Sofosbuvir-Velpatasvir in HCV Genotype 1, 2, 4, 5, or 6
ASTRAL-1

Source: Feld JJ, et al. N Engl J Med. 2015;373:2599-607.

Sofosbuvir-Velpatasvir in HCV Genotype 1, 2, 4, 5, or 6
ASTRAL-1: Study Features

- **Design**: Randomized, placebo-controlled, phase 3 trial using a fixed-dose combination of sofosbuvir-velpatasvir for 12 weeks in treatment-naïve and treatment-experienced patients with GT 1, 2, 4, 5, or 6 chronic HCV
- **Setting**: 81 sites in United States, Europe, and Hong Kong
- **Entry Criteria**
  - Chronic HCV GT 1, 2, 4, 5, or 6
  - HCV RNA ≥10,000 IU/mL at screening
  - Prior treatment failure with interferon allowed (but no prior NS5A or NS5B)
  - Patients with compensated cirrhosis allowed
- **Primary End Point**: SVR12

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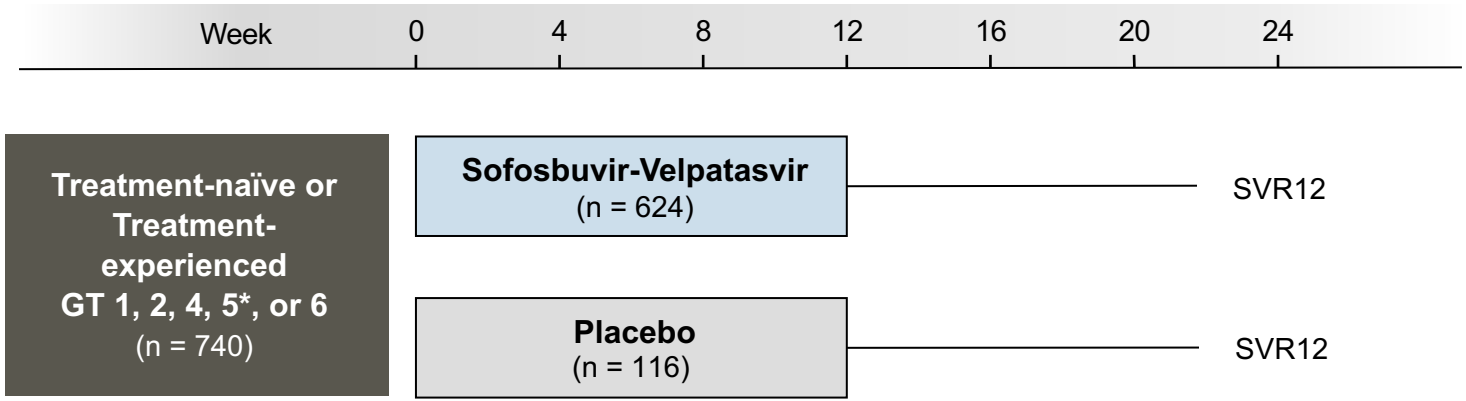
Sofosbuvir-Velpatasvir in HCV Genotype 1, 2, 4, 5, or 6
ASTRAL-1: Study Design



Randomized 5:1 ratio for treatment to placebo. Stratified by cirrhosis and HCV genotype.
*Genotype 5 patients (n = 6) were assigned to active arm (and not randomized)
Placebo recipients were eligible for deferred treatment with sofosbuvir-velpatasvir

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

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Sofosbuvir-Velpatasvir in HCV Genotype 1, 2, 4, 5, or 6
ASTRAL-1: Baseline Characteristics

