Treatment Experienced

Sofosbuvir-Velpatasvir-Voxilaprevir in NS5A-Experienced GT 1-6

POLARIS-1

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

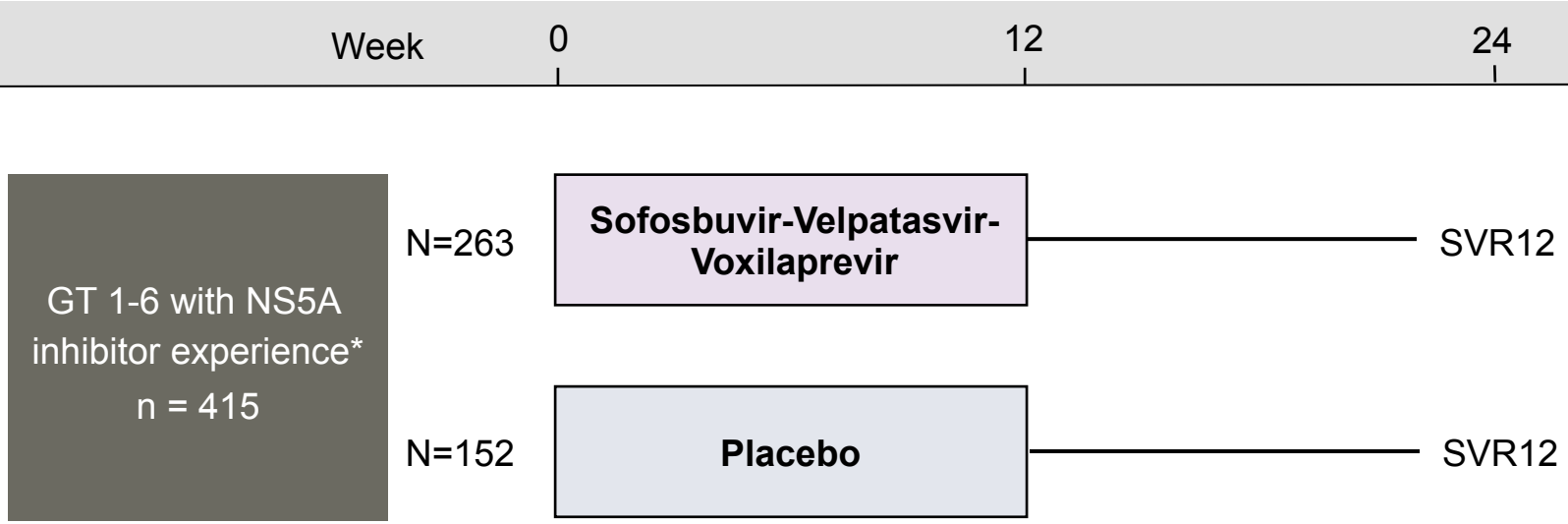
Sofosbuvir-Velpatasvir-Voxilaprevir in NS5A-Experienced GT 1-6
POLARIS-1: Study Features

POLARIS-1 Trial

- **Design**: Randomized, placebo-controlled, phase 3 trial to evaluate the efficacy of a fixed-dose combination of sofosbuvir-velpatasvir-voxilaprevir for 12 weeks in NS5A-inhibitor-experienced patients with GT 1-6 chronic HCV infection
- **Setting**:
  - 108 sites in United States, Canada, New Zealand, Australia, France, Germany, and United Kingdom
- **Entry Criteria**
  - Age >18 years
  - Chronic HCV (any genotype)
  - HCV RNA ≥10,000 IU/mL at screening
  - Prior treatment failure with DAA that contained NS5A inhibitor
  - 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 NS5A-Experienced GT 1-6
POLARIS-1: Study Design



- GT 1 patients randomized 2:1 ratio (active:placebo). Stratified by presence of cirrhosis (target ≥30%).
- Genotypes 2-6 were assigned to active arm (and not randomized).
- Placebo recipients were eligible for deferred treatment with sofosbuvir-velpatasvir-voxilaprevir

Drug Dosing

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

Placebo: one pill once daily

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Sofosbuvir-Velpatasvir-Voxilaprevir in NS5A-Experienced GT 1-6
POLARIS-1: Baseline Characteristics

