HCV Drug Combo Promising All on Its Own

By Michael Smith, North American Correspondent, MedPage Today
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BOSTON – A three-drug regimen that eliminated both standard hepatitis C drugs has yielded positive early results in hard-to-treat patients, a researcher reported.

In treatment-naive patients with viral genotype 1 – most of them with the difficult 1a variant – the virus was undetectable in 94% of patients at 4 and 12 weeks after the end of therapy, according to Gregory Everson, MD, of the University of Colorado in Aurora.

There have so far been no viral breakthroughs on treatment or relapses afterward, Everson told a late-breaker session at the annual meeting here of the American Association for the Study of Liver Diseases.

But he cautioned that the findings are interim results of a small trial with the three drugs: once-daily daclatasvir, an NS5A replication complex inhibitor; twice daily asunaprevir, an NS3 protease inhibitor; and twice-a-day BMS-791325, a non-nucleos(t)ide NS5B polymerase inhibitor.

The three-drug combination is intended to overcome a perceived failure of the first two – daclatasvir and asunaprevir – to treat patients with genotype 1a in the absence of the standard therapy, pegylated interferon and ribavirin.

The standard therapy yields sustained virologic responses in no more than half of patients with genotype 1, although adding either of the approved direct-acting agents – telaprevir (Incivek) and boceprevir (Victrelis) – improves those outcomes markedly, at least in clinical trials.

But regimens with interferon and ribavirin are difficult to follow, so that real-world effectiveness is much lower, leading to a growing interest in other agents that can be used without the old standbys.

To see if the earlier results can be improved, the researchers are testing the novel three-drug combination – with either 12 or 24 weeks of therapy and at two doses of the BMS-791325.

The primary endpoint of the study is the so-called SVR12 – viral levels too low to be quantified 12 weeks after the end of treatment.

Everson presented results from the first part of the trial, with a 75-mg dose of BMS-791325, in 16 patients treated for 12 weeks and 16 treated for 24 weeks. Three-quarters of each group had genotype 1a virus and the remainder had genotype 1b.

Four weeks after the end of treatment, 94% of patients in both treatment groups had undetectable virus, Everson reported. It's still too early to report SVR12 rates for those in the

24-week treatment group, but all patients who had 12 weeks of therapy maintained their undetectable status out to the SVR12 mark.

Importantly, he said, all of the patients with genotype 1a were undetectable at week four after treatment, although data was missing for one participant in the 24-week treatment group.

The treatment was well tolerated, Everson said, with no discontinuations owing to therapy and no serious adverse events related to the study drugs.

The only disadvantage of the regimen is the twice daily dosing, commented Paul Pockros, MD, of Scripps Clinic in La Jolla, Calif., who was not involved in the study.

The three drugs are well tolerated, especially "compared with what we are used to" with interferon and ribavirin, Pockros told MedPage Today.

And he added that the efficacy results give positive answers to two important questions: Can patients with genotype 1a be treated effectively and can the treatment duration be shortened to 12 weeks?

"It's a viable regimen," he concluded.