Precise Assignment of HCV Genotypes

Simultaneous calling of RAVs for Clinicians

The *Sentosa*® SQ HCV Genotyping Assay is a clinically validated Next-Generation Sequencing (NGS) test for genotyping and variant calling for Hepatitis C Virus (HCV) in clinical samples.

- Achieves 100% genotyping correctness[1]
- Simultaneous detection and reporting of genotypes and RAVs on a single platform[2]
- Greatly minimizes the occurrences of indeterminate results, as compared to probe-based genotyping assays[1,3]
- Validated and approved for *in vitro* diagnostic use (CE-IVD)

The *Sentosa*® NGS Workflow- Automated from sample-to-variant call

- Full workflow, ready-to-use platform with LIS connectivity
- Setup and implementation for routine diagnostics in two weeks
- Integrated platform for HCV Quantitative RT-PCR Test and HCV Genotyping Test
- Reagent rental model available

Table 1: Common HCV direct-acting antiviral agents & respective drug targets. Active ingredients in combinatory drug treatment regimen for HCV-positive individuals based on U.S. Food and Drug Administration (FDA) approved therapies. [7]

Active Ingredients	Targets
Grazoprevir	NS3
Simeprevir	NS3
Paritaprevir	NS3
Elbasavir	NS5A
Daclatasvir	NS5A
Velpatasvir	NS5A
Ledipasvir	NS5A
Ombitasvir	NS5A
Sofosbuvir	NS5B
Dasabuvir	NS5B

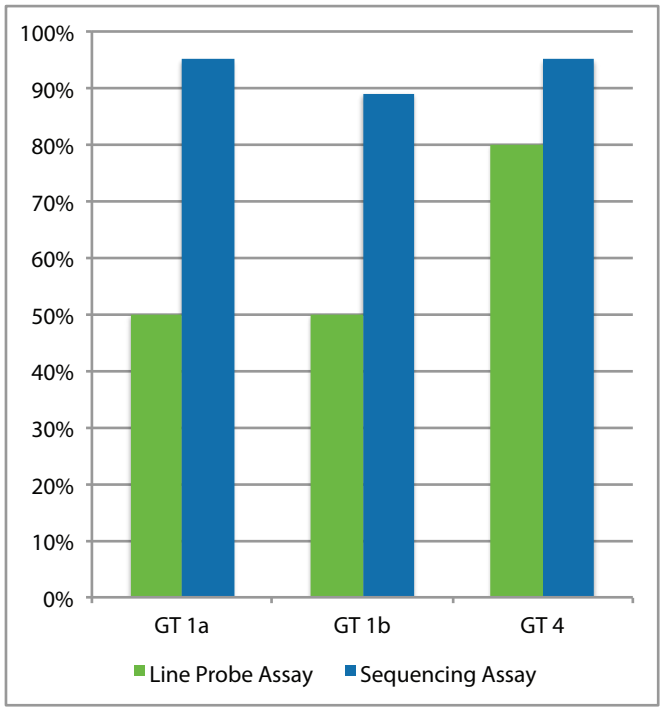
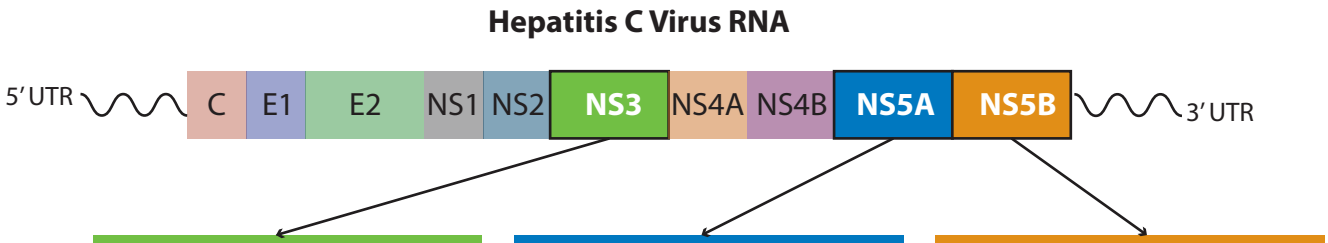


Figure 1: Estimated efficacy of treatment prescribed based on line probe genotyping results as compared to deep sequence analysis results. Genotyping methods that are based on either reverse hybridization targeting 5'UTR/ core regions or real-time PCR targeting 5'UTR/ NS5B have been reported to cause up to 10% of inaccurate and incomplete genotype assignment.[4,5,6] This leads to risk of treatment failure and consequently undue pharmacological costs driven by inappropriate genotype characterization.[5]

