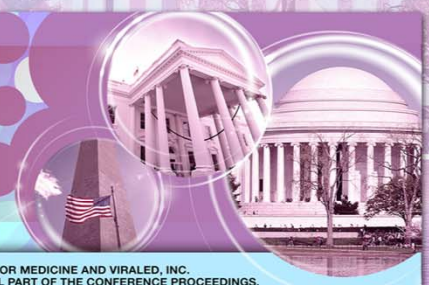
REPORTING ON AASLD 2017

ADVANCES IN CHRONIC HEPATITIS C:
MANAGEMENT AND TREATMENT

COMPREHENSIVE EXPERT REVIEW AND
DISCUSSION OF KEY PRESENTATIONS



REPORTING ON AASLD 2017

ADVANCES IN CHRONIC HEPATITIS C:
MANAGEMENT AND TREATMENT

COMPREHENSIVE EXPERT REVIEW AND
DISCUSSION OF KEY PRESENTATIONS

AN INDEPENDENT CME ACTIVITY JOINTLY PROVIDED BY POSTGRADUATE INSTITUTE FOR MEDICINE AND VIRALED, INC.
THE COVERAGE IS NOT SANCTIONED BY THE CONFERENCE ORGANIZERS AND IS NOT AN OFFICIAL PART OF THE CONFERENCE PROCEEDINGS.

CURRENT DAAS INCLUDING TREATMENT OF DAA NON-RESPONDERS AND RASS

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

REPORTING ON AASLD 2017

ADVANCES IN CHRONIC HEPATITIS C: MANAGEMENT AND TREATMENT

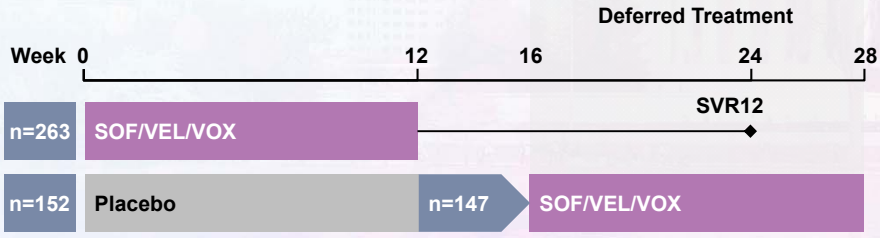
COMPREHENSIVE EXPERT REVIEW AND DISCUSSION OF KEY PRESENTATIONS

SOF/VEL/VOX FOR 12 WEEKS IN NS5A-INHIBITOR-EXPERIENCED HCV-INFECTED PATIENTS: RESULTS OF THE DEFERRED TREATMENT GROUP IN THE PHASE 3 POLARIS-1 STUDY

Marc Bourlière, Stuart C. Gordon, Eugene R. Schiff, Tram T. Tran, Natarajan Ravendhran, Charles S. Landis, Robert H. Hyland, Jie Zhang, Hadas Dvory-Sobol, Luisa M. Stamm, Diana M. Brainard, John G. McHutchison, Lawrence Serfaty, Alex J. Thompson, Thomas E. Sepe, Michael P. Curry, K. Rajender Reddy, Michael P. Manns

Abstract 1178

POLARIS-1 STUDY: PATIENT POPULATION



- Primary study was a double-blind, randomized, placebo-controlled trial in NS5A inhibitor-experienced HCV GT 1–6 patients
- Patients who received placebo in the primary study were eligible to receive open-label SOF/VEL/VOX for 12 weeks in the deferred treatment substudy following completion of the post-treatment Week 4 visit and unblinding

