Major Liver Meeting Points to Continued Progress in Hep C Fight

Highlights from presentations at the Annual Meeting of the American Association for the Study of Liver Diseases (AASLD) in San Francisco.

December 14, 2015 By Benjamin Ryan

For the last several years, the Annual Meeting of the American Association for the Study of Liver Diseases (AASLD) has heralded exciting scientific developments in hepatitis C virus (HCV) treatment. Today, as many such advancements have come to fruition and hep C is increasingly easy to treat, news of further scientific progress continues to roll in.

The major pharmaceutical players in the field, including Gilead Sciences, AbbVie, Bristol-Myers Squibb (BMS), and Merck, all presented findings at the conference about drug regimens that fine-tune treatment for the virus and address the needs of certain segments of the hep C population that still don't respond as well to therapy as the majority.

In addition, researchers presented results from research that adds greater understanding to the liver health-related benefits of a hep C cure.

Below is a summary of major research presented at the conference. To read about each study in greater detail, click the hyperlinks.

Liver Health

Two studies in particular illuminated how curing hep C may improve the health of the liver and dial back some of the damage inflicted by the virus. One found that people with advanced fibrosis or cirrhosis who kick the virus to the curb often see their fibrosis score drop by at least one point. (Fibrosis has five stages in the so-called Metavir scoring system, from F0 to F4. F3 means advanced fibrosis and F4 is synonymous with cirrhosis.) Other researchers concluded that curing hep C may keep people with decompensated cirrhosis, the more advanced form of cirrhosis, from needing a liver transplant.

Gilead Sciences

Hep C industry kingpin Gilead flexed its muscles at the conference, showing considerable evidence

that the company will continue to dominate the field in 2016. In September, Gilead released an overview of findings from its four-part Phase III research program, called ASTRAL, investigating the once-daily, fixed-dose combination of the nucleotide analog polymerase inhibitor Sovaldi (sofosbuvir) and the investigational pangenotypic NS5A inhibitor velpatasvir for the treatment of genotypes 1 through 6. This combo tablet is essentially an upgrade of Gilead's Harvoni (ledipasvir/sofosbuvir), swapping velpatasvir for ledipasvir to allow treatment of all the major genotypes of the virus.

Gilead applied for FDA approval for the new tablet in October.

The trial results provided in September showed that Sovaldi/velpatasvir essentially works as well as Harvoni (which is approved for genotypes 1, 4, 5, and 6), curing most study participant groups 94 to 100 percent of the time.

The AASLD conference saw more detailed results from the ASTRAL trials, including the ASTRAL-4 study, which included 267 participants with decompensated cirrhosis who had all genotypes except 5. They were randomized to take: 12 weeks of Sovaldi/velpatasvir; the tablet plus ribavirin for 12 weeks; or 24 weeks of the tablet alone. Eighty-three percent of the first group was cured, compared with 94 percent in the second group, and 86 percent in the third. There was no statistically significant difference between these results, however, meaning that the difference between them could have occurred by chance.

Results were also presented at the conference from a study of Harvoni paired with Gilead's investigational NS3/4A protease inhibitor vendroprevir, with or without ribavirin, given for eight weeks to people with genotype 1 and advanced liver disease. The regimen boasted a 96 percent cure rate.

AbbVie
To follow up on Viekira Pak (ombitasvir/paritaprevir/ritonavir; dasabuvir), AbbVie is developing a regimen including the NS3/4A protease inhibitor ABT-493 and the NS5A inhibitor ABT-530. Researchers presented selected findings at AASLD from the ongoing Phase II SURVEYOR-I and -II trials of eight- and 12-weeks of the regimen, given with or without ribavirin. Both presentations only looked at results of those treated for 12 weeks.

The SURVEYOR-I study results focused on people with genotype 1, both with and without cirrhosis. Between 97 and 100 percent of them were cured. The SURVEYOR-II results looked at people with genotype 2 or 3 who did not have cirrhosis. Between 96 and 100 percent of those with genotype 2 were cured, as were 93 to 94 percent of those with genotype 3.

Bristol-Myers Squibb
In July, the U.S. Food and Drug Administration (FDA) approved a combination of BMS's Daklinza (daclatasvir) and Sovaldi to treat genotype 3, the first treatment regimen green-lit for that genotype.

At AASLD, researchers presented findings from the Phase IIIb ALLY-3+ study of 12 or 16 weeks of Daklinza and Sovaldi plus ribavirin among hard-to-treat people with advanced fibrosis or cirrhosis. All those with F3 fibrosis were cured, regardless of treatment length, while a respective 83 percent and 89 percent of those with cirrhosis were cured when treated for 12 and 16 weeks.

Looking at treatment for those coinfected with hep C and HIV, researchers conducted a systematic literature review of the ALLY-2 trial of Daklinza and Sovaldi and the PHOTON-1 and PHOTON-2 studies of Sovaldi and ribavirin. After pooling the results, and adjusting the pool to account for differences between the various groups of participants, the researchers found that 12 weeks of Daklinza and Sovaldi cured HCV in 99.99 percent of coinfected individuals, while the cure rate after 12 weeks of Sovaldi and ribavirin was only 84.6 percent.

Merck

Merck applied for FDA approval in June of the fixed-dose combination of the NS3/4A protease inhibitor grazoprevir and the NS5A replication complex inhibitor elbasvir to treat those with genotypes 1, 4 and 6 of the virus. A decision is likely in the coming weeks.

At AASLD, researchers presented findings from the double-blind, placebo-controlled Phase III C-EDGE CO-STAR study of elbasvir/grazoprevir among people with genotypes 1, 4 or 6 who inject drugs and who are receiving opioid agonist therapy. In a modified analysis, 96 percent of those with genotype 1a, 97 percent of those with genotype 1b, 100 percent of those with genotype 4 and 60 percent of those with genotype 6 were cured. (There were only five people with genotype 6 in the study, so the cure rate for that group is not the most statistically reliable.)

Three-Week Treatment

It may be possible for some individuals who respond very quickly to hep C drugs to get away with just three weeks of treatment. Researchers presented findings from the pilot, response-guided, open-label SODAPI study of triple therapy involving an NS3 protease inhibitor plus dual NS5A-NS5B nucleoside inhibitors, given to 26 non-cirrhotic individuals with genotype 1b. They were treated with: Harvoni and BMS's experimental asunaprevir; Sovaldi, Daklinza and Janssen's Olysio (simeprevir); or Sovaldi, Daklinza and asunaprevir.

Eighteen participants whose viral loads dropped below 500 after 48 hours of first being treated received just three weeks of treatment. All of them were cured. The other participants were treated for eight or 12 weeks.

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