Sofosbuvir-Velpatasvir-Voxilaprevir in DAA-Experienced GT 1-4
POLARIS-4

Note: POLARIS-4 published in tandem with POLARIS-1

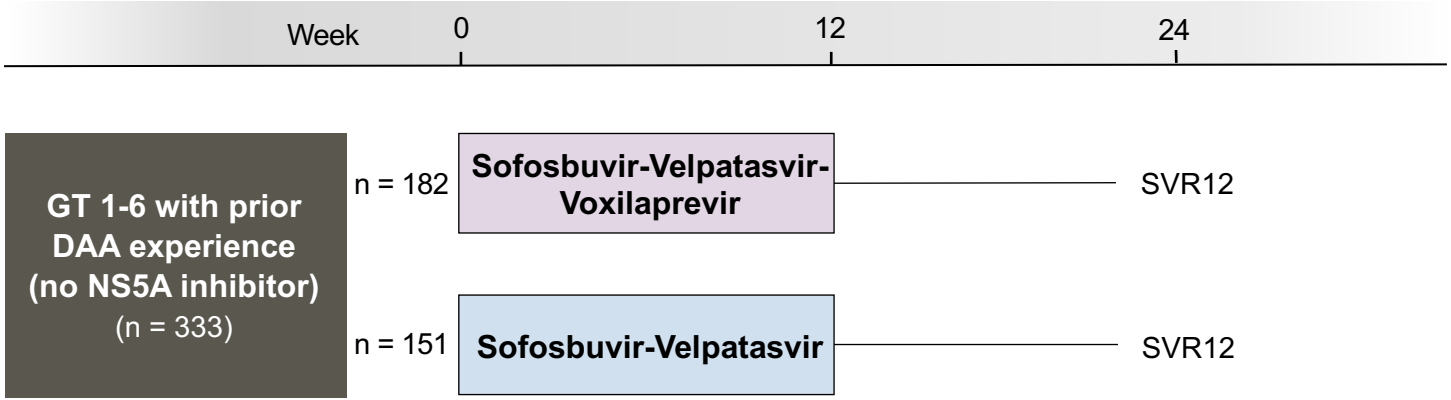
Bourlière M, et al. N Engl J Med. 2017;376:2134-46.

Sofosbuvir-Velpatasvir-Voxilaprevir in DAA-Experienced GT 1-4 POLARIS-4: Study Features

- **Design**: Open-label, randomized, active-comparator, phase 3 trial to compare efficacy of a fixed-dose combination of sofosbuvir-velpatasvir-voxilaprevir versus sofosbuvir-velpatasvir for 12 weeks in DAA-experienced patients who had not received prior NS5A inhibitor.
- **Setting**: 102 sites in United States, Canada, Europe, Australia, and New Zealand
- **Entry Criteria**
  - Age ≥18 years
  - Chronic HCV GT 1-6 (enrolled only GT 1-4)
  - HCV RNA ≥10,000 IU/mL at screening
  - DAA experienced (excluding prior NS5A use)
  - Patients with compensated cirrhosis allowed
- **Primary End Point**: SVR12

Source: Bourlière M, et al. N Engl J Med. 2017;376:2134-46.

Sofosbuvir-Velpatasvir-Voxilaprevir in DAA-Experienced GT 1-6 POLARIS-4: Study Design



GT 1, 2, 3 participants randomized 1:1. Stratified by presence of cirrhosis.
GT4 participants were assigned to active arm (and not randomized).
No GT 5, 6 participants were enrolled.

Drug Dosing
Sofosbuvir-Velpatasvir-Voxilaprevir (400/100/100 mg): fixed dose combination; one pill once daily
Sofosbuvir-Velpatasvir (400/100 mg): fixed dose combination; one pill once daily

