Interleukin 28B (IL28B) testing to predict response to treatment of hepatitis C virus (HCV) infection

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Authors’ conclusions
Hepatitis C virus (HCV) infections, which cause inflammation of the liver and may result in liver fibrosis and cirrhosis, are estimated to affect 2% to 3% of the world’s population, including 2.7 to 4.1 million individuals in the United States. Most individuals with HCV become infected after needlestick injuries, the sharing of hypodermic needles, blood transfusions prior to standard HCV screening, or insufficient infection control in healthcare settings. Many patients with acute HCV infections do not initially exhibit clinical symptoms, and up to 25% will clear the virus spontaneously. However, 75% to 85% of infected individuals progress to having chronic HCV. Clinically, chronic HCV may be associated with abdominal pain, abdominal swelling, jaundice, itching, fatigue, changes in urine or stool color, and nausea or vomiting. Moreover, chronic HCV infections result in a significantly increased risk for liver fibrosis, cirrhosis, and hepatocellular carcinoma, and are the most common reason for liver transplantation. HCV is classified based on the DNA sequence of the virus, since this sequence may be highly variable between HCV patients. HCV is grouped into 6 major genotypes (different versions of DNA sequence), each of which has a different geographic distribution. HCV genotypes 1, 2, and 3 account for the vast majority of HCV cases in the United States and Europe, with genotype 1 being the most common. Until recently, the standard treatment for HCV infections of all genotypes was a combination of pegylated interferon alpha (PegIFN) and ribavirin (RBV). Treatment with PegIFN/RBV results in a sustained viral response (SVR; no evidence of the virus 24 weeks after treatment cessation) in up to 50% of patients with HCV genotype 1, and in 80% to 90% of patients with HCV genotype 2 or 3. However, newer treatment regimens involving PegIFN, RBV, and a direct-acting protease inhibitor—a combination referred to as “triple therapy”—increase the chance of viral response in patients with HCV genotype 1. Recently, studies designed to identify genetic variants associated with an increased likelihood of response to PegIFN/RBV therapy have been conducted with the goal of identifying the most appropriate candidates for treatment with these medications. These studies identified 2 single nucleotide polymorphisms (SNPs; single base pair changes in DNA sequence) near the interleukin 28B gene (IL28B). IL28B is located on chromosome 19 at band q13.13 and encodes the cytokine interferon lambda 3. Specifically, the genotypes of the rs12979860 C/T and rs8099917 T/G SNPs showed a significant correlation with the likelihood of PegIFN/RBV treatment response in patients with chronic HCV. Based on these associations, tests examining 1 or both IL28B SNPs are now clinically available and may be used in patients being considered for treatment with PegIFN/RBV. It is suggested that IL28B SNP testing may provide information to help avoid potentially ineffective therapies and increase the chance of SVR.

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