ADVANCES IN CHRONIC HEPATITIS C:
MANAGEMENT AND TREATMENT

INDEPENDENT REPORTING ON AASLD 2016

COMPREHENSIVE EXPERT REVIEW AND DISCUSSION OF KEY PRESENTATIONS

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Sofosbuvir/Velpatasvir/Voxilaprevir for 12 Weeks as a Salvage Regimen in NS5A Inhibitor-Experienced Patients with Genotype 1–6 Infection: The Phase 3 POLARIS-1 Study

Marc Bourlière, Stuart C. Gordon, Alnoor Ramji, Natarajan Ravendhran, Tram T. Tran, Robert H. Hyland, Jie Zhang, Hadas Dvory-Sobol, Luisa M. Stamm, Diana M. Brainard, G. Mani Subramanian, John G. McHutchison, Ziad H. Younes, Michael P. Curry, Eugene R. Schiff, K. Rajender Reddy, Michael P. Manns

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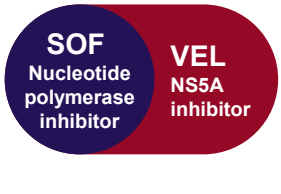
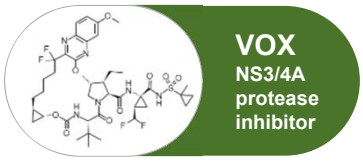
POLARIS-1: Pangenotypic Single Tablet Regimen with Inhibitors of HCV NS5B (Nucleotide) + NS5A + NS3





Sofosbuvir (SOF)/Velpatasvir (VEL)

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

Voxilaprevir (VOX)

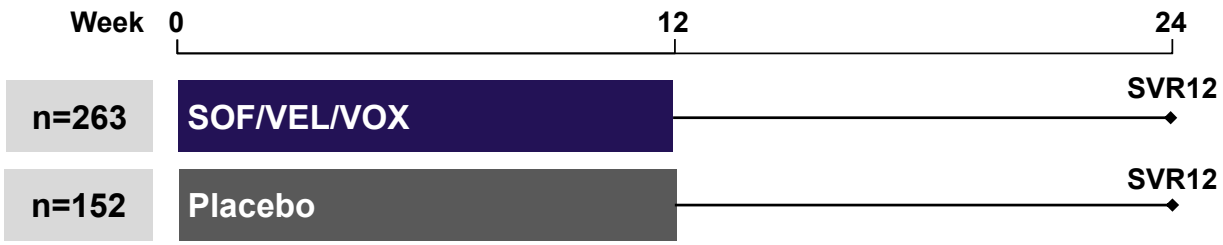
- HCV NS3/4A PI with potent antiviral activity against GT 1-6, including most RASs

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-1: Study Design



- Double-blind, randomized, placebo-controlled trial in NS5A-experienced GT 1–6 patients conducted at 109 sites (USA, Canada, France, Germany, UK, Australia, New Zealand)
- Patients with GT 1 at screening randomized equally to SOF/VEL/VOX or matching placebo (all other GTs assigned to SOF/VEL/VOX)
  - Stratified by presence of cirrhosis