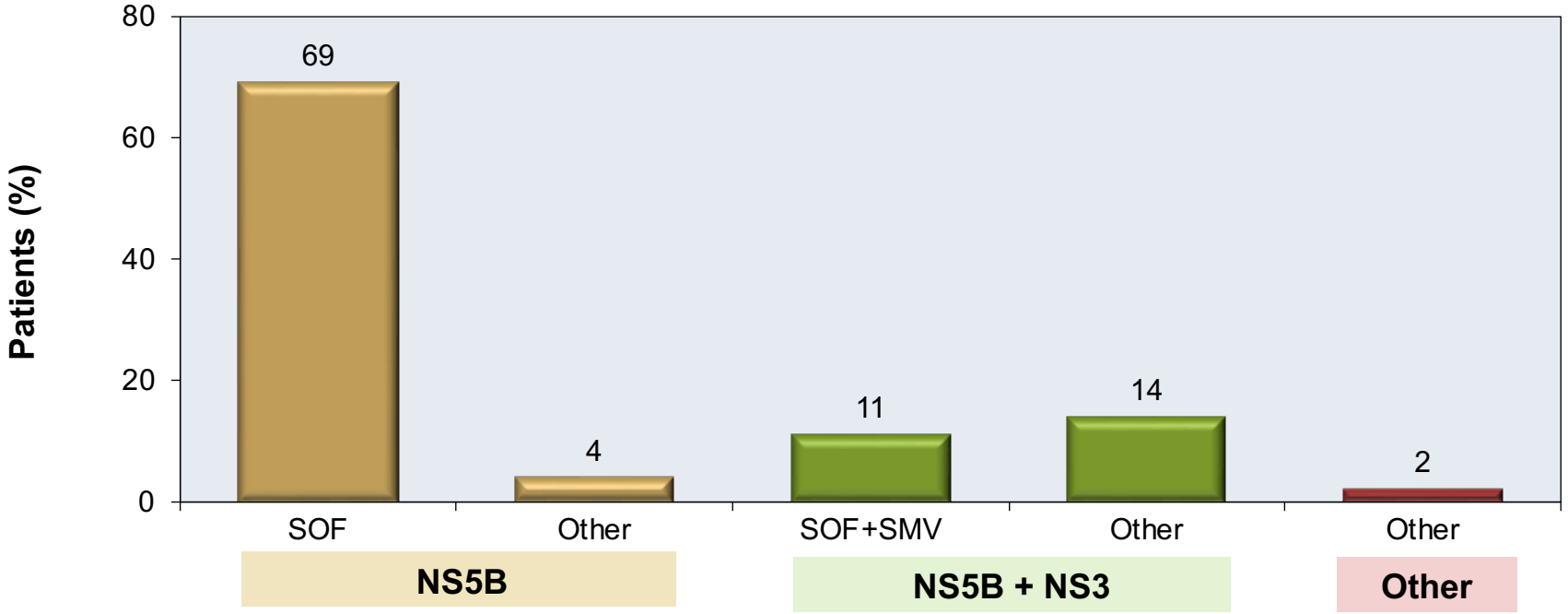
Source: Bourlière M, et al. N Engl J Med. 2017;376:2134-46.

Sofosbuvir-Velpatasvir-Voxilaprevir in DAA-Experienced GT 1-3 POLARIS-4: Baseline Characteristics

Baseline Characteristics	SOF-VEL-VOX x 12 weeks (n = 182)	SOF-VEL x 12 weeks (n = 151)
Age, mean (range)	57 (25-85)	57 (24-80)
Male, n (%)	143 (79)	114 (75)
White, n (%)	160 (88)	131 (87)
Genotype, % 1 1a 1b 2 3 4	 78 (43) 54 (30) 24 (13) 31 (17) 54 (30) 19 (10)	 66 (44) 44 (29) 22 (15) 33 (22) 52 (34) 0
Body mass index, mean, kg/m^2 (range)	29 (18-45)	29 (18-53)
Mean HCV RNA, log_{10} IU/mL (range)	6.3 ± 0.6	6.3 ± 0.7
IL28B CC, n (%)	33 (18)	29 (19)
Cirrhosis, n (%)	84 (46)	69 (46)

Source: Bourlière M, et al. N Engl J Med. 2017;376:2134-46.

Sofosbuvir-Velpatasvir-Voxilaprevir in DAA-Experienced GT 1-3 POLARIS-4: Prior HCV Treatment

