ADVANCES IN CHRONIC HEPATITIS C:
MANAGEMENT AND TREATMENT

INDEPENDENT REPORTING ON AASLD 2016

COMPREHENSIVE EXPERT REVIEW AND DISCUSSION OF KEY PRESENTATIONS

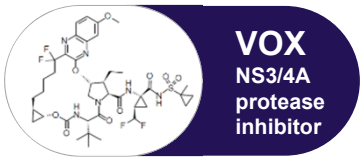
AN INDEPENDENT CME ACTIVITY JOINTLY PROVIDED BY POSTGRADUATE INSTITUTE FOR MEDICINE AND VIRALED, INC.
THE COVERAGE IS NOT SANCTIONED BY THE CONFERENCE ORGANIZERS AND IS NOT AN OFFICIAL PART OF THE CONFERENCE PROCEEDINGS.

A Randomized Phase 3 Trial of Sofosbuvir/Velpatasvir/Voxilaprevir for 8 Weeks Compared to Sofosbuvir/Velpatasvir for 12 Weeks in DAA-Naïve Genotype 1–6 HCV Infected Patients: The POLARIS-2 Study

Ira M. Jacobson, Tarik Asselah, Ronald Nahass, Bal R. Bhandari, Albert Tran, Robert H. Hyland, Luisa M. Stamm, Hadas Dvory-Sobol, Yanni Zhu, Diana M. Brainard, G. Mani Subramanian, John G. McHutchison, Stephen Shafran, Mitchell Davis, Catherine A. Stedman, Eric Lawitz, Edward J. Gane

Abstract LB-12

POLARIS-2: Pangenotypic Single Tablet Regimen with Inhibitors of HCV NS5B (Nucleotide) + NS5A + NS3



Sofosbuvir (SOF)/Velpatasvir (VEL)

- SOF: Nucleoside polymerase inhibitor with activity against HCV GT 1-6
- VEL: Potent pangenotypic NS5A inhibitor

Voxilaprevir (VOX)

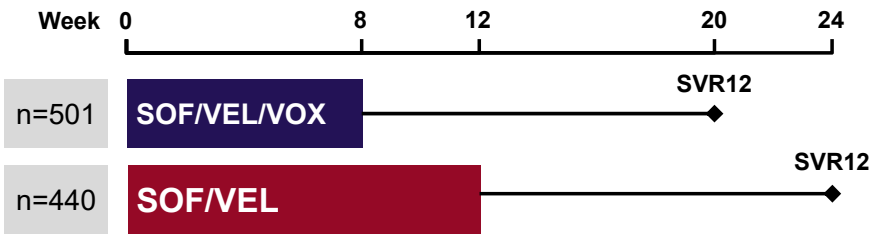
- HCV NS3/4A PI with potent antiviral activity against GT 1-6, including most RASs

SOF/VEL/VOX

- Once daily, oral, fixed-dose combination (400/100/100 mg) for GT 1-6

Bourlière M, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. 194.

POLARIS-2: Study Design



- Open-label, randomized, active-comparator trial at 117 sites (USA, Canada, France, Germany, UK, Australia, and New Zealand)
- Genotypes 1–6 with and without compensated cirrhosis
  - GT 3 patients with cirrhosis were enrolled in a separate study (POLARIS-3)
- 1:1 randomization for GT 1–4 (other GTs assigned to SOF/VEL/VOX)
  - Stratified by GT, cirrhosis, and prior treatment experience (naïve or IFN experienced)

Bourlière M, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. 194.

