ADVANCES IN CHRONIC HEPATITIS C:
MANAGEMENT AND TREATMENT
INDEPENDENT REPORTING ON AASLD 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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ENDURANCE-1: A Phase 3 Evaluation of the Efficacy and Safety of 8- versus 12-week Treatment with Glecaprevir/ Pibrentasvir (formerly ABT-493/ABT-530) in HCV Genotype 1 Infected Patients with or without HIV-1 Co-infection and without Cirrhosis

Stefan Zeuzem, Jordan J. Feld, Stanley Wang, Marc Bourlière, Heiner Wedemeyer, Edward J. Gane, Robert Flisiak, Wan- Long Chuang, Steven L. Flamm, Paul Y. Kwo, Gladys Sepulveda, Ruth Soto-Malave, Massimo Puoti, Edward Tam, Rafael Bruck, Francisco Fuster, Seung Woon Paik, Franco Felizarta, Bo Fu, Teresa Ng, Chih-Wei Lin, Federico Mensa

Abstract 253

Next Generation Direct-Acting Antivirals

Glecaprevir (formerly ABT-493)
pangenotypic NS3/4A protease inhibitor

Pibrentasvir (formerly ABT-530)
pangenotypic NS5A inhibitor

Collectively: G/P

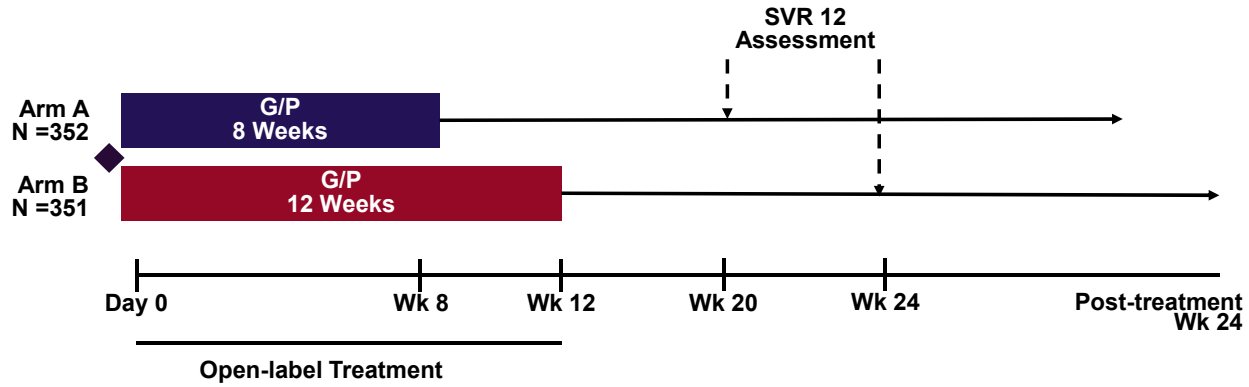
In vitro:[1,2]
- Additive/synergistic antiviral activity
- High barrier to resistance
- Potent against common NS3 polymorphisms (eg., positions 80, 155, and 168) and NS5A polymorphisms (eg., positions 28, 30, 31 and 93)

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

G/P is co-formulated and dosed once daily as three 100 mg/40 mg pills for a total dose of 300 mg/120 mg.
Glecaprevir was identified by AbbVie and Enanta.

Zeuzem S, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. 258. Ng TI, et al. Abstract 636. CROI, 2014. Ng TI, et al. Abstract 639. CROI, 2014.

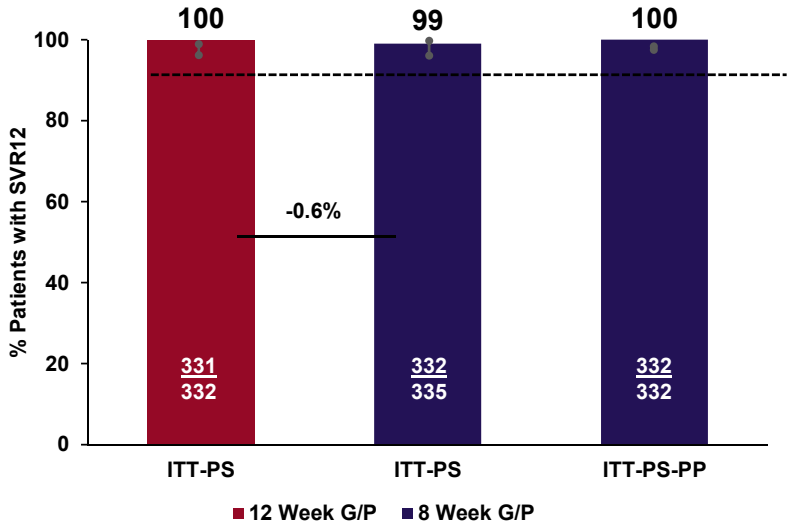
ENDURANCE-1: Study Design and Patient Population



- GT1 non-cirrhotics (n=703)
- Treatment naïve or treatment-experienced with IFN or PEG +/- RBV or SOF + RBV +/- PEG (excluded any prior experience with HCV DAA other than SOF)
- HCV monoinfected or HCV/HIV coinfected (ART naïve or on stable ART regimen)

Zeuzem S, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. 253.

