ADVANCES IN CHRONIC HEPATITIS C:
MANAGEMENT AND TREATMENT
REPORTING ON EASL 2016
COMPREHENSIVE EXPERT REVIEW AND DISCUSSION OF KEY PRESENTATIONS

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SHORT DURATION TREATMENT WITH SOFOSBUVIR/VELPATASVIR PLUS GS-9857 IN TREATMENT-NAIVE GENOTYPE 1-6 HCV-INFECTED PATIENTS WITH OR WITHOUT CIRRHOSIS

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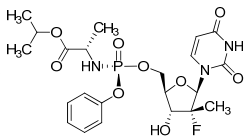
Abstract SAT-138

SOF
NS5B Nucleotide Polymerase Inhibitor



VEL
NS5A Inhibitor

SOF **VEL** + **GS-9857 NS3/4A PI**

Sofosbuvir (SOF)[1,2]

- Potent antiviral activity against HCV GT 1–6
- Once-daily, oral, 400-mg tablet

Velpatasvir (GS-5816; VEL)[3-5]

- Picomolar potency against GT 1–6
- 2nd-generation NS5A inhibitor with improved resistance profile

SOF/VEL FDC

- Once-daily, oral, FDC (400/100mg) for HCV

GS-9857

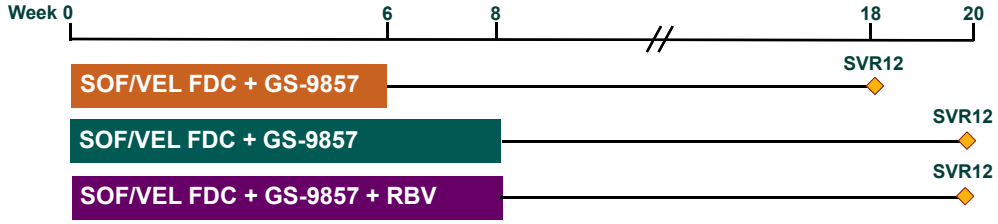
- HCV NS3/4A PI with potent antiviral activity against GT 1–6[6]
- Improved resistance profile vs other HCV PIs[6]
- Safety and pharmacokinetic data from Phase 1 study in healthy subjects support evaluation in HCV patients[7]

FDC, fixed-dose combination; GT, genotype; HCV, hepatitis C virus; PI, protease inhibitor.

Gane E, et al. 51st EASL; Barcelona, Spain; April 13-17, 2016. Abst. SAT-138.

To Evaluate the Safety and Efficacy of SOF/VEL (400/100 mg) + GS-9857 (100 mg) for 6 or 8 Weeks in Treatment-naïve, HCV Patients

Study Design



HCV GT, n (%)			
1	35 (52)	69 (70)	31 (100)
2	6 (9)	6 (6)	0
3	21 (31)	18 (18)	0
4	5 (7)	5 (5)	0
5	0	0	0
6	0	1 (1)	0

RBV, ribavirin; SVR12, sustained virologic response 12 wk after treatment end.

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Predefined RAVs*

HCV GT	NS3 RAVs	NS5A RAVs	NS5B RAVs
1a	V36A/G/L/M, Q41R, F43I/L/S/V, T54A/C/G/S, V55A/I, Y56H, Q80H/K/L/R, S122R, R155any, A156any, D168any, I/V170A/L/T	K24G/N/R, K26E, M28A/G/T/V, Q30C/E/G/H/I/L/K/R/S/T/Y, L31I/F/M/V, P32L, S38F, H58D/L, A92K/T, Y93C/F/H/L/N/R/S/T/W	None
1b		L28M, L31I/F/M/V, P32L, P58D, A92K, Y93C/H/N/S	None
2a	None	T24G/N/R/S, F28A/C/G/L/T, K30E/G/H/R/T, L31I/F/M/V, P32L, S38F, P58D/S, C92K/N/S/T, Y93C/F/H/N/S	S96T, N142T, L159F, E237G, S282any, C289I/L
2b	None	S24G/N/R, L28A/G/T, K30E/G/H/R/T, L31F/I/M, P32L, S38F, P58D, C92K/T, Y93C/F/H/N/S	L320F/I/V, V321A/I
3	None	S24G/N/R, M28A/G/T, A30E/G/H/K/R, L31I/F/M/V, P32L, S38F, P58D, E92T, Y93C/F/H/N/S	None
4	None	K24G/N/R, L28A/G/M/T/V, L30E/G/H/K/R/S/T, M31F/V, P32L, S38F, P58D/L/S, A92K/T, Y93C/F/H/N/S	None

*NS3 RAVs are any variant known to confer susceptibly to any PI in vitro; NS5As RAVs are variants that confer >2.5-fold reduced susceptibly to ledipasvir in vitro.