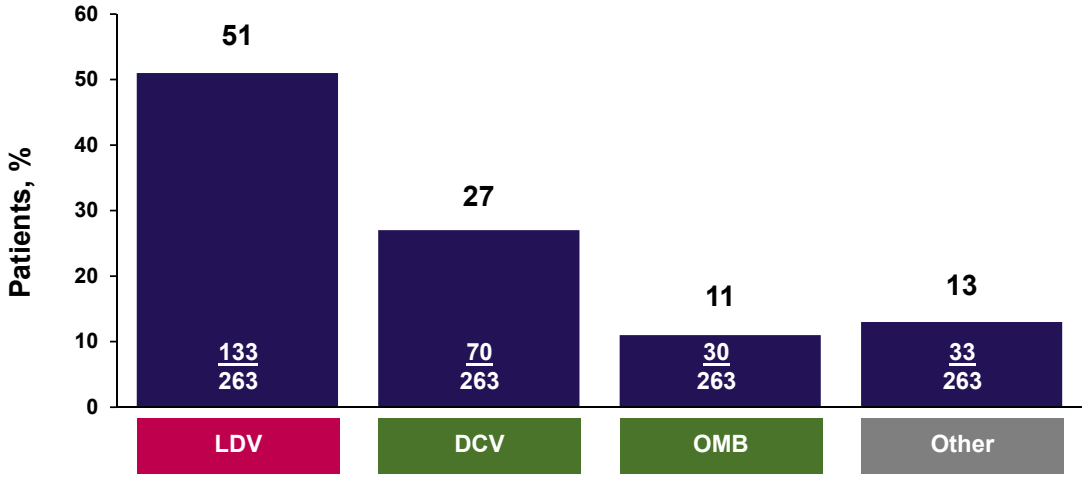
Bourlière M, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. 194.

POLARIS-1: Demographics

		SOF/VEL/VOX 12 weeks n=263	Placebo 12 weeks n=152
Mean age, y (range)		58 (27–84)	59 (29–80)
Male, n (%)		200 (76)	121 (80)
White, n (%)		211 (80)	124 (82)
Mean BMI, kg/m^2 (range)		29 (18–67)	29 (18–61)
Cirrhosis, n (%)		121 (46)	51 (34)
Genotype, n (%)	1a / 1b / Other	101 (38) / 45 (17) / 4 (2)	117 (77) / 31 (20) / 2 (1)
	2	5 (2)	—
	3	78 (30)	—
	4	22 (8)	—
	5 / 6 / Unknown	1 (<1) / 6 (2) / 1 (<1)	0 / 2 (1) /0
IL28B CC, n (%)		47 (18)	27 (18)
Mean HCV RNA, $\log_{10}$ IU/mL (range)		6.3 (1.6–7.7)	6.3 (3.7–7.6)

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

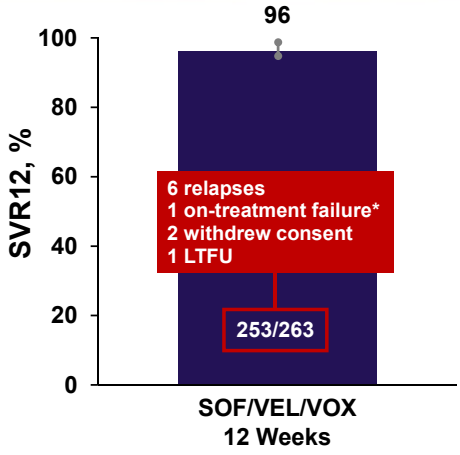
POLARIS-1: Results: Prior NS5A Treatment



3 patients received both LDV and DCV; DCV, daclatasvir; LDV, ledipasvir; OMB, ombitasvir.