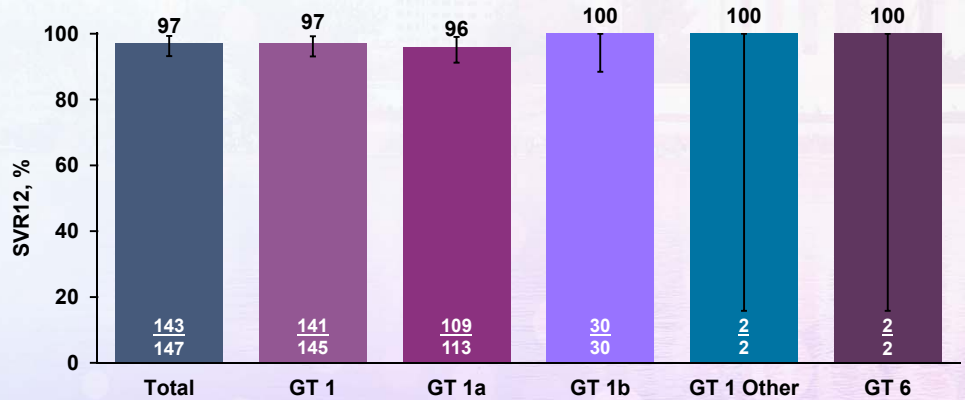
POLARIS-1 STUDY: PATIENT DEMOGRAPHICS

	SOF/VEL/VOX 12 Weeks n=147
Mean age, y (range)	59 (29–80)
Male, n (%)	116 (79)
White, n (%)	121 (82)
Mean BMI, kg/m^2 (range)	29 (18–62)
Cirrhosis, n (%)	49 (33)
HCV GT, n (%)	
1 (Total)	145 (99)
1a	113 (77)
1b	30 (20)
Other	2 (1)
6	2 (1)
IL28B CC, n (%)	26 (18)

	SOF/VEL/VOX 12 Weeks n=147
Mean HCV RNA, $\log_{10}$ IU/mL (range)	6.3 (4.5–7.6)
Prior treatment experience	
NS5A + NS5B	76 (52)
NS5A + NS3 ± NS5B	61 (41)
NS5A ± Others	9 (6)
Others	1 (<1)
Baseline RASs	
NS3 only	10 (7)
NS5A only	60 (41)
NS3 and NS5A	61 (41)
None	14 (10)
Not available	2 (1)

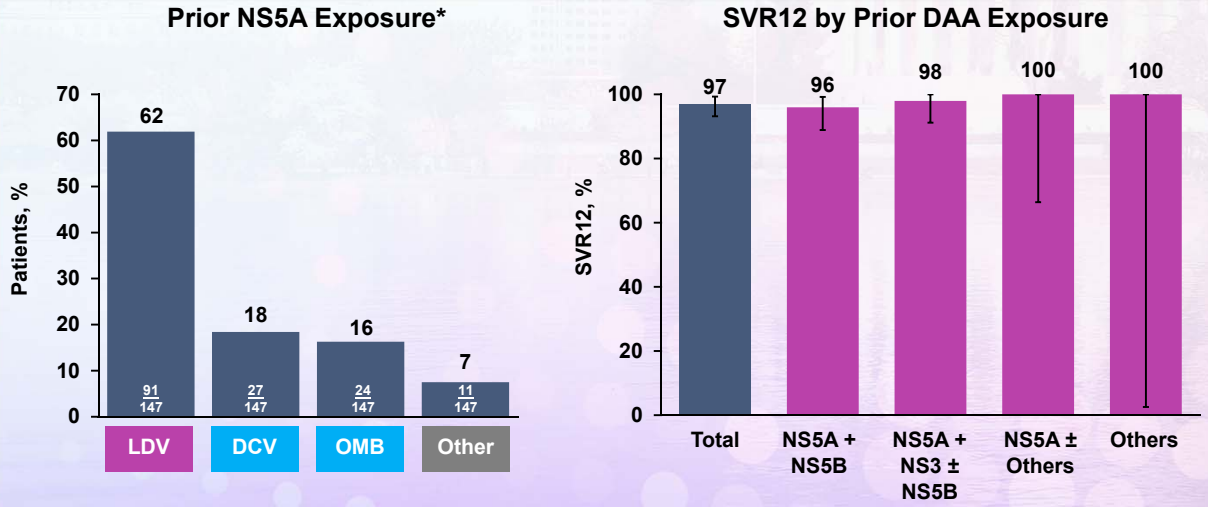
Bourliere M, et al. 68th AASLD; Washington, DC; October 20-24, 2017; Abst. 1178.

POLARIS-1 STUDY: SVR12 BY GENOTYPE/SUBTYPE



Bourliere M, et al. 68th AASLD; Washington, DC; October 20-24, 2017; Abst. 1178.

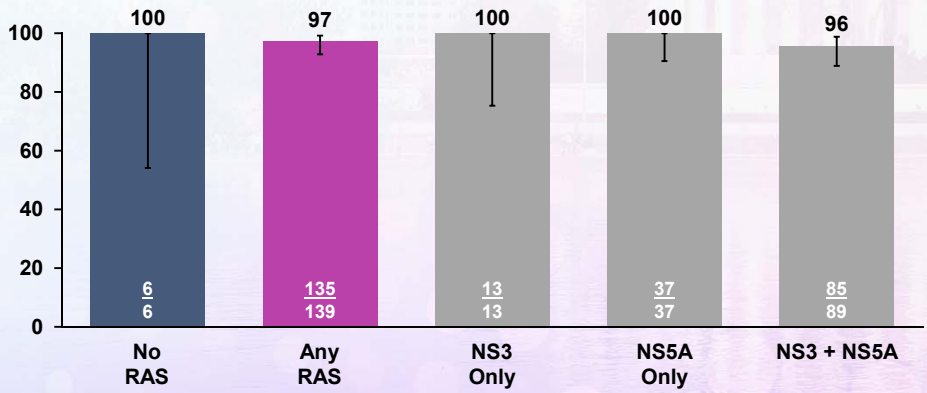
POLARIS-1 STUDY: PRIOR NS5A EXPOSURE AND SVR12