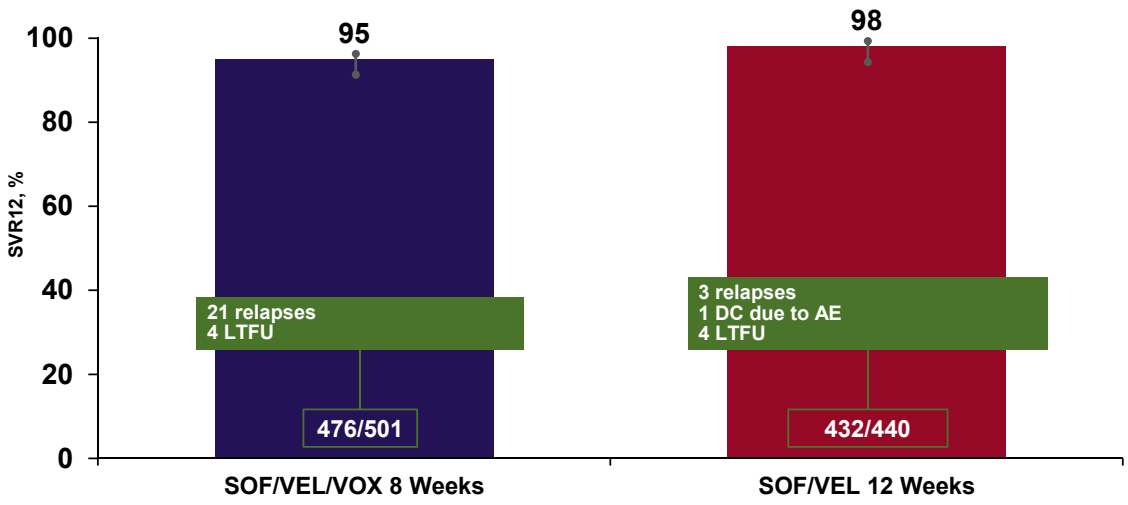
POLARIS-2: Randomized Controlled Trial of SOF/VEL/VOX for 8 Weeks versus SOF/VEL for 12 Weeks

- Open-label
- Treatment-naïve and experienced (interferon/ribavirin only)
- HCV genotype 1, 2, 3, 4, 5, 6

		SOF/VEL/VOX 8 Weeks n=501	SOF/VEL 12 Weeks n=440
Mean age, y (range)		53 (18–78)	52 (19–82)
Male, n (%)		255 (51)	237 (54)
White, n (%)		391 (78)	365 (83)
Mean BMI, kg/m^2 (range)		27 (17–57)	27 (18–54)
Cirrhosis, n (%)		90 (18)	84 (19)
Genotype, n (%)*	**1a / 1b / Other**	169 (34) / 63 (13) / 1 (<1)	172 (39) / 59 (13) / 1 (<1)
	2	63 (13)	53 (12)
	3	92 (18)	89 (20)
	4	63 (13)	57 (13)
	5 / 6 / Unknown	18 (4) / 30 (6) / 2 (<1)	0 / 9 (2) / 0
IFN experienced, n (%)		118 (24)	100 (31)
IL28B CC, n (%)		166 (33)	136 (31)
Mean HCV RNA, $\log_{10}$ IU/mL (range)		6.1 (2.7–7.6)	6.2 (4.0–7.6)

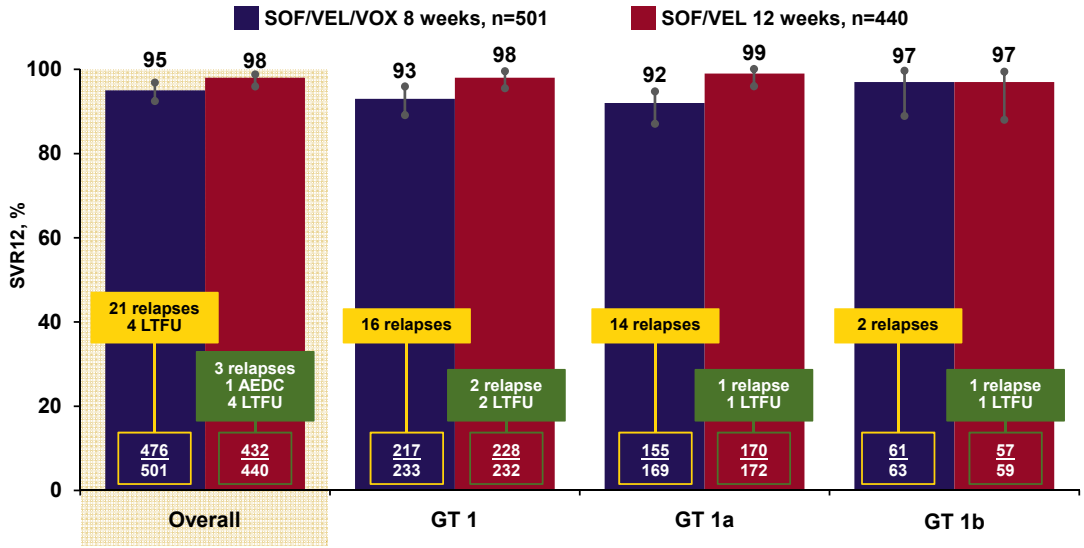
Jacobson I, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. LB-12.

