Oral HCV Combos Promising

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WASHINGTON -- All-oral combinations of two novel drugs for hepatitis C (HCV) demonstrated promising efficacy in a small clinical trial, a researcher said here.

Combinations of two and three drugs yielded viral cures in 89% or more of patients with HCV genotype, regarded as difficult to treat, according to Eric Lawitz, MD, of the University of Texas Health Science Center in San Antonio.

And the regimens were well tolerated and safe over a 12-week treatment period, Lawitz reported at the annual meeting of the American Association for the Study of Liver Diseases.

Lawitz was reporting on two drugs that so far have no formal names -- MK-5172, an HCV NS3/4A protease inhibitor, and MK-8742, which block the activity of the NS5A replication complex.

The so-called C-WORTHY study compared outcomes in three groups of patients:

- 25 patients with HCV genotypes 1a and 1b, assigned to daily therapy with 100 milligrams of MK-5172, 50 milligrams of MK-8742, and ribavirin, at doses ranging from 600 to 1,400 milligrams.
- 27 patients with the same genotypes, assigned to the same doses of MK-5172 and ribavirin, but a higher dose -- 50 milligrams daily -- of MK-8742.
- 13 patients -- all with genotype 1b -- given MK-5127 and MK-8742, at 100 and 50 milligrams, respectively, but no ribavirin.

The primary endpoint of the study was the proportion of patients who had undetectable virus 12 weeks after the end of treatment, the so-called SVR_{12}.

In the first group, that proportion was 96%; one patient stopped treatment early, Lawitz said.

In the second group, the proportion reaching SVR_{12} was 89%; two patients stopped early and one relapsed after having undetectable virus at the end of treatment.

In the smallest group, all 13 patients reached an SVR_{12}.

The one patient who relapsed, a 51-year-old woman, had low levels of the drugs in her system, perhaps indicating a "compliance issue," Lawitz said, but she also had viral mutations consistent with drug resistance.

Lawitz said the main adverse effects of the three regimens were fatigue, headache, and nausea. No patients stopped therapy because of adverse events, and there were no grade 3 and 4 lab abnormalities.

The findings support further study of the two drugs in regimens that avoid the two mainstays of current HCV therapy -- intravenous pegylated interferon and oral ribavirin

Standard therapy for HCV has been based for several years on the two drugs, with the recent addition of the protease inhibitors telaprevir (Incivek) and boceprevir (Victrelis).

But because they are regarded as hard to tolerate, investigators have been searching for so-called direct-acting agents -- drugs that target aspects of the virus itself -- that would be sufficiently powerful to cure the disease without them.

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