ADVANCES IN CHRONIC HEPATITIS C:
MANAGEMENT AND TREATMENT
REPORTING ON EASL 2016

COMPREHENSIVE EXPERT REVIEW AND DISCUSSION OF KEY PRESENTATIONS

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HIGH SVR RATES WITH ABT-493 + ABT-530 CO-ADMINISTERED FOR 8 WEEKS IN NON-CIRRHOTIC PATIENTS WITH HCV GENOTYPE 3 INFECTION

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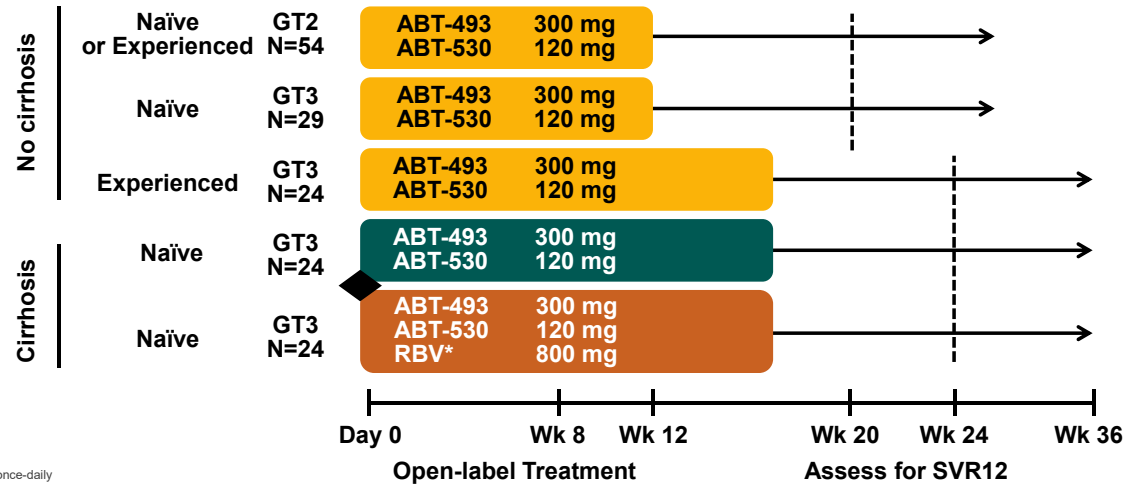
Abstract PS098

SURVEYOR-II Part 2 Study Design

- Partially randomised, open-label, multicentre phase 2 trial evaluating the dose combination of ABT-493 and ABT-530 identified in the dose-ranging part 1 of this study



*RBV dosed once-daily

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Demographics and Patient Characteristics

	ABT-493 + ABT-530 (N = 29)
Male, n (%)	15 (52)
Race, n (%)	
White	26 (90)
Black	1 (3)
Hispanic/Latino, n (%)	2 (7)
Age, mean years (range)	47 (27 – 66)
BMI, mean kg/m^2, ± SD	26 ± 3.8
HCV RNA, median $\log_{10}$ IU/mL (range)	6.5 (5.0 – 7.5)
HCV GT3a*, n (%)	25 (86)
Baseline fibrosis stage, n (%)	
F0 – F1	20 (69)
F2	2 (7)
F3	7 (24)

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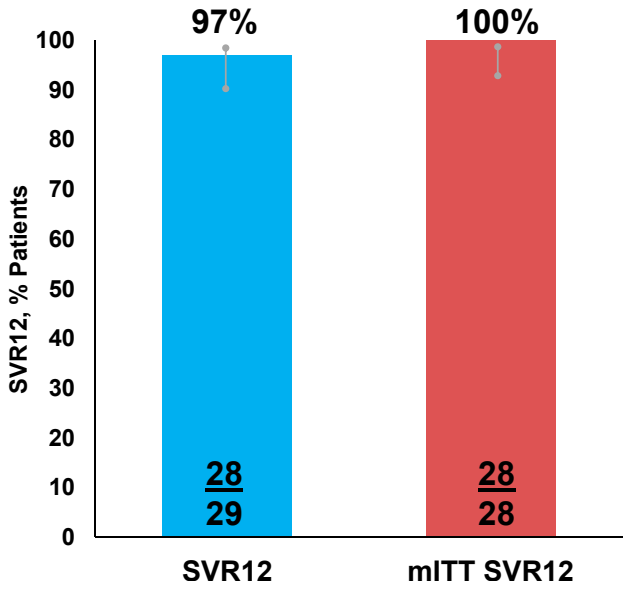
SVR12 Analysis

