AASLD 2013: AbbVie's Dual Interferon-free Combination Cures Genotype 1b Hepatitis C in 95%

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by Keith Alcorn

A 2-drug combination of direct-acting antivirals developed by AbbVie achieved sustained virological response (SVR) in 95% of previously untreated patients with genotype 1b hepatitis C infection after 12 weeks of treatment, without the need for pegylated interferon or ribavirin, Eric Lawitz from the Texas Liver Institute reported Sunday at the 64th AASLD Liver Meeting in Washington, DC. In people who had failed to respond to a previous course of pegylated interferon and ribavirin, the same combination achieved SVR in 90%.

AbbVie is already testing ABT-450, an HCV protease inhibitor boosted by ritonavir, and ABT-267, an NS5A inhibitor, in several Phase 3 clinical studies in combination with a third drug, the non-nucleoside polymerase inhibitor ABT-333. These trials will begin to report results by the end of 2013, and it is likely that AbbVie will submit a licensing application in early 2014 for this 3-drug, interferon-free combination in order to achieve marketing approval in the second half of 2014.

The results presented on Sunday came from a Phase 2 study designed to determine whether a 2-drug combination of a protease inhibitor and an NS5A inhibitor would be sufficiently potent to achieve a high cure rate in patients with genotype 1b hepatitis C infection. HCV subtype 1b has a higher barrier to resistance than subtype 1a. This raises the possibility that patients with genotype 1b may be able to use 2 highly potent direct-acting antivirals instead of 3 to achieve a cure with 12 weeks of treatment, potentially reducing the risk of side effects and drug-drug interactions with other medications.

The PEARL-1 study was a Phase 2 trial that enrolled 42 previously untreated patients with hepatitis C infection and 40 previous null responders. Previously untreated patients were 60% male and 26% African American; prior null responders were 38% male and 3% African American.

All participants received 12 weeks of treatment with ABT-450 (150 mg once-daily boosted with 100 mg of ritonavir in order to maintain high drug levels) and ABT-267 (25 mg once-daily).

The primary endpoint of the study was the proportion of patients with sustained virologic response 12 weeks after completion of a 12-week course of treatment (SVR12).

In the previously untreated group, 95% of patients (40 out of 42) achieved SVR 12 weeks after completion of treatment. There were 2 patients were lost to follow-up but no recorded virological failures among previously untreated patients.

In the previous null responder group, 90% of patients (36 out of 40) achieved SVR 12 weeks after completing treatment. A total of 4 virological failures occurred in this group: 1 viral breakthrough during treatment after an initial treatment response, and 3 post-treatment viral relapses.

The study drugs were fairly well-tolerated. The most commonly reported adverse effects reported during the study were headache (33% of previously untreated patients and 25% of prior null responders) and nausea (19% of previously untreated patients but no prior null responders). There were 2 serious adverse events that were not considered to be related to the study drug, and 1 patient temporarily interrupted treatment after a grade 3 liver enzyme (ALT) elevation.

This combination will now go forward into further studies.

Questioned regarding the potential for drug interactions between the ritonavir booster used in this combination and other classes of medication, Lawitz said that in his view, the interaction between ritonavir and other drugs metabolized by the CYP3A4 enzyme was "manageable."

However, use of 100 mg ritonavir -- which is also used to boost antiretroviral drug levels in HIV treatment -- with at least 18 drugs from 10 different classes is contraindicated; these include commonly prescribed medications such as anti-arrhthymics, ergot alkaloids used in migraine treatment, and the statins simvastatin and lovastatin.

E Lawitz, C Hezode, P Varunok, et al. Interferon- and Ribavirin-free Regimen of ABT-450/r + ABT-267 in HCV Genotype 1b-infected Treatment-naive Patients and Prior Null Responders. 64th Annual Meeting of the American Association for the Study of Liver Diseases (AASLD 2013). Washington, DC, November 1-5, 2013. Abstract 74.