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

POLARIS-1: Results: SVR12

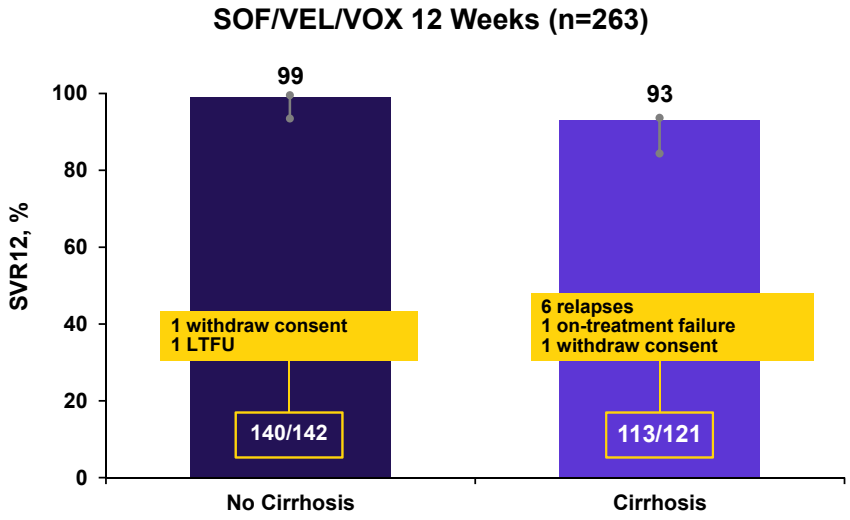


- No patients who received placebo achieved SVR
- p <0.001 for superiority compared with prespecified 85% performance goal for SOF/VEL/VOX

* Exposure was consistent with non-adherence.

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

POLARIS-1: Results (SVR12) by Cirrhosis Status



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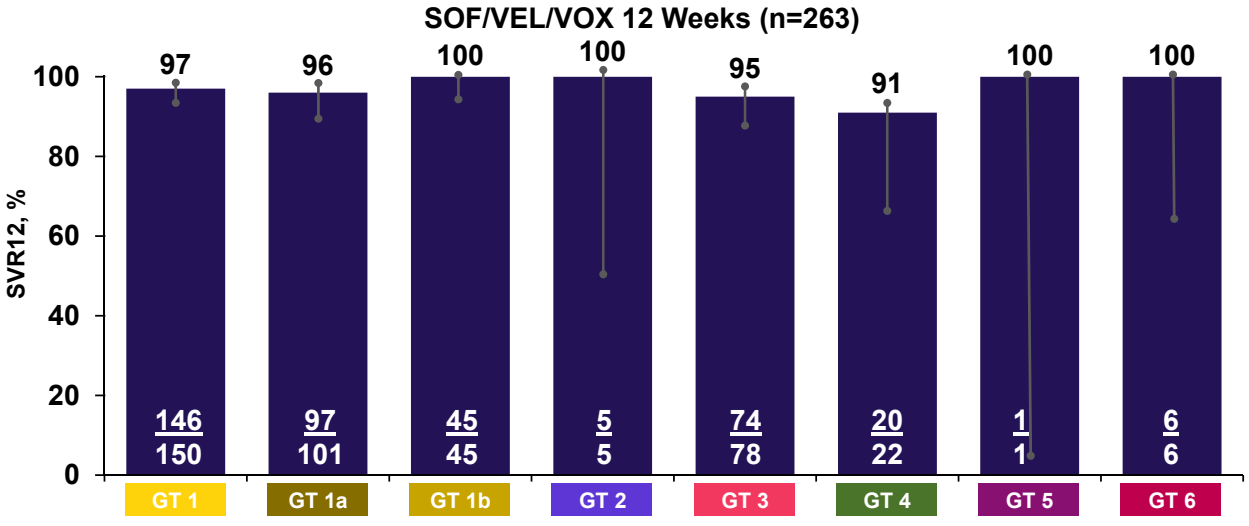
POLARIS-1: Results (SVR12) by Subtype/Genotype



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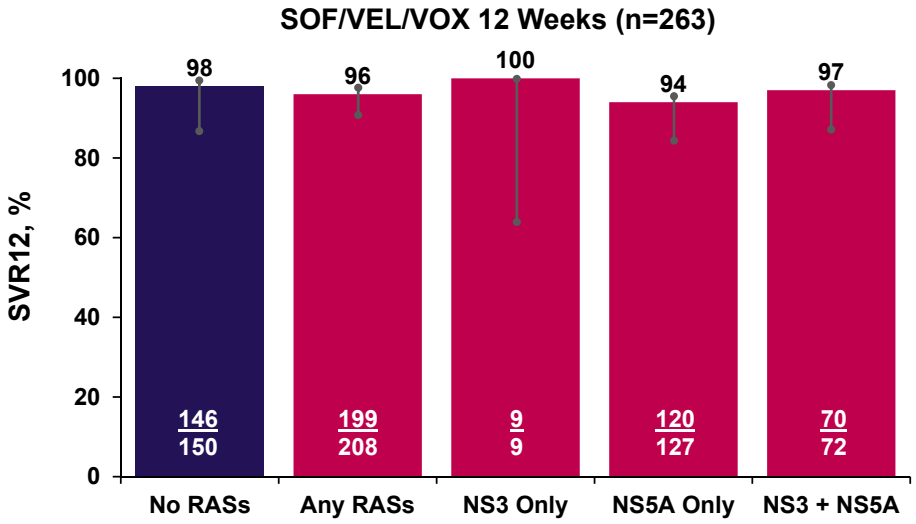
POLARIS-1 : Results (SVR12)