Baseline Characteristic	Sofosbuvir-Velpatasvir (n = 624)	Placebo (n = 116)
Age, mean (range)	54 (18-82)	53 (25-74)
Male, n (%)	374 (60)	68 (59)
Race, n (%) White Black Asian	 493 (79) 52 (8) 62 (10)	 90 (78) 11 (9) 11 (9)
HCV genotype, % 1a 1b 2 4 5 6	 210 (34) 118 (19) 104 (17) 116 (19) 35 (6) 41 (7)	 46 (40) 19 (16) 21 (18) 22 (19) 0 8 (7)
Body mass index, mean (range)	27 (17-57)	26 (18-40)
HCV RNA ≥800,000 IU/mL, n (%)	461 (74)	87 (75)
IL28B non-CC, n (%)	433 (69)	79 (68)

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Sofosbuvir-Velpatasvir in HCV Genotype 1, 2, 4, 5, or 6
ASTRAL-1: Baseline Characteristics

Baseline Characteristics	Sofosbuvir-Velpatasvir (n = 624)	Placebo (n = 116)
Cirrhosis, n (%)	121 (19)	21 (18)
Treatment experienced, n (%)	201 (32)	33 (28)
Prior therapy, n (%)		
Peginterferon + Ribavirin	122 (61)	24 (73)
Peginterferon + Ribavirin + Protease Inhibitor	56 (28)	6 (18)
Standard Interferon +/- Ribavirin	23 (11)	3 (9)

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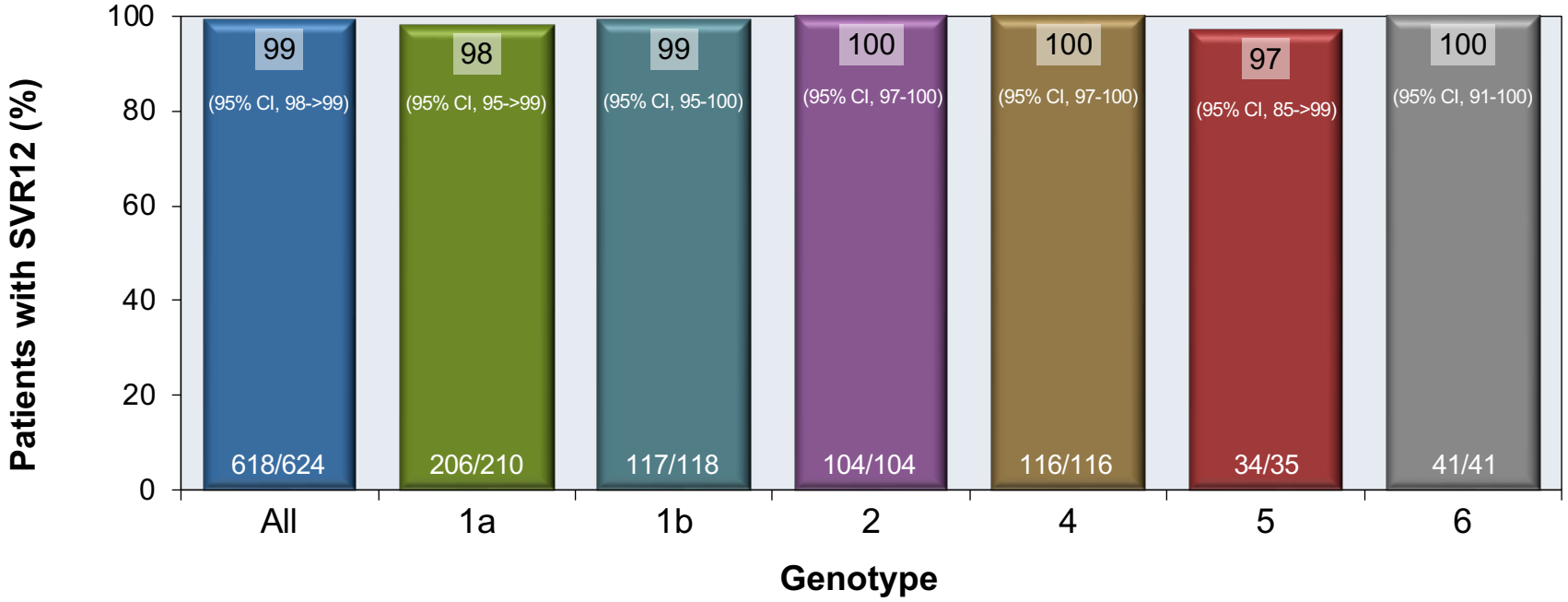
Sofosbuvir-Velpatasvir in HCV Genotype 1, 2, 4, 5, or 6
ASTRAL-1: Results

