Ledipasvir Sofosbuvir Combination Cuts Cirrhotic Hepatitis C

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BOSTON — Nearly all patients with cirrhotic chronic hepatitis C infection who failed previous protease-inhibitor-based therapy responded to a fixed-dose combination of ledipasvir and sofosbuvir (Harvoni, Gilead Sciences), with or without ribavirin, investigators report.

The rate of sustained viral response 12 weeks after treatment with the three drugs was 96%, said principal investigator Marc Bourlière, MD, from Hospital Saint Joseph in Marseilles, France. Without ribavirin, the rate was 97%.

Dr Bourlière presented the study results here at The Liver Meeting 2014.

All the patients had hepatitis C genotype 1, compensated cirrhosis, and lower responses to conventional hepatitis C therapies. They had already been unsuccessfully treated with a sequential regimen of pegylated interferon and ribavirin followed by pegylated interferon and ribavirin plus an NS3-4A protease inhibitor — telaprevir (Incivek) or boceprevir (Victrelis).

"When we compare the safety issue with the triple regimen to the treatment with telaprevir or boceprevir, everything changes. For the patients, it's a new life; everything is easy for them," Dr Bourlière said in an interview with Medscape Medical News.

The ledipasvir and sofosbuvir combination is the first oral regimen for the treatment of chronic hepatitis C genotype 1 to be approved by the US Food and Drug Administration. It is also the first approved regimen that does not need to be administered with interferon or ribavirin.

Ledipasvir inhibits NS5A, a nonstructural protein involved in hepatitis C RNA replication. Sofosbuvir is an hepatitis C nucleotide polymerase inhibitor.

The 154 patients who completed the trial were randomized to one of two regimens. Half received the ledipasvir and sofosbuvir combination plus placebo for 24 weeks. The other half received placebo for 12 weeks followed by the ledipasvir and sofosbuvir combination plus ribavirin for 12 weeks.

Shorter Regimen in Hard-to-Treat Patients

The sustained viral response 12 weeks after treatment was 96% for the 24-week combination and 97% for the 12-week combination plus ribavirin. There were three relapses in the 12-week group and two in the 24-week group.

A patient in the 12-week group who withdrew because of sepsis that occurred during the placebo phase was excluded from the efficacy analysis.

The combination was relatively well tolerated, with or without ribavirin. Only two adverse events, headache and fatigue, occurred more frequently with the ledipasvir and sofosbuvir combination than with placebo. Most adverse events were mild to moderate in severity.

The possibility of having an effective but shorter regimen for this hard-to-treat population is particularly appealing, said session comoderator Keith Lindor, MD, from the College of Health Solutions at Arizona State University in Tempe.

"The biggest issue for many of us treating these patients is the cost. What this study shows is that using a third drug that is relatively cheap — ribavirin — for 12 weeks gave similar results to using a more expensive combination for 24 weeks," he told Medscape Medical News.

This study was supported by Gilead Sciences. Dr Bourlière is an advisor and speaker for the company. Dr Lindor has disclosed no relevant financial relationships.

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