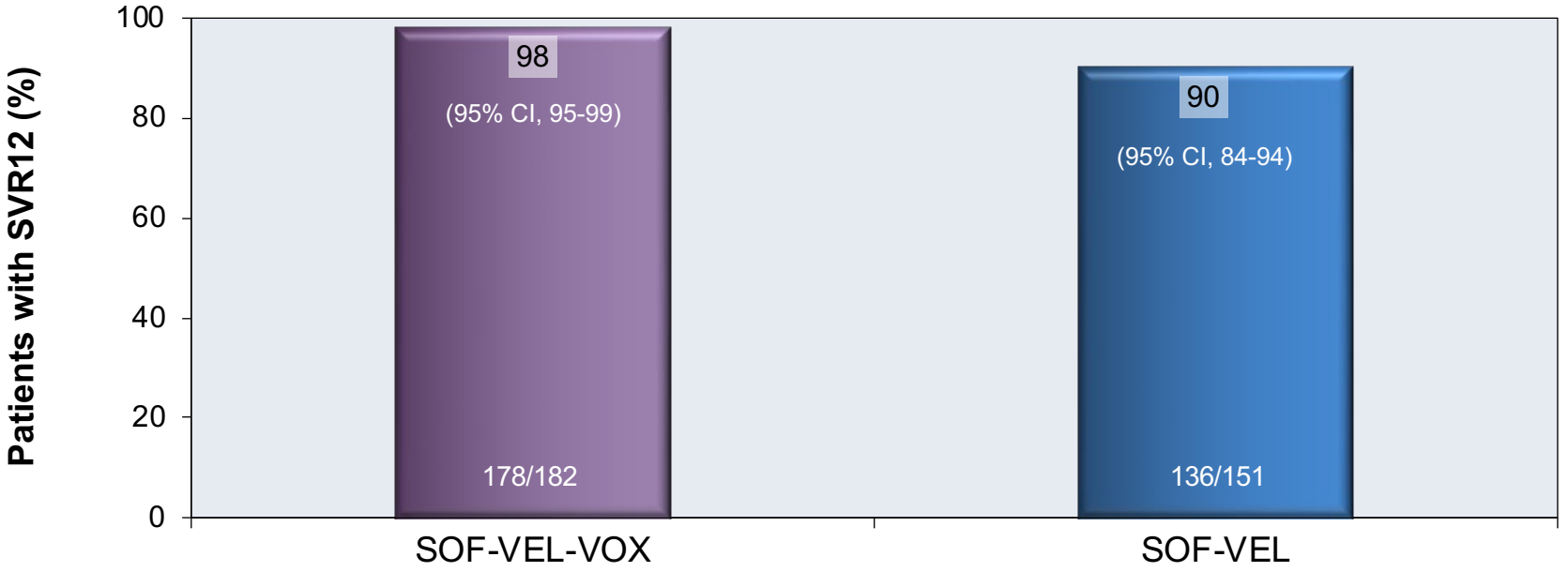


Other NS5B included mericitabine (n = 7); other NS5B plus NS3 included deleobuvir plus faldaprevir (n = 14), mericitabine plus danoprevir (n = 8), and sofosbuvir plus telaprevir (n = 6); one patient without prior DAA exposure is excluded.

Source: Bourlière M, et al. N Engl J Med. 2017;376:2134-46.

