Liver Conference Previews the Future of Hep C Treatment

Highlights from the 50th Annual Meeting of the European Association for the Study of the Liver.

May 18, 2015 By Benjamin Ryan

In the fast-changing field of hepatitis C virus (HCV) treatment, pharmaceutical companies are in a mad dash to develop improved therapies as they seek to tap into the hugely lucrative market. The annual International Liver Congress, which this year took place in Vienna, Austria, from April 22 to 26, gives a picture of what the future of hep C treatment may look like.

While meetings in recent years provided a more general hope that interferon would fall by the wayside and that cure rates would rise above 90 percent for many people with hep C, the 2015 gathering focused more on fine-tuning the armamentarium against the virus. After all, Gilead Sciences' Harvoni (ledipasvir/sofosbuvir), approved by the U.S. Food and Drug Administration (FDA) in October 2014, already boasts near-perfect cure rates. But the fixed-dose combination pill is thus far only approved for genotype 1 in the United States. (It is also approved for genotype 4 in Europe.) So the current research battle is for highly effective treatments targeting other genotypes, as well as for those who have advanced liver disease, who have had liver transplants, or who have other serious health problems. In addition, pharma companies are seeking to chisel away at the treatment times required to K.O. the virus.

To follow are major highlights from the treatment front, as reported at the conference. Click on the hyperlinks for more information about any of the studies.

Daclatasvir:

The combination of Bristol-Myers Squibb's daclatasvir and Gilead's Sovaldi (sofosbuvir), plus or minus ribavirin, is likely to gain FDA approval to treat genotype 3 of hep C in the fall. As reported at the liver conference, the regimen has shown varying degrees of promise in a wide array of treatment groups.

Researchers reported promising preliminary results of a trial of daclatasvir and Sovaldi, given with or without ribavirin, among people with genotype 3 who had advanced liver disease or other serious complications related to hep C. A relatively high proportion of those with this difficult-to-treat genotype achieved a sustained virologic response four weeks after completing therapy.

Known as an SVR4, this milestone indicates a high likelihood that these individuals will make it another eight weeks to achieve an SVR12, which is considered a cure. Out of those treated for 12 weeks, 76 percent of the cirrhotic participants and 92 percent of the non-cirrhotic participants achieved an SVR4. In the 24-week treatment group, 88 percent of the cirrhotic participants and 83 percent of the non-cirrhotic participants achieved an SVR4.

In the phase III ALLY-1 trial, which included people with any genotype as well as those with advanced liver disease or recurring virus after a liver transplant, the participants took all three drugs for 12 weeks. Eighty-three percent of those with cirrhosis achieved an SVR12. While over 90 percent of participants with Child-Pugh class A or B were cured, those with the more advanced class C had only a 56 percent cure rate. Ninety-four percent of the post-transplant group was cured.

The Phase III ALLY-2 trial comprised HIV/HCV coinfected people with genotypes 1 through 4, including those with cirrhosis, who were treated without ribavirin for 12 or eight weeks. Overall, 97 percent of those who took 12 weeks of treatment were cured, including all of the small groups of people with genotypes 2, 3 and 4. Just 76 percent of those who took eight weeks of therapy, all of whom had genotype 1, were cured.

A large trial of people with genotype 1 of the virus, including people with cirrhosis, showed largely excellent cure rates. Among those who took ribavirin in the trial, a respective 100 percent and 97 percent of those treated for 12 and 24 weeks achieved an SVR4. For those who did not take ribavirin, the respective SVR4 rates after 12 and 24 weeks of treatment were 82 percent and 94 percent.

Grazoprevir/Elbasvir:

Merck's investigatory direct-acting antivirals, grazoprevir and elbasvir, which the company hopes to market as a fixed-dose combination tablet, showed largely excellent cure rates in various groups of participants.

In the C-EDGE trial, 12 or 16 weeks of grazoprevir and elbasvir, given with or without ribavirin, cured over 90 percent of an array of subgroups of people with genotypes 1, 4 or 6 of hepatitis C. The study included those coinfected with HIV and those with and without cirrhosis. Exceptions to the high cure rates included: those with genotype 6 treated for 12 weeks without ribavirin, who had an 80 percent cure rate; those with cirrhosis treated for 12 weeks, who had an 89 percent cure rate regardless of whether they took ribavirin; those with genotype 4 treated for 12 weeks without ribavirin, who had a 78 percent cure rate; and those treated for 16 weeks without ribavirin, among whom 60 percent were cured if they had genotype 4 and 75 percent were cured if they had genotype 6.

The Phase II C-SALVAGE trial saw a 96 percent cure rate following 12 weeks of all three drugs given to treatment-experienced people with genotype 1, including those with cirrhosis. Ninety-four percent of those with compensated cirrhosis were cured.

In the Phase II/III C-SURFER trial, 12 weeks of grazoprevir and elbasvir cured 99 percent of those with genotype 1 of hep C and advanced kidney disease, including those with stages 4 and 5 of chronic kidney disease who were either treatment experienced or treatment naive. The trial included those with and without cirrhosis.

Shorter Treatment Lengths:

The Phase II C-SWIFT study gave grazoprevir/elbasvir and Sovaldi to participants for various lengths of time, curing high rates of treatment-naive people with genotype 1 or 3 after eight weeks of treatment. Ninety-four percent of those with genotype 1 and cirrhosis were cured, as were 93 percent of the non-cirrhotic participants with genotype 3.

Gilead Sciences had success with a six-week regimen in a Phase II study of a fixed-dose combination of Sovaldi and GS-5816 plus GS-9857 among easier-to-treat people with genotype 1. However, the regimen was less successful among those with cirrhosis and especially people who had failed a previous treatment. Ninety-three percent of the treatment-naive, non-cirrhotic participants were cured, as were 87 percent of the treatment-naive cirrhotic participants and 67 percent of the treatment-experienced group.
