

Treatment Naïve & Experienced

Sofosbuvir-Velpatasvir in Genotype 3 ASTRAL-3

*Published in tandem with ASTRAL-2 Trial

Foster GR, et al. N Engl J Med. 2015;373:2608-17.

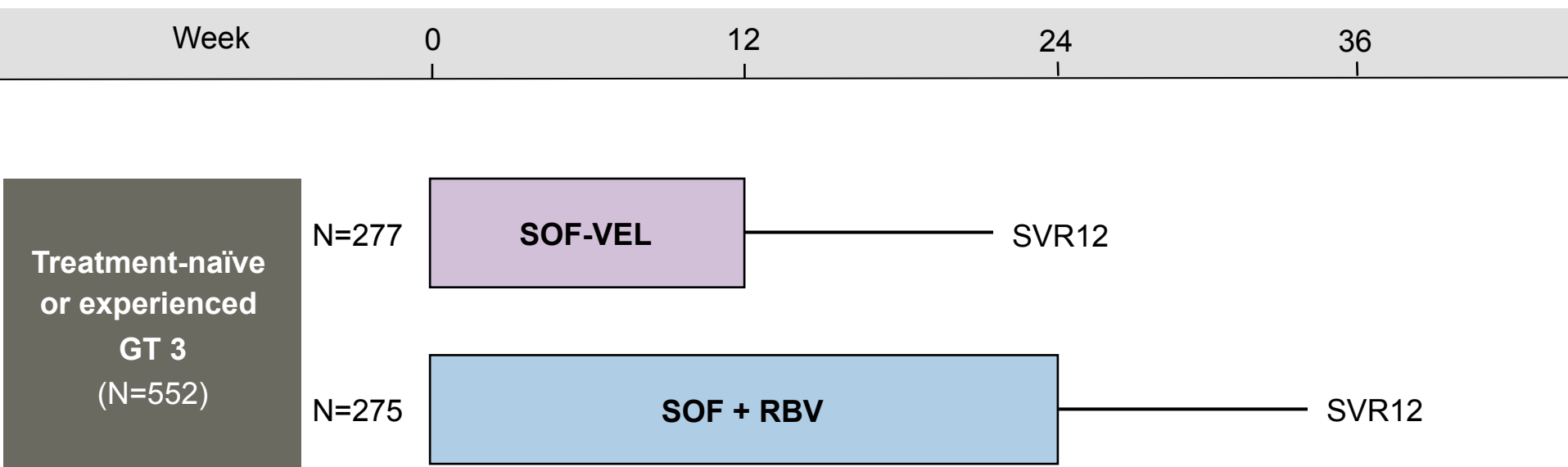
Sofosbuvir-Velpatasvir in HCV Genotype 3

ASTRAL-3: Study Features

ASTRAL-3 Trial

- **Design:** Randomized, placebo-controlled, phase 3 trial using a fixed-dose combination of sofosbuvir-velpatasvir for 12 weeks (compared with sofosbuvir + ribavirin) in treatment-naïve and treatment-experienced patients with GT 3 chronic HCV
- **Setting:** 76 sites in US, Canada, Europe, Australia, New Zealand
- **Entry Criteria**
 - Chronic HCV GT 3
 - HCV RNA $\geq 10,000$ 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

Sofosbuvir-Velpatasvir in HCV Genotype 3 ASTRAL-3: Study Design



*Randomization stratified by treatment experience and cirrhosis status.

