Hepatitis C Vaccine Boosted Immune Response

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BOSTON – A therapeutic vaccine against the hepatitis C virus was associated with a significantly higher sustained virologic response rate when added to standard-of-care treatment, and the findings justify further development of the vaccine, Dr. Paul Pockros reported at the meeting.

In the proof-of-concept trial, 133 patients infected with hepatitis C virus (HCV) genotype 1 were randomized to either triple therapy comprising the experimental GI-5005 vaccine, which is designed to elicit a T-cell response specific to HCV, along with pegylated interferon alfa-2b plus ribavirin (P/R), or the standard P/R therapy alone.

The primary outcome measure was sustained virologic response (SVR), defined as undetectable HCV RNA at 6 months after treatment, said Dr. Pockros of the Scripps Clinic in La Jolla, Calif.

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DR. POCKROS

The 68 patients in the experimental group initially received monotherapy with the vaccine, consisting of five weekly injections followed by two monthly injections for a 12-week lead-in period, before progressing to the standard-of-care P/R treatment and once-monthly injections. The 65 patients in the control group received standard-of-care P/R treatment alone.

In both groups, the treatment duration was 48 weeks for treatment-naive patients and 72 weeks for those who had a poor or partial response to prior P/R treatment, said Dr. Pockros. Patients in whom prior P/R therapy induced no notable decrease in HCV viral load, as well as those in whom prior treatment initially resulted in undetectable HCV RNA followed by a viral rebound, were excluded from the analysis.

Among the study's treatment-naive patients, 58% of those who received the vaccine achieved SVR, compared with 48% of those who received P/R alone. Among the prior poor and partial responders, the respective SVR rates in the vaccine and control groups were 17% and 5%, Dr. Pockros reported.

"There was a slight benefit in the treatment-naive and nonresponders, [but] this was numerical only and was not statistically significant," he said. However, the overall benefit in the vaccine vs. control groups was statistically significant, with respective SVR rates of 47% and 35%.

The vaccine strategy appears to be safe. "The most common associated adverse events were mild, transient injection-site reactions," said Dr. Pockros. In addition, "the discontinuation rates due to adverse events were comparable [13%] in both the triple-therapy and standard-of-care arms."

Of particular interest, Dr. Pockros noted, was the T-cell response in a subgroup of difficult-to-treat patients receiving the vaccine. Previous studies have suggested that patients carrying the T allele of the IL28 gene are at high risk of treatment failure with the standard interferon-based therapy. The T-cell response in vaccine-treated patients, as measured by interferon-gamma enzyme-linked ImmunoSpot assay, "mimicked what we saw with a virologic response," he said.

"Four of five T/T allele patients had a T-cell response – one did not actually get treated – but none of the patients who received standard of care had a T-cell response."

Although the findings need to be confirmed in additional studies with larger patient populations, the vaccine will likely be genotype specific, he noted. Future studies will evaluate the efficacy of monotherapy with the vaccine in genotype-specific patients, Dr. Pockros said.

The proof-of-concept study was funded by GlobeImmune, manufacturer of the vaccine. Dr. Pockros disclosed a financial relationship with GlobeImmune. ■