POLARIS-2: Results (SVR12)



Jacobson I, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. LB-12.

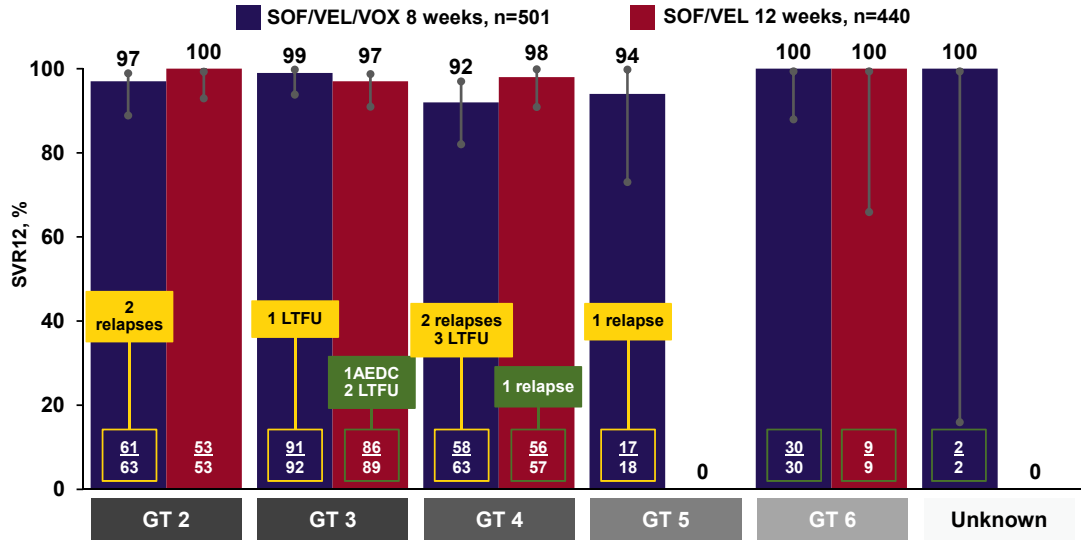
POLARIS-2: Results - SVR12 by Genotype (GT 1)



AEDC, Discontinuation due to AE. Error bars represent 95% confidence intervals.
2 of 2 patients (100%) with GT 1 Other achieved SVR12 (1 each in the SOF/VEL/VOX and SOF/VEL groups).

Bourlière M, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. 194.