Two patients had S282T at baseline, both achieved SVR12

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ADVANCES IN CHRONIC HEPATITIS C: MANAGEMENT AND TREATMENT

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COMPREHENSIVE EXPERT REVIEW AND DISCUSSION OF KEY PRESENTATIONS

A Randomized, Controlled, Phase 3 Trial of Sofosbuvir/Velpatasvir/Voxilaprevir or Sofosbuvir/Velpatasvir for 12 Weeks in Direct-Acting Antiviral-Experienced Patients with Genotype 1–6 HCV Infection: The POLARIS-4 Study

Stefan Zeuzem, Steven L. Flamm, Myron Tong, John M. Vierling, Stephen Pianko, Peter Buggisch, Victor de Lédinghen[7] Robert H. Hyland, Xiaoru Wu, KC Huang, Evguenia S. Svarovskaia, Luisa M. Stamm, Diana M. Brainard, G. Mani Subramanian, John G. McHutchison, Elizabeth C. Verna, Meena B. Bansal, Charles S. Landis, Simone I. Strasser, Curtis L. Cooper, Kris Kowdley

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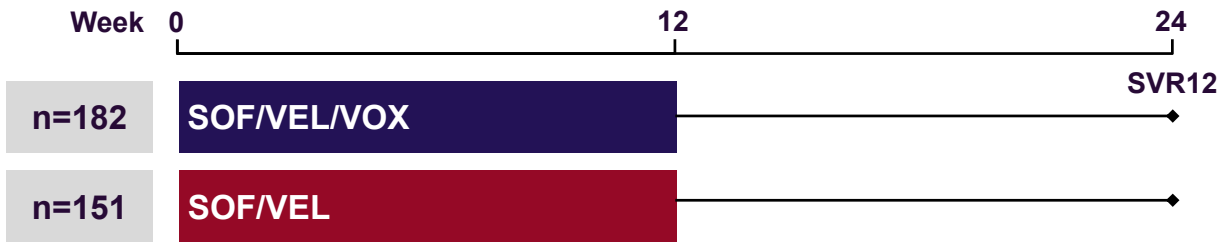
POLARIS-4: Study Design



- Open-label, randomized, active-comparator trial in DAA-experienced GT 1–6 patients without prior NS5A inhibitor experience conducted at 102 sites (USA, Canada, France, Germany, UK, Australia, New Zealand)
- Patients with HCV GT 1, 2, and 3 at screening were randomized equally to SOF/VEL/VOX or SOF/VEL (all other GTs assigned to SOF/VEL/VOX)
  - Stratified by GT and presence of cirrhosis

Zeuzum S, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. 109.

