The ASTRAL Program

SOF
Nucleotide polymerase inhibitor

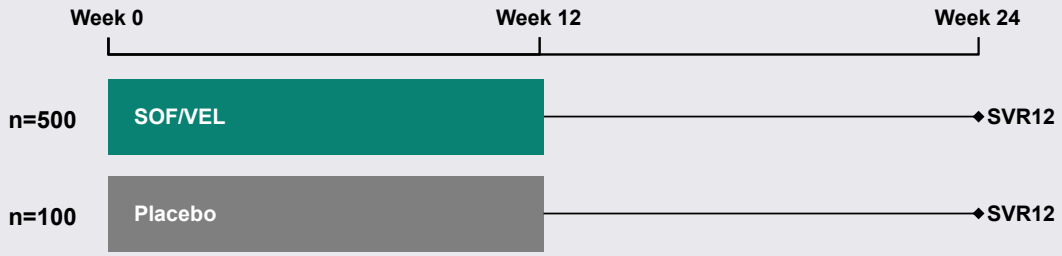
VEL
NS5A inhibitor

- **SOF/VEL FDC**
  - Once daily, oral, FDC (400/100 mg)
  - 12 weeks of Treatment

ASTRAL[1]	ASTRAL[2]	ASTRAL[3]	ASTRAL[4]
GT[1, 2, 4–6]	GT[2]	GT[3]	GT[1–6] CPT-B Cirrhosis

1. Jacobson IM, et al. N Engl J Med 2013;368:1867-77
2. Lawitz E, et al. N Engl J Med 2013;368:1878-87
3. Cheng G, et al. EASL 2013, poster 1191
4. German P, et al. EASL 2013, poster 1195
5. Lawitz E, et al. EASL 2013, poster 1082.

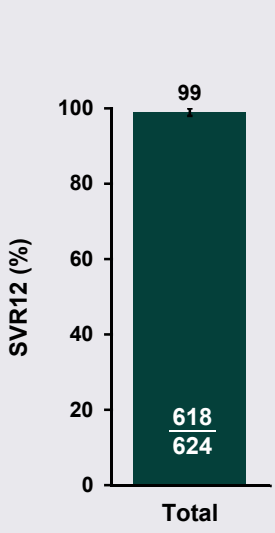
ASTRAL-1: Study Design



- Double blind, placebo controlled
- Broad inclusion criteria
- 5:1 randomization to SOF/VEL or placebo
  - Stratified by HCV genotype and cirrhosis (presence/absence)
  - GT 5 patients not randomized
- Conducted at 81 sites in US, Canada, UK, Germany, France, Italy, Belgium, and Hong Kong

Feld J, et al. 66th AASLD; San Francisco, CA; November 13-17, 2015; Abst. LB-2.

