Efficacy of 12-Week GS-7977/Ribavirin Combo for Hep C Geno 1 Varies by IL-28B Status

April 23, 2012

Early follow-up data from small evaluations of Gilead Sciences' nucleotide analog GS-7977 plus ribavirin in people with genotype 1 hepatitis C virus (HCV) infection starting therapy for the first time indicate that the experimental nucleotide analog continues to show promise as a cornerstone of interferon-free treatment.

Preliminary data from the ELECTRON clinical trial was presented Saturday, April 21, at the 47th Annual Meeting of the European Association for the Study of the Liver (EASL) in Barcelona. According to the findings, 88 percent of genotype 1 patients starting therapy for the first time with a 12-week course of GS-7977 plus ribavirin had undetectable viral loads about a month after completing treatment; in other words, they had a sustained virologic response at week 4 (SVR 4).

Separately, Gilead issued a press release noting less robust preliminary data in another group of people living with genotype 1 HCV infection. In the QUANTUM study, the SVR 4 rate was only 59 percent.

ELECTRON was originally designed to test 12 weeks of GS-7977 therapy with and without pegylated interferon and/or ribavirin in people living with genotype 2 or 3 HCV infection. The encouraging results were reported in November 2011 at the 62nd Annual Meeting of the American Association for the Study of Liver Diseases (AASLD) in San Francisco.

Four additional groups were eventually added to the study, including two exploring 12 weeks of GS-7977 plus ribavirin, without pegylated interferon, in genotype 1 patients.

One group of 10 patients who were prior hepatitis C treatment null responders—minimal viral load reductions while on a previous regimen consisting of pegylated interferon and ribavirin. In these patients, only 11 percent had an SVR 4, as reported at the 19th annual Conference on Retroviruses and Opportunistic Infections in March in Seattle.

A second group of 25 patients who were starting HCV therapy for the first time.
Long-awaited follow-up data from the group of genotype 1 patients initiating therapy for the first time were reported at EASL by Eric Gane, MD, of Auckland City Hospital in Aukland, New Zealand,

and his colleagues.

The 25 ELECTRON study volunteers with genotype 1 starting therapy for the first time were, on average, 48 years old. Seventy-six percent were male and most were white. Eighty-eight percent had HCV genotype 1a.

All patients (100 percent) had undetectable viral loads after four weeks of treatment. Similarly and encouragingly, all patients ended their 12-week treatment course with undetectable viral loads—a perfect end-of-treatment response in the group.

Four weeks after stopping treatment, 22 of the 25 (88 percent) first-time treatment takers had undetectable viral loads. the three remaining patients saw their HCV viral loads rebound soon after completing therapy.

In the QUANTUM study, in which 19 first-time treatment takers with genotype 1 HCV took an a course of treatment identical to the one used in ELECTRON, SVR 4 was achieved in only 10 of 17 patients (59 percent; two volunteers discontinued treatment prematurely). Seven patients, or 41 percent, experienced viral relapse after treatment was completed.

A likely reason for the SVR 4 difference between the groups in ELECTRON and QUANTUM is the prevalence of key IL-28B polymorphisms. Whereas 11 of the 25 (44 percent) of patients in ELECTRON had the IL-28B CC polymorphism—which has historically been associated with better hepatitis C treatment responses, usually to pegylated interferon-based regimens—CC was the IL-28B type in only three of 19 (16 percent) patients in QUANTUM.

Each of the three patients who relapsed in the ELECTRON study had a different IL-28B polymorphism—one had CC, another had CT and the third had TT. The seven patients who relapsed in the QUANTUM study either had IL28B C/T (four patients) or IL28B T/T (three patients).

Patients in both studies will continue to be observed to determine sustained virologic response rates at weeks 12 and 24 of follow-up (SVR 12 and SVR 24). Additionally, some genotype 1 patients starting therapy for the first time in QUANTUM are receiving a total of 24 weeks of treatment with GS-7977 plus ribavirin. These data, along with a full review of the 12-week treatment results in QUANTUM, have not yet been formally presented.

In concluding his ELECTRON presentation, Gane reiterated that 88 percent of genotype 1 patients starting therapy for the first time achieved SVR 4 following 12 weeks of therapy with GS-7977 plus ribavirin. “This result,” he noted, “suggests that 12 weeks of GS-7977 plus ribavirin can potentially provide higher rates of SVR in treatment-naive genotype 1 patients than those achieved with longer durations of protease inhibitor plus pegylated interferon and ribavirin therapy.”

The combination of GS-7977 plus ribavirin, he added, was well tolerated. The most common side effects, occurring in no more than 4 percent of genotype 1 patients starting therapy for the first time, were fatigue, dizziness, headache, lymphocyte abnormalities and white blood cell count

changes.

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