Baseline Characteristic	SOF-VEL-VOX (n = 263)	Placebo (n =152)
Age, mean (range)	58 (27-84)	59 (29-80)
Male, n (%)	200 (76)	121 (80)
White, n (%)	211 (80)	124 (82)
HCV genotype—no. (%)		
1	150 (57)	150 (99)
1a	101 (38)	117 (77)
1b	45 (17)	31 (20)
1 (other)	4 (2)	2 (1)
2	5 (2)	0
3	78 (30)	0
4	22 (8)	0
5	1 (<1)	0
6	6 (2)	2 (1)
Mean HCV RNA, $\log_{10}$ IU/mL (range)	6.3 ± 0.7	6.3 ± 0.6
IL28B CC, n (%)	47 (18)	27 (18)
Cirrhosis, n (%)	121 (46)	51 (34)

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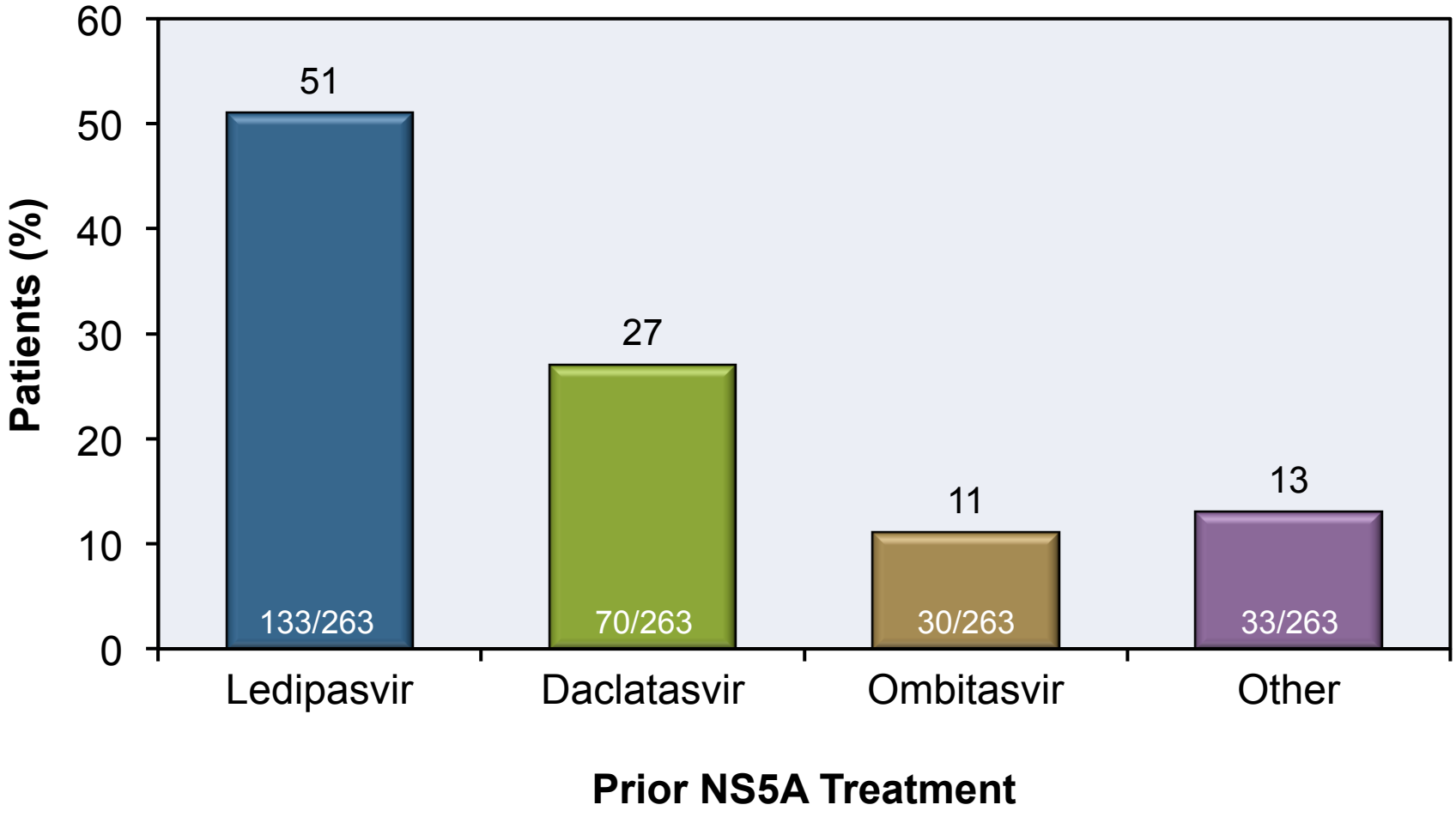
Sofosbuvir-Velpatasvir-Voxilaprevir in NS5A-Experienced GT 1-6
POLARIS-1: Prior NS5A Treatment



