Sofosbuvir-Velpatasvir versus Sofosbuvir-Velpatasvir-Voxilaprevir in DAA-Naïve GT 1-6

POLARIS-2

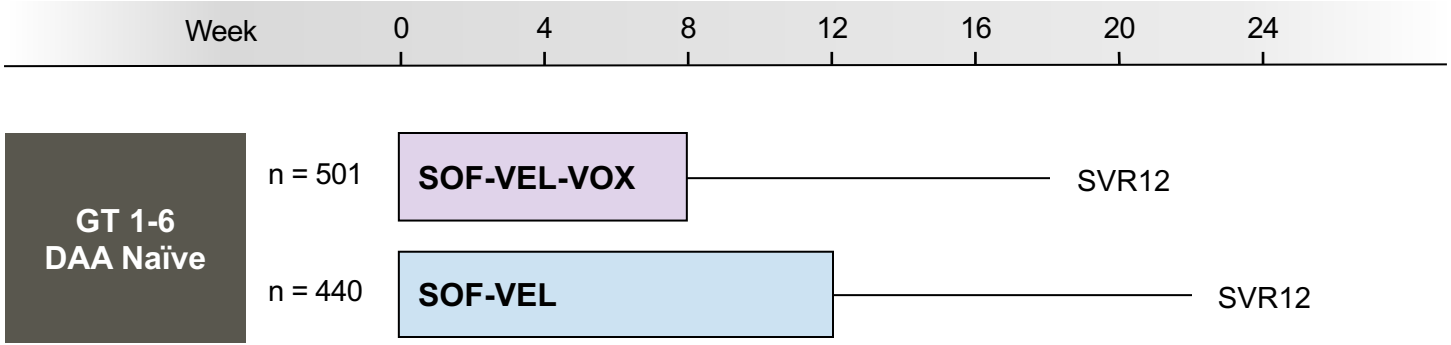
Source: Jacobson IM, et al. Gastroenterology. 2017;153:113-22.

SOF-VEL-VOX versus SOF-VEL in DAA-Naïve HCV GT 1-6
POLARIS-2: Study Features

- **Design**: Randomized, open-label, phase 3 trial to compare efficacy of sofosbuvir-velpatasvir-voxilaprevir (SOF-VEL-VOX) for 8 weeks versus sofosbuvir-velpatasvir (SOF-VEL) for 12 weeks in DAA-naïve patients with GT 1-6 chronic HCV infection.
- **Setting**: 117 sites in United States, Canada, New Zealand, Australia, France, Germany, and United Kingdom
- **Entry Criteria**
  - Age ≥18 years
  - Chronic HCV GT 1-6 (all GT 5, 6 assigned to SOF-VEL-VOX)
  - HCV RNA ≥10,000 IU/mL at screening
  - No prior treatment with DAA; prior peginterferon + ribavirin allowed
  - Patients with compensated cirrhosis allowed except if GT3
- **Primary End Point**: SVR12

Source: Jacobson IM, et al. Gastroenterology. 2017;153:113-22.

SOF-VEL-VOX versus SOF-VEL in DAA-Naïve HCV GT 1-6
POLARIS-2: Study Design



GT 3 patients with cirrhosis were enrolled in separate study (POLARIS-3)
GT 1-4 randomized 1:1; all GT 5, 6 assigned to SOF-VEL-VOX
Stratified by GT, cirrhosis, and prior treatment experience

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

Drug Dosing
SOF-VEL-VOX (400/100/100 mg): fixed dose combination; one pill once daily
SOF-VEL (400/100 mg): fixed dose combination; one pill once daily

Source: Jacobson IM, et al. Gastroenterology. 2017;153:113-22.

