The 2016 Hepatitis C Treatment Research Pipeline

What *new therapies are the major players in hepatitis C pharmaceuticals developing?*

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The extraordinarily lucrative hepatitis C virus (HCV) treatment market has inspired a frantic level of competition between a handful of pharmaceutical companies. Since releasing Sovaldi (sofosbuvir) in late 2013 and Harvoni (ledipasvir/sofosbuvir) in late 2014, Gilead has dominated the field, and appears poised to continue doing so in 2016 as the company awaits the U.S. Food and Drug Administration's (FDA) mid-year decision about yet another new treatment.

Meanwhile, several other companies are nipping at Gilead's heels, and at the very least are eager to develop therapies that have been well-studied in subpopulations of people with hep C who still have a need for improved treatments. Another major goal is a shorter treatment length. Many people can take Harvoni for just eight weeks; otherwise 12 or sometimes 24 weeks are in order. Pharmaceutical companies are looking for more eight-week treatments, and are even trying to develop six-week therapies.

To read a feature article on all of the hep C drugs, and expanded uses for existing treatments, that are awaiting FDA approval, click here.

Gilead Sciences:

Gilead is waiting on U.S. Food and Drug Administration (FDA) approval of its fixed-dose, once-daily, pangenotypic (meaning it works on all genotypes) combination tablet that includes Sovaldi and the investigational pangenotypic NS5A inhibitor velpatasvir. A decision is expected June 28.

Otherwise, the company is studying the Sovaldi/velpatasvir tablet in combination with the investigational pangenotypic NS3/4A protease inhibitor GS-9857. Gilead recent moved the triple combo treatment into Phase III trials, which include people with genotypes 1 or 3 of hep C.

At the November 2015 Annual Meeting of the American Association for the Study of Liver Diseases (AASLD) in San Francisco, Gilead presented findings from the Phase II trials of Sovaldi/velpatasvir plus GS-9857. The results offered hope for the development of shorter treatments, and also for difficult-to-treat individuals who have been treated before. Among those trial participants with cirrhosis and genotype 1 or 3 who had previously been treated with an interferon and ribavirin

combination, 100 percent were cured after eight weeks of treatment. The cure rate was 89 percent among people with genotype 1 who had previously been treated with a protease inhibitor.

AbbVie:

Viekira Pak (ombitasvir/paritaprevir/ritonavir; dasabuvir) and Technivie (ombitasvir/paritaprevir/ritonavir) comprise AbbVie's portfolio of approved therapies.

AbbVie is currently enrolling participants in six global Phase III clinical trials of a once-daily pangenotypic regimen including the NS3/4A protease inhibitor ABT-493 and the NS5A inhibitor ABT-530. They are testing eight or 12 weeks of the regimen among people with genotypes 1 through 6, and plan to recruit 1,600 participants from 27 countries. Four of the studies, collectively called ENDURANCE, will include people without cirrhosis who are treated with regimens up to 12 weeks long. The two EXPEDITION trials will include difficult-to-treat groups, all of them treated for 12 weeks. One trial will include those with compensated cirrhosis and all of the six genotypes but genotype 3. (AbbVie is evaluating treatment of genotype 3 cirrhotics in the separate SURVEYOR-2 study.) The other trial will include people with all genotypes who have severe kidney impairment or end-stage kidney disease, including some participants with compensated cirrhosis.

The company presented results at the AASLD conference from the ongoing Phase II SURVEYOR-1 and -2 studies of eight or 12 weeks of ABT-493 and ABT-530. Ninety-seven to 100 percent of those with genotype 1 were cured, as were 96 percent to 100 percent of those with genotype 2, and 83 percent to 94 percent of those with genotype 3.

Merck:

The FDA recently approved Merck's once-daily combination tablet Zepatier (grazoprevir/elbasvir) to treat genotypes 1 and 4 of hep C.

At AASLD, Merck announced results from Part A of two Phase II trials, C-CREST-1 and -2, in which a combination of grazoprevir, MK-3682 (at either 300 milligrams or 450 mg) and either elbasvir or MK-8408, given for eight weeks, for the most part cured more than 90 percent of participants who did not have cirrhosis and had not been treated before. Those with genotype 2 had a 94 percent cure rate when taking grazoprevir, MK-8408 and MK-3682 (450 mg), but only 60 percent to 71 percent with other combination treatments.

Merck is moving into Part B of C-CREST-1 and -2 with the triple combination regimen of grazoprevir, MK-3682 and MK-8408. C-CREST-1 will evaluate eight, 12 or 16 weeks of grazoprevir, MK-3682, and MK-8404, with or without ribavirin, among people with genotype 1 or 2, some of whom have cirrhosis. C-CREST-2 will test eight, 12 or 16 weeks of grazoprevir, MK-3682, and MK-8408, with or without ribavirin, among those with genotype 3, some of whom have been treated before and some of whom have cirrhosis. Lastly, Merck is studying grazoprevir, MK-3682 and MK-8408, given for 16 weeks with ribavirin or 24 weeks without ribavirin among cirrhotic and non-cirrhotic people with genotype 1 or genotype 3 who have failed a direct-acting antiviral regimen (the modern class of hep C drugs that were first introduced in 2011).

Bristol-Myers Squibb:

The manufacturer of Daklinza (daclatasvir), Bristol-Myers Squibb (BMS), recently received FDA approval for an expansion of the indicated uses for the drug, which is used in combination with Sovaldi. Now, in addition to being approved to treat those with genotype 3, the two-drug regimen may be used by those with genotype 1, as well as those with advanced cirrhosis and individuals with hep C that has returned following a liver transplant.

According to BMS spokesperson Robert Perry, the company has chosen not to develop new hep C treatments, instead focusing on research of the real-world effectiveness of Daklinza and on clinical trials that expand the populations of those approved to take the therapy.

Janssen and Achillion:

Janssen's Olysio (simeprevir) is approved to treat genotype 1 or 4 of hep c in combination with Sovaldi.

In May 2015, Janssen and Achillion announced a collaboration to develop hep C drugs with the hopes of producing a treatment that works on multiple genotypes and requires a shorter treatment time. Drugs included as part of the collaboration are the NS5A inhibitor odalasvir, the NS3/4A protease inhibitor sovaprevir and the NS5B polymerase inhibitor and ACH-3422 for the treatment of genotype 1.

One ongoing Phase II trial includes Olysio (simeprevir), odalasvir and the nucleotide analog NS5B polymerase inhibitor ALS-335, given to those with genotype 1. The plan is to get this combination into Phase III trials by 2017.

Interim results from a Phase II trial showed that all 18 people with genotype 1, none of whom had been treated before, were cured after six weeks of once-daily odalasvir and Sovaldi.

Janssen will have the exclusive, worldwide right to develop the drugs studied in collaboration with Achillion. And if hep C therapies from the collaboration are approved, Janssen will have the exclusive right to commercialize them globally.
