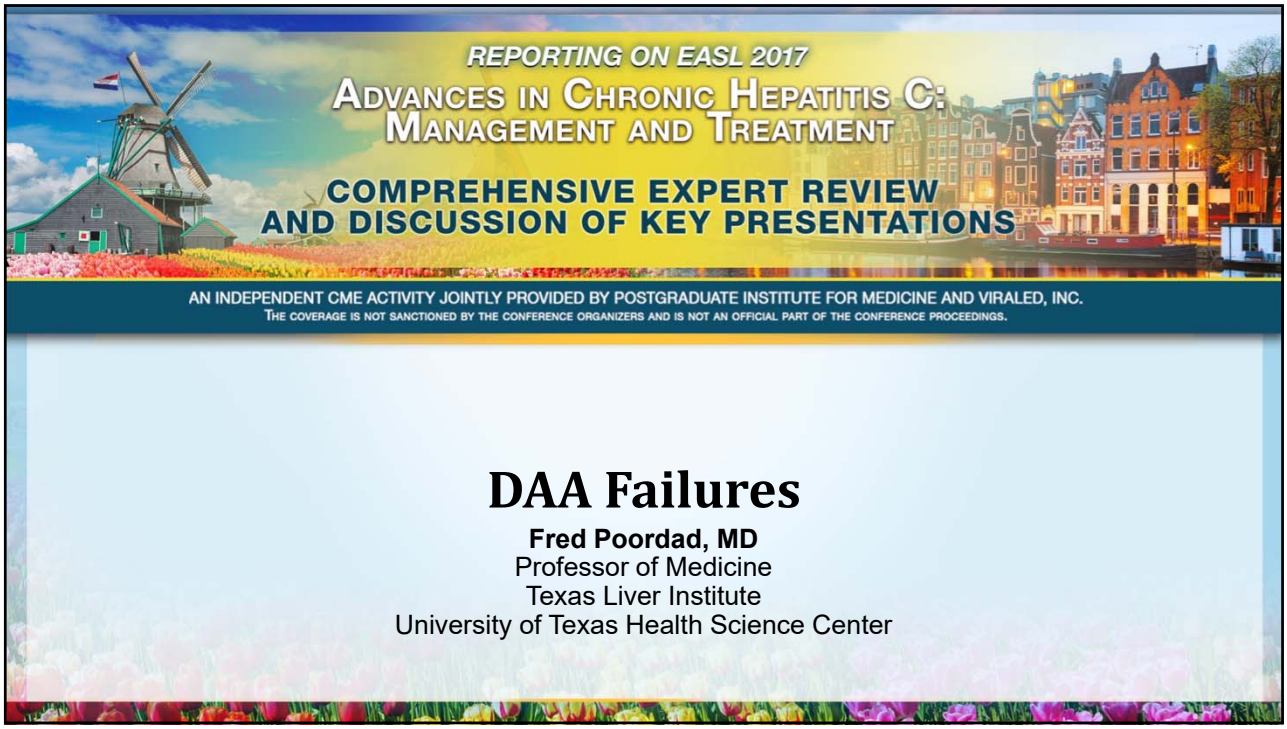


DAA Failures

Fred Poordad, MD
Professor of Medicine
Texas Liver Institute
University of Texas Health Science Center

MAGELLAN-1, Part 2: Glecaprevir/Pibrentasvir for 12 or 16 Weeks in Patients with Chronic HCV Genotype 1 or 4 and Prior Direct-Acting Antiviral Treatment Failure

Fred Poordad, Stanislas Pol, Armen Asatryan, Maria Buti, David Shaw, Christophe Hézode, Franco Felizarta, Stuart C Gordon, Stephen Pianko, Michael W Fried, David E Bernstein, Joel Gallant, Chih-Wei Lin, Yang Lei, Teresa I Ng, Tami Pilot-Matias, Jens Kort, Federico Mensa