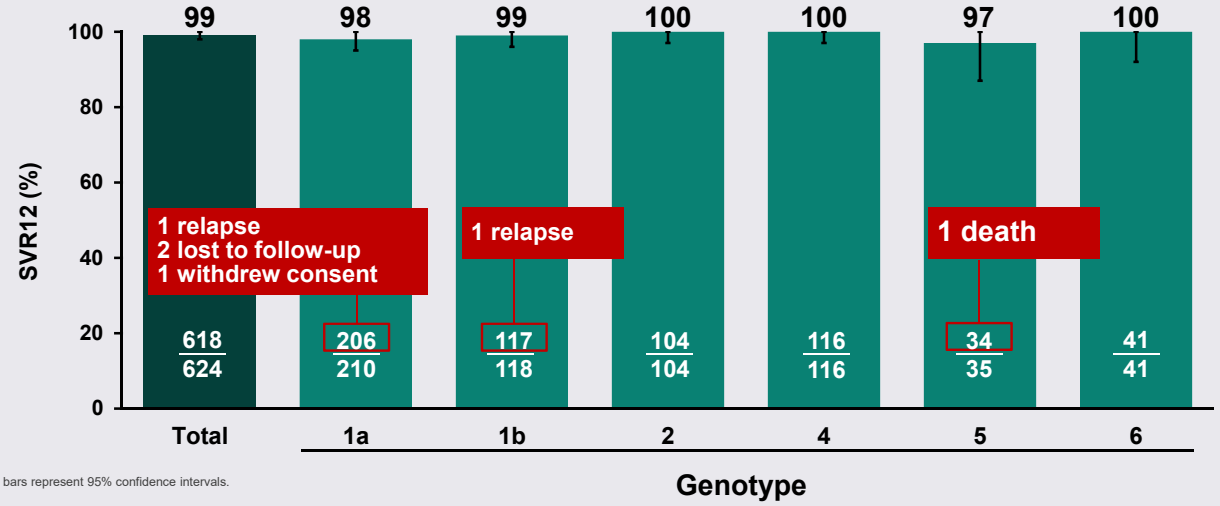
ASTRAL-1: Total SVR12



Error bars represent 95% confidence intervals.

Feld J, et al. 66th AASLD; San Francisco, CA; Novembe

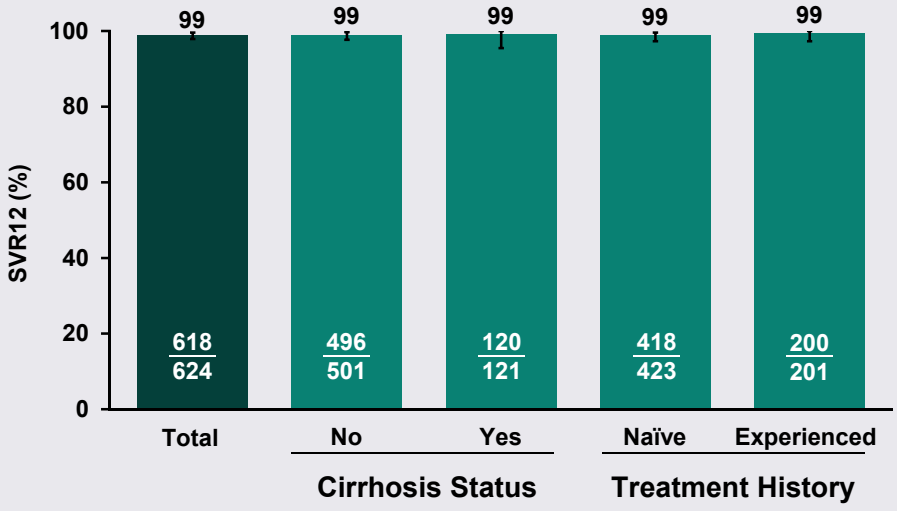
ASTRAL-1: SVR12 by HCV Genotype



Error bars represent 95% confidence intervals.

Feld J, et al. 66th AASLD; San Francisco, CA; November 13-17, 2015; Abst. LB-2.

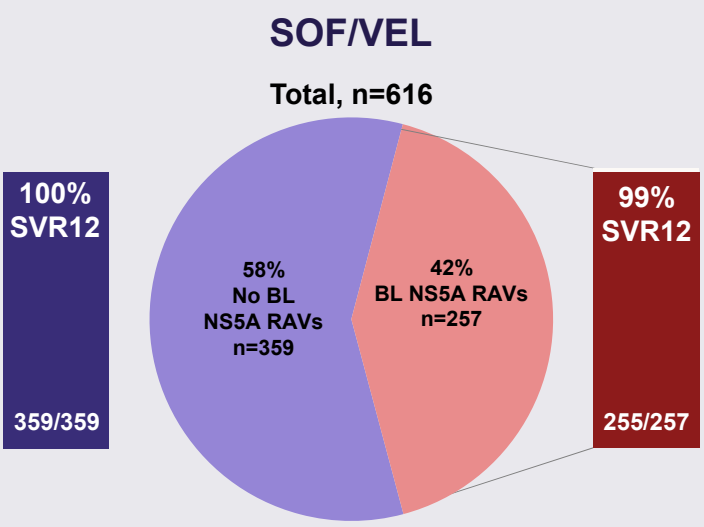
ASTRAL-1: SVR12 by Cirrhosis Status and Treatment History (SOF/VEL)



Error bars represent 95% confidence intervals.

Feld J, et al. 66th AASLD; San Francisco, CA; November 13-17, 2015; Abst. LB-2.