- No virologic failures
- 1 patient withdrew consent after treatment week 6 due to intolerance of blood draws and had an undetectable HCV RNA at the time of discontinuation



mITT SVR12 rate excludes non-virologic failures

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Laboratory Abnormalities

Event, n	ABT-493 + ABT-530 (N = 29)
ALT, grade ≥2 (>3 × ULN)	0
AST, grade ≥2 (>3 × ULN)	0
Total bilirubin	
Grade 2 (>1.5 – 3 × ULN)	1
Grade ≥3 (>3 × ULN)	0
Alk phos, grade ≥2 (>2.5 × ULN)	0
Hemoglobin, grade ≥2 (<10 g/dL)	0

- In all patients with baseline ALT elevations, ALT levels normalized with treatment and no on-treatment ALT elevations were observed
- No grade 3 or 4 abnormalities were observed

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Cirrhosis Cohort Key Eligibility Criteria and Endpoints

- Key inclusion criteria
  - 18 to 70 years of age, inclusive
  - HCV GT3 infection, HCV RNA >10,000 IU/mL
  - Presence of compensated cirrhosis (Child-Pugh score ≤6)
    - Liver biopsy (eg., METAVIR >3 or Ishak >4), or
    - FibroScan ≥14.6 kPa, or
    - FibroTest ≥0.75 with APRI >2
- Key exclusion criteria
  - Any prior HCV treatment
  - Any prior history of hepatic decompensation
  - HIV co-infection, albumin <LLN, platelet count <90 × 109/L
  - Herbal supplements and potent P-gp inducers were prohibited
- Endpoints
  - Efficacy: SVR12 (primary) and virologic failure
  - Safety: adverse events (AEs) and laboratory abnormalities

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Cirrhosis Cohort Demographics and Patient Characteristics

	ABT-493 + ABT-530 (N = 24)	ABT-493 + ABT-530 + RBV (N = 24)
Male, n (%)	13 (54)	18 (75)
White race, n (%)	23 (96)	22 (92)
Age, median years (range)	55 (36 – 68)	57 (30 – 65)
BMI, median kg/m^2 (range)	27 (19 – 37)	27 (21 – 35)
HCV GT3a*, n (%)	22 (92)	24 (100)
HCV RNA, median $\log_{10}$ IU/mL (range)	6.4 (5.3 – 7.2)	6.3 (4.2 – 7.3)
ALT, median U/L (range)	100 (22 – 198)	116 (28 – 218)
Platelets, median $\times$ 10^9/L (range)	140 (86 – 245)	157 (109 – 291)
Albumin, median g/dL (range)	4.1 (3.1 – 4.4)	4.2 (3.2 – 4.7)
Child-Pugh score = 6, n (%)	5 (21)	3 (13)

* Genotype and subtype were determined by the Versant HCV Genotype Inno-LiPA Assay Version 2.0 or higher