ASTRAL-1: SVR12 Results by Genotype



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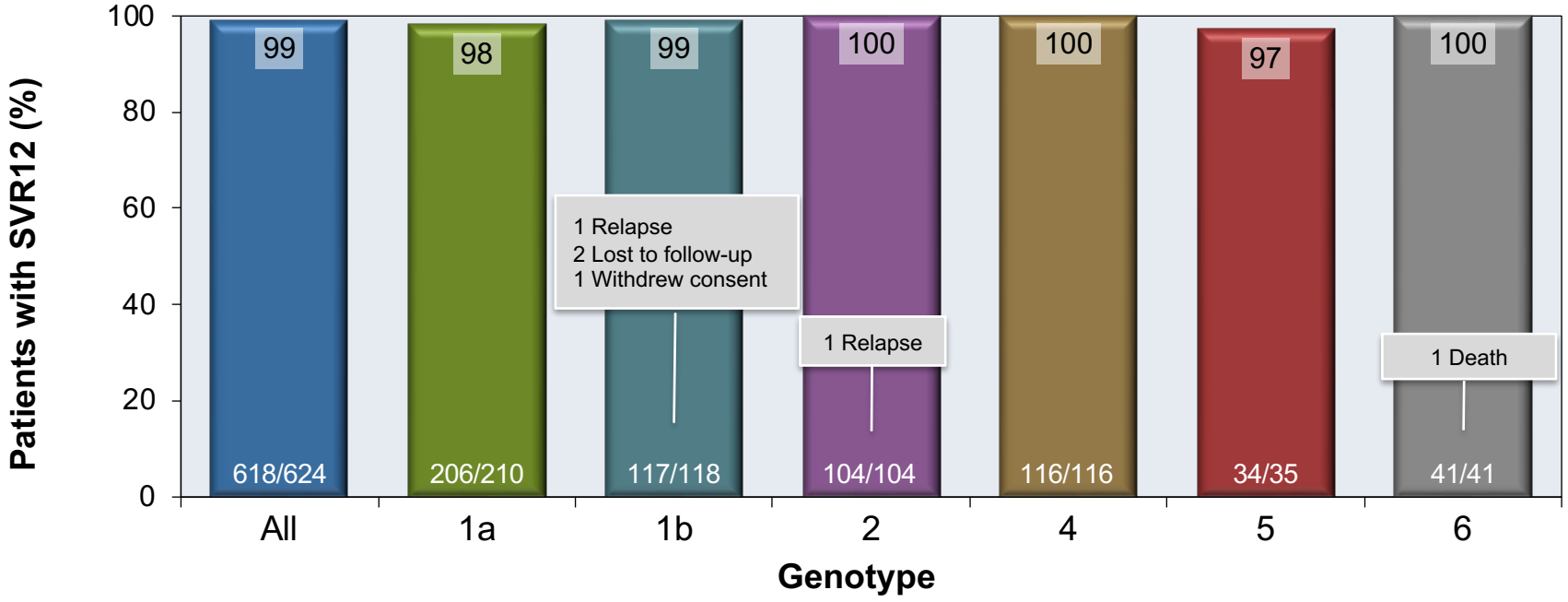
Sofosbuvir-Velpatasvir in HCV Genotype 1, 2, 4, 5, or 6
ASTRAL-1: Results

