BMS Oral Hep C Drug Combo Cures 90% of Null Responders With Genotype 1b in Japanese Study

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Combining two experimental oral hepatitis C drugs from Bristol-Myers Squibb (BMS)—daclatasvir, a once-daily NS5a inhibitor, and asunaprevir, a twice-daily protease inhibitor—cured nine of 10 previously treated "null" responders after 24 weeks of treatment. Kazuaki Chayama, MD, PhD, of Hiroshima University and his colleagues presented these results from a Japanese Phase IIa study on Monday, November 7, at the 62nd annual meeting of the American Association for the Study of Liver Diseases (AASLD) in San Francisco.

The encouraging report follows the groundbreaking results of an earlier trial of daclatasvir and asunaprevir presented at the 46th Annual Meeting of the European Association for the Study of the Liver earlier this year in Berlin. That study was among the first to prove that hepatitis C could be cured without pegylated interferon and ribavirin.

All of the study participants in the most recent trial reported by Chayama's team had had hepatitis C virus (HCV) genotype 1b, and none of them had cirrhosis.

Remarkably, although one study participant discontinued daclatasvir and asunaprevir after only 16 days, she was cured. According to Chayama's report, she was hospitalized for gastroenteritis—which was considered unrelated to the study drugs—two weeks after starting the study medications, and treated with antibiotics. Even though she discontinued treatment with a detectable HCV viral load, her HCV viral load became undetectable two weeks later; she has been followed for 24 weeks and remains undetectable.

The duo of direct-acting antivirals (DAAs) worked quickly for the remaining 90 percent of study participants; by week four, hepatitis C viral load had dropped to less than 15 international unites per milliliter (IU/mL), and all of them were undetectable by week eight.

According to Chayama and his colleagues, there was no association between pre-treatment resistance and treatment outcome. Before starting treatment, eight of 10 study participants had evidence of daclatasvir resistance, and three of 10 had evidence of resistance to HCV protease inhibitors; one had evidence of resistance to both drugs. However, all were cured.

Initially, study participants were treated with 600 milligrams (mg) of asunaprevir twice daily, but the dose was reduced to 200 mg after an ongoing study found that the higher dose caused serious—but reversible—liver enzyme elevations. At the 200 mg dose, liver enzyme elevations were still documented, but they were mild to moderate in intensity and resolved during treatment or after it was stopped.

Other side effects were considered mild or moderate as well. The most common side effects were diarrhea and headache.

In summary, Chayama noted, “High cure rates are possible with dual oral DAA therapy in patients with genotype 1b infection.”

Additional clinical trials are looking at different combinations of daclatasvir, asunaprevir, ribavirin and pegylated interferon—both alfa and lambda versions—in both first-time treatment takers and null responders.