SOF-VEL-VOX versus SOF-VEL in DAA-Naïve HCV GT 1-6
POLARIS-2: Baseline Characteristics

Baseline Characteristic	SOF-VEL-VOX x 8 weeks (n = 501)	SOF-VEL x 12 weeks (n = 440)
Age, mean (range)	53 (18-78)	55 (19-82)
Male, n (%)	255 (51)	237 (54)
White, n (%)	391 (78)	365 (83)
HCV genotype—no. (%) 1a 1b 2 3 4 5 6	 169 (34) 63 (13) 63 (13) 92 (18) 63 (13) 18 (4) 30 (6)	 172 (39) 59 (13) 53 (12) 89 (20) 57 (13) 0 9 (2)*
Body mass index, mean kg/m^2 (range)	26.9 (16.9-57.3)	27.1 (17.9-54.0)
Mean HCV RNA, $\log_{10}$ IU/mL (SD)	6.1 (0.75)	6.2 (0.66)
IL28B CC, n (%)	166 (33)	136 (31)
Cirrhosis, n (%)	90 (18)	84 (19)

Abbreviations: SD, standard deviation
* 9 patients with GT6 were assigned to SOF-VEL and initially misclassified as GT1

Source: Jacobson IM, et al. Gastroenterology. 2017;153:113-22.

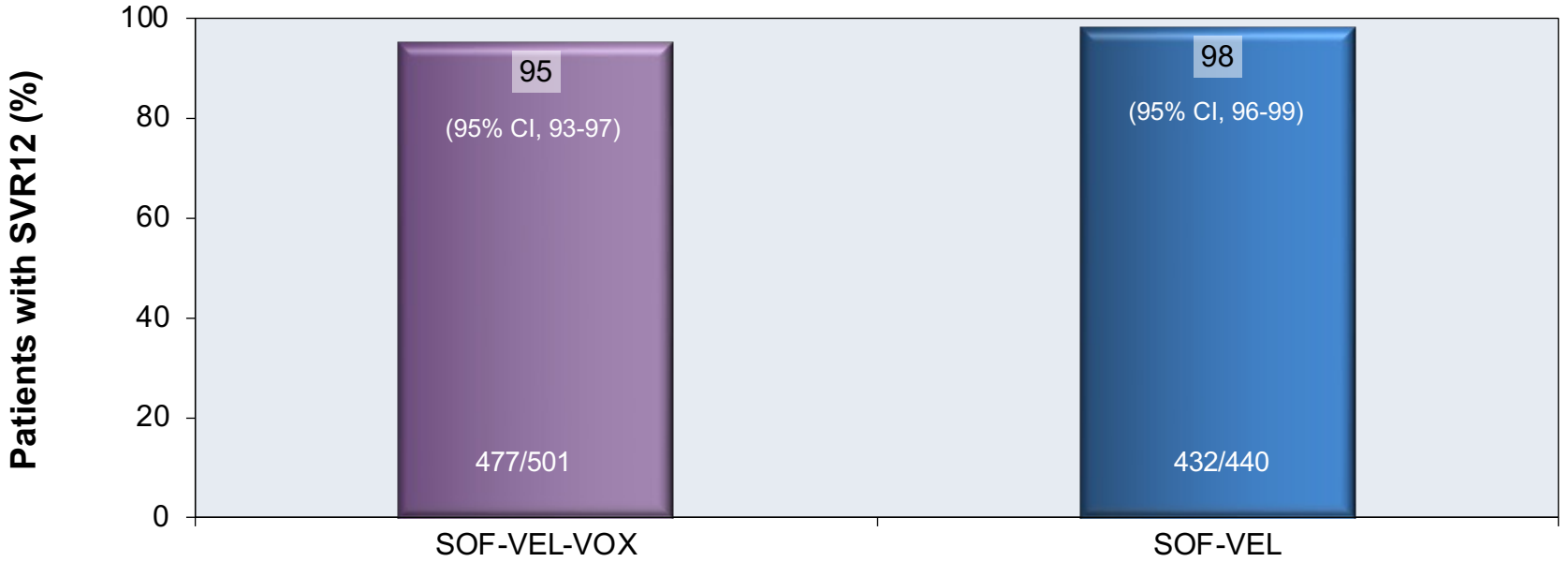
SOF-VEL-VOX versus SOF-VEL in DAA-Naïve HCV GT 1-6
POLARIS-2: Baseline Characteristics

Information on Prior Treatment	**SOF-VEL-VOX** x 8 weeks (n = 501)	**SOF-VEL** x 12 weeks (n = 440)
Treatment-Naïve	383 (76)	340 (77)
Treatment-Experienced	118 (24)	100 (23)
Peginterferon + Ribavirin	93 (79)	81 (81)
Other	25 (21)	19 (19)
Most Recent Treatment Response		
Nonresponder	50 (42)	47 (47)
Relapse	55 (47)	44 (44)
Other	13 (11)	9 (9)

Source: Jacobson IM, et al. Gastroenterology. 2017;153:113-22.