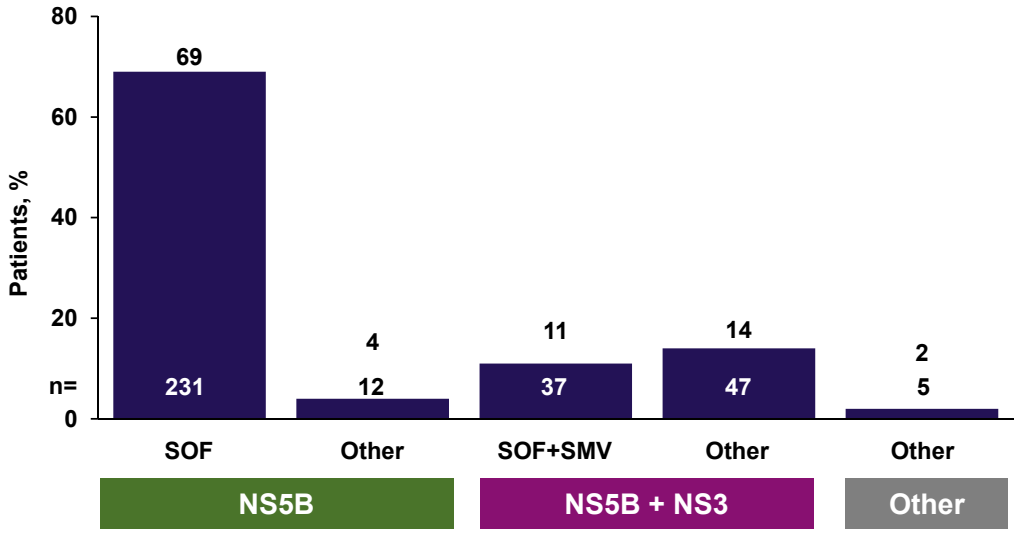
POLARIS-4: Demographics

- Randomized controlled trial of persons who failed non-NS5A containing DAA regimens (SOF 73% or SOF+RBV/IFN)
  - SOF/VEL/VOX for 12 weeks (n=182) versus SOF/VEL for 12 weeks (n=151)

		SOF/VEL/VOX 12 Weeks n=182	SOF/VEL 12 Weeks n=151
Mean age, y (range)		57 (25-85)	57 (24-80)
Male, n (%)		143 (79)	114 (75)
White, n (%)		160 (88)	131 (87)
Mean BMI, kg/m^2 (range)		29 (18-45)	29 (18-53)
Cirrhosis, n (%)		84 (46)	69 (46)
Genotype, n (%)	1a / 1b	54 (30) / 24 (13)	44 (29) / 22 (14)
	2	31 (71)	33 (22)
	3	54 (30)	52 (34)
	4	19 (10)	-
IL28B CC, n (%)		33 (18)	29 (19)
Mean HCV RNA, $\log_{10}$ IU/mL (range)		6.3 (5.0 – 7.5)	6.3 (3.6 - 7.3)

Zeuzum S, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. 109.

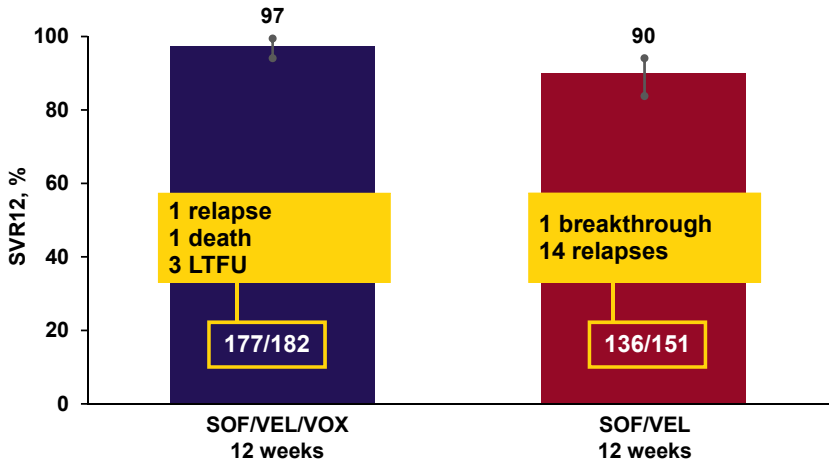
POLARIS-4: Prior HCV Treatment



Other NS5B included mericitabine (n=7); other NS5B+NS3 included deleobuvir+faldaprevir (n=14), mercitabine+danoprevir (n=8), and SOF+telaprevir (n=6); one patient without prior DAA exposure is excluded; SMV, simeprevir; SOF, sofosbuvir

Zeuzum S, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. 109.

