Success for Gilead’s New Experimental Hepatitis C Tablet

A fixed-dose tablet of the two drugs in Epclusa plus voxilaprevir could become the first treatment approved for those who have failed hep C treatment.

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Gilead Sciences has announced successful top-line results of four large trials of an experimental fixed-dose combination hepatitis C virus (HCV) tablet containing the components of Epclusa (sofosbuvir/velpatasvir) plus the investigational voxilaprevir. All participant groups had a 95 or 96 percent cure rate.

If green-lighted by the U.S. Food and Drug Administration (FDA), the triple-drug tablet would be the first hep C treatment approved for those who have failed a previous cure attempt with oral direct-acting antiviral (DAA) treatment.

The international, Phase III POLARIS-1, -2, -3 and -4 trials tested the efficacy of a fixed-dose combination of the nucleotide analog NS5B polymerase inhibitor sofosbuvir, the pangenotypic (meaning it applies to all genotypes) NS5A inhibitor velpatasvir and the investigational pangenotypic NS3/4A protease inhibitor voxilaprevir (formerly known as GS-9857) among those with genotypes 1 through 6 of hep C.

The POLARIS-1 and -4 studies included 445 people with genotypes 1 through 6 who had been previously treated with DAAs. They received 12 weeks of sofosbuvir/velpatasvir/voxilaprevir. The participants of POLARIS-1 failed a previous treatment with an NS5A inhibitor, while the POLARIS-4 participants failed treatment with other classes of DAAs.

The POLARIS-2 and -3 studies included 611 people who underwent their first treatment with DAAs and who received eight weeks of sofosbuvir/velpatasvir/voxilaprevir. The POLARIS-2 study included participants with genotypes 1 through 6 of hep C with or without cirrhosis. The POLARIS-3 study included people with genotype 3 of hep C and compensated cirrhosis.

In POLARIS-1, a double-blind, placebo-controlled study, 96 percent (253 of 263) of those with genotypes 1 through 6 who took sofosbuvir/velpatasvir/voxilaprevir for 12 weeks achieved a sustained virologic response 12 weeks after completing therapy (SVR12, considered a cure), compared with none of those who were randomized into the placebo group (0 of 152). Forty-one percent (172 of 415) of the overall group in POLARIS-1 had cirrhosis.
In POLARIS-4, individuals with genotypes 1 through 4 who had taken other, non-NS5A inhibitors before were divided into two groups. Those in the first group received 12 weeks of sofosbuvir/velpatasvir/voxilaprevir and were cured at a rate of 97 percent (177 of 182); those in the second group received 12 weeks of Epclusa and were cured at a rate of 90 percent (136 of 151). Forty-six percent (153 of 333) of all those in POLARIS-4 had cirrhosis.

In POLARIS-2, individuals with genotypes 1 through 6 who had not taken DAAs before were divided into two groups. Those in the first group were treated with sofosbuvir/velpatasvir/voxilaprevir for eight weeks and were cured at a rate of 95 percent (476 of 501); those in the second group were treated with Epclusa for 12 weeks and were cured at a rate of 98 percent (432 of 440). Eighteen percent of all those in POLARIS-2 had cirrhosis, while 23 percent had previously failed treatment with an interferon-based regimen.

Because the two cure rates in POLARIS-2 were within 5 percentage points of each other, the researchers judged the newer treatment non-inferior to Epclusa, meaning that the two tablets’ response rates are essentially comparable.

POLARIS-3 randomized people who had not been treated with DAAs before and who had cirrhosis to receive eight weeks of sofosbuvir/velpatasvir/voxilaprevir or 12 weeks of Epclusa. Ninety-six percent (106 of 110) of those who received the triple-drug combo were cured, as were 96 percent (105 of 109) of those who received Epclusa.

Those who were treated with the triple-combination tablet, whether for eight or 12 weeks, had a similar incidence of adverse health events compared with those treated with a placebo or Epclusa. The most common adverse events among those on the triple combo were headache, fatigue, diarrhea and nausea. One person out of the 1,056 who received the triple combo across the four studies stopped treatment—this person was in a 12-week-treatment group—because of an adverse health event.

Gilead will present more detailed results from these studies at the Liver Meeting 2016 in Boston in November.

To read a press release about the study, click here.