SOF-VEL-VOX versus SOF-VEL in DAA-Naïve HCV GT 1-6
POLARIS-2: Results

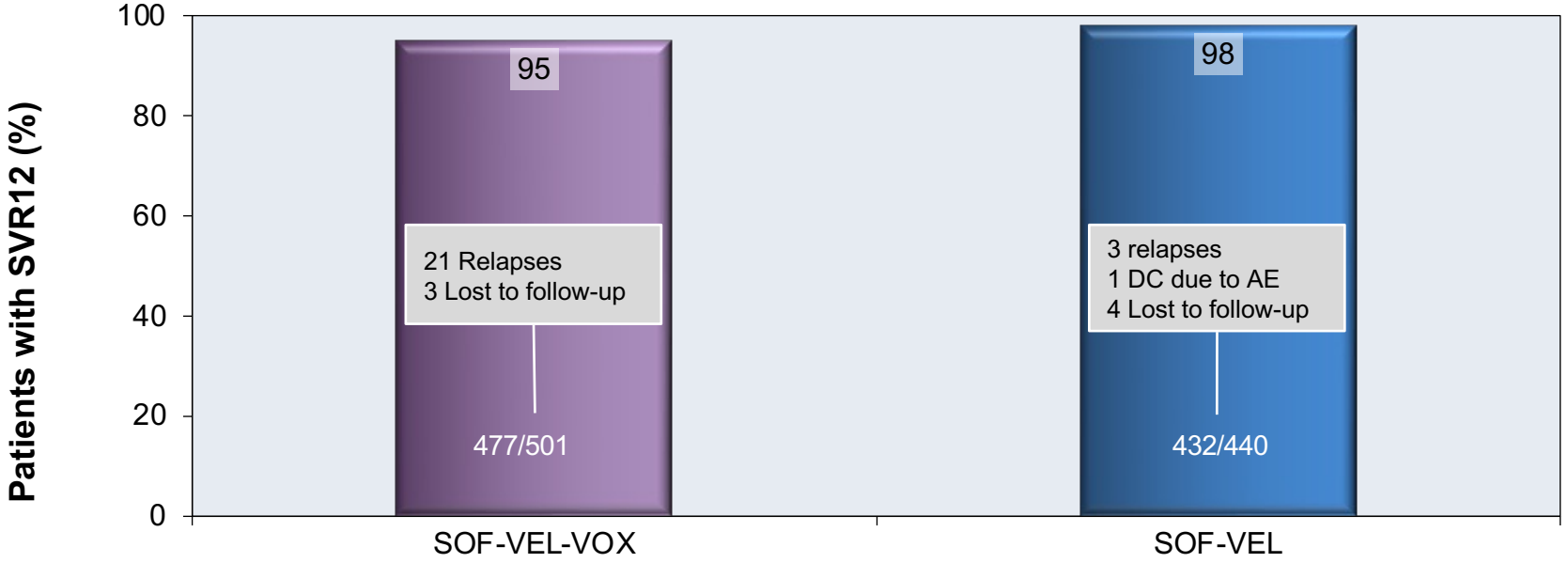
POLARIS-2: Overall SVR12 by Treatment Arm



Source: Jacobson IM, et al. Gastroenterology. 2017;153:113-22.

