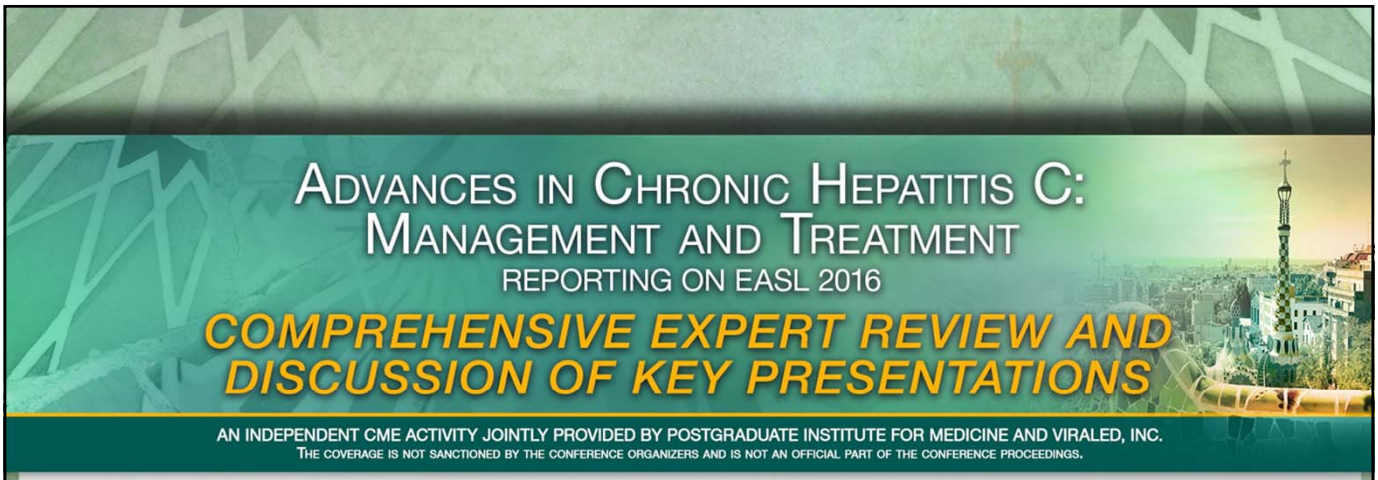


HIGH EFFICACY OF ABT-493 AND ABT-530 IN HCV GENOTYPE 1-INFECTED PATIENTS WHO HAVE FAILED DIRECT-ACTING ANTIVIRAL-CONTAINING REGIMENS: THE MAGELLAN-I STUDY

Fred Poordad, Stuart C Gordon, Armen Asatryan, Franco Felizarta, Robert W Reindollar, Charles Landis, Michael W Fried, David E Bernstein, Teresa I Ng, Chih-Wei Lin, Ran Liu, Jens Kort, Federico J Mensa

Abstract GS11

Next Generation Direct-acting Antivirals

ABT-493[1]
Pangenotypic NS3/4A protease inhibitor

ABT-530[3]
Pangenotypic NS5A inhibitor

***In vitro*:**[1,3]
- High barrier to resistance
- Potent against common NS3 variants (eg., positions 80, 155, 168) and NS5A variants (eg., positions 28, 30, 31 and 93)
- Additive/synergistic antiviral activity

Clinical PK & Metabolism:
- Once-daily oral dosing
- Minimal metabolism and primary biliary excretion
- Negligible renal excretion (<1%)

1. ABT-493 identified by AbbVie and Enanta. 2. Ng TI, et al. Abstract 636. CROI, 2014. 3. Ng TI, et al. Abstract 639. CROI, 2014; Poordad F, et al. 51st EASL; Barcelona, Spain; April 13-17, 2016. Abst. GS11.