ASTRAL-1: Resistance Analysis (1% Cut-off)



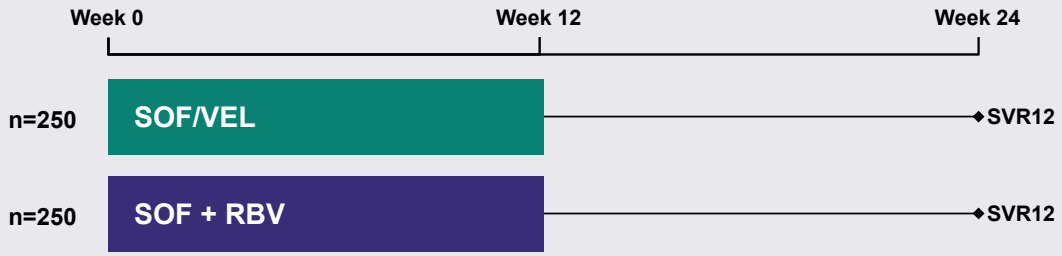
Feld J, et al. 66th AASLD; San Francisco, CA; November 13-17, 2015; Abst. LB-2.

ASTRAL-1: Safety

Adverse Event, n (%)	Placebo n=116	SOF/VEL n=624
Headache	33 (28)	182 (29)
Fatigue	23 (20)	126 (20)
Nasopharyngitis	12 (10)	79 (13)
Nausea	13 (11)	75 (12)

Feld J, et al. 66th AASLD; San Francisco, CA; November 13-17, 2015; Abst. LB-2.

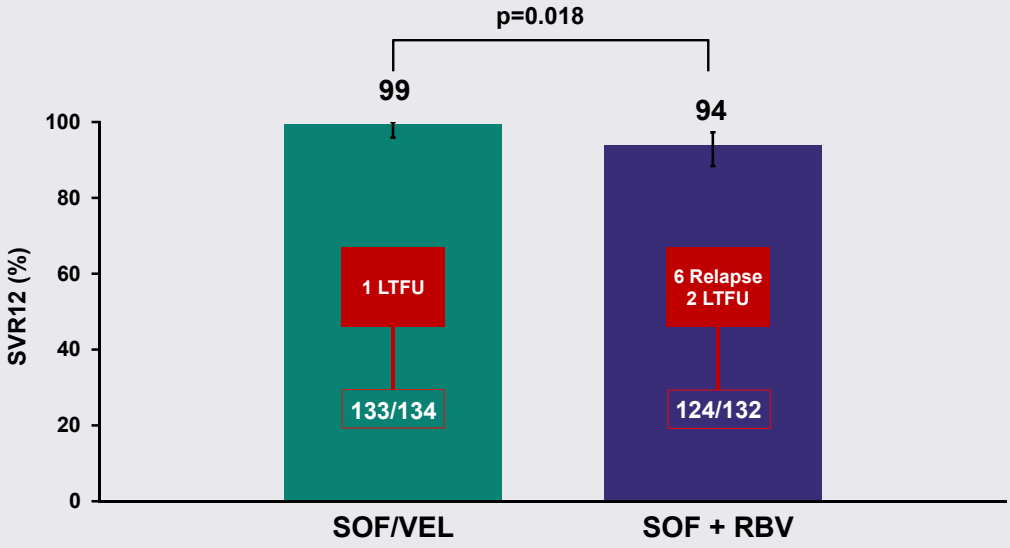
ASTRAL-2: Study Design



- Open-label, active-comparator trial
- Broad inclusion criteria
- 1:1 randomization to SOF/VEL or SOF + RBV
  - Stratified by prior treatment (TN/TE) and cirrhosis (presence/absence)
- Conducted at 51 sites in US

Sulkowski M, et al. 66th AASLD; San Francisco, CA; November 13-17, 2015; Abst. 205.

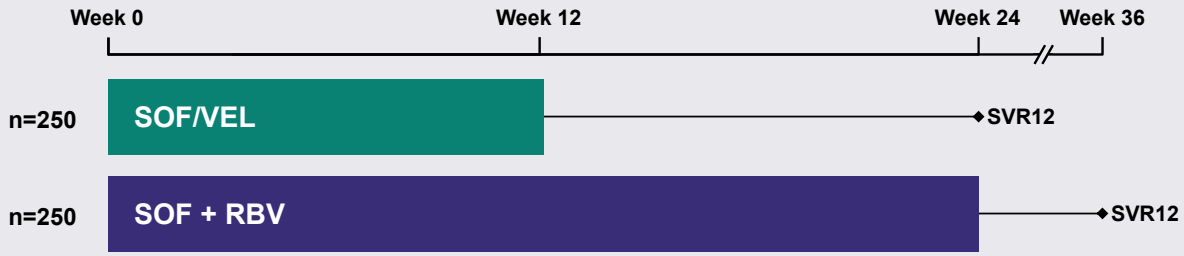
ASTRAL-2: SVR12 by Treatment Arm



Error bars represent 95% confidence intervals.