GLE/PIB x 8 Weeks or 12 Weeks in GT1 Noncirrhotics



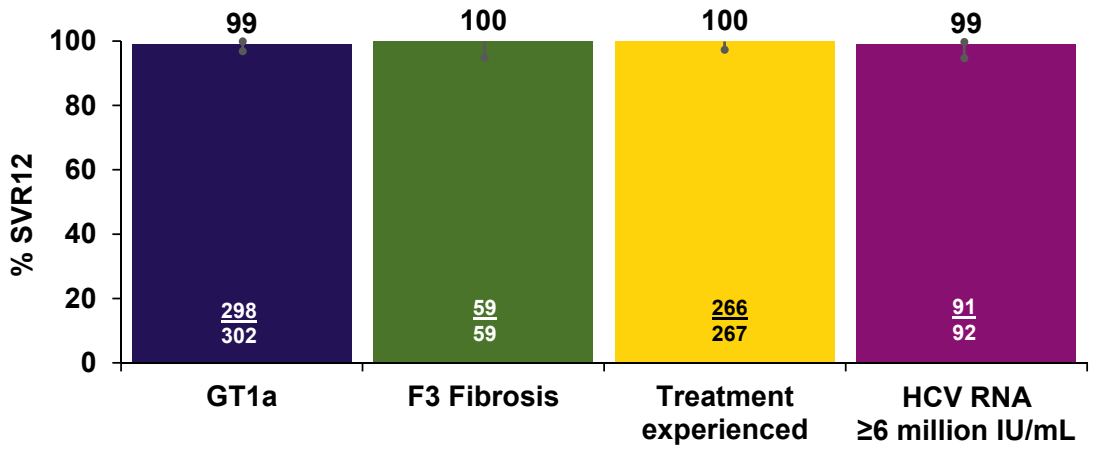
Primary endpoint threshold: 91%

ITT-PS: ITT population, excluding HIV co-infected *and* SOF experienced patients

ITT-PS-PP: ITT-PS population excluding patients with premature D/C or virologic failure prior to week 8, and missing data in the SVR12 window

Zeuzem S, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. 253.

Subgroup Analysis: Pooled ITT Population



ITT Population: All patients receiving study drug

Zeuzem S, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. 258.

Summary of Laboratory Abnormalities

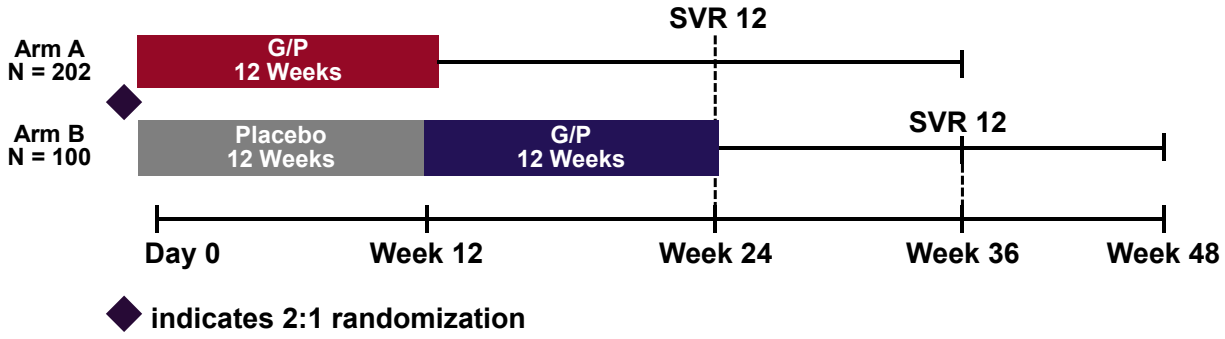
Characteristic, n (%)	G/P 8 Weeks N = 352	G/P 12 Weeks N = 351
AST*		
Grade 2 (>3 × ULN)	0	0
Grade ≥3 (>5 × ULN)	1 (0.3)	0
ALT*		
Grade 2 (>3 × ULN)	1 (0.3)	0
Grade ≥3 (>5 × ULN)	0	0
Total Bilirubin Grade 3 (3-5 × ULN)†	1 (0.3)	2 (0.6)