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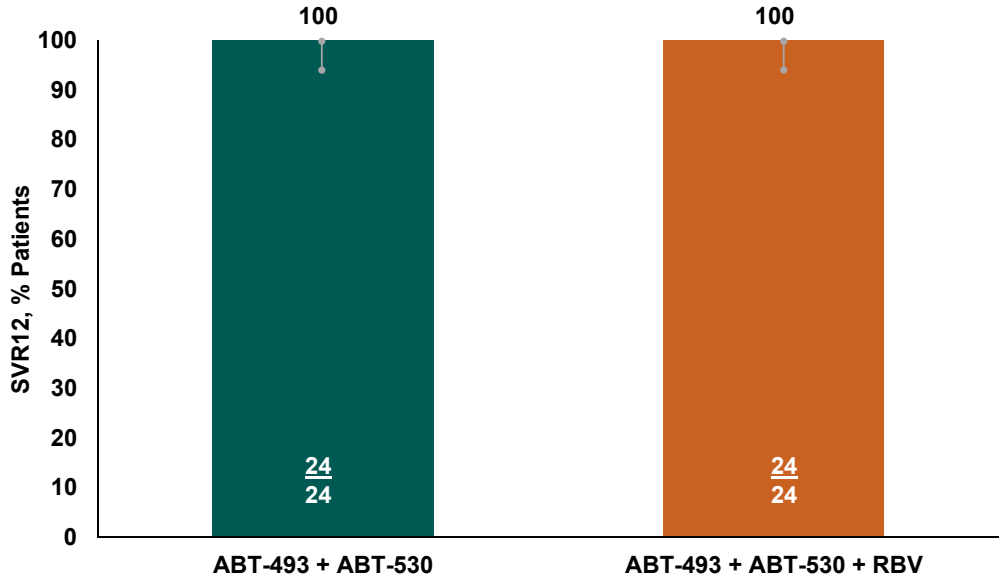
100% SVR12 by ITT Analysis



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Cirrhosis Cohort: Laboratory Abnormalities

Event, n	ABT-493 + ABT-530 (n = 24)	ABT-493 + ABT-530 + RBV (n = 24)
ALT, grade ≥2 (>3 × ULN)*	0	0
AST, grade ≥2 (>3 × ULN)*	0	0
Total bilirubin		
Grade 2 (>1.5 – 3 × ULN)	1	7
Grade 3 (>3 – 10 × ULN)	1	0
Alk phos, grade ≥2 (>2.5 × ULN)	0	0
Haemoglobin		
Grade 2 (<10 – 8 g/dL)	0	1
Grade ≥3 (<8 g/dL)	0	0

- No ALT elevations
- 1 patient with elevated baseline bilirubin had a grade 3 total bilirubin elevation on day 44 that resolved post treatment

* Post nadir

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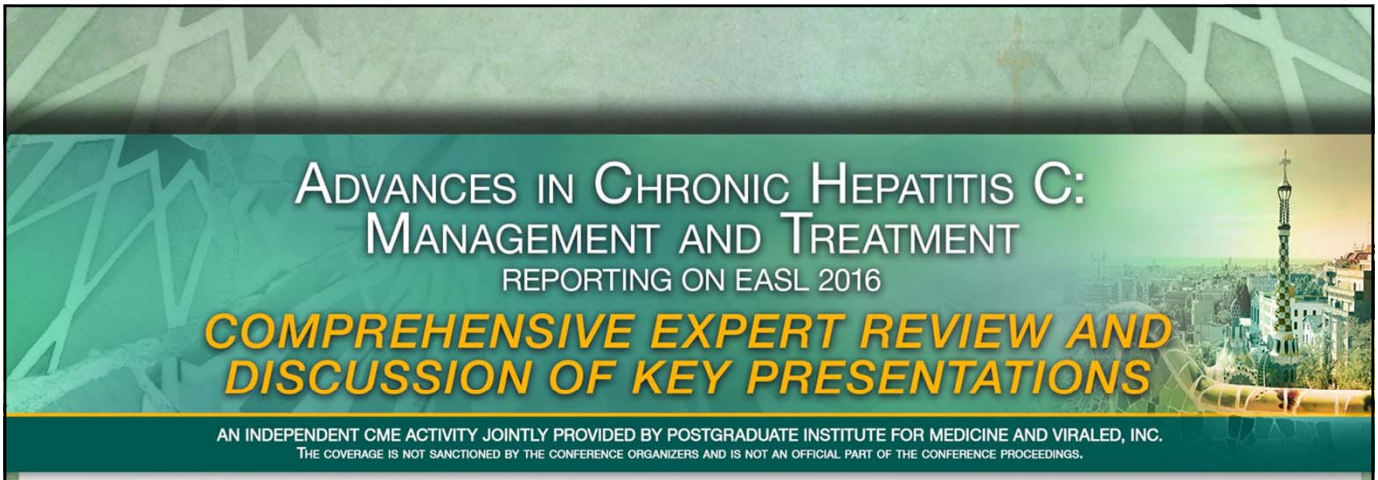