Sofosbuvir-Velpatasvir-Voxilaprevir in DAA-Experienced GT 1-6 POLARIS-4: Results

POLARIS-4: Overall SVR12 by Treatment Arm

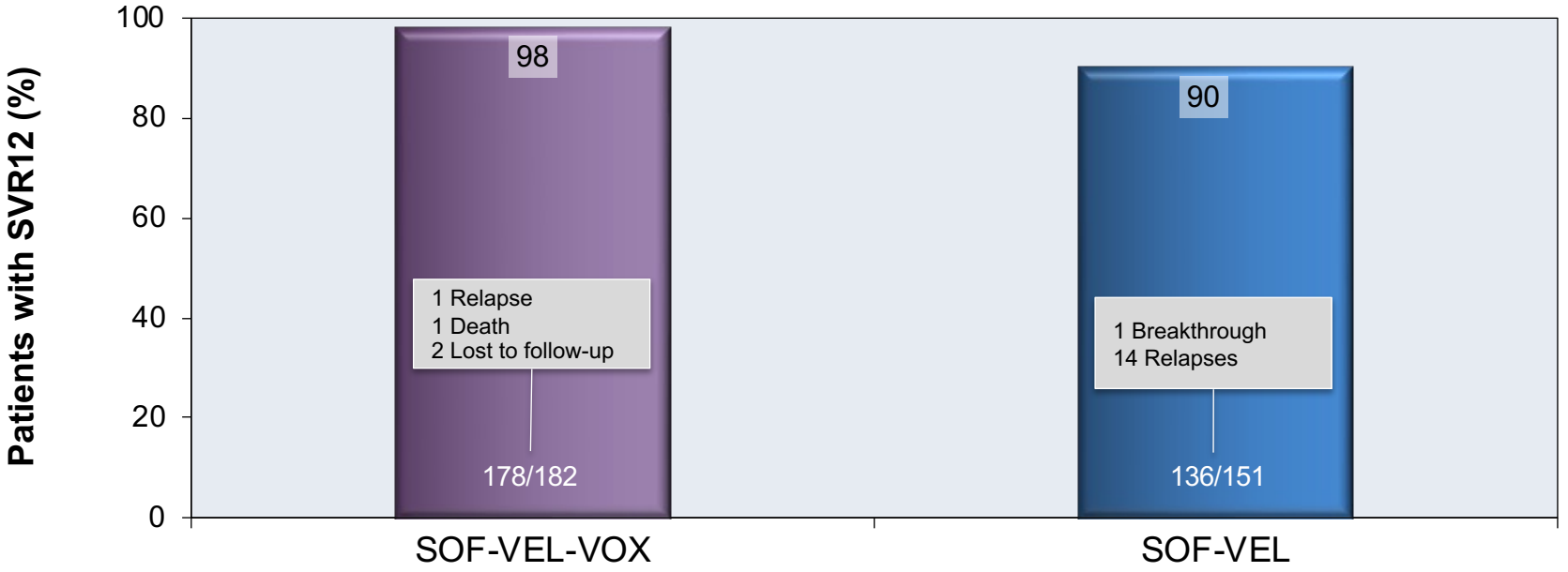


Abbreviations: SOF, sofosbuvir; VEL, velpatasvir; VOX, voxilaprevir
P<0.001 for superiority compared with prespecified 85% performance goal for SOF-VEL-VOX

Source: Bourlière M, et al. N Engl J Med. 2017;376:2134-46.

Sofosbuvir-Velpatasvir-Voxilaprevir in DAA-Experienced GT 1-6 POLARIS-4: Results

POLARIS-4: Overall SVR12 by Treatment Arm



Abbreviations: SOF, sofosbuvir; VEL, velpatasvir; VOX, voxilaprevir
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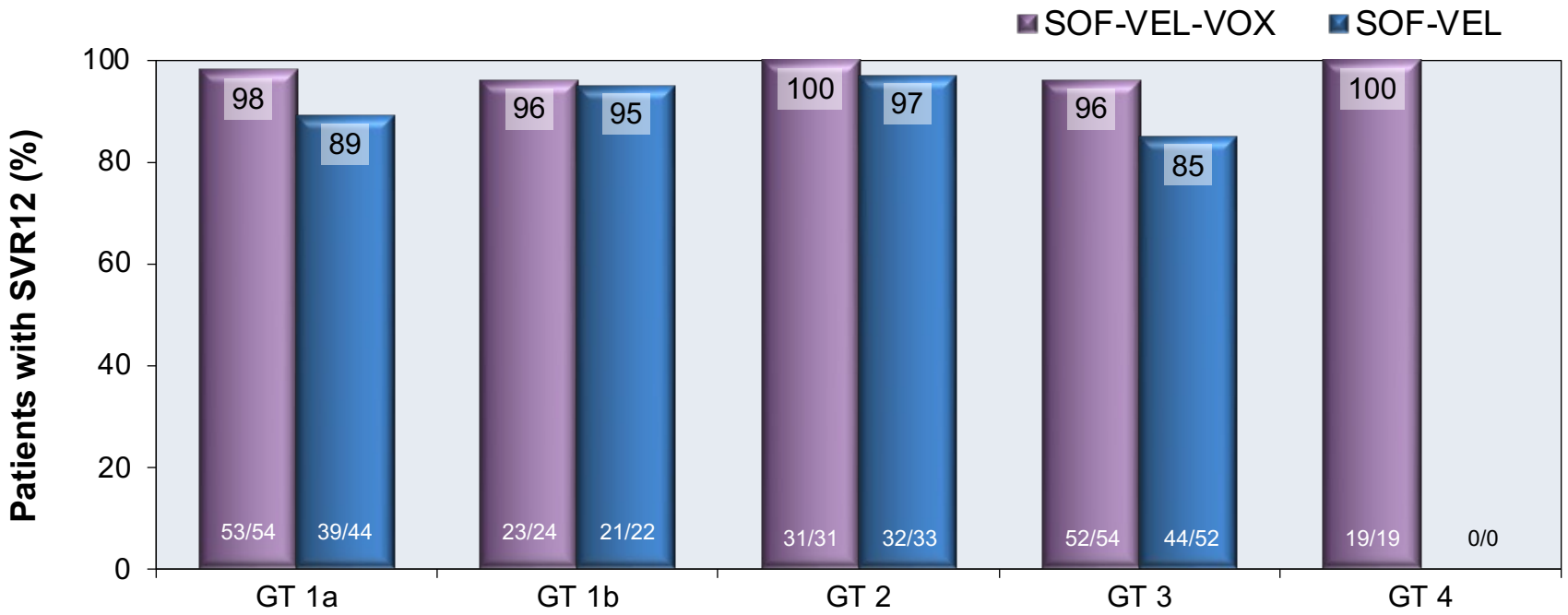
Source: Bourlière M, et al. N Engl J Med. 2017;376:2134-46.