POLARIS-4: Results SVR12

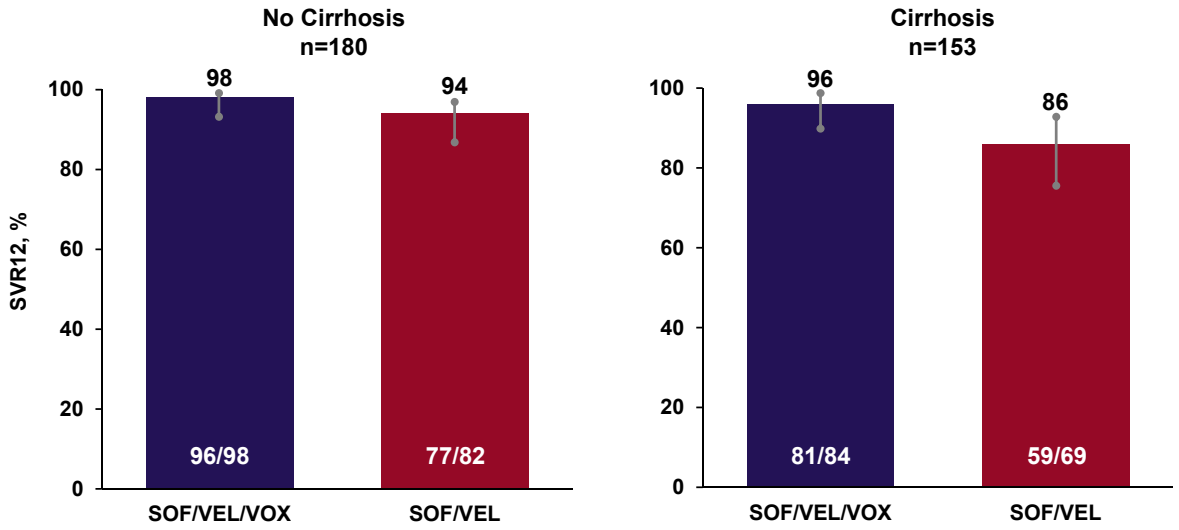


- p <0.001 for superiority compared with prespecified 85% performance goal for SOF/VEL/VOX
- p=0.092 for SOF/VEL

Error bars represent 95% confidence intervals.

Zeuzum S, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. 109.

POLARIS-4: Results SVR12 by Cirrhosis Status



Error bars represent 95% confidence intervals.