100% SVR4 WITH ABT-493 AND ABT-530 WITH OR WITHOUT RIBAVIRIN IN TREATMENT-NAÏVE HCV GENOTYPE 3-INFECTED PATIENTS WITH CIRRHOSIS

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Abstract LB01

Next Generation Direct-acting Antivirals

ABT-493
Pangenotypic NS3/4A protease inhibitor

ABT-493 **ABT-530**

ABT-530
Pangenotypic NS5A inhibitor

In vitro:[1,2]	High barrier to resistance
	Potent against common NS3 variants (eg., positions 80, 155, 168) andNS5A variants (eg., positions 28, 30, 31, and 93)
Clinical PK & metabolism:	Additive/synergistic antiviral activity
	Once-daily oral dosing
	Minimal metabolism and primary biliary excretion
	Negligible renal excretion (<1%)

ABT-493 identified by AbbVie and Enanta.
1. Ng TI, et al. Abstract 636. CROI, 2014.
2. Ng TI, et al. Abstract 639. CROI, 2014.

Kwo P, et al. 51st EASL; Barcelona, Spain; April 13-17, 2016. Abst. LB01.

ABT-493 and ABT-530 Have Potent Activities Against All HCV Genotypes, Including GT3

Stable HCV GT3a Replicon EC_{50}			
NS3/4A Protease Inhibitor	**nM**	**NS5A Inhibitor**	**pM**
ABT-493	**1.6**	**ABT-530**	**2**
Grazoprevir[1]	35	Elbasvir[7]	140
GS-9857[2]	6.1	Velpatasvir[8]	20
Simeprevir[3,4]	472	Ledipasvir[9]	168,000
Paritaprevir	19	Ombitasvir	19
Asunaprevir[5]	1162	Daclatasvir[10]	530
		Odalasvir	48
		MK-8408[11]	2

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3. Olysio prescribing information.
4. Chase R, et al. IAPAC, 2013.
5. McPhee F, et al. AAC, 2012.
6. Yang H, et al. AAC, 2014.
7. Liu R, et al. AAC doi:10.1128/AAC.01390-15
8. Cheng G, et al. EASL, 2013.
9. Cheng G, et al. EASL, 2012
10. Wang C, et al. AAC, 2014.
11. http://files.shareholder.com/downloads/ACHN/0x0x602481/8b28c708-13b6-420d-9325-401c57b89001/ACHN_R_D_Day_Final.pdf
12. Asante-Appiah E, AASLD, 2014.

Kwo P, et al. 51st EASL; Barcelona, Spain; April 13-17, 2016. Abst. LB01.

ABT-530 Retains Antiviral Activity Against Common GT3 Single-Position NS5A Variants

NS5A Inhibitor	Fold Change in EC50 for GT3 NS5A Variants		
	M28T	A30K	Y93H
ABT-530	**0.4**	**1.1**	**2.5**
Ledipasvir[1]	NA	>1000	>1000
Velpatasvir[2]	NA	10 – 100	>100
Daclatasvir[3]	46	56 - 62	2738 – 2752
Elbasvir[4]	NA	50	486
Ombitasvir[5]	423	NA	6728
MK-8408	NA	NA	NA

NA, not available

1. Hernandez D, et al. J Clin Virol, 2013.
2. Doehle BP, et al. EASL, 2015.
3. Wang C, et al. AAC, 2013:57:611-3.
4. Gane E, et al. EASL, 2015.
5. Krishnan P, et al. AAC, 2015.

Kwo P, et al. 51st EASL; Barcelona, Spain; April 13-17, 2016. Abst. LB01.