SOF-VEL-VOX versus SOF-VEL in DAA-Naïve HCV GT 1-6
POLARIS-2: Results

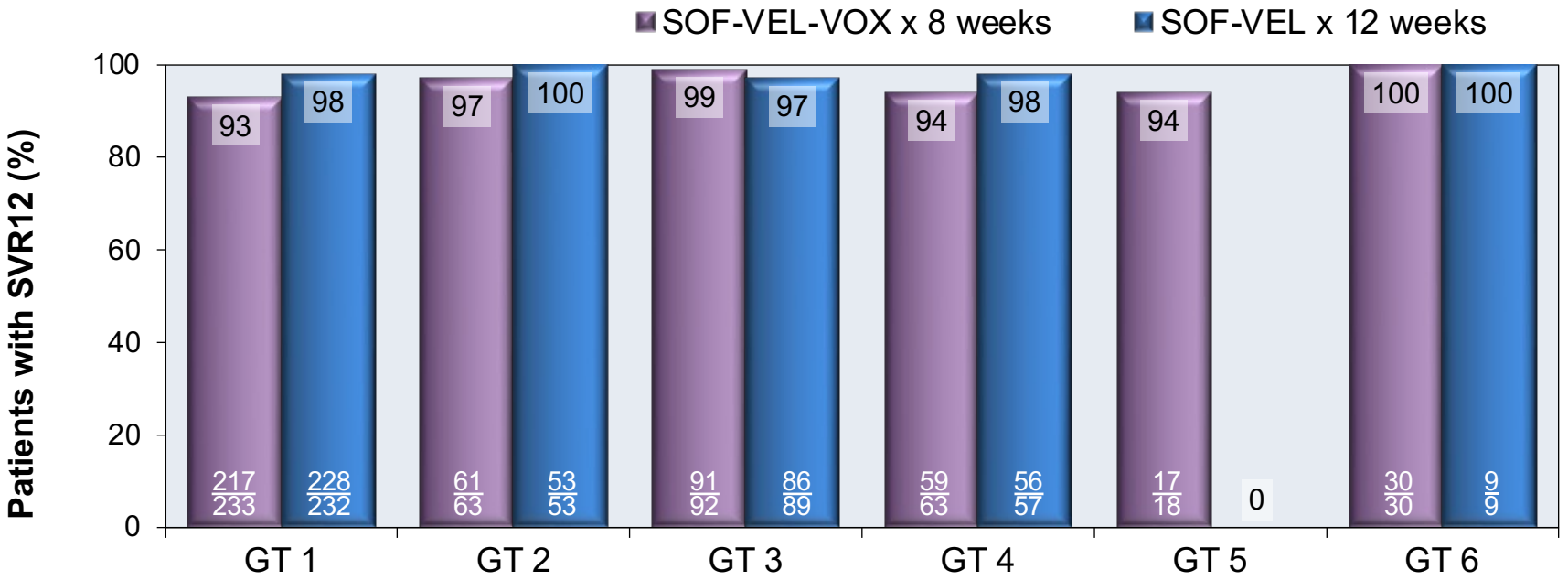
POLARIS-2: Overall SVR12 by Treatment Arm



Source: Jacobson IM, et al. Gastroenterology. 2017;153:113-22.

