1. Purpose

This study evaluated the antiviral activity of TMC435, administered once daily as monotherapy or in combination with pegylated interferon (PegIFN) and ribavirin (RBV), in a phase 1B study of treatment-naive and -experienced genotype-1b HCV-infected patients.

2. Methods

2.1 Study Design

Patients were randomized to one of three groups: monotherapy with TMC435 at doses of 25 mg, 75 mg, or 200 mg qd, or placebo, followed by triple therapy with TMC435 or placebo in combination with PegIFN and RBV. The presence of Q80K and R155K mutations at baseline did not affect the antiviral activity of TMC435.

3. Results

3.1 Virological Analysis

HCV RNA levels of 1000 IU/mL, 100 IU/mL, and 50 IU/mL were achieved in 100% of patients at Day 28.

3.2 Breakthrough and Associated Mutations

Virological analysis was performed on patients with viral breakthrough during four weeks of treatment with TMC435 plus PegIFN and RBV, respectively, during the phase 1B study.

3.3 Conclusions

TMC435 demonstrated potent, dose-dependent antiviral activity in both treatment-naive and -experienced patients, with a 50% effective concentration (EC50) value of 8 nM.

4. Acknowledgments

All authors are employees of Tibotec.

References

1. Manns M et al. Presented at the 44th Annual Meeting of European Association for the Study of the Liver (EASL), Copenhagen, Denmark, April 22-26, 2009.

2. The OPERA-1 study design is summarized in Figure 1.

3. Baseline mutations in NS3 protease domain (aa 1-181) are indicated in each graph at the time points with sequence information available.

4. Conclusions

- TMC435 demonstrated potent, dose-dependent antiviral activity in both treatment-naive and -experienced patients.
- Baseline mutations in NS3 protease domain (aa 1-181) are indicated in each graph at the time points with sequence information available.

Disclosure: all authors are employees of Tibotec.