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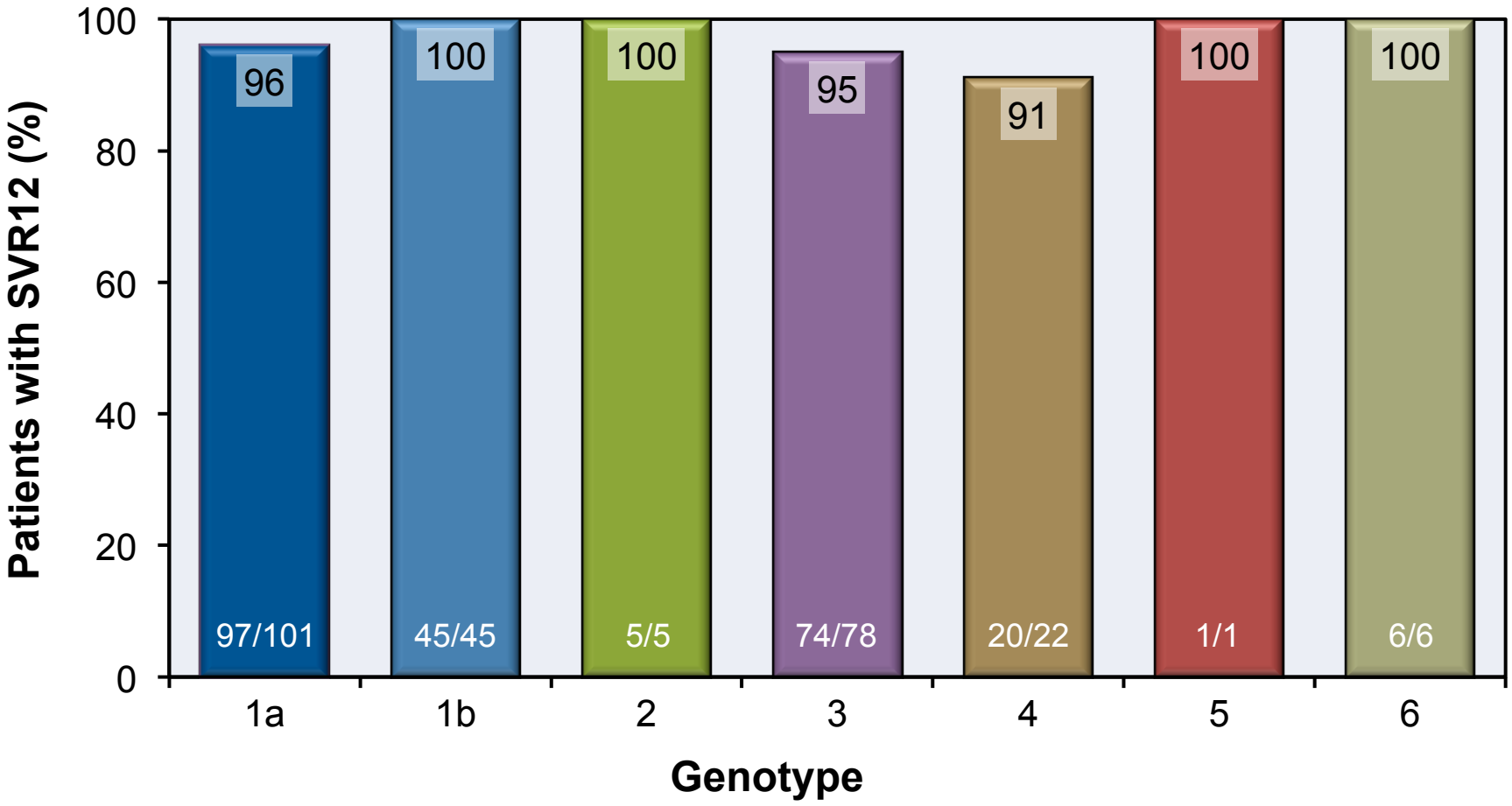
Sofosbuvir-Velpatasvir-Voxilaprevir in NS5A-Experienced GT 1-6
POLARIS-1: Results

