TMC435 Boosts Cure Rates in Previously Treated Geno 1 HCV Patients

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Up to 80 percent of people with genotype 1 hepatitis C virus (HCV) who didn't respond successfully to earlier therapy were cured of their infection using Janssen Pharmaceuticals' and Medivir AB's once-daily HCV protease inhibitor TMC435 plus pegylated interferon and ribavirin (peg-IFN/RBV), according to final data from the Phase II ASPIRE clinical trial presented Thursday, April 19, at the 47th Annual Meeting of the European Association for the Study of the Liver (EASL) in Barcelona.

The ASPIRE study, reviewed in detail at EASL by Stefan Zeuzem, MD, of Goethe University Hospital in Frankfurt, Germany, and his colleagues, randomized 462 people living with genotype 1 HCV infection to one of seven groups, six of which involved different doses (100 or 150 milligrams) of TMC435 taken once daily for 12, 24 or 48 weeks plus 48 weeks of peg-IFN/RBV. The seventh group—each group consisted of roughly 66 people—served as controls and received 48 weeks of peg-IFN/RBV alone.

All patients in the study were either relapsers (their HCV viral loads become detectable after successfully completing an earlier course of treatment), partial responders (their viral loads dropped but were not undetectable at the end of an earlier course of treatment) or null responders (their viral loads decreased very little during an earlier course of treatment). Relapsers are the most likely to respond with retreatment, notably with the addition of a third drug, whereas null responders are typically less likely to respond to retreatment with a three-drug regimen.

Nineteen percent of those enrolled in the study had advanced fibrosis or cirrhosis; 41 percent were infected with genotype 1a HCV; and 58 percent were infected with genotype 1b HCV.

In the TMC435 groups, 61 to 80 percent had a sustained virologic response 24 weeks after finishing therapy (SVR 24)—they were cured of their infections. In the control group, only 23 percent achieved an SVR 24. The differences in the SVR 24 rates in all of the TMC435 groups, compared with that in the control group, were statistically significant, meaning they were too great to have occurred by chance.

Among those in the TMC435 groups, the SVR 24 rate appeared lowest among those who took 100

mg TMC435 plus peg-IFN/RBV for 48 weeks and highest among those who took 150 mg TMC435 plus peg-IFN/RBV for 48 weeks.

Looking specifically at results among those receiving 150 mg plus peg-IFN/RBV for 48 weeks, 10 of 17 (59 percent) null responders, 19 of 22 (86 percent) partial responders and 23 of 26 (89 percent) relapsers achieved SVR 12 in the clinical trial.

Rates of treatment discontinuation due to viral breakthrough or lack of virologic response in the study were between 9 and 17 percent in the TMC435 group, compared with 53 percent in the control group. Viral relapse rates among those who completed their assigned treatment regimen were between 6 and 18 percent in the TMC435 groups, compared with 44 percent in the control group.

As for side effects, the most common ones included headache, fatigue, flulike symptoms and a drop in neutrophils (a type of white blood cell), occurring in one-third to nearly one-half of all patients, with little differences between those in the TMC435 groups and control group. Pruritis (itching) was more common among those in the TMC435 groups, compared with the control group (35 versus 17 percent, respectively), as were increases in bilirubin (a yellowish pigment produced when the liver breaks down old red blood cells).

Side effects leading to treatment discontinuation occurred in 7 to 9 percent of those in the TMC435 group, compared with 5 percent in the control group.

“Following treatment with TMC435 plus [peg-IFN/RBV],” Zeuzem and his colleagues conclude, “patients who failed previous [peg-IFN/RBV] treatment exhibited significantly higher SVR 24 rates compared with [control], including difficult-to-treat prior null responders with cirrhosis. TMC435 was well tolerated in this population.”