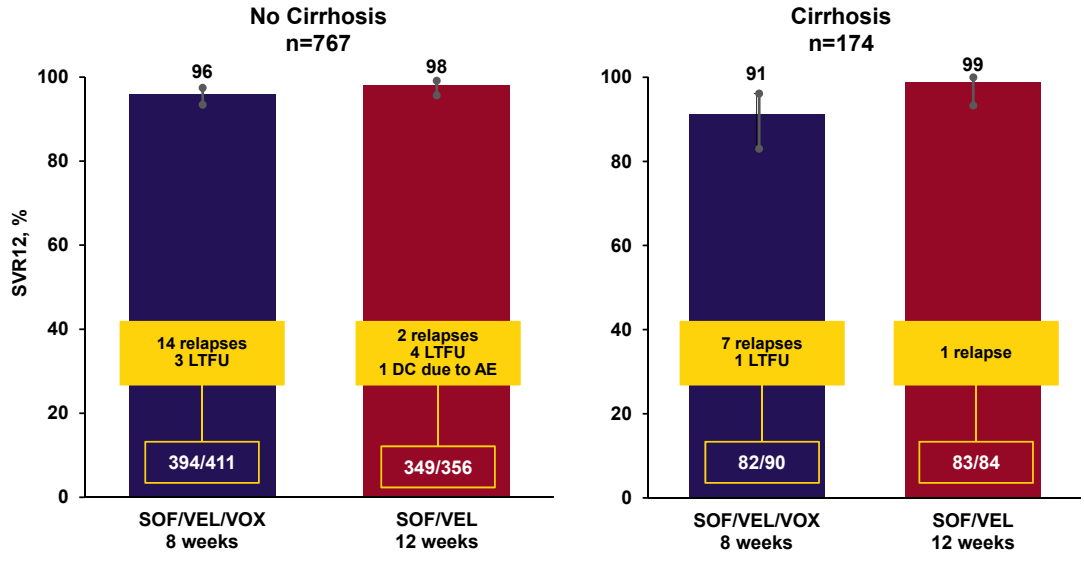
POLARIS-2:
Results - SVR12 by Genotype (GT 2–6)



AEDC, Discontinuation due to AE. Error bars represent 95% confidence intervals.

Bourlière M, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. 194.

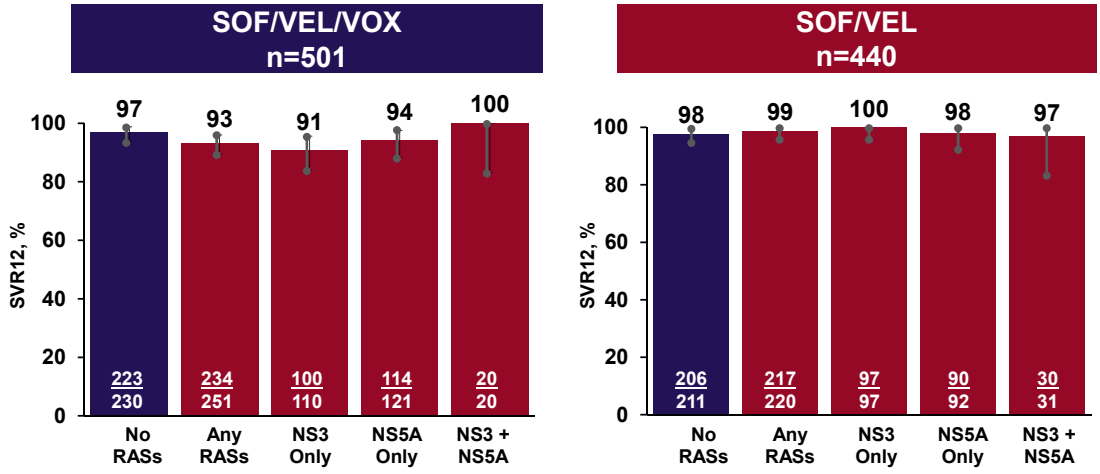
POLARIS-2:
Results - SVR12 by Cirrhosis Status



Error bars represent 95% confidence intervals.

Bourlière M, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. 194.

POLARIS-2:
Results - SVR12 by Baseline RASs



- All 64 patients with baseline NS5B nucleoside inhibitor RASs achieved SVR12

20 patients in the SOF/VEL/VOX group and 9 patients in the SOF/VEL group were excluded due to incomplete RAS data; RASs were analyzed using a 15% cut off; error bars represent 95% confidence intervals.