POLARIS-1: SVR12 Results by Genotype



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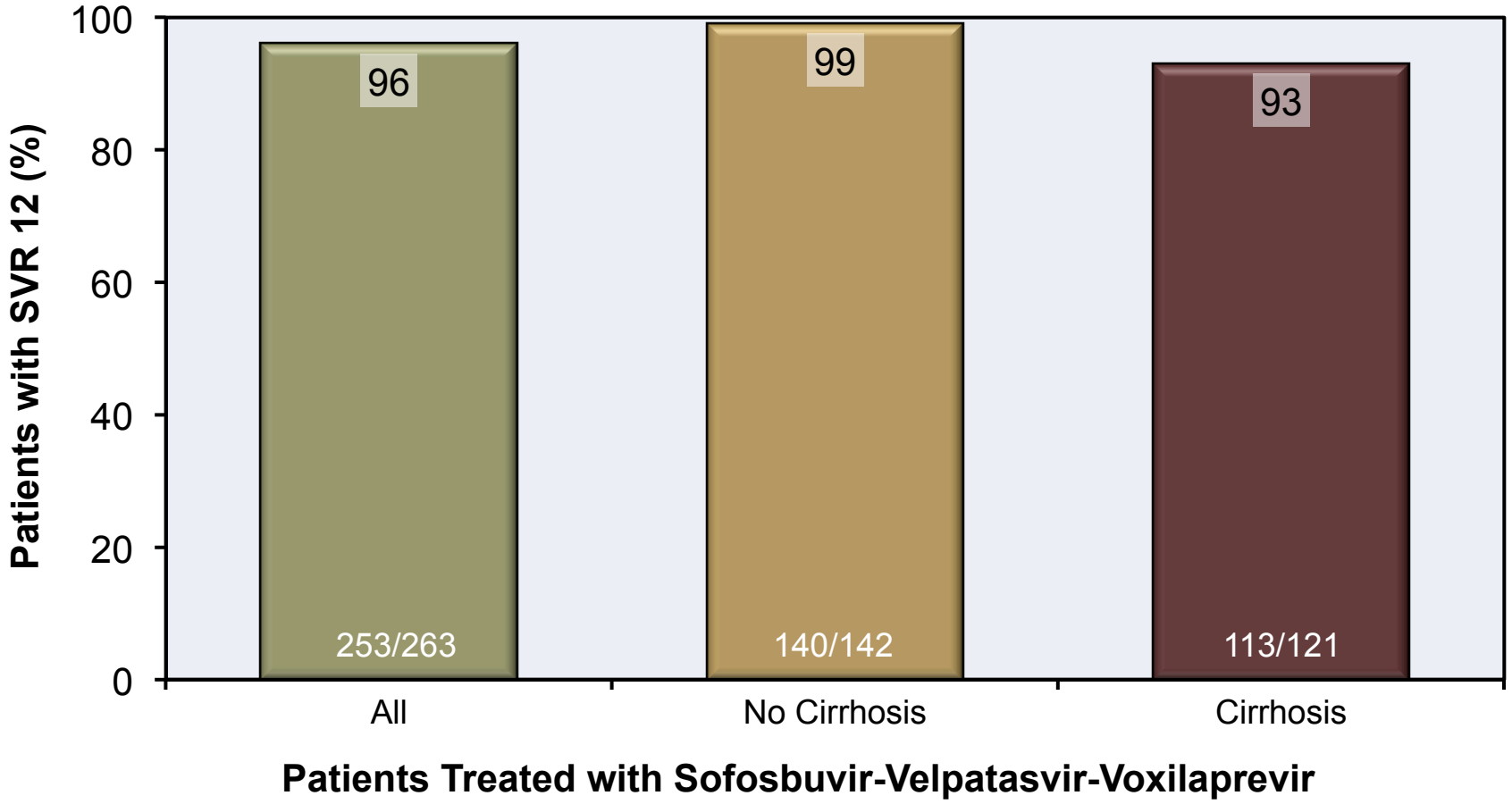
Sofosbuvir-Velpatasvir-Voxilaprevir in NS5A-Experienced GT 1-6
POLARIS-1: Results