Abbreviations: SOF-VEL = sofosbuvir-velpatasvir; RBV = ribavirin

Drug Dosing

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

Sofosbuvir: 400 mg once daily

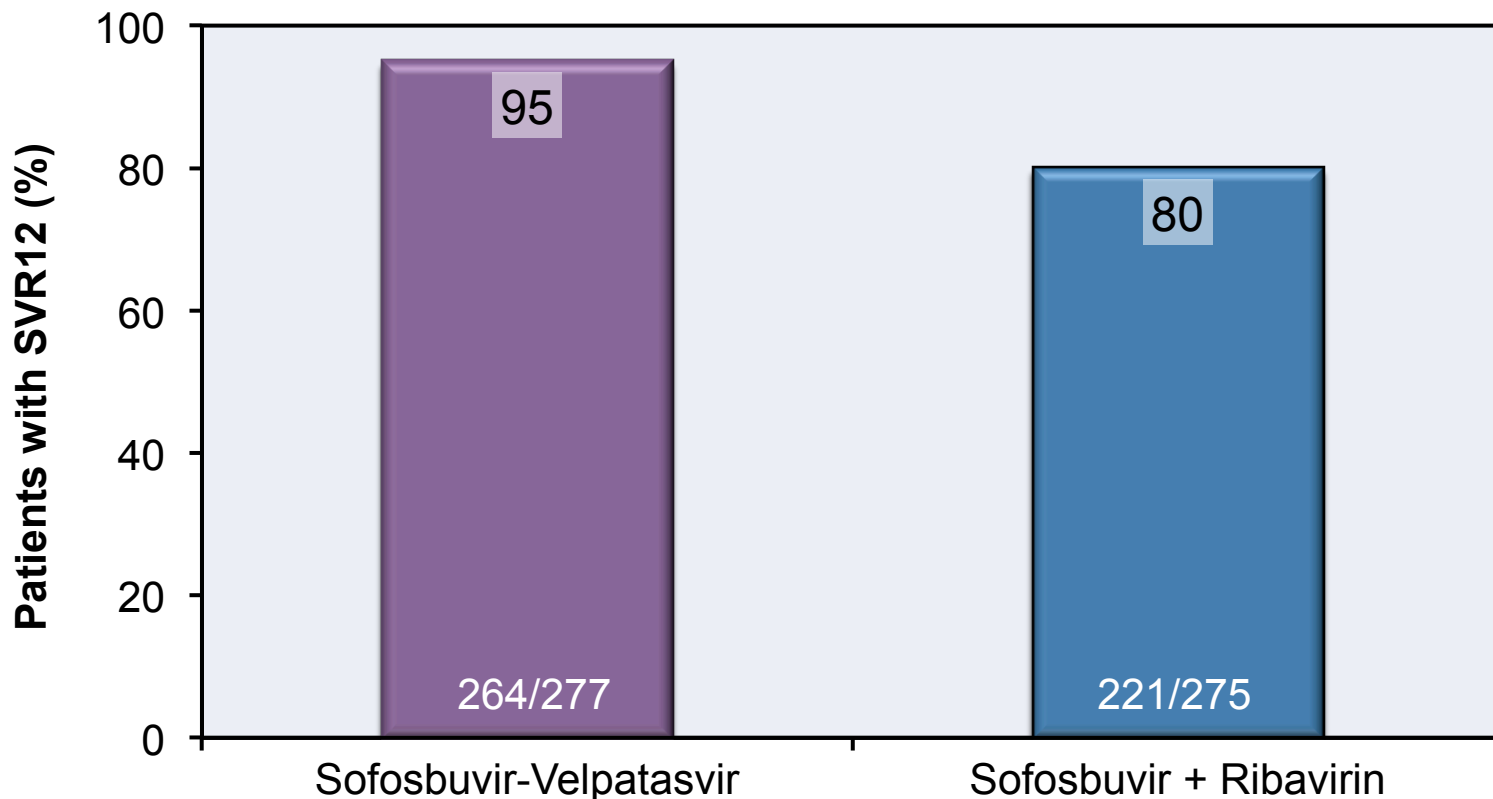
Ribavirin (weight-based and divided bid): 1000 mg/day if < 75 kg or 1200 mg/day if ≥ 75 kg

Sofosbuvir-Velpatasvir in HCV Genotype 3 ASTRAL-3: Baseline Characteristics

Baseline Characteristic	Sofosbuvir-Velpatasvir (N=277)	Sofosbuvir + Ribavirin (N=275)
Age, mean (range)	49 (21-76)	50 (19-74)
Male, n (%)	170 (61)	174 (63)
Race, n (%)		
White	250 (90)	239 (87)
Black	3 (1)	1 (<1)
Asian	23 (8)	29 (11)
Body mass index, mean (range)	26 (17-48)	27 (17-56)
HCV RNA \geq 800,000 IU/mL, n (%)	191 (69)	194 (71)
IL28B non-CC, n (%)	172 (62)	164 (60)
Cirrhosis, n (%)	80 (29)	83 (30)
Treatment-experienced, n (%)	71 (26)	71 (26)
Prior response, no./total (%)		
Non-response	20/71 (28)	24/71 (34)
Relapse or breakthrough	51/71 (72)	47/71 (66)

