TMC435 Effective in the Treatment of HCV Genotype 1 Infection

Written by Eric Butterman

Michael W Fried, MD, University of North Carolina, Chapel Hill, North Carolina, USA, presented the results of the PILLAR [TMC435-C205; NCT00882908 and ASPIRE [TMC435-C206; NCT00980330] trials. Both studies demonstrated that TMC435 (an oral inhibitor of the hepatitis C virus [HCV] NS3/4A protease) administered once-daily with pegylated interferon alpha-2a (PegIFNa-2a) and ribavirin (RBV) is safe, has potent antiviral activity, and shortens total treatment by 24 weeks compared with PegIFNa-2a/RBV alone.

The two trials were international, randomized, double-blind studies that enrolled men and women, aged 18 to 70 years who were chronically infected with HCV genotype 1 (plasma HCV RNA >100,000 IU/mL at screening). In the PILLAR trial, patients were HCV treatment-naïve and received TMC435 for 12 or 24 weeks with PegIFNa-2a/RBV. In the ASPIRE trial, patients were HCV treatment-experienced, although naïve to direct-acting antivirals. The participants were stratified by prior virological response (relapsers, partial responders, null responders). TMC435 with PegIFNa-2a/RBV was administered for 12, 24, or 48 weeks.

The primary efficacy endpoint, which was the same in both studies, was the proportion of patients with undetectable HCV RNA (<25 IU/mL) 24 weeks after the planned end of treatment. Secondary objectives included an evaluation of the safety and tolerability of TMC435 plus PegIFNa-2a/RBV compared with PegIFNa-2a/RBV/placebo over the trial period. Virologic response rates and 95% confidence intervals were calculated using a logistic regression model, including baseline HCV RNA and the stratification factors as covariates. The results of planned interim 24-week efficacy and safety analyses, including the proportion of patients with undetectable HCV RNA (<25 IU/mL) at Weeks 4, 12, and 24, from both studies were reported.

In the PILLAR trial, 68 to 79% of patients who were treated with TMC435 achieved a rapid virologic response (HCV RNA <25 IU/mL) compared with 5% in the control arm at Week 4.

At Week 12, rapid virologic response was 91% to 97% for the TMC435 arms compared with 58% in the control arm, and at Week 24, rapid virologic response was 94% to 97% for the TMC435 arms compared with 82% in the control arm. In the TMC435 arms, 79% to 86% of subjects were eligible to stop treatment by Week 24.

In the ASPIRE trial, at Weeks 4, 12, and 24, significantly higher virologic response rates were observed following active treatment compared with placebo plus PegIFNa-2a/RBV. In null and partial responders, higher virologic response rates were observed in the TMC435 150-mg dose arms, compared with 100-mg dose arms, at early time points.

The distribution of the IL28B genotype (TT, CC, and CT) was similar across treatment groups with the higher responses rates for the CC genotype in the placebo arms. In the TMC435 groups, higher-than placebo responses were observed in the TT, CC, and CT categories, with no major differences between IL28B genotypes.

Given in combination with PegIFNa-2a/RBV, the safety and tolerability profile of TMC435 was generally similar to those of the placebo control. In treatment-naïve and treatment-experienced patients, TMC435, administered once-daily with PegIFNa-2a/RBV, has potent antiviral activity, rapidly achieving undetectable HCV RNA levels in the majority of patients.