

Hepatitis C Viral RNA Genotype 1 NS5B Drug Resistance

Test Code: 906679

Specimen Requirements: 2 mL frozen plasma from an EDTA lavender-top tube (0.6 mL minimum).

CPT Code*: 87902

CLINICAL USE

- Identify resistance-associated mutation as potential cause of NS5B inhibitor (sofosbuvir) failure

CLINICAL BACKGROUND

HCV infection affects more than 3.5 million individuals in the United States.¹ Left untreated, it can lead to progressive liver injury, cirrhosis, hepatocellular carcinoma, and the need for liver transplantation. Of the 6 major HCV genotypes, genotype 1 (including subtypes 1a and 1b) is the most prevalent by far in the United States.² Combination therapy with pegylated interferon (PEG) plus ribavirin was the mainstay of treatment for all genotypes, but resulted in low sustained virologic response rates of approximately 40% to 50% in HCV genotype 1-infected patients.^{3,4} In addition, severe adverse effects remain a limitation of PEG-based therapy.

The availability of direct-acting antivirals (DAAs) has led to PEG-free treatment options for all HCV genotypes.⁵ DAAs interrupt HCV replication by targeting specific HCV proteins, such as the NS5A protein, NS5B polymerase, and NS3/4A protease.⁶ DAAs that inhibit NS3/4A (simeprevir, paritaprevir), NS5A (daclatasvir, ledipasvir, ombitasvir), and NS5B (sofosbuvir, dasabuvir) have been approved for treatment of HCV infection and are available in fixed-dose combinations.^{7,8} Additional DAAs in development may expand such options.⁹

The high mutation rate of the HCV genome, combined with selective pressure from ongoing therapy, can lead to selection of HCV variants that are resistant to DAAs.^{10,11} Rare resistance-associated substitutions at codon 282 in the NS5B region have been detected following treatment of genotype 1a or 1b HCV infection with sofosbuvir.¹¹ Additional rare mutations conferring resistance to other anti-NS5B agents have been reported.^{6,12}

The Hepatitis C Viral RNA Genotype 1 NS5B Drug Resistance assay determines the HCV genotype (1a, 1b, or 1) and detects mutations associated with resistance to sofosbuvir. The identification of specific mutations or polymorphisms may be useful to optimize treatment selection.

INDIVIDUALS SUITABLE FOR TESTING

- Individuals with genotype 1 HCV infection who experience treatment failure with sofosbuvir

METHOD

- Reverse transcription polymerase chain reaction (PCR) and DNA sequencing of NS5B codons 270 to 530
- Analytical sensitivity: >95% for viral loads ≥ 700 IU/mL
- Results reported:
 - HCV genotype: 1a, 1b, 1, or not detected (genotypes other than 1 may not be detected)
 - Sofosbuvir resistance: predicted or not predicted

INTERPRETIVE INFORMATION

An interpretation of “resistance predicted” suggests that treatment failure with sofosbuvir may be due to the presence of an NS5B mutation (S282T). An interpretation of “resistance not predicted” indicates that the S282T sofosbuvir resistance mutation was not detected.⁶

Resistance may also be affected by as yet uncharacterized mutations and interactions among mutations. Failure to obtain a genotype may be due to insufficient virus, a non-1 genotype, mutations in the viral genome at the assay priming sites, or the presence of an inhibitory substance in the sample.

References

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* The CPT code provided is based on AMA guidelines and is for informational purposes only. CPT coding is the sole responsibility of the billing party. Please direct any questions regarding coding to the payer being billed.

This test was developed and its performance characteristics have been determined by Focus Diagnostics. Performance characteristics refer to the analytical performance of the test.