ASTRAL-1: SVR12 Results by HCV Genotype



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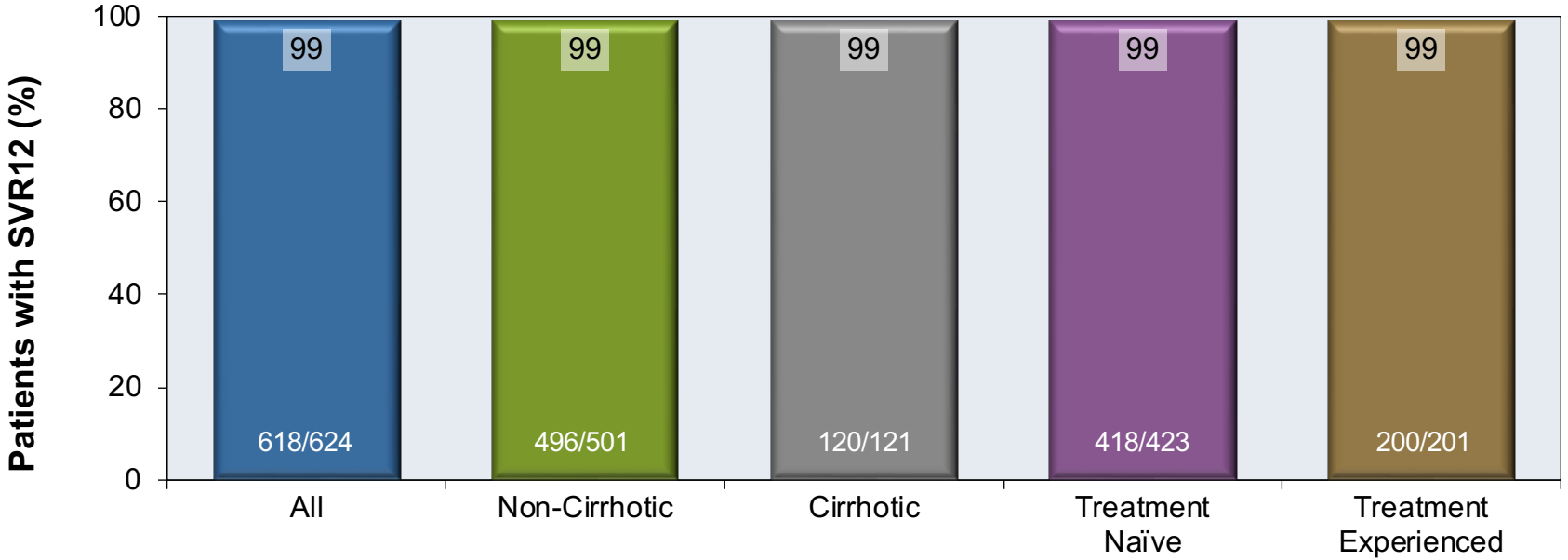
Sofosbuvir-Velpatasvir in HCV Genotype 1, 2, 4, 5, or 6
ASTRAL-1: Results

