Shorter Treatment Strategy Beats Hepatitis C

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By Ed Susman , Contributing Writer, MedPage Today

BOSTON -- A 6-week treatment regimen appeared to be as effective as the more standard 12 weeks of therapy for patients with hepatitis C virus infection, researchers reported here at the annual Conference on Retroviruses and Opportunistic Infections.

In a pilot study that treated 20 patients in each of three arms, all patients treated with the combination of sofosbuvir (Sovaldi, nucleotide NS5B inhibitor) 400 mg with ledipasvir (NS5A inhibitor) 90 mg once daily for 12 weeks achieved a sustained virologic response at 12 weeks' post-treatment (SVR12), reported Anita Kohli, MD, an infectious disease fellow at the National Institutes of Health Clinical Center in Bethesda, Md.

But she also noted that two regimens using the same backbone and adding either the investigative agent GS-9669 (non-nucleoside NS5B inhibitor) 500 mg once daily or GS-9451 (a protease/NS3/4 inhibitor) 80 mg once daily for 6 weeks had similar outcomes: 95% of patients on GS-9669 achieving an SVR12, and 100% of patients on GS-9451 achieving an SVR12.

The one patient in the study who failed to achieve an SVR12 relapsed before SVR4; that individual had stage 3 liver disease, a high viral load, and unfavorable genotype, Kohli said.

All patients in all 3 arms were naive to treatment for hepatitis C virus. All patients were included in the 12-week arm, but patients diagnosed with cirrhosis were excluded from the 6-week trials.

"These results are not statistically significantly different from each other," Kohli told *MedPage Today* at a press briefing sponsored by the conference organizers.

"We find these results very promising. This was a pilot study," Kohli said. "We will follow these patients out to 48 weeks to see if the results are maintained."

A cure in the context of HCV is a sustained virologic response -- defined as undetectable viral RNA at some prespecified point after ending therapy, usually 12 or 24 weeks.

"What we have learned from this trial is that we can treat patients for shorter durations of therapy and we see that 6 weeks is effective," Kohli said.

"Secondly, these regimens are very simple -- 1, 2, or 3 pills a day. Third, our patient population is one that is historically very difficult to treat -- more than 80% of the patients were African American, most had genotype 1a, most had high viral loads, 25% to 30% of the patients had advanced-stage liver disease.

"The reason we wanted to look at the short-duration therapies is because we think it is very important in treatment of hepatitis C globally in limited resource settings. We really need very simple treatments for the 150 million to 180 million people globally," she said.

All the treatment regimens avoided the use of interferon, once the mainstay of treatment of hepatitis C virus, but a therapy that is difficult to tolerate for many patients. The use of interferon-free directly acting

antiviral agents is an emerging approach to improve the efficacy and tolerability of therapy for hepatitis C virus, Kohli said.

However, she noted that the efficacy of interferon and ribavirin-free regimens shorter than 8 to 12 weeks has not been reported. One study evaluating sofosbuvir, ledipasvir, and ribavirin for 6 weeks showed an SVR12 rate of only 68%, she said. She also noted that the optimal combination of directly acting antiviral agents not been established.

Press conference moderator Jean-Michel Pawlotsky, MD, PhD, professor of medicine at Hopital Henri Mondor Creteil/University of Paris-Est, told *MedPage Today* that, while the results of the SYNERGY trial look interesting, they are not ready for routine implementation.

"There are very small numbers in this study," he said. "We have to see how this will apply to real-life patients. The danger is always to undertreat patients. If the time is too short and it works in a trial and you start treating real-life patients you can have failures. So we really need to extend this trial. It is interesting because it shows that some people can be cured in a very short duration of treatment."

Pawlotsky said he would not be comfortable treating his patients in this manner without more extensive studies.

Ledipasvir is not currently approved in the U.S. Its manufacturer, Gilead, filed last month for FDA approval of the drug in a fixed-dose combination with sofosbuvir.