SOF-VEL-VOX versus SOF-VEL in DAA-Naïve HCV GT 1-6
POLARIS-2: Results

POLARIS-2: SVR by Treatment Arm and Genotype

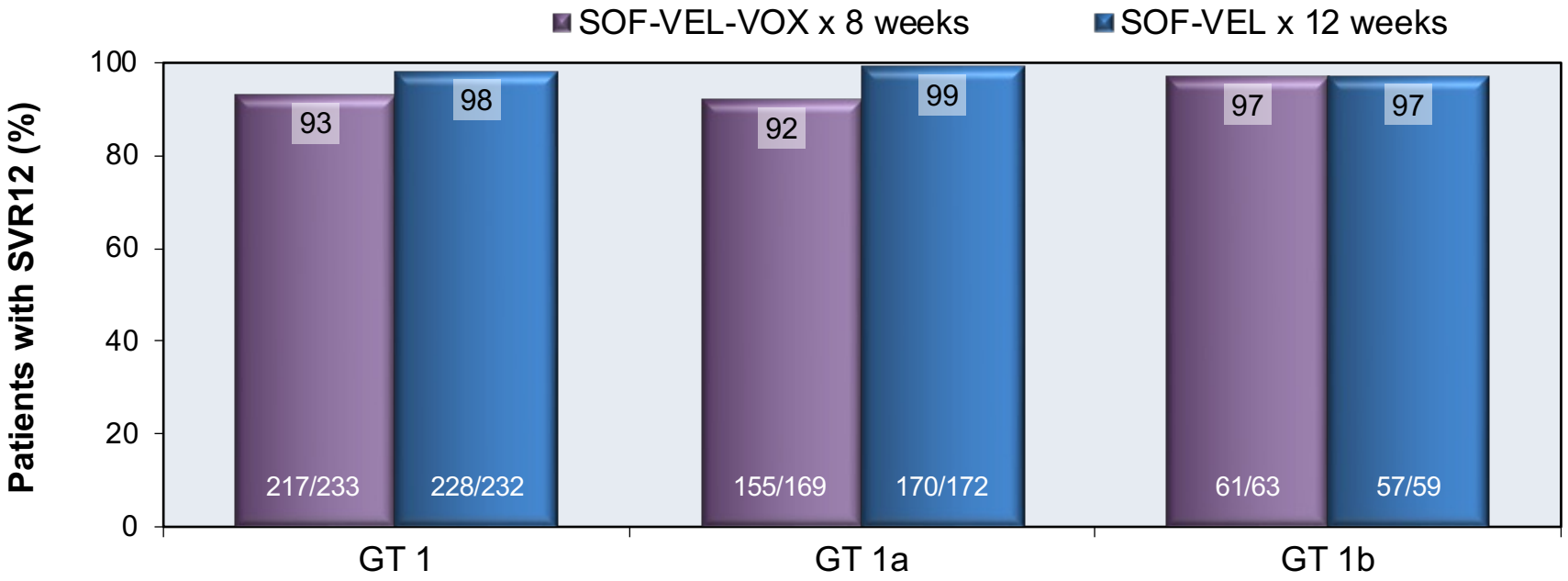


Abbreviations: DCAE, Discontinuation due to AE; LTFU, Lost to follow-up.
Two patients had unknown genotype were assigned to SOF-VEL-VOX and went on to achieve SVR12

Source: Jacobson IM, et al. Gastroenterology. 2017;153:113-22.

SOF-VEL-VOX versus SOF-VEL in DAA-Naïve HCV GT 1-6 POLARIS-2: Results

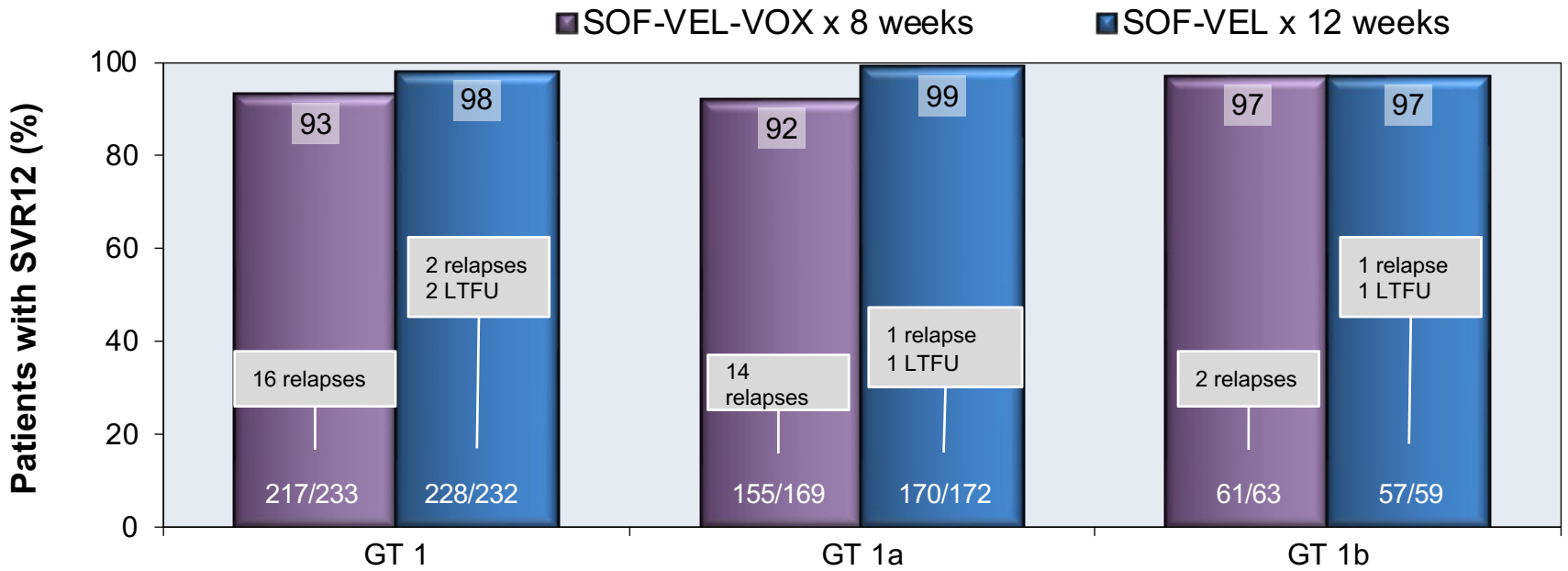
POLARIS-2: SVR by Treatment Arm and Genotype 1 Subtype