Sofosbuvir-Velpatasvir-Voxilaprevir in DAA-Experienced GT 1-6 POLARIS-4: Results

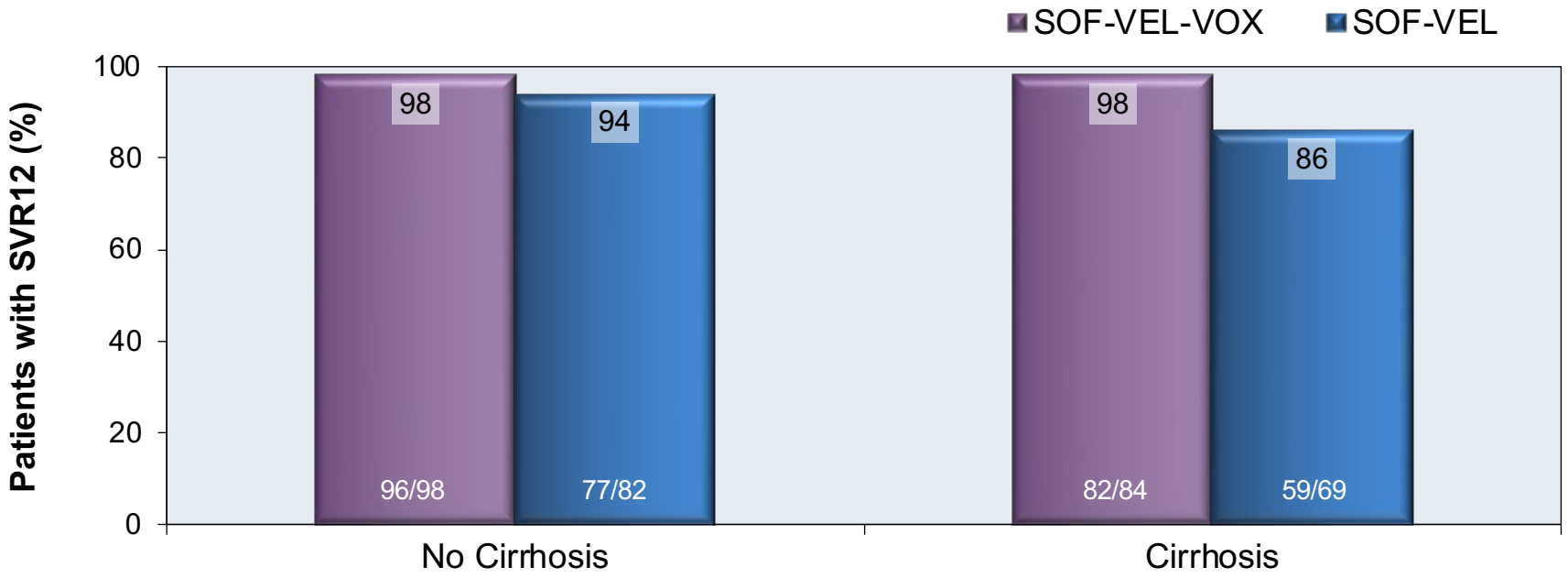
POLARIS-4: SVR12 by Genotype



Source: Bourlière M, et al. N Engl J Med. 2017;376:2134-46.