AST, aspartate aminotransferase; ALT, alanine aminotransferase; ULN, upper limit of normal
*Post-nadir
†Grade 3 bilirubin elevations observed at baseline; all primarily indirect
No Grade 4 laboratory abnormalities were observed
Safety was similar in HCV GT1 mono-infected and HIV-1/HCV GT1 co-infected patients
All co-infected patients maintained HIV-1 RNA suppression during the treatment period

Zeuzem S, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. 258.

ENDURANCE-2 Study Design

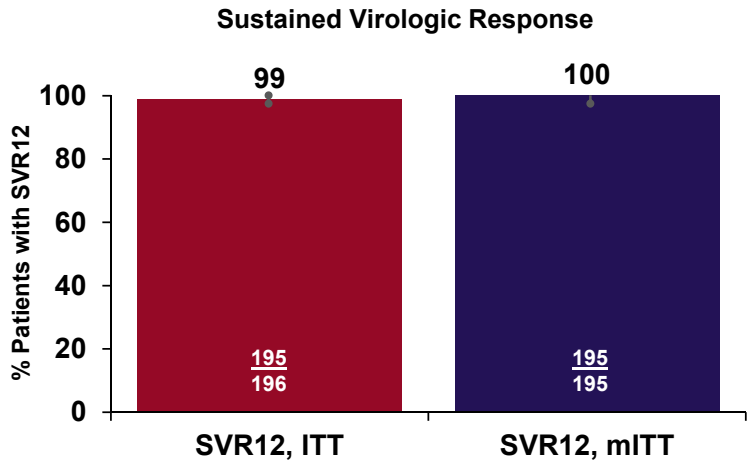
- In Phase 2 trials, 98% (53/54) SVR12 in GT2-infected patients treated for 8 weeks (no virologic failures); favorable safety with no ALT elevations or dose-dependent AEs
- ENDURANCE-2 (NCT02640482) is a randomized, double-blind, placebo-controlled, multicenter, phase 3 study investigating the safety and efficacy of 12-week G/P in treatment-naïve or treatment-experienced patients with chronic HCV GT2 infection without cirrhosis



G/P is co-formulated and dosed once daily as three 100 mg/40 mg pills for a total dose of 300 mg/120 mg.

Kowdley K, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. 73.

ENDURANCE-2: Efficacy, ITT & mITT Populations



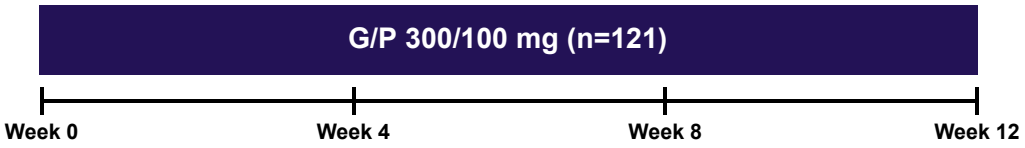
ITT population: excludes 6 SOF-experienced patients, all of whom achieved SVR12

mITT population: ITT population excluding 1 non-virologic failure who achieved SVR4

Kowdley K, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. 73.

ENDURANCE-4: Study Design

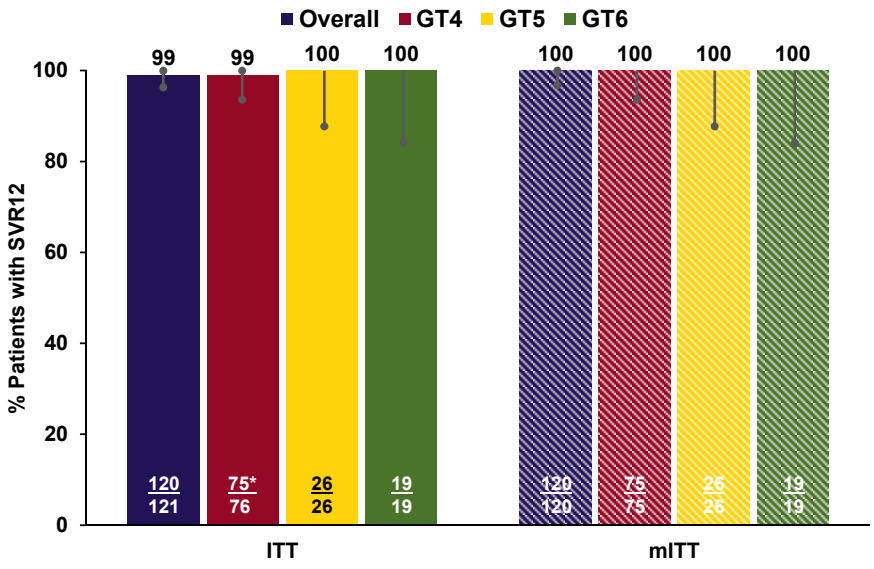
Open-label, multicenter, single-arm study to evaluate the efficacy and safety of 12-week G/P in HCV FT4, 5, or 6-incefected, non-cirrhotic patients