Source: Jacobson IM, et al. Gastroenterology. 2017;153:113-22.

SOF-VEL-VOX versus SOF-VEL in DAA-Naïve HCV GT 1-6
POLARIS-2: Results

POLARIS-2: SVR by Treatment Arm & Genotype 1 Subtype

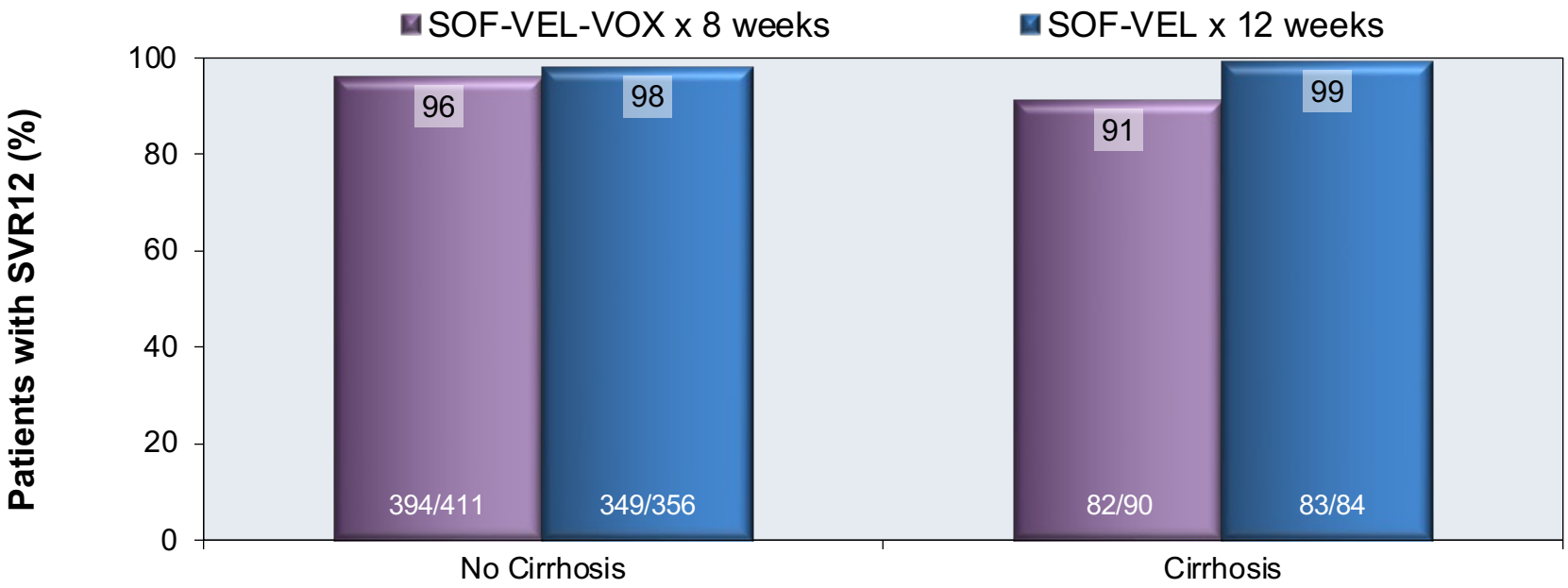


Abbreviations: LTFU, Lost to follow-up

Source: Jacobson IM, et al. Gastroenterology. 2017;153:113-22.