Sulkowski M, et al. 66th AASLD; San Francisco, CA; November 13-17, 2015; Abst. 205.

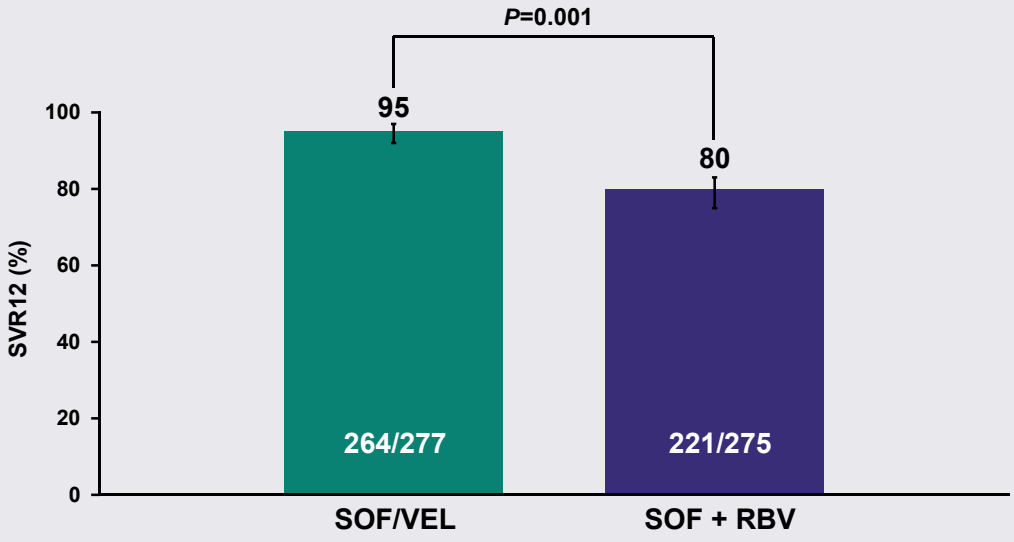
ASTRAL-3: Study Design



- Open-label, active-comparator trial
- Broad inclusion criteria
- 1:1 randomization to SOF/VEL or SOF + RBV
  - Stratified by prior treatment (TN/TE) and cirrhosis (presence/absence)
- Conducted at 76 sites in US, Canada, UK, Germany, France, Italy, Australia, and New Zealand

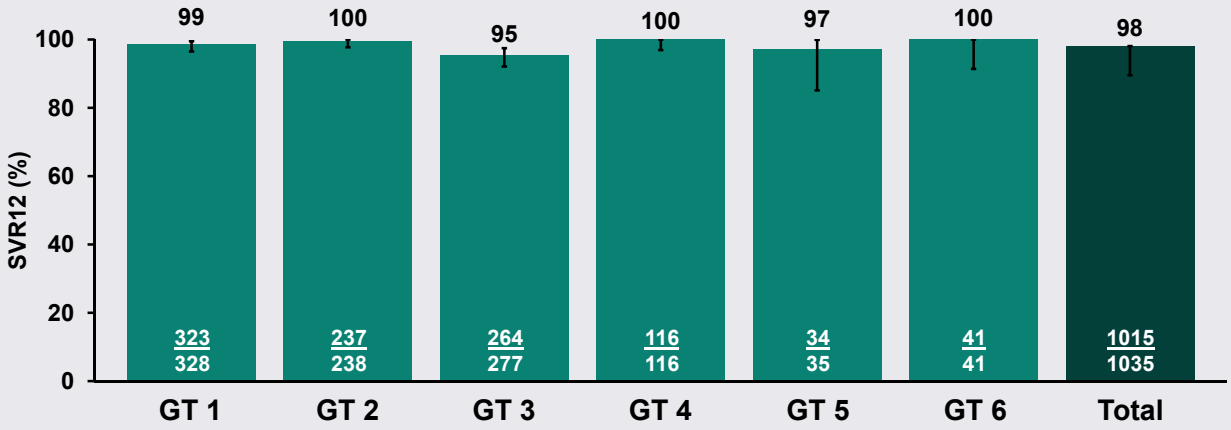
Mangia A, et al. 66th AASLD; San Francisco, CA; November 13-17, 2015; Abst. 249.