**6 patients had received either prior ledipasvir (LDV) and daclatasvir (DCV) or LDV and ombitasvir (OMB).

Bourliere M, et al. 68th AASLD; Washington, DC; October 20-24, 2017; Abst. 1178.

POLARIS-1 STUDY: SVR12 BY BASELINE RAS



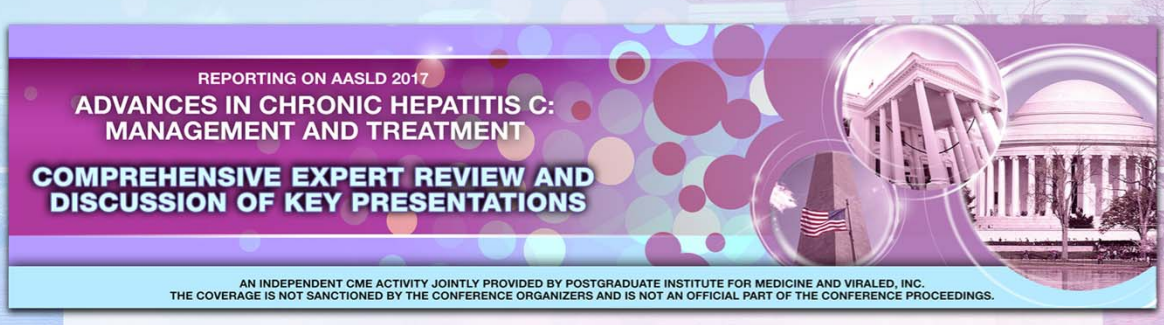
- Of the 4 patients who relapsed, 2 developed treatment-emergent resistance
  - 1 had treatment-emergent NS3 Y56H, D168A/V, and NS5A L31L/M
  - 1 had treatment-emergent NS3 V36V/A

Bourliere M, et al. 68th AASLD; Washington, DC; October 20-24, 2017; Abst. 1178.

POLARIS-1 STUDY: SUMMARY

- Baseline RASs were very common but did not impact SVR12
- High SVR12 rates were observed in NS5A inhibitor-experienced patients treated with SOF/VEL/VOX for 12 weeks
  - 96% in NS5A+NS5B-exposed patients
  - 98% in NS5A+NS3+/−NS5B-exposed patients

Bourliere M, et al. 68th AASLD; Washington, DC; October 20-24, 2017; Abst. 1178.

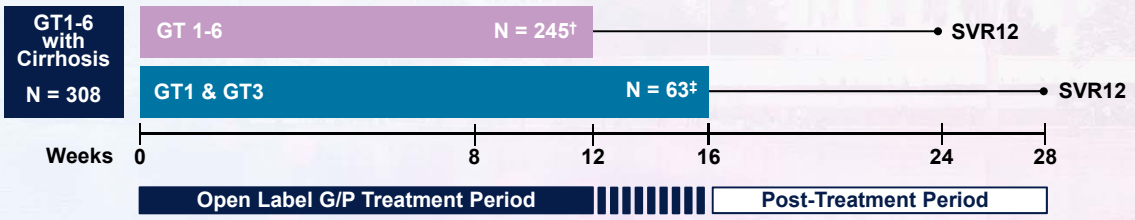


EFFICACY, SAFETY, AND PHARMACOKINETICS OF GLECAPREVIR/PIBRENTASVIR IN ADULTS WITH CHRONIC GENOTYPE 1-6 HEPATITIS C VIRUS INFECTION AND COMPENSATED CIRRHOSIS: AN INTEGRATED ANALYSIS

Edward J. Gane, Fred Poordad, Neddie Zadeikis, Joaquin M. Valdes, Chih-Wei Lin, Wei Liu, Armen Asatryan, Stanley Wang, Catherine A. Stedman, Susan Greenbloom, Tuan T. Nguyen, Magdy Elkhashab, William R. Harlan, Marcus A. Woerns, Albert Tran, Jean-Pierre Mulkay, Yao Yu, Tami Pilot-Matias, Ariel R. Porcalla, Federico J. Mensa