POLARIS-1: SVR 12 by Cirrhosis Status



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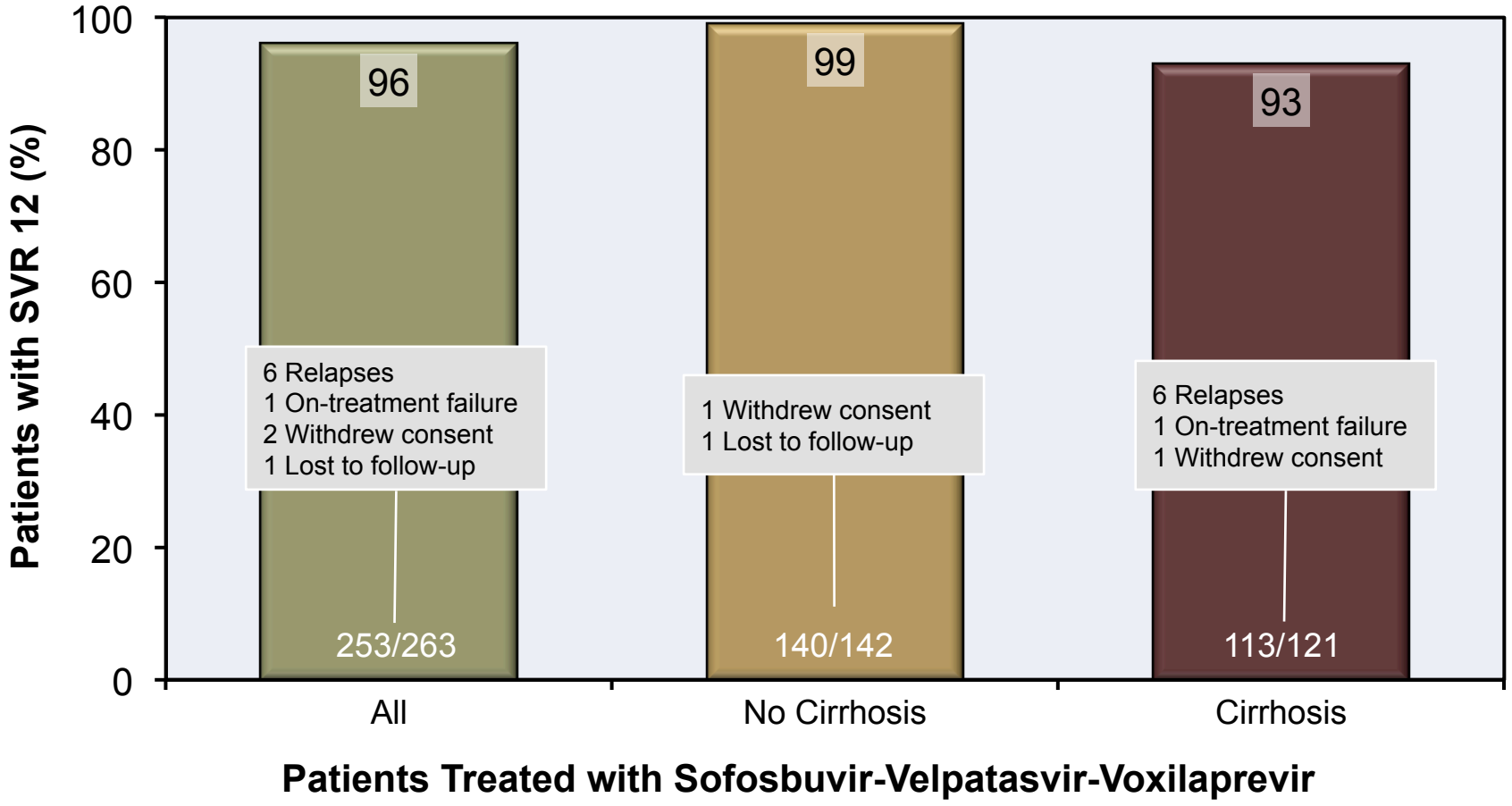
Sofosbuvir-Velpatasvir-Voxilaprevir in NS5A-Experienced GT 1-6
POLARIS-1: Results

