2014 AASLD Liver Conference Round-Up

The Annual Meeting of the American Association for the Study of Liver Diseases (AASLD) in Boston included a trove of good news for people with hep C.

December 15, 2014 By Benjamin Ryan

Each year liver experts converge for a major conference that for the past few years has heralded major advancements in hepatitis C virus (HCV) care and treatment. The 2014 Annual Meeting of the American Association for the Study of Liver Diseases in Boston, also known as the Liver Meeting, was no different. Here are some highlights and major themes from the hep C research presented at the conference.

Harvoni keeps going strong

Gilead Sciences' single-pill, once-daily combination regimen Harvoni (ledipasvir/sofosbuvir), which the U.S. Food and Drug Administration (FDA) approved in October, cured high rates of several key demographics of people with hep C in various studies. The pill contains the NS5A inhibitor ledipasvir and the nucleotide analog polymerase inhibitor sofosbuvir, the latter of which is FDA approved as an individual agent under the brand name Sovaldi.

In the ERADICATE trial, 12 weeks of Harvoni led to a sustained virologic response 12 weeks after completing therapy (SVR12, considered a cure) in 49 out of 50, or 98 percent, of people with genotype 1 of hep C who were coinfected with HIV. About a quarter of the participants had advanced fibrosis.

In another study, of 155 cirrhotic people with genotype 1 of hep C, all of whom had failed at least two previous cure attempts, 96 percent of those randomized to take Harvoni and ribavirin for 12 weeks were cured, as were 97 percent of those assigned to 24 weeks of just Harvoni. (In other words, ribavirin cut treatment time in half without sacrificing efficacy.)

In a third trial, 12 weeks of Harvoni plus ribavirin cured a respective 73 percent and 89 percent of 50 cirrhotic and noncirrhotic treatment-experienced people with genotype 3 of the virus (which has emerged as the new difficult-to-treat genotype). Meanwhile 12 weeks of the drug without ribavirin cured 96 percent of 25 treatment-naive and treatment-experienced people with genotype 6.

Good news for genotype 4

A pair of studies showed promise that genotype 4 of hep C should be easier to treat. In the SYNERGY trial, 21 people with genotype 4 took Harvoni for 12 weeks. Thirty-eight percent of them had been treated before (but not with direct-acting antivirals). Ten percent had advance fibrosis and 33 percent had compensated cirrhosis. Twenty of the participants were cured, for an SVR12 rate of 95 percent. The cure rate likely would have been 100 percent, but one person stopped treatment after the first dose.

AbbVie's "3D" regimen also posted high marks in the PEARL-1 study. Forty-two treatment-naive and 49 treatment-experienced people with genotype 4 of hep C took 3D plus ribavirin for 12 weeks. In addition, 44 treatment-naive people with genotype 4 took just 3D for 12 weeks.

The 3D regimen consists of a coformulated, once-daily pill of the protease inhibitor paritaprevir (ABT-450), the NS5A inhibitor ombitasvir (ABT-267) and Norvir (ritonavir), which is taken with the twice-daily non-nucleoside polymerase inhibitor dasabuvir (ABT-333).

All 91 of those who took ribavirin were cured, compared with 40 out of 44 (91 percent) of those who did not take ribavirin.

The U.S. Food and Drug Administration is expected to issue a decision about 3D's approval in the coming days.

Short treatment times

The race to develop hep C therapies requiring less than 12 weeks of treatment is gathering steam. Some people with hep C may already be able to take Harvoni for just eight weeks. And three new studies presented at the liver conference showed promise that other combination therapies may also succeed with such a short treatment time. However, attempts at curing the virus in just six or four weeks generally came up short.

Eight weeks of Achillion's NS5A inhibitor ACH-3102 plus Sovaldi cured all 12 participants with genotype 1 of hep C in recent trial.

The same treatment length for Sovaldi and Gilead's NS5A inhibitor GS-5816 (given at either 25 milligrams or 100 mg), cured 81 percent of participants on the higher dose who also took ribavirin and 90 percent those taking the higher dose of GS-5816 with no ribavirin. Eighty-eight percent of genotype 2s were cured with the high-dose regimen, regardless of whether they took ribavirin. In another study with an identical design, among people with genotype 3 who took ribavirin, 88 percent of those taking the low dose and 100 percent of those the high dose of GS-5816 were cured. The respective cure rates were 96 percent and 100 percent among those who did not take ribavirin.

A four-week regimen of Merck's fixed-dose combination therapy of the NS3/4A protease inhibitor grazoprevir and the NS5A replication complex inhibitor elbasvir, plus Sovaldi, given to treatment-naive people with genotype 1, posted very poor interim data in the C-SWIFT trial, with just 39

percent on a likely path to a cure. Data for those taking the combination for six weeks were more promising, with 80 and 87 percent of cirrhotic and noncirrhotic participants, respectively, likely to be certified cured. The good news was that 95 percent of cirrhotic participants treated for eight weeks will probably be cured by the end of the trial.

Post-liver transplant outlook

After a liver transplant, if someone hasn't already been cured of hep C, the virus will invariably reinfect the new liver. New research shows that treating post-transplant individuals with Sovaldi and Janssen's NS3/4A protease inhibitor Olysio (simeprevir)—a combination the FDA recently approved—means a very good chance at a cure, according to preliminary results from one study. A total of 109 people are being treated for 12 weeks with the two drugs, with about a quarter of the participants also receiving ribavirin.

Of the 101 participants who finished treatment at the time the data was assessed, 99 (98 percent) had an undetectable viral load upon completion. Eighty-three out of 90 participants (92 percent) who made it four weeks after completing therapy achieved a sustained virologic response (SVR4), which indicates a high likelihood that they will eventually be pronounced cured. Sixty out of 66 participants (91 percent) who made it 12 weeks past the end of therapy achieved an SVR12, indicating they are cured.

BMS tries to stay competitive

Bristol-Myers Squibb (BMS), which recently withdrew its application to the FDA for approval of a combination regimen of asunaprevir and daclatasvir to treat genotype 1b—presumably because the combination fared poorly in comparison with the current crop of drugs that are either on the market or near the end of the pipeline—has reason to hope it can stay in the hep C game, according to research presented in the conference.

In the UNITY-1 trial, 312 treatment-naive participants and 103 treatment-experienced participants took 12 weeks of BMS's "TRIO" regimen: a fixed-dose combination pill of the NS5A replication complex inhibitor daclatasvir, the NS3 protease inhibitor asunaprevir and the non-nucleoside NS5B polymerase inhibitor beclabuvir. Ninety-one percent of the participants were cured, including 92 percent of the treatment-naive participants and 89 percent of the treatment-experienced participants.

BMS is working with the FDA on providing evidence of the effects of daclatasvir in combination with other hep C drugs, such as the results of the ALLY-3 trial: A total of 152 people with genotype 3 took daclatasvir and Sovaldi for 12 weeks; 101 participants were treatment naive and 51 were treatment experienced. Ninety percent of the treatment-naive participants and 86 percent of the treatment-experienced participants were cured.