ABT-530 Retains Antiviral Activity Against Common GT1a Single-Position NS5A Variants

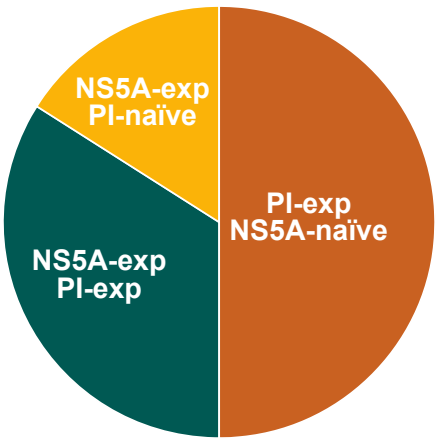
NS5A Inhibitor	Fold Change in EC_{50} for GT1a NS5A Variants			
	Q30E	L31M/V	H58D	Y93H/N
ABT-530	**2.4**	**1.1 – 1.3**	**1.1**	**6.7 – 7.1**
Ledipasvir[1,2]	3279	393 – 2787	>1000	4918
Velpatasvir[3,4]	37	2.1 – 9	NA	81 – 609
Daclatasvir[5]	25205	341 – 3386	500	5432 – 47477
Elbasvir[4,6]	50	125	NA	600 – 2000
Ombitasvir[7]	1326	2	243	41383 – 66740
Odalasvir[1,4]	71	1 – 2.4	8	5083
MK-8408	NA	NA	NA	NA

1. Patel D, et al. EASL, 2015. 2. http://www.accessdata.fda.gov/drugsatfda_docs/nda/2014/205834Orig1s000MicroR.pdf 3. Doehle BP, et al. EASL, 2015.
4. Gao M, et al. Curr Opin Virol ; 3:514-20.5. Fridell RA, et al. Hepatology,54:1924-35. 6. Gane E, et al. EASL, 2015. 7. Krishnan P, et al. AAC, 2015, Poordad F, et al. 51st EASL; Barcelona, Spain; April 13-17, 2016. Abst. GS11.

Prior DAA Treatment Regimens Among Enrolled

Prior Regimen	n
LDV/SOF	8
SMV + SOF ± RBV	8
OBV/PTV/r + DSV ± RBV	4
DBV + FDV + RDV ± RBV	4
SAM + SMV	2
TVR + PR	8
BOC + PR	10
DCV ± PR	2
Other	9

Treatment Experience by DAA Class:



25 (50%) NS5A-experienced
42 (84%) PI-experienced

4 patients were treated more than once with DAA-containing regimens.

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Baseline RAVs by Deep Sequencing Detection Threshold: 1% vs 15%

ABT-493 dose ABT-530 dose RBV dose	200 mg 80 mg (N = 6)	300 mg 120 mg 800 mg (N = 22)	300 mg 120 mg (N = 22)
Any NS3 or NS5A RAVs, n (%)	**5 (83) 4 [67]**	**19 (86) 18 [82]**	**17 (77) 5 [68]**
NS3 only, n	2, 1	6, 7	7, 7
NS5A only, n	3, 3	6, 6	1, 1
Both NS3 and NS5A RAVs, n	0, 0	7, 5	9, 7

Most Common

NS3 RAV Positions:	NS5A RAV Positions:
Q80 (n = 22, **21**)	Q30 (n = 14, **11**)
R155 (n = 4, **1**)	Y93 (n = 10, **8**)
D168 (n = 4, **4**)	

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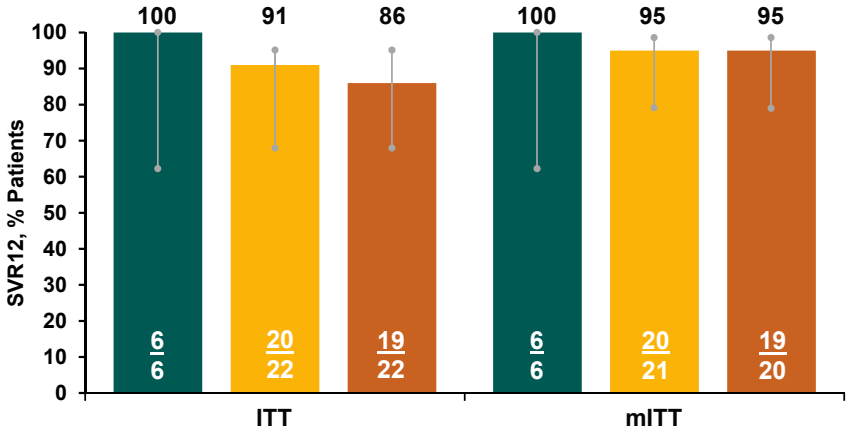
SVR12 by ITT and mITT Analysis