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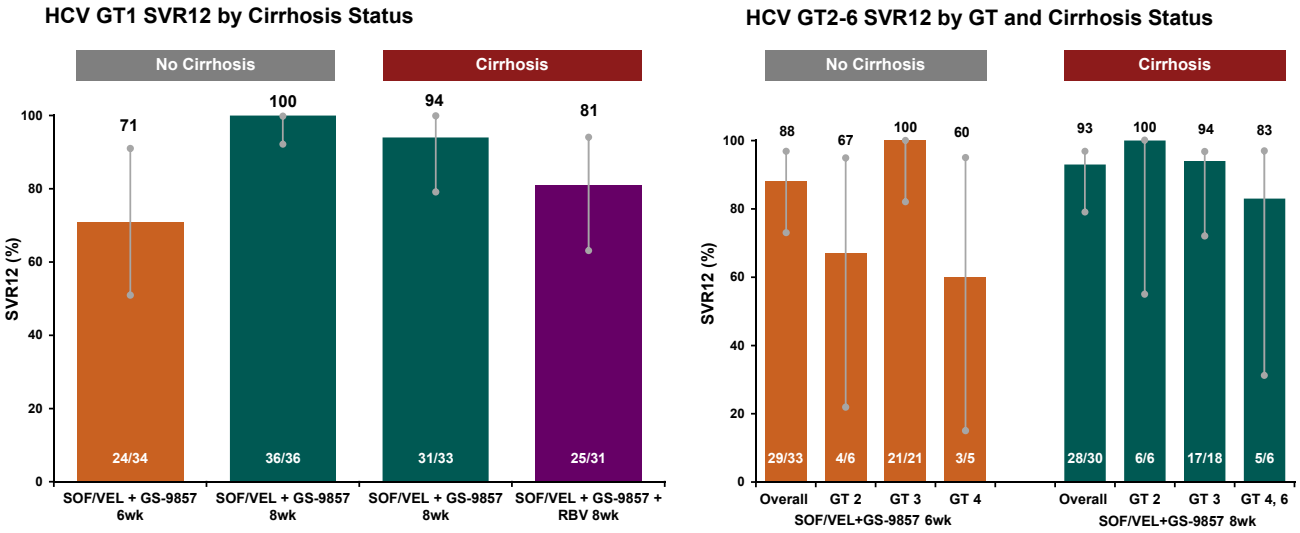
Results



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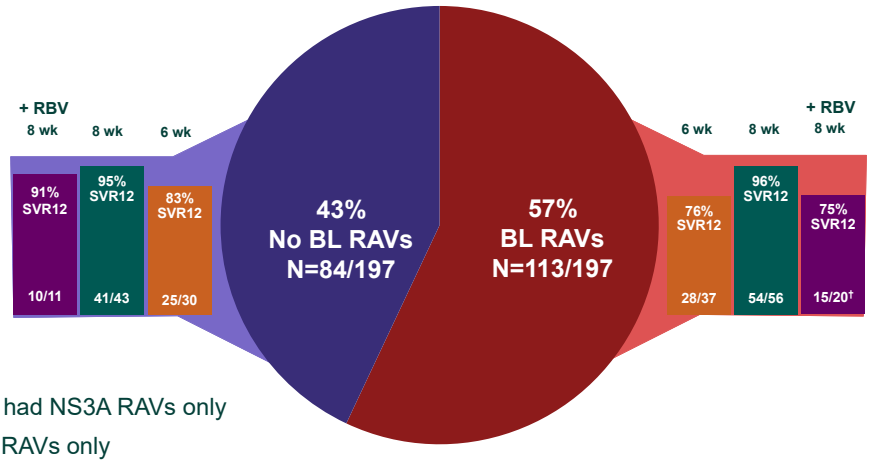
Baseline RAVs* and SVR12 in HCV GT 1-6



- 22% of patients had NS3A RAVs only
- 20% had NS5A RAVs only
- 4% had NS5B RAVs only
- 11% had multiple-class RAVs

*Deep sequencing with 1% assay cutoff; 1includes 1 patient who did not complete treatment.

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Overall Safety Summary

	Patients, n (%)	SOF/VEL+GS-9857 6 wk n=67	SOF/VEL+GS-9857 8 wk n=99	SOF/VEL+GS-9857+RBV 8 wk n=31
Overall Safety	Any AE	44 (66)	68 (69)	25 (81)
	Grade 3/4 AE	1 (1)	2 (2)	0
	Serious AE	0	2 (2)	0
	Discontinuation due to AE of regimen	0	2 (2)	2 (6)
Laboratory Abnormalities	Grade 3/4 laboratory abnormality	3 (4)	4 (4)	11 (35)

- Serious AEs of atrial flutter (n=1) and vertigo (n=1) were considered unrelated to study drug
- AEs leading to discontinuation of study drugs were alanine/aspartate aminotransferase elevation at Week 2 (n=1); diarrhea, nausea, and vomiting (n=2); and fatigue (n=1)
- Grade 3/4 laboratory abnormalities:
  - Without RBV: none observed in >1 patient
  - With RBV: anemia, hyperglycemia, and elevated lipase observed in >1 patient

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