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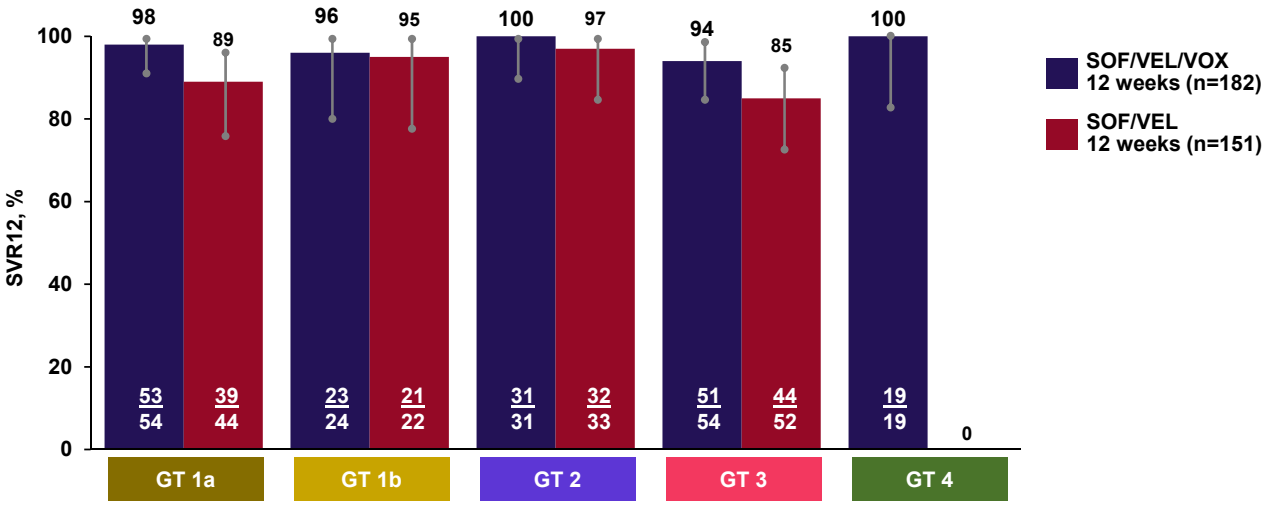
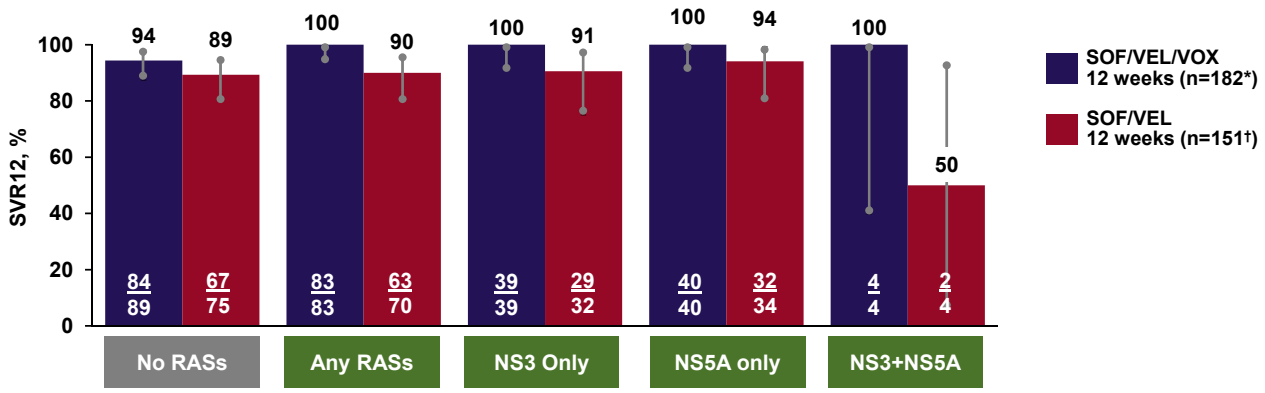
POLARIS-4: Results SVR12 by Genotype



Error bars represent 95% confidence intervals.

Zeuzum S, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. 109.

POLARIS-4: Results SVR12 by Baseline RASs



- Twenty-two patients had NS5B RASs – all achieved SVR12
- No treatment-emergent RASs were observed in the patient who relapsed following SOF/VEL/VOX
- In the SOF/VEL group, 10 of the 15 patients with virologic failure developed Y93H or Y93C

*10 patients and †6 patients were excluded due to incomplete RAS data; RASs were analyzed using a 15% cut off; error bars represent 95% confidence intervals.

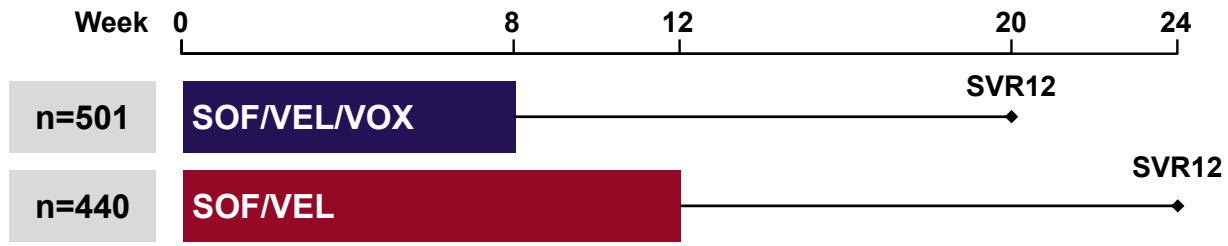
Zeuzum S, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. 109.