ABT-493	200	300	300	200	300	300
ABT-530	120	120	120	120	120	120
RBV		800			800	
Breakthrough	0	0	1	0	0	1
Relapse	0	1	0	0	1	0
LTFU	0	1	2	--	--	--

- 1 LTFU after week 6 with HCV RNA undetectable
- 2 patients LTFU after completing treatment (1 death); both achieved SVR8

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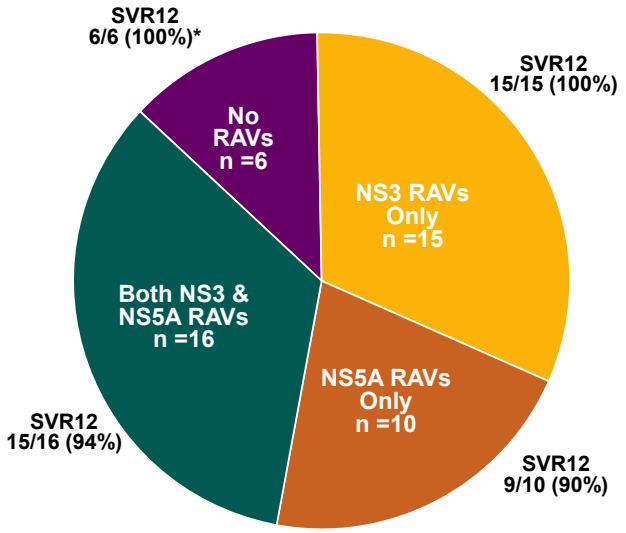
mITT SVR12 Rates in Patients with Baseline RAVs



- 100% SVR12 in 10 patients with Y93 NS5A RAVs
- 100% SVR12 in 26 patients with Q80 or R155 NS3 RAVs
- 100% SVR12 in 17 patients with prior failure of a SOF-containing regimen

* 3 patients with no baseline RAVs were lost to follow-up and are excluded from the mITT analysis. Baseline RAVs based on deep sequencing 1% threshold.

Poordad F, et al. 51st EASL; Barcelona, Spain; April 13-17, 2016. Abst. GS11.

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

AN INDEPENDENT CME ACTIVITY JOINTLY PROVIDED BY POSTGRADUATE INSTITUTE FOR MEDICINE AND VIRALED, INC.
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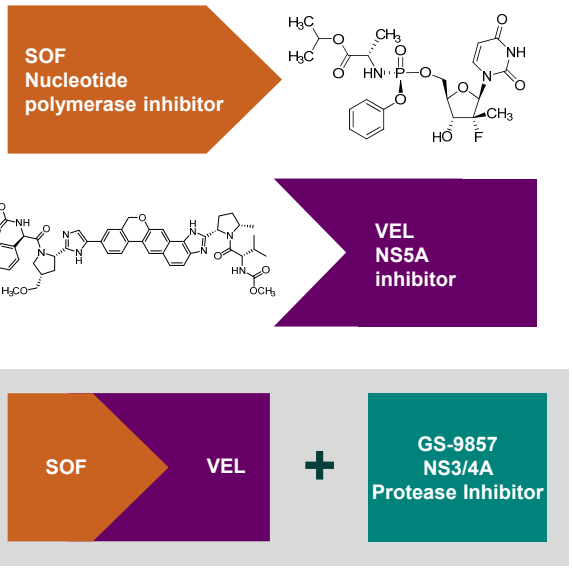
HIGH EFFICACY OF SOFOSBUVIR/VELPATASVIR PLUS GS-9857 FOR 12 WEEKS IN TREATMENT-EXPERIENCED GENOTYPE 1-6 HCV-INFECTED PATIENTS, INCLUDING THOSE PREVIOUSLY TREATED WITH DIRECT-ACTING ANTIVIRALS

Eric Lawitz, Kris Kowdley, Michael Curry, Nancy Reau, Mindie Nguyen, Paul Kwo, Ira Jacobson, Tram T. Tran, Ronald Nahass, Federico Hinestrosa, Robert Herring Jr., Michael Bennet, Jenny C. Yang, Luisa M. Stamm, Di An, Hadas Dvory-Sobol, Diana M. Brainard, John G. McHutchison, Eugene Schiff, Mitchell Davis, Kyle Etzkorn, Raymond T. Chung, David Pound, Maribel Rodriguez-Torres, K. Rajender Reddy, Ziad Younes, Edward J. Gane