Sofosbuvir-Velpatasvir in HCV Genotype 3 ASTRAL-3: Results

ASTRAL-3: SVR12 Results

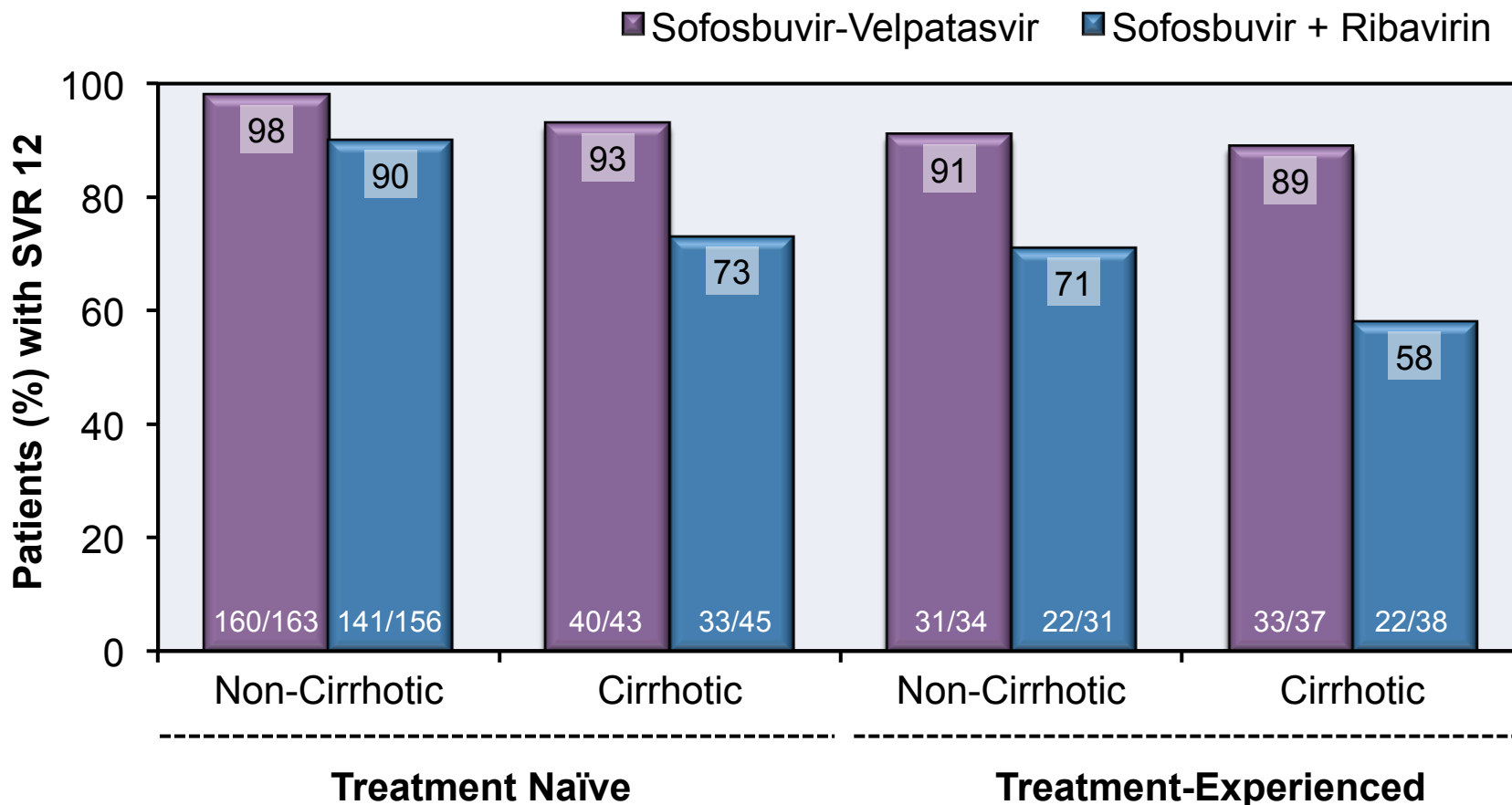


$P < 0.001$ for superiority of Sofosbuvir-Velpatasvir compared with Sofosbuvir + Ribavirin

Source: Foster GR, et al. N Engl J Med. 2015;373:2608-17.