Targeted Regions- Simultaneous Genotyping & Calling of RAVs in Accordance with Guidelines

- Providing holistic insights into all 1st line drug treatment options
- Designed in accordance with American Association for the Study of Liver Diseases (AASLD)[8] and European Association for the Study of the Liver (EASL) recommended HCV testing guidelines[9]
- Simultaneous call out of Genotype 1 to 6, subtype 1a and 1b and resistance associated variants (RAVs) in a single sample



Target Region

Detection

Baseline RAVs only. For full list of RAVs visit link below.

Codon 1 to 267	Codon 14 to 201	Codon 346 to 559
RAV Detection for GT 1a & 1b	RAV Detection for GT 1a & 1b	RAV Detection for GT 1a & 1b and Detection for GT 1, 2, 3, 4, 5, 6

NS3 Codon	RAVs	Detected by Vela Diagnostics	AASLD Guidelines GT 1a & 3	EASL Guidelines GT 1a	EASL Guidelines GT 1b
Q80	Q80H	✓		✓	✓
	Q80K	✓		✓	✓
	Q80R	✓		✓	✓

NS3 Codon	RAVs	Detected by Vela Diagnostics	AASLD Guidelines GT 1a & 3	EASL Guidelines GT 1a	EASL Guidelines GT 1b
M28	M28A	✓	✓	✓	
	M28G	✓	✓	✓	
	M28T	✓	✓	✓	
Q30	Q30D	✓	✓	✓	
	Q30E	✓	✓	✓	
	Q30G	✓	✓	✓	
	Q30H	✓	✓	✓	
	Q30K	✓	✓	✓	
	Q30L	✓	✓	✓	
	Q30R	✓	✓	✓	
L31	L31F	✓	✓	✓	✓
	L31M	✓	✓	✓	✓
	L31V	✓	✓	✓	✓
P32	P32L	✓		✓	✓
	P32S	✓		✓	✓
H58	H58D	✓		✓	
Y93	Y93C	✓	✓	✓	✓
	Y93H	✓	✓	✓	✓
	Y93N	✓	✓	✓	✓
	Y93S	✓	✓	✓	✓

NS3 Codon	RAVs	Detected by Vela Diagnostics	AASLD Guidelines GT 1a & 3	EASL Guidelines GT 1a	EASL Guidelines GT 1b
L159	L159F			✓	✓
C316	C316N				✓

Figure 2: Illustration of Hepatitis C Virus RNA gene regions targeted by *Sentosa*® SQ HCV Genotyping Assay and major baseline RAVs called out by *Sentosa*® SQ Reporter software in accordance with AASLD and EASL's recommended guidelines. Testing of baseline RAVs is strongly recommended prior to first-line drug treatment of NS5A or NS3 inhibitors.

Visit www.veladx.com/NGS-Virology for more information

References
[1,2,3] Data on file
[4] Chronic Hepatitis C Virus Infection: Developing Direct-Acting Antiviral Drugs for Treatment Guidance for Industry, by FDA/CDER, Revision 2, published May 2016
[5] Polilli, Ennio et al. Consequences of Inaacurate Hepatitis C Virus Genotyping on the Costs of Prescription of Direct Antiviral Agents in an Italian District. ClinicoEconomics and Outcomes Research: CEOR 8 (2016): PMC. Web. 8 Nov 2016.
[6] Ceccherini-Silberstein F, Di Maio VC, Aragri M, Ciotti M, Cento V, Perno CF. Hepatitis C virus gene sequencing as a tool for precise genotyping in the era of new direct antiviral agents. Hepatology. (2016) 63 (3):1058-1059
[7] U.S Food and Drug Administration. 2016. A complete list of currently approved FDA therapies to treat Hepatitis B and C, accessed 8 December, 2016. <http://www.fda.gov/forpatients/illness/hepatitisbc/ucm408658.htm>
[8] AASLD-IDSA. 2016. Recommendations for testing, managing, and treating hepatitis C, accessed 5 December, 2016. <http://www.hcvguidelines.org>
[9] EASL Recommendations on Treatment of Hepatitis C 2016. J Hepatol (2016), accessed 12 October 2016 <http://dx.doi.org/10.1016/j. jhep.2016.09.001>

IVD: For *in-vitro* diagnostic use. Not for distribution in US.

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