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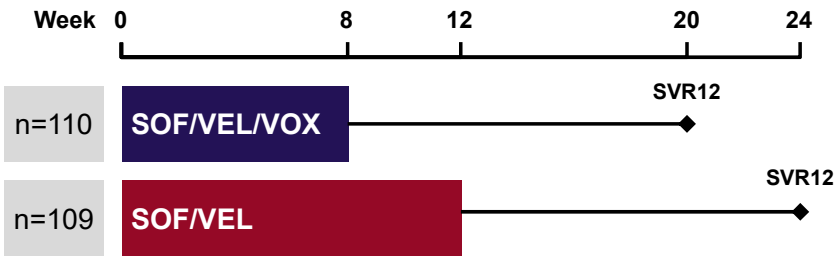
A Randomized, Phase 3 Trial of Sofosbuvir/Velpatasvir/Voxilaprevir for 8 Weeks and Sofosbuvir/Velpatasvir for 12 Weeks for Patients with Genotype 3 HCV Infection and Cirrhosis: The POLARIS-3 Study

Graham R. Foster, Alexander Thompson, Peter J. Ruane, Sergio Borgia, Gregory Dore, Kimberly Workowski, Robert H. Hyland, Jing Wang, Evguenia S. Svarovskaia, Luisa M. Stamm, Diana M. Brainard, G. Mani Subramanian, John G. McHutchison, Thomas Berg, Kosh Agarwal, Brian Conway, Jordan Feld, Bernard Willems, Stuart K. Roberts, Eric Gane

Abstract 258

POLARIS-3: Study Design



- Open-label, randomized, active-comparator trial conducted at 84 sites (USA, Canada, France, Germany, UK, Australia, New Zealand)
- Patients with GT 3, all of whom had cirrhosis
- 1:1 randomization
  - Stratified by prior treatment experience (IFN experienced or naïve)

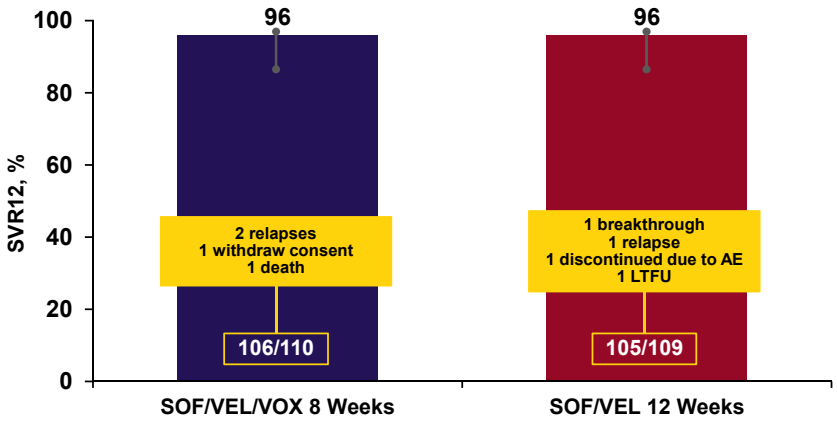
Foster G, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. 258.

POLARIS-3: Randomized Controlled Trial of SOF/VEL/VOX for 8 Weeks Versus SOF/VEL for 12 Weeks in Patients with HCV Genotype 3 and Cirrhosis

	SOF/VEL/VOX 8 Weeks n=110	SOF/VEL 12 Weeks n=109
Mean Age, y (range)	54 (25–75)	55 (31–69)
Male, n (%)	74 (67)	83 (76)
White, n (%)	100 (91)	97 (89)
Mean BMI, kg/m^2 (range)	28 (20–50)	27 (18–46)
Mean Platelets, x10^3/μL (range)	14 (37–351)	150 (51–292)
IFN Experienced, n (%)	35 (32)	32 (29)
IL28B CC, n (%)	41 (37)	52 (48)
Mean HCV RNA, log$_{10}$ IU/mL (range)	6.0 (1.6–7.6)	6.3 (4.1–7.5)