Sofosbuvir-Velpatasvir-Voxilaprevir in DAA-Experienced GT 1-6 POLARIS-4: Results

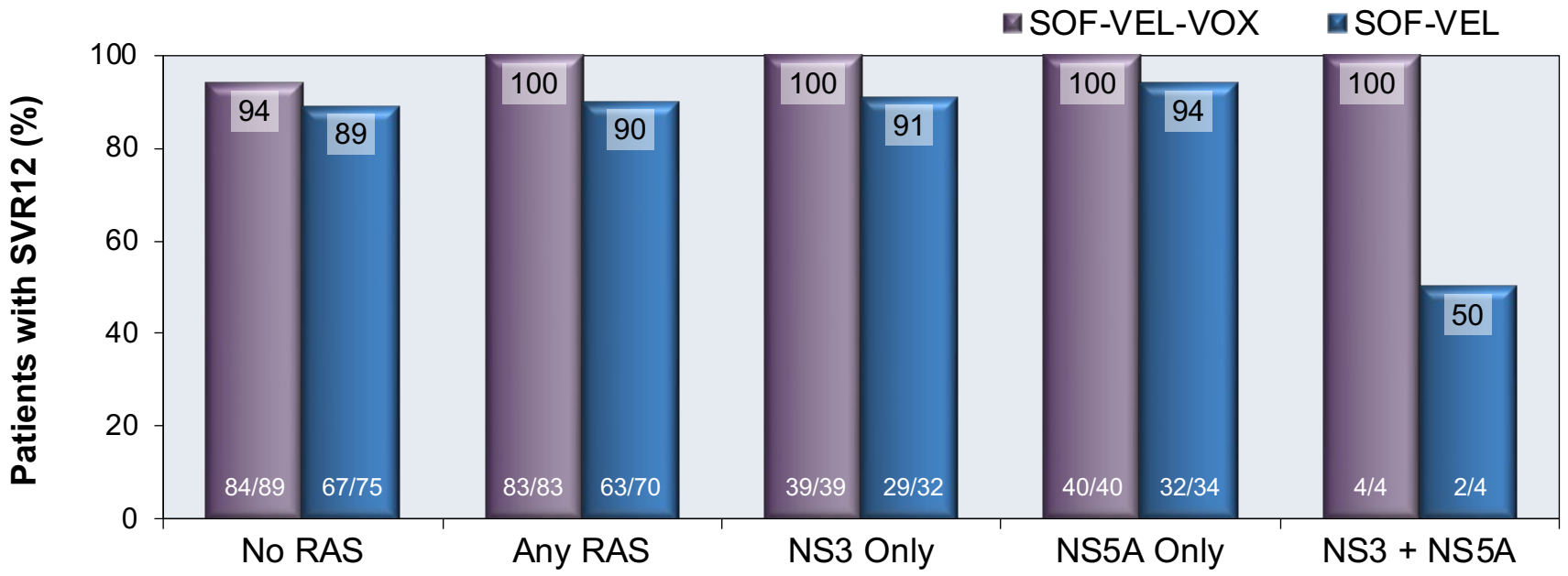
POLARIS-4: SVR12 by Cirrhosis Status



Source: Bourlière M, et al. N Engl J Med. 2017;376:2134-46.

Sofosbuvir-Velpatasvir-Voxilaprevir in DAA-Experienced GT 1-6 POLARIS-4: Results

POLARIS-4: Overall SVR by Baseline RAS



n = 22 patients had NS5B RASs – all went on to achieve SVR12.
No treatment-emergent RASs noted in the viral relapser on SOF-VEL-VOX. In SOF-VEL group, 10/15 developed Y93H or Y93C.

Source: Bourlière M, et al. N Engl J Med. 2017;376:2134-46.

Sofosbuvir-Velpatasvir-Voxilaprevir in DAA-Experienced GT 1-3 POLARIS-4: Adverse Events

Adverse Event (AE), n (%)	**SOF-VEL-VOX** x 12 weeks (n = 182)	**SOF-VEL** x 12 weeks (n = 151)
Discontinuation due to AE	0	1 (<1)
Serious AE	4 (2)	4 (3)
Deaths	1 (1)	0
AE in ≥5% of patients Headache Fatigue Diarrhea Nausea	 50 (27) 43 (24) 36 (20) 22 (12)	 43 (28) 43 (28) 7 (5) 12 (8)
Laboratory AEs (Grade 3-4)	11 (6)	10 (7)

Abbreviations: SOF, sofosbuvir; VEL, velpatasvir; VOX, voxilaprevir

§ One death in SOF-VEL-VOX group due to illicit drug overdose.

Source: Bourlière M, et al. N Engl J Med. 2017;376:2134-46.

Sofosbuvir-Velpatasvir-Voxilaprevir in DAA-Experienced GT 1-3 POLARIS-1 and POLARIS-4: Conclusions

Conclusions: “Sofosbuvir-velpatasvir-voxilaprevir taken for 12 weeks provided high rates of sustained virologic response among patients across HCV genotypes in whom treatment with a DAA regimen had previously failed.”

Source: Bourlière M, et al. N Engl J Med. 2017;376:2134-46.

Acknowledgments

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HEPATITIS B ONLINE

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