HCV GenoSure® Drug Resistance Assay NS3/4A

Monogram BIOSCIENCES
LabCorp Specialty Testing Group

Samuel H. Pepkowitz, MD, Medical Director
345 Oyster Point Blvd
South San Francisco, CA 94080 - Tel: (800) 777-0177

Patient Name	DOB	Patient ID/Medical Record #	Gender	Monogram Accession #
Date Collected	Date Received	Date Reported	Mode	Report Status
Referring Physician			Reference Lab ID/Order #	
Comments				

	Drug		HCV GenoSure® NS3/4A		Assessment		Comments
	Generic Name	Brand/ Regimen	Region	Drug Resistance Associated Variants* Detected	Drug		
PI	**Glecaprevir**	Mavyret	NS3	None	GLE	**None/Undetermined**	
PI	**Grazoprevir**	Zepatier	NS3	None	GZR	**None/Undetermined**	
PI	**Paritaprevir**	Viekira Pak	NS3	Q80K	PTV/r	**None/Undetermined**	
PI	**Simeprevir**	Olysio	NS3	Q80K	SMV	**Resistance Possible**	
PI	**Voxilaprevir**	Vosevi	NS3	None	VOX	**None/Undetermined**	

Important Definitions

- **Resistance Possible -** Resistance Associated Variants (RAVs) detected that (a) represent naturally-occurring polymorphisms or treatment-emergent variants associated with reductions in sustained virologic response (SVR) rates, (b) emerge during direct-acting antiviral (DAA)-treatment or relapse, and/or (c) may confer reductions in susceptibility based on *in vitro* data. Refer to prescribing information for specific details regarding the impact of these variants on treatment response in defined patient populations and when administered in combination with other antiviral agents.
- **None/Undetermined -** None; no RAVs detected. Undetermined; variants detected that have a subtle or uncertain impact on DAA-treatment responses.

Notes:

- All variants are reported relative to the HCV genotype/subtype specific reference H77
- Assessment is based on a rules-based algorithm (version 6)
- Naturally-occurring polymorphisms may impact the emergence of resistance, leading to failure of DAA combination therapy
- Naturally-occurring DAA resistance-associated polymorphisms identified at baseline may impact SVR if the treatment regimen, or adherence, is suboptimal. The impact of these polymorphisms may vary in treatment-naïve and treatment-experienced patients and with varying disease states (e.g. non-cirrhotic vs cirrhotic)
- Reduced susceptibility to any one component of a DAA-containing regimen may be overcome by the activity of the other components of the regimen and/or longer treatment duration
- Treatment emergent RAVs may persist for prolonged periods of time and may impact subsequent treatment regimens

Region		Genotype	Summary of All Variants Observed
NS3	Protease: aa 1-181 Helicase: aa 182-644	1a	Q80K, S91T, T98A, S125A, L153I, V248I, S332P, S410A, F418Y, F557L, V609I
NS4A	Protease cofactor: aa 1-54		Q46Q/R

Comments: **Q80K DETECTED**. The Q80K polymorphism significantly impacts sustained virologic response in HCV GT 1a infected patients that (a) are treated with simeprevir in combination with pegylated interferon and ribavirin, or (b) have compensated cirrhosis and are treated with simeprevir plus sofosbuvir. In these clinical settings, a regimen that does not include simeprevir should be considered.

For more information on interpreting this report, please call Monogram Customer Service at 800-777-0177 between the hours of 6:30am to 5:00pm Pacific Time Monday through Friday.

This assay is performed using a next-generation sequencing platform that analyzes the specified non-structural coding regions of HCV. Variants are reported at a sensitivity that has been demonstrated to be equivalent to that of Sanger/population sequencing. Genotype assignment is determined from the sequence of the specified regions that are derived using subtype specific methodology, and should not be used to establish or confirm the HCV genotype. HCV genotype determination should only be done with an assay intended for that purpose. This assay was validated by testing samples with viral loads equal to or above 2000 IU/mL and should be interpreted only on such specimens. This assay meets the standards for performance characteristics and all other quality control and assurance requirements established by CLIA. The results should not be used as the sole criteria for patient management. This test was developed and its performance characteristics determined by Monogram Biosciences. It has not been cleared or approved by the FDA. The results have been disclosed to you from confidential records protected by law and are not to be disclosed to unauthorized persons. Further disclosure of these results is prohibited without specific consent of the persons to whom it pertains, or as permitted by law.