ASTRAL-1: SVR12 Results by Cirrhosis Status and Treatment Experience



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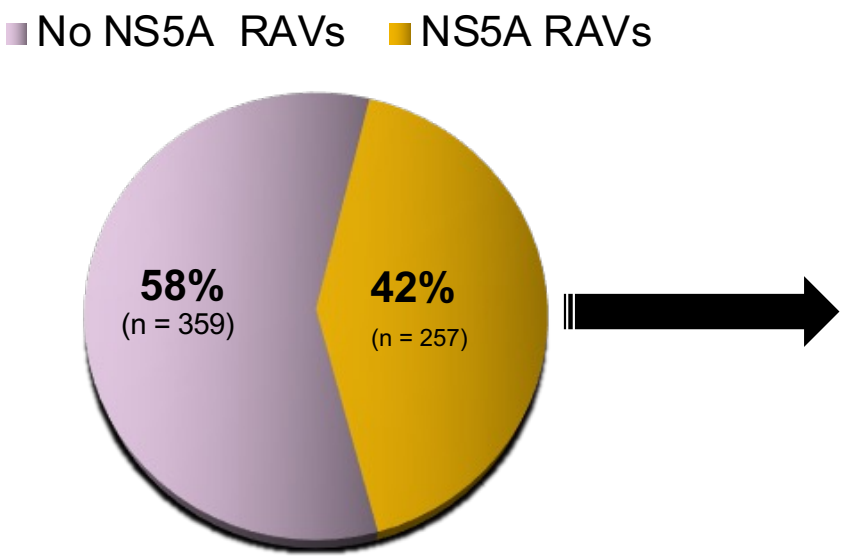
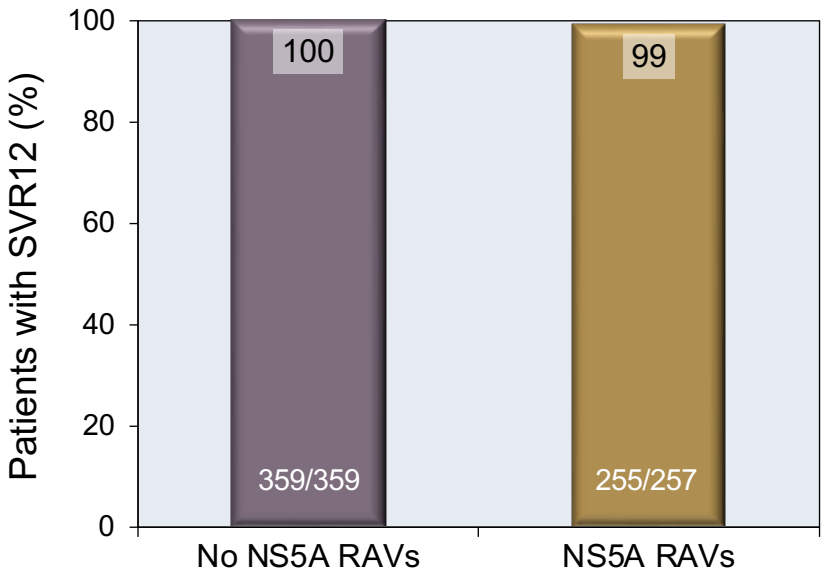
Sofosbuvir-Velpatasvir in HCV Genotype 1, 2, 4, 5, or 6
ASTRAL-1: Resistance

Baseline Resistance-Associated Variants (RAVs)



Response to Treatment (SVR12)



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Sofosbuvir-Velpatasvir in HCV Genotype 1, 2, 4, 5, or 6
ASTRAL-1: Adverse Events

Adverse Event (AE), n (%)	Sofosbuvir-Velpatasvir (n = 624)	Placebo (n = 116)
Discontinuation due to AE	1 (<1)	2 (2)
Serious AEs	15 (2)	0
Deaths	1[§] (<1)	0
Any AE in ≥10% of patients		
Headache	182 (29)	33 (28)
Fatigue	126 (20)	23 (20)
Nasopharyngitis	79 (13)	12 (10)
Nausea	75 (12)	13 (11)
Laboratory AEs		
Hemoglobin <10 g/dL	2 (<1)	0
Lymphocyte count 350 to <500/mm^3	3 (<1)	0
Neutrophil count 500 to <750/mm^3	4 (1)	0
Platelet count 25K to <50K/mm^3	1 (<1)	0

[§]This death was not considered to be study-related.

Source: Feld JJ, et al. N Engl J Med. 2015;373:2599-607.

Sofosbuvir-Velpatasvir in HCV Genotype 1, 2, 4, 5, or 6
ASTRAL-1: Conclusion

Conclusions: “Once-daily sofosbuvir–velpatasvir for 12 weeks provided high rates of sustained virologic response among both previously treated and untreated patients infected with HCV genotype 1, 2, 4, 5, or 6, including those with compensated cirrhosis.”

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Acknowledgments

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HEPATITIS B ONLINE

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