Abstract 74

OBJECTIVE AND STUDY DESIGN



- **Objective:** Evaluate the efficacy, safety and pharmacokinetics of 12 and 16 weeks of G/P treatment in patients with chronic HCV GT1-6 infection and compensated cirrhosis in an integrated analysis across 4 phase 2 and 3 studies*

*patients pooled from the EXPEDITION-1, EXPEDITION-4, SURVEYOR-2, and MAGELLAN-1 studies
†includes 20 HCV GT1-6 patients with renal impairment; GT3 were HCV treatment-naïve only
‡includes GT3 treatment-experienced (IFN/pegIFN±RBV or SOF+RBV±pegIFN) patients and GT1 patients experienced with NS5A and/or protease inhibitors

Gane E, et al. 68th AASLD; Washington, DC; October 20-24, 2017; Abst. 74.

BASELINE CHARACTERISTICS

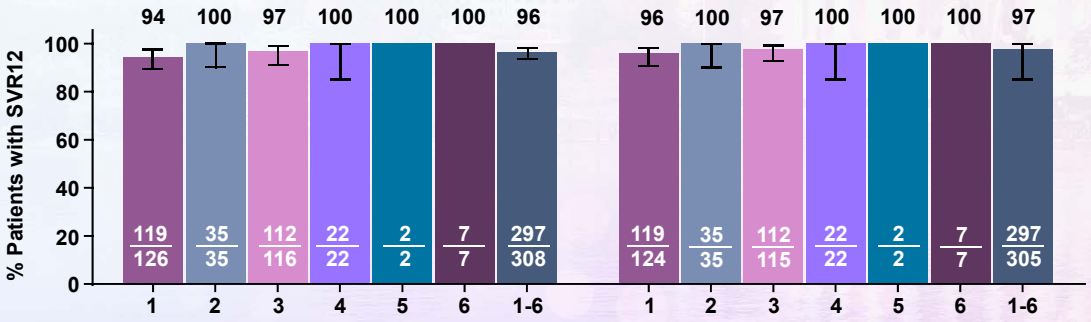
Characteristic	G/P, N = 308
Male, n (%)	199 (65)
White race, n (%)	261 (85)
Age, median (range), years	58.5 (26–88)
BMI, median (range), kg/m^2	28.2 (18.0–55.4)
HCV genotype, n (%)	
1	123 (40)
2	38 (12)
3	116 (38)
4	22 (7)
5	2 (1)
6	7 (2)
HCV RNA, $\log_{10}$ IU/mL median (range)	6.2 (3–7)
Cirrhosis diagnosed by liver biopsy, n (%)	47 (15)
Cirrhosis diagnosed by Fibroscan, n (%)	215 (70)
Cirrhosis diagnosed by FibroTest + APRI, n (%)	46 (15)

Characteristic, n (%)	G/P, N = 308
Treatment-naive	182 (59)
Treatment-experienced PRS-experienced NS5A inhibitor- and/or PI-experienced	126 (41) 99 (32) 27 (9)
Baseline Child-Pugh Score* 5 6 7	 264 (86) 41 (13) 2 (<1)
Platelet counts, ×10^9/L <100 ≥100	 70 (23) 238 (77)
Albumin, g/dL <3.5 ≥3.5	 23 (7) 285 (93)

BMI, body mass index , APRI, aspartate aminotransferase-to-platelet ratio index.
PRS, experienced with IFN or pegIFN ± RBV, or SOF + RBV + pegIFN; PI, protease inhibitor.
*1 patient missing data

Gane E, et al. 68th AASLD; Washington, DC; October 20-24, 2017; Abst. 74.

SVR12: ITT AND MITT ANALYSES



Reason for Non-response, n (%)	N=308
Breakthrough	5 (2)
Relapse	3 (1)
Missing data	2 (<1)
Discontinuation	1 (<1)

Reason for Non-response, n (%)	N=305
Breakthrough	5 (2)
Relapse	3 (1)

Gane E, et al. 68th AASLD; Washington, DC; October 20-24, 2017; Abst. 74.

SUMMARY

- G/P for 12 and 16 weeks achieved high efficacy in patients with HCV GT 1–6 infection and compensated cirrhosis, including those with renal impairment
  - 96% (ITT) and 97% (mITT) overall SVR12

Gane E, et al. 68th AASLD; Washington, DC; October 20-24, 2017; Abst. 74.