Selgantolimod Shows Promise as Treatment for Hepatitis B

In a Phase II study, the drug was safe and well tolerated, and a small number of people achieved benchmarks of success against the virus.

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Gilead Sciences' selgantolimod (GS-9688), a potent and selective oral agonist of toll-like receptor 8 (TLR8) was safe and well tolerated as a treatment for hepatitis B virus (HBV) in a mid-stage trial, with a small number of participants experiencing key benchmarks of combatting the virus.

Edward Gane, MD, of the Auckland City Hospital in New Zealand, presented findings from a randomized, double-blind, placebo-controlled, multicenter Phase II trial of selgantolimod at The Liver Meeting, the annual meeting of the American Association for the Study of Liver Diseases, this month in Boston.

The study enrolled 48 people with HBV who were virally suppressed thanks to treatment with oral antivirals such as Vemlidy (tenofovir alafenamide), Viread (tenofovir disoproxil fumarate) or Baraclude (entecavir). Of these, 24 were hepatitis B surface antigen (HBeAg) positive and 24 were HBeAg negative.

The participants were randomized into three groups. In addition to their oral antiviral, nine people received a placebo, 20 people received 1.5 milligrams of selgantolimod and 19 people received 3 mg of selgantolimod. After 24 weeks, all participants received an additional 24 weeks of oral antiviral treatment alone.

There were six groups in total, since each of the three treatment groups were further broken into a pair of groups based on HBeAg status. The baseline characteristics of the study groups were similar. Between 50% and 90% of the groups were men, 50% to70% were Asian, 0% to 10% were white, 10% to 44% were Native Hawaiian or Pacific Islander and 0% to 30% were Black. The average HBV viral load was 20 to 25, the average ALT liver enzyme level was 20 to 31 and the average FibroTest fibrosis score was 0.18 to 0.34.

At week 24, all of those in the placebo group experienced less than a 0.1 log10 (20.5%) decline in

hepatitis B surface antigen (HBsAg). Of those in the 1.5 mg group, 80% of the HBeAg-positive individuals and 80% of the HBeAg-negative individuals experienced less than a 0.1 log01 decline, a respective 20% and 10% experienced a 0.1 log10 to 0.3 log10 (20.5% to 50%) decline and 0% and 10% experienced a 1.0 log10 (90%) or greater decline in HBsAg. Of those in the 3 mg group, 100% of the HBeAg-positive individuals and 70% of the HBeAg-negative individuals experienced less than a 0.1 log10 decline in HBsAg; the other 30% of the latter group experienced a 0.1 to 0.3 log10 decline.

At 24 weeks, 10% of the HBeAg-negative 3 mg group experienced HBsAg loss. and 10% of the HBeAg-positive 1.5 mg group experienced HBeAg loss. No one in the placebo group experienced HBsAg or HBeAg loss.

None of the study participants experienced virologic breakthrough, defined as two consecutive study visits in which their viral load was at least 69.

The greater the dose of selgantolimod, the greater the induction of the cytokines interleukin 11p40 (IL011p40), IL-1RA and interferon-gamma.

After adjusting the data to account for various differences between the participants, the study authors found that baseline predictors of having a higher IL-12p30 response, specifically a greater than 5-fold increase, included: receiving the 3 mg versus 1.5 mg dose of selgantolimod (associated with a 31-fold greater likelihood of a response); having a body mass index (BMI) of below 25, indicating being below overweight, compared with an obese BMI of at least 30 (19-fold greater likelihood); having an overweight BMI of 25 to 29.9 versus a BMI of at least 30 (40-fold greater likelihood); and having a HBsAg level greater than 100 versus 100 or less (9.7-fold greater likelihood).

There were no significant associations between HBsAg decline and levels of interferon-gamma, IL-12p40 or IL1RA.

The investigators concluded that selgantolimod was safe and well tolerated.

In the placebo, 1.5 mg and 3 mg groups, a respective 100%, 90% and 100% experienced adverse health events that emerged during the study; a respective 0%, 10% and 0% experienced severe (Grade 3 or higher) adverse health events; a respective 0%, 15% and 5% experienced serious adverse health events; and a respective 0%, 5% and 0% experienced adverse health events that led participants to discontinue treatment.

The most common adverse health events in the placebo, 1.5 mg and 3 mg groups were nausea (experienced by a respective 0%, 35% and 58%), vomiting (0%, 20% and 26%), fatigue (11%, 15% and 26%), chills (11%, 5% and 21%), urinary tract infection (33%, 25% and 21%) and headache (44%, 25% and 16%).

“Oral [selgantolimod] is safe, well-tolerated and induced dose-dependent changes in [chronic hepatitis B] patients,” the researchers concluded, adding that 5% of patients experienced either at

least a 1 log10 decline in HBsAg levels or HBsAg loss at week 24.

A separate ongoing study is evaluating selgantolimod at both doses in those without viral suppression.

To read the study abstract, click here.

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