Abstract PS-156

Next Generation Direct-Acting Antivirals

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

Pibrentasvir
(formerly ABT-530)
pangenotypic NS5A inhibitor

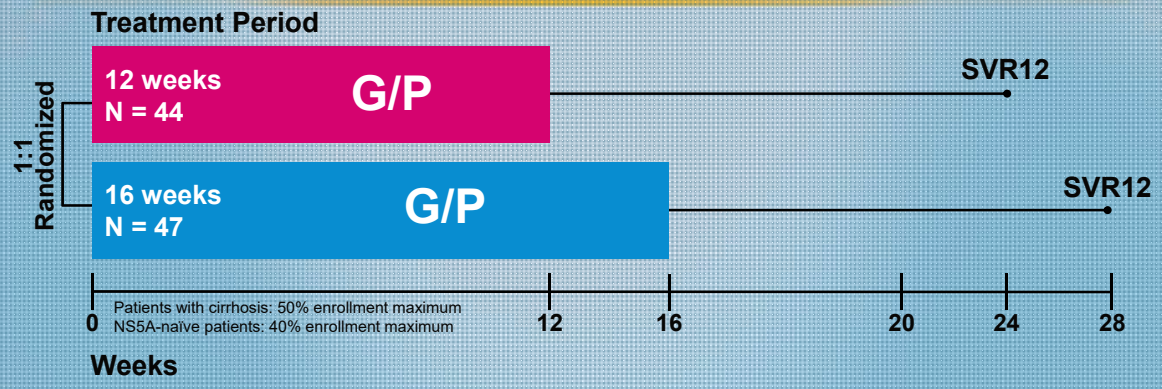
Coformulated: G/P

- Once-daily oral dosing with food
- Potent against common NS3 and NS5A polymorphisms[1]
- Minimal metabolism, primary biliary excretion, and negligible renal excretion (<1%)
  - Favorable safety profile: mostly mild AEs with few Grade ≥3 lab abnormalities[2]
  - Concomitant PPI use allowed
  - Phase 2 (12 weeks): 95% mITT SVR12 rate in patients with prior NS5A and/or PI failure[3]

G/P is coformulated 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

1. Ng TI, et al. Antimicrobial Agents and Chemotherapy. 2017.
2. DuFour, J-F et al. EASL 2017; FRI-238
3. Poordad F, et al. Hepatology 2017; DOI: 10.1002/hep.29081.
Poordad F, et al. 52nd EASL, Amsterdam, Netherlands; April 19-23, 2017. Abst. PS-156.

MAGELLAN-1, Part 2 Study: Objective and Study Design



- Objective
  - Determine the efficacy and safety of G/P for 12 or 16 weeks in patients with chronic HCV GT1, 4, 5 or 6 infection and prior DAA failure, including those with compensated cirrhosis

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MAGELLAN-1, Part 2: Registrational Study

MAGELLAN-1, Part 2 Study: Baseline Demographics and Clinical Characteristics

Characteristic	G/P 12 weeks N = 44	G/P 16 weeks N = 47
Male, n (%)	31 (70)	33 (70)
White race, n (%)	34 (77)	35 (75)
Black race, n (%)	9 (20)	11 (23)
Age, median years (range)	57 (22 – 67)	56 (36 – 70)
BMI, median kg/m^2 (range)	28 (21 – 41)	29 (20 – 52)
HCV RNA, median $\log_{10}$ IU/mL (range)	6.1 (4.7 – 7.2)	6.3 (4.7 – 7.1)
Compensated cirrhosis, n (%)	15 (34)	12 (26)
HCV subtype*, n (%)		
1a	35 (80)	32 (71)
1b	8 (18)	10 (22)
1e	0	1 (2)
4	1 (2)	3 (6)
1 (not subtyped)	0	1† (2)

*Genotype and subtype determined by phylogenetic analysis for samples with available sequences
†One patient had GT1, based on LiPA analysis, but was not subtyped

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MAGELLAN-1, Part 2 Study: Clinical Characteristics (Cont'd)

Characteristic , n (%)	G/P 12 weeks N = 44	G/P 16 weeks N = 47
Previous DAA regimen class*		
NS3/4A PI only (NS5A inhibitor-naïve)	14 (32)	13 (28)
NS5A inhibitor only (PI-naïve)	16 (36)	18 (38)
NS3/4A PI + NS5A inhibitor	14 (32)	16 (34)
Prior DAA treatment response		
On-treatment failure	14 (32)	13 (28)
Virologic relapse	30 (68)	34 (72)
Presence of key baseline substitutions†		
None	13 (30)	13 (30)
NS3 only	2 (5)	4 (9)
NS5A only	24 (55)	23 (52)
NS3 + NS5A	5 (11)	4 (9)