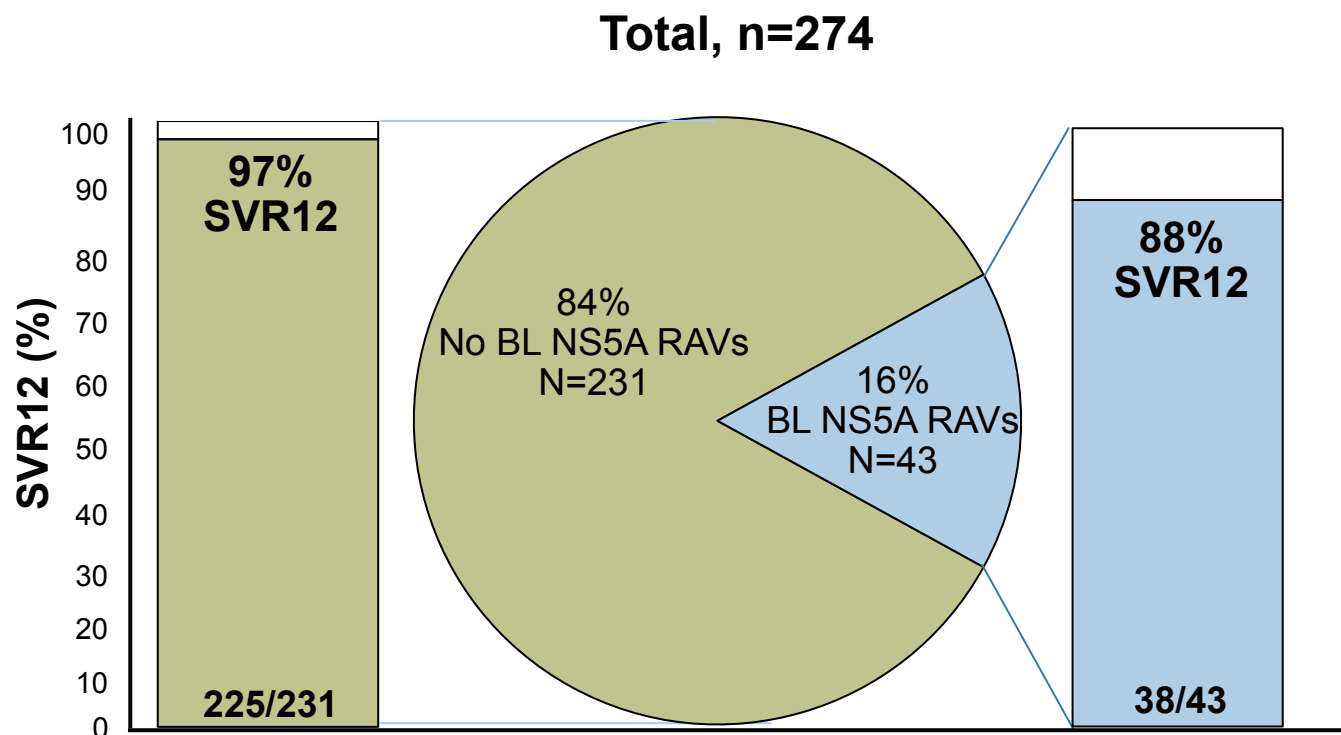
Sofosbuvir-Velpatasvir in HCV Genotype 3 ASTRAL-3: Results

ASTRAL-3: SVR12 Results by Cirrhosis & Treatment Experience



Sofosbuvir-Velpatasvir in HCV Genotype 3 ASTRAL-3: Resistance

Baseline NS5A Resistance-Associated Variants and SVR12



- SVR12 was 84% (21/25) in patients with Y93H

Sofosbuvir-Velpatasvir in HCV Genotype 3 ASTRAL-3: Adverse Events

Adverse Event (AE), n (%)	Sofosbuvir-Velpatasvir (n=277)	Sofosbuvir + Ribavirin (n=275)
Discontinuation due to AE	0	9 (3)
Serious AEs	6 (2)	15 (5)
Deaths	0	3 (1)
Any AE in $\geq 10\%$ of patients		
Fatigue	71 (26)	105 (38)
Headache	90 (32)	89 (32)
Nausea	46 (17)	58 (21)
Insomnia	31 (11)	74 (27)
Laboratory AEs		
Hemoglobin <10 g/dl	0	10 (4)
Total bilirubin >2.5 to 3 mg/dl	0	2 (1)
Platelet count 25K to <50K/mm ³	1 (<1)	1 (<1)

Sofosbuvir-Velpatasvir in HCV Genotype 3 ASTRAL-3: Conclusions

Conclusions: “Among patients with HCV genotype [2 or] 3 with or without previous treatment, including those with compensated cirrhosis, 12 weeks of treatment with sofosbuvir-velpatasvir resulted in rates of sustained virologic response that were superior to those with standard treatment with sofosbuvir-ribavirin.”