SOF-VEL-VOX versus SOF-VEL in DAA-Naïve HCV GT 1-6 POLARIS-2: Results

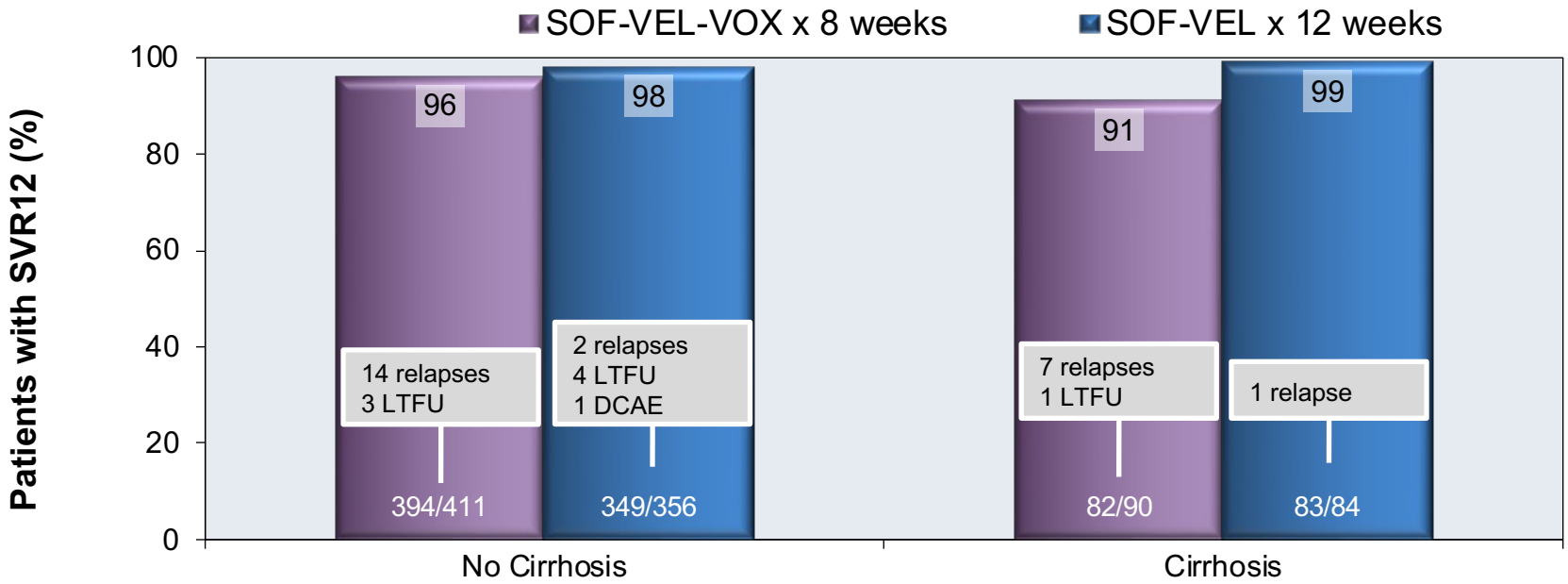
POLARIS-2: SVR12 by Cirrhosis Status



Source: Jacobson IM, et al. Gastroenterology. 2017;153:113-22.