ASTRAL-3: SVR12 By Treatment Arm



Mangia A, et al. 66th AASLD; San Francisco, CA; November 13-17, 2015; Abst. 249.

Pooled ASTRAL, SOF/VEL 12 Weeks: SVR12

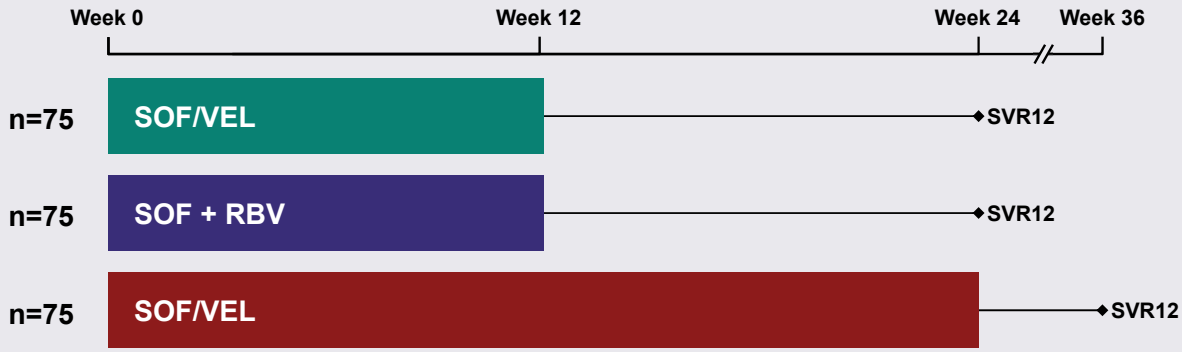


Of the 20 patients who did not achieve SVR12

- 12 had relapse
- 1 had re-infection
- 7 did not have a SVR12 assessment

Mangia A, et al. 66th AASLD; San Francisco, CA; November 13-17, 2015; Abst. 249.

ASTRAL-4: SOF/VEL in Patients with Decompensated Liver Disease



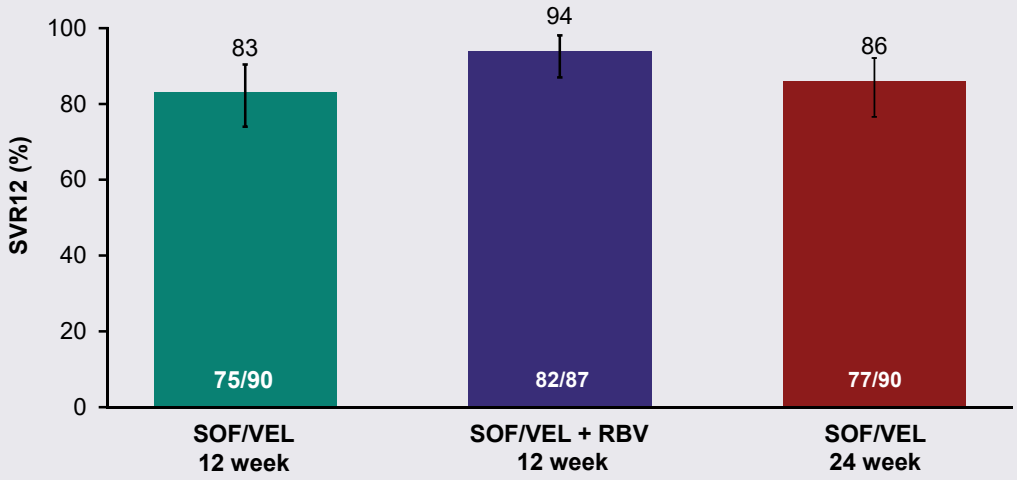
- Open-label, randomized (1:1:1) US study (NCT02201901)
- HCV GT 1–6 treatment-naïve or -experienced patients with Child-Pugh-Turcotte (CPT) B cirrhosis
- Key