirrhosis, or were positive for HBsAg.

- The study was approved by the ethics committee at each site.

- All patients provided written informed consent before participation.

Results

- Baseline demographic and characteristics: Table 1 shows the baseline demographics and characteristics of the study population.

- Week-4 virologic response: Figure 2 shows the mean decrease in plasma HCV RNA over time for each treatment group.

- Safety and tolerability: Table 2 presents the most common adverse events reported during the study.

- Week-4 virologic response: Figure 3 shows the change in alanine aminotransferase (ALT) levels from baseline for each treatment group.

Conclusions

- TMC435 in combination with PEGIFN and RBV was well tolerated and demonstrated antiviral activity.

- The combination of TMC435, PEGIFN, and RBV was demonstrated to be effective in treatment-naïve and treatment-experienced patients.

- The combination was well tolerated, with no new safety signals observed.

- These results support the development of TMC435 for the treatment of HCV genotype-1 infection in combination with PEGIFN and RBV.

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References


- TMC435 + PEGIFN has compensated liver disease.