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: 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)

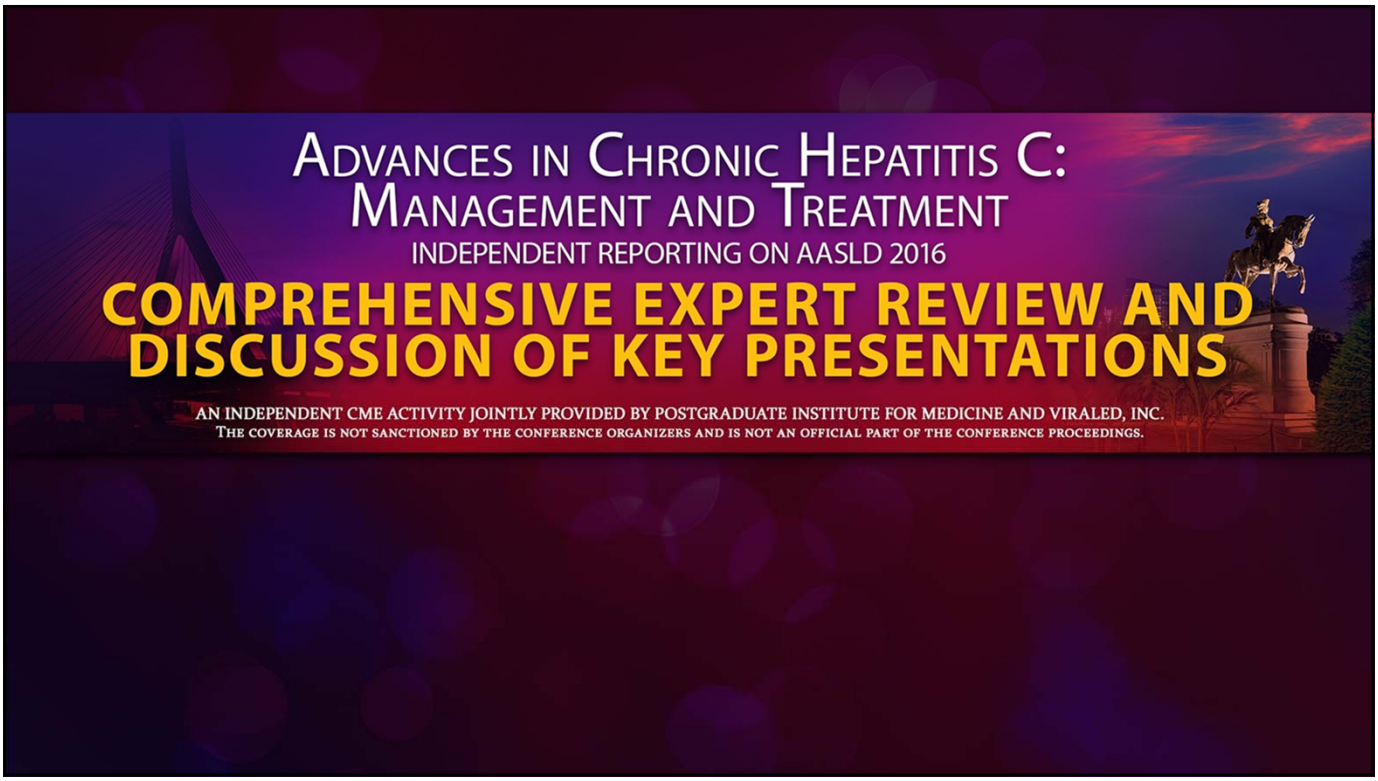
Jacobson I, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. LB-12.

POLARIS-2: Demographics

- 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.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