Abstract PS008

Background



Sofosbuvir (SOF)[1,2]

- Potent antiviral activity against HCV GT 1–6

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

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

GS-9857 [6,7]

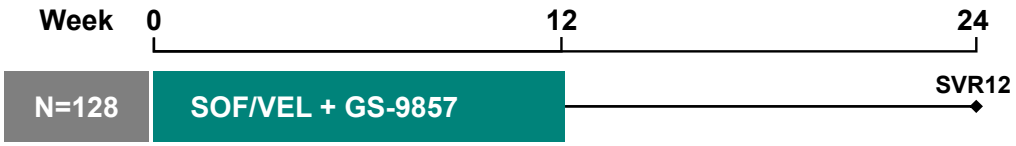
- HCV NS3/4A protease inhibitor with potent antiviral activity against HCV GT 1–6
- Improved resistance profile compared with other HCV protease inhibitors

SOF/VEL + GS-9857

- SOF/VEL FDC (400/100 mg) tablet plus GS-9857 100-mg tablet is taken orally, once daily

1. Jacobson IM, et al. N Engl J Med 2013;368:1867-77; 2. Lawitz E, et al. N Engl J Med 2013;368:1878-87; 3. Cheng G, et al. EASL 2013, poster 1191; 4. German P, et al. EASL 2013, poster 1195; 5. Lawitz E, et al. J Viral Hepat 2015;22:1011-9; 6. Taylor JG, et al. EASL 2015, poster 899; 7. Kirby B, et al. EASL 2015, poster 861, Lawitz E, et al. 51st EASL; Barcelona, Spain; April 13-17, 2016. Abst. PS008.

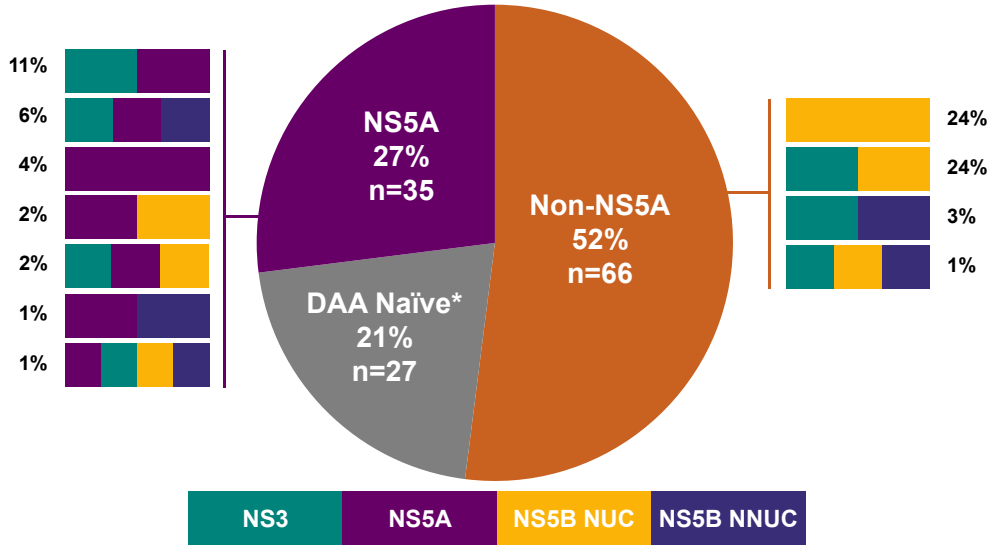
Study Designs GS-US-367-1168 and GS-US-367-1169



- Two Phase 2, multicenter, open-label studies (US, New Zealand)
  - GS-US-367-1168: GT 1
  - GS-US-367-1169: GT 2, 3, 4, 5, 6
- Broad inclusion criteria
  - HCV treatment experienced, including DAA experienced
    - GT 1: NS5A inhibitor or ≥2 DAA classes
    - GT 2–6: Peg-IFN + RBV or any DAA
  - 50% with compensated cirrhosis

Lawitz E, et al. 51st EASL; Barcelona, Spain; April 13-17, 2016. Abst. PS008.

Results: Prior Treatment Experience (N=128)



*GT 2-6 patients who failed prior Peg-IFN + RBV regimens.

