The FDA Makes Hepatitis C a Priority

Recognizing that investigational drugs from three pharmaceutical companies show advantages over existing hepatitis C therapies, the FDA has sped up its development and review process for the therapies.

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With pharmaceutical companies clamoring to bring to market second-generation direct acting antivirals (DAAs) for the treatment of hepatitis C virus (HCV), the U.S. Food and Drug Administration (FDA) has recently given a trio of companies a significant leg up. Two promising investigational agents—Gilead Sciences' nucleotide analogue inhibitor sofosbuvir and Janssen's protease inhibitor simeprevir—each received what is known as a priority review status from the FDA over the past few weeks. And in early May, the FDA tapped AbbVie's interferon-free combination therapy, ABT-450/r, ABT-267 and ABT-333 (which has been studied both with and without ribavirin) as a "breakthrough therapy," qualifying those drugs for an expedited development and review process in preparation for FDA approval.

The FDA grants priority review to drugs in development that appear to offer significant advantages over available therapies. As of now, there are two FDA-approved DAAs to treat hep C: Incivek (telaprevir) and Victrelis (boceprevir), each of which cures about 50 to 75 percent of those who undergo therapy lasting between 24 and 48 weeks. Both must be taken with ribavirin and also interferon, an injectable drug that often causes difficult, flu-like side effects. So at this stage, the FDA's imprimatur for the investigational therapies, while not necessarily a promise of the final stamp of approval, marks an official recognition that the research indicates these new drugs will likely improve on the current crop of therapeutic options on various fronts.

Simeprevir, for one, has shown in clinical trials to have somewhat higher cure rates than today's DAAs, but its major advancements are in its once-a-day dosing, its reduction of side effects and its shorter duration of therapy. Sofosbuvir, meanwhile, has been a champion of sorts throughout the clinical trials process, consistently boasting high cure rates when used in combination with other drugs in development: either Bristol-Myers Squibb's daclatasvir or Gilead's own ledipasvir (the company has longer-range plans to develop sofosbuvir and ledipasvir as a fixed-dose pill).

For practical purposes, the priority review is intended to cut down the FDA's review process, which begins 60 days after a new drug application (NDA) is filed, from the standard 10 months to six. Companies that receive priority review also get additional guidance from the FDA to expedite the development and approval process. On March 28, Janssen filed its NDA for simeprevir, to be taken

with ribavirin and interferon for treatment of those with genotype 1 of hep C; as such, the company expects an answer from the FDA in late November. Gilead is just a couple weeks behind in the same process; it's seeking approval for sofosbuvir to be administered as an all-oral therapy with ribavirin among those with genotype 2 or 3, and in combination with ribavirin and interferon for genotypes 1, 4, 5 and 6.

By comparison, Incivek and Victrelis each received priority review designation in January 2011 and were approved in May that same year.

Achieving breakthrough therapy status, on the other hand, promises a more dynamic range of benefits to AbbVie, which is the first company developing an HCV therapy that has received the designation. Intended to expedite the development and review of investigational drugs when clinical trial data shows they promise at least one significant improvement over currently available treatments, the designation means AbbVie receives, for starters, fast track designation. This allows a pharmaceutical company to submit elements of its marketing application before submitting its complete application for the drug. Among other benefits, the breakthrough therapy designation also grants AbbVie more FDA involvement in the combo therapy development—for example, by providing increased access to the agency's senior management, as well as giving practical advice and helping design clinical trials that are as efficient as possible.

Alan Franciscus, executive director of the Hepatitis C Support Project in San Francisco, said that AbbVie's breakthrough status was awarded "clearly because of the less frequent dosing and pill burden, lower side effects and high cure rates" when compared with Incivek and Victrelis.

"I believe that this will greatly accelerate the approval process, especially if the FDA has stated that they will provide guidance during the development and approval process," Franciscus says.

But even with all this extra help, AbbVie's combo is still running behind its competitors, not having submitted an NDA. Furthermore, sofosbuvir and simeprevir have been researched as an interferon-free combination therapy with one another: Taken with or without ribavirin, they were found in a recent study to boast high cure rates among those with genotype 1 of hep C. If both drugs receive FDA approval, clinicians are free to prescribe them together off-label, providing yet another option outside the FDA-sanctioned uses for people with hep C.

Daniel Fierer, MD, an assistant professor of medicine in infectious diseases at Mount Sinai School of Medicine in New York City, projects that "since simeprevir and sofosbuvir were already expected to hit the market soonest, probably at the same time, the only thing I can see is that maybe AbbVie moves up its timeline a little. But if it doesn't move it up to being out before [Janssen's simeprevir and Gilead's sofosbuvir] come to the table, they will start eating without AbbVie, and then it'll be leftovers for lunch."

Indeed, there is much excitement over these drugs in the pipeline, as well as over the larger wave of interferon-free regimens that should arrive a bit further down the line. Franciscus acknowledges this but also hopes that the hubbub doesn't distract physicians from the hep C patients who have

urgent therapeutic needs.

“What really scares me is that people with HCV and their medical providers are waiting for the interferon-free drug approval, but there are definitely some people who should be treated now—it could be dangerous to wait,” he says. “There is never a guarantee that the interferon-free drugs will work for everyone.”

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