POLARIS-1: SVR 12 by Cirrhosis Status



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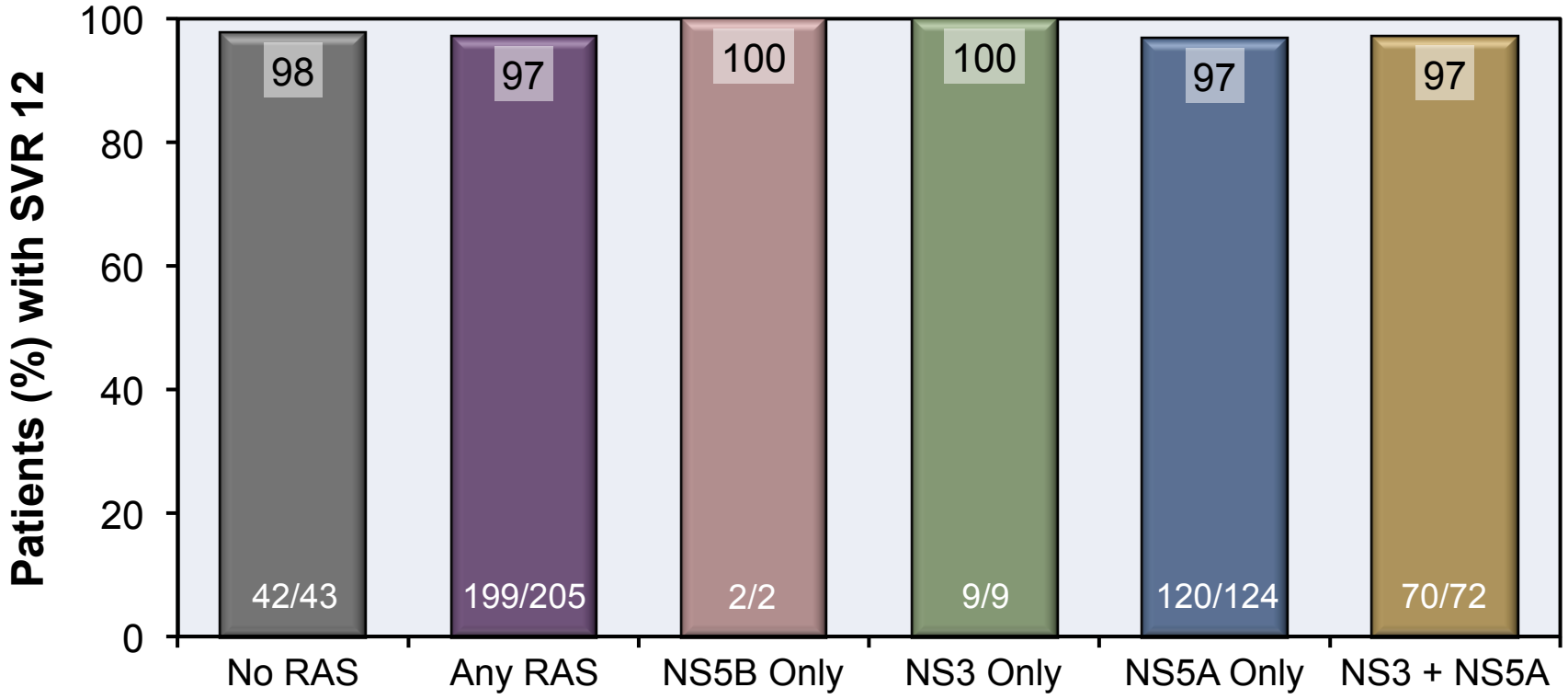
Sofosbuvir-Velpatasvir-Voxilaprevir in NS5A-Experienced GT 1-6
POLARIS-1: Results

POLARIS-1: SVR12 by Baseline Resistance-Associated Substitutions (RAS)



83% of patients had baseline resistance-associated substitutions (RASs); 79% had NS5A RASs.
None who relapsed had treatment-emergent RASs.

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

Sofosbuvir-Velpatasvir-Voxilaprevir in NS5A-Experienced GT 1-6
POLARIS-1: Adverse Events

Adverse Event (AE)	SOF-VEL-VOX (n = 263)	Placebo (n = 152)
Discontinuation due to AE—no. (%)	1 (<1) §	3 (2)
Serious AEs—no. (%)	5 (2)	7 (5)
Deaths—no.	0	0
Any AE in ≥5% of patients—no. (%)		
Headache	66 (25)	26 (17)
Fatigue	56 (21)	30 (20)
Diarrhea	47 (18)	19 (12)
Nausea	37 (14)	12 (8)
Laboratory AEs Grade 3 or Above—no. (%)	18 (6.9%)	22 (14.5%)

§ One patient in active arm discontinued due to angioedema attributed to ramipril.

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

Sofosbuvir-Velpatasvir-Voxilaprevir in DAA-Experienced GT 1-6 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.