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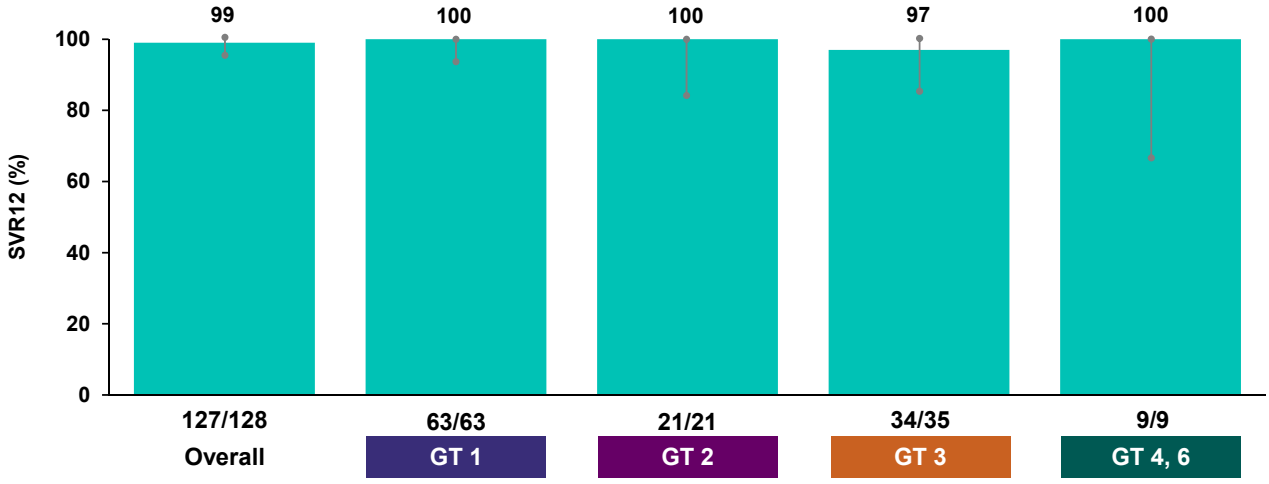
Results: SVR12 Overall and by Genotype

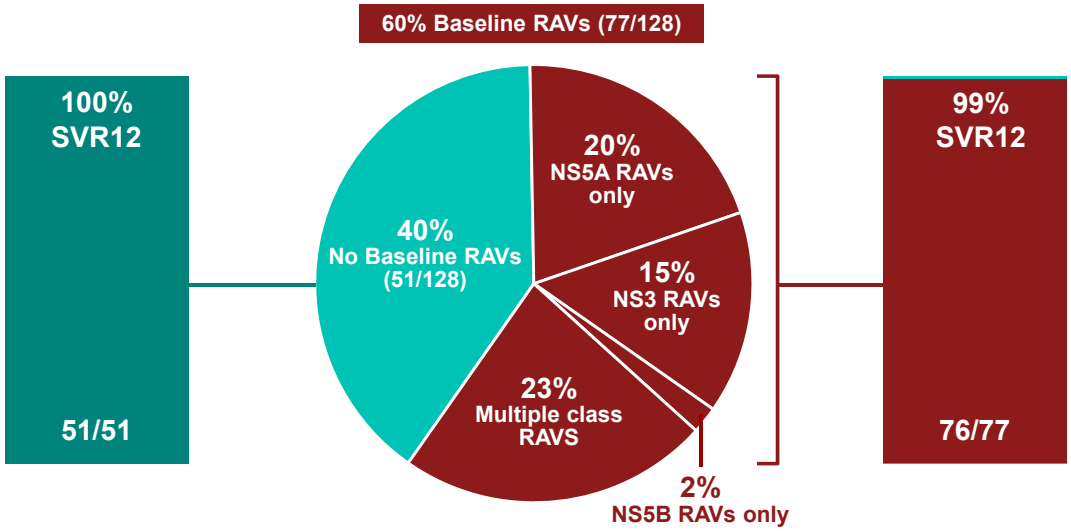


One Patient Relapsed at Post-treatment Week 8

Error bars represent 95% confidence intervals.

Lawitz E, et al. 51st EASL; Barcelona, Spain; April 13-17, 2016. Abst. PS008.

Results: Resistance Analysis



Deep sequencing with 1% assay cutoff.

Lawitz E, et al. 51st EASL; Barcelona, Spain; April 13-17, 2016. Abst. PS008.