NS3 PIs included: PTV, SMV, ASV, TVR, or BOC; NS5A inhibitors included: DCV, LDV, or OBV
*Sofosbuvir (NS5B inhibitor) could be included in any prior treatment regimen
†Only 44 patients had sequencing data available in each arm; percentages are based on N = 44; substitutions detected by next generation sequencing using 15% detection threshold at positions 155, 156, and 168 in NS3, and 24, 28, 30, 31, 58, 92, and 93 in NS5A

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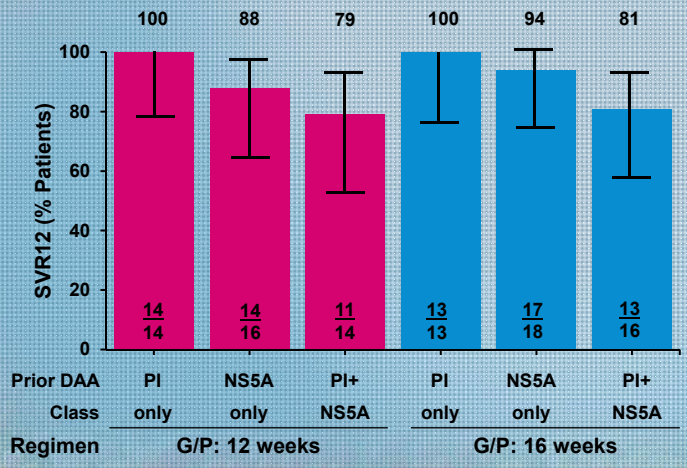
MAGELLAN-1, Part 2 Study: Results
SVR12 by DAA Class in Prior Therapy



Overall SVR12:

- 12-week: 89% (39/44)
  - 1 OTVF; 4 relapse
- 16-week: 91% (43/47)
  - 1 OTVF; 0 relapse

Prior Treatment History

- PI: TVR, SMV, BOC
- NS5A: LDV, DCV
- NS5A+PI: OBV and PTV, or other combinations
- OTVF, on-treatment virologic failure

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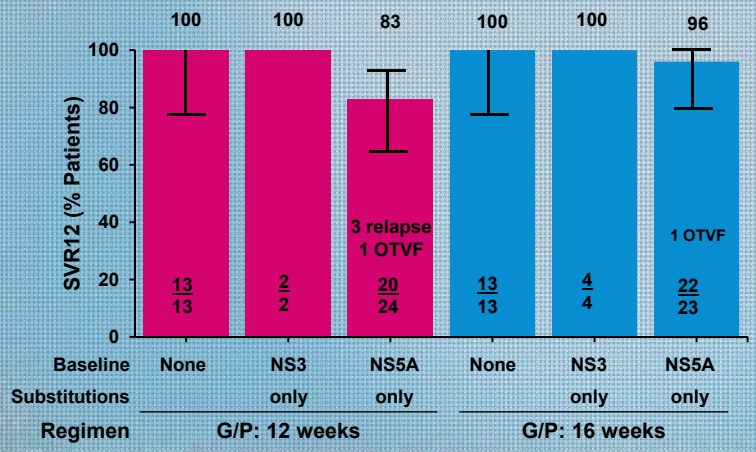
MAGELLAN-1, Part 2 Study: Results
SVR12 by Key NS3 and NS5A Baseline Substitutions



Key baseline NS3 and NS5A substitutions were only present in patients with prior failure to both PI and NS5A inhibitors

- 5/9 of these patients achieved SVR12
- Key NS3 positions:
  - 155, 156, 168
- Key NS5A positions:
  - 24, 28, 30, 31, 58, 92, 93
- OTVF:
  - on-treatment virologic failure

Y93H/N at baseline: 100% (13/13) SVR12 in patients with NS5A inhibitor experience (PI-naïve)

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MAGELLAN-1, Part 2 Study: Conclusions

- Patients with prior failure to PI containing regimens (NS5A inhibitor-naïve):
  - 100% SVR12 with 12 or 16 weeks of G/P treatment
- Patients with prior failure to both PI- and NS5A inhibitor-containing regimens had lower SVR12 rates
- Patients with prior failure to NS5A inhibitors (i.e., LDV or DCV); NS3/4A PI-naïve:
  - 94% SVR12 with 16 weeks of G/P treatment with no relapse
  - No impact of baseline NS5A substitutions on SVR12
- G/P for 12 or 16 weeks was well tolerated; Grade 3 lab abnormalities were rare, with no discontinuations due to AEs, and no DAA-related serious AEs

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