- Key Study Endpoints
  - SVR12
  - Percentage of participants with on-treatment virologic failure or post-treatment relapse
  - Adverse events (AEs) and lab abnormalities

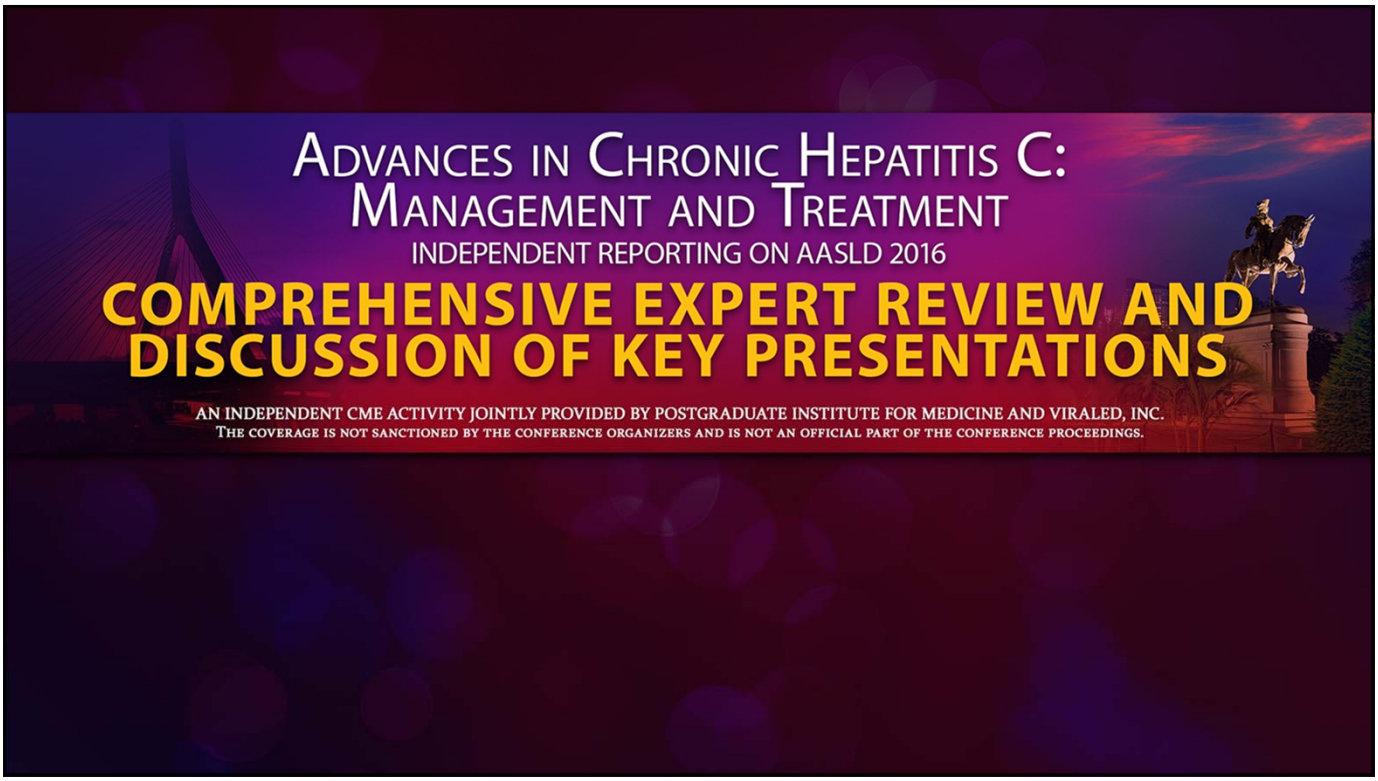
Asselah T, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. 114..

EDURANCE-4 Study: Efficacy Results



G/P is unapproved. The efficacy and safety of the regimen has not been established.
*One GT4 patient discontinued treatment on day 12 and did not achieve SVR12

Asselah T, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. 114..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