SOF-VEL-VOX versus SOF-VEL in DAA-Naïve HCV GT 1-6 POLARIS-2: Results

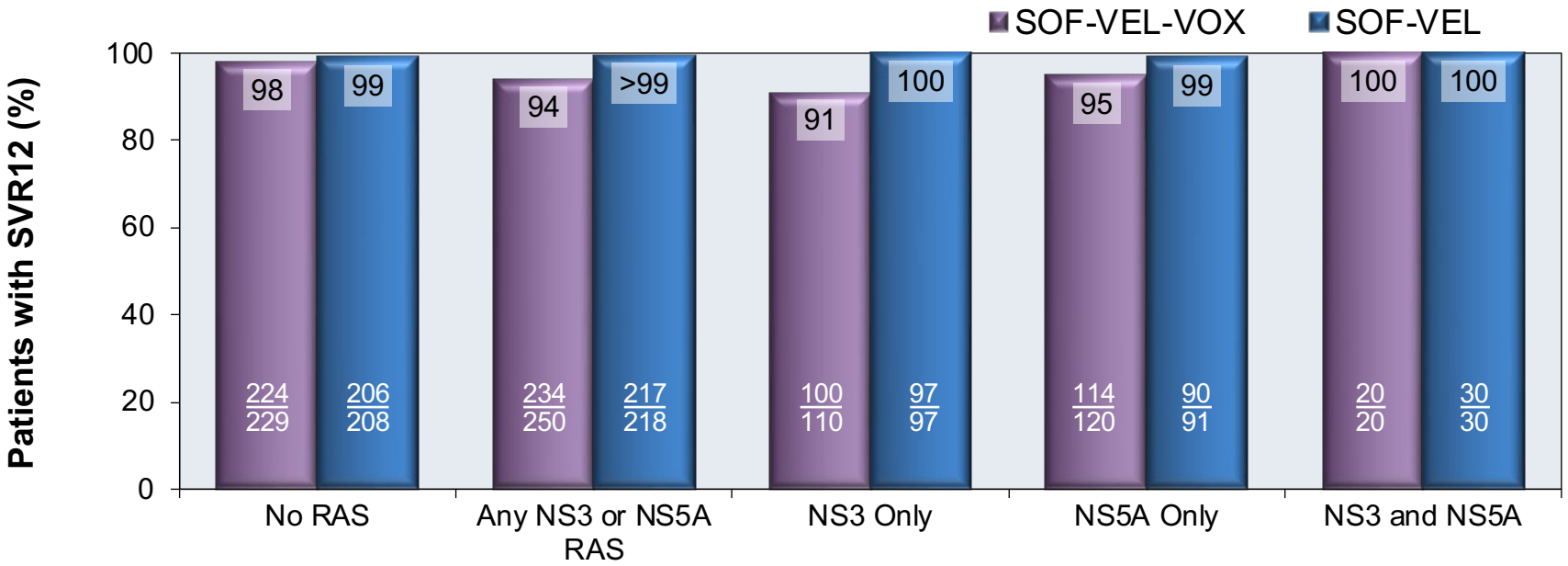
POLARIS-2: SVR12 by Cirrhosis Status



Source: Jacobson IM, et al. Gastroenterology. 2017;153:113-22.

SOF-VEL-VOX versus SOF-VEL in DAA-Naïve HCV GT 1-6
POLARIS-2: Results

POLARIS-2: SVR12 by Baseline RASs*



* Using a 15% reporting threshold

Source: Jacobson IM, et al. Gastroenterology. 2017;153:113-22.

SOF-VEL-VOX versus SOF-VEL in DAA-Naïve HCV GT 1-6
POLARIS-2: Adverse Events

Adverse Event (AE), n (%)	**SOF-VEL-VOX** x 8 weeks (n = 501)	**SOF-VEL** x 12 weeks (n = 440)
Discontinuation due to AE	0	2 (<1) [§]
Serious AE	15 (3)	7 (2)
Serious Related AE	0	0
Deaths	0	0
Any AE in >10% of patients		
Headache	134 (27)	99 (23)
Fatigue	106 (21)	90 (20)
Diarrhea	88 (18)	32 (7)
Nausea	80 (16)	40 (9)
Laboratory AEs (Grade 3-4)	24 (5)	16 (4)

[§] One patient discontinued due to upper respiratory infection; 1 patient due to C. difficile infection. Neither were considered related to study medication by investigator.

Source: Jacobson IM, et al. Gastroenterology. 2017;153:113-22.

SOF-VEL-VOX versus SOF-VEL in DAA-Naïve HCV GT 1-6
POLARIS-2: Conclusions

Conclusions: “In phase 3 trials of patients with HCV infection, we did not establish that sofosbuvir-velpatasvir-voxilaprevir for 8 weeks was noninferior to sofosbuvir-velpatasvir for 12 weeks, but the 2 regimens had similar rates of SVR in patients with HCV genotype 3 and cirrhosis. Mild gastrointestinal adverse events were associated with treatment regimens that included voxilaprevir.”

Source: Jacobson IM, et al. Gastroenterology. 2017;153:113-22.

Acknowledgments

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HEPATITIS B ONLINE

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