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

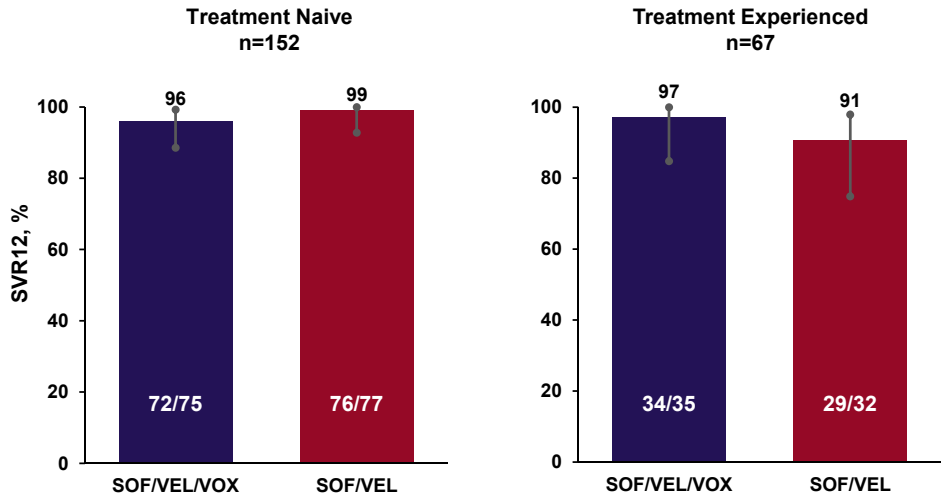
POLARIS-3: Results (SVR12)



- There were 6 patients with Y93H in the SOF/VEL/VOX group and 4 in the SOF/VEL group; all achieved SVR12
- No treatment emergent RASs in the SOF/VEL/VOX group. In the SOF/VEL group, both virologic failures had Y93H

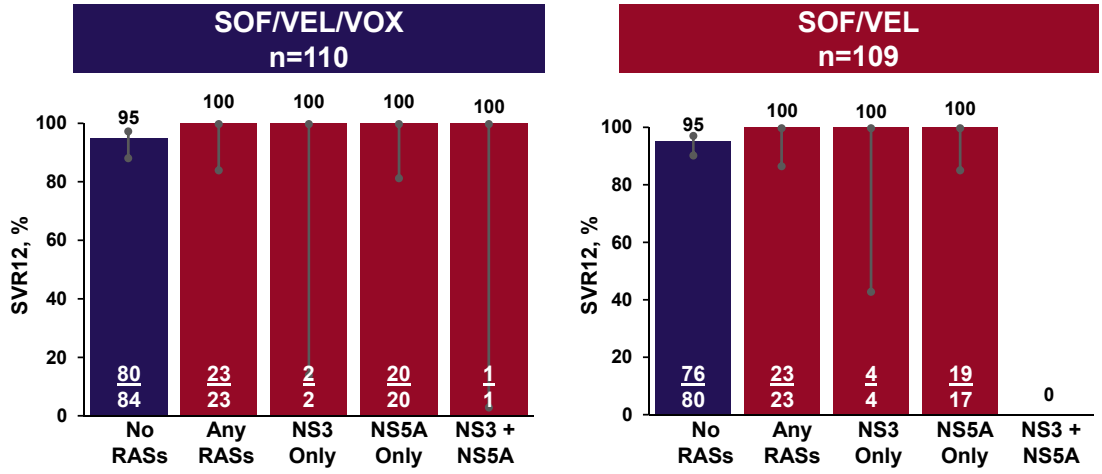
Foster G, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. 258.

POLARIS-3: Results - SVR12 by Prior Treatment



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

POLARIS-3:
Results - SVR12 by Baseline RASs



- There were 6 patients with Y93H in the SOF/VEL/VOX group and 4 in the SOF/VEL group; all achieved SVR12
- No treatment emergent RASs in the SOF/VEL/VOX group; in the SOF/VEL group, both virologic failures had Y93H

3 patients in the SOF/VEL/VOX group and 6 patients in the SOF/VEL group were excluded due to incomplete RAS data; RASs were analyzed using a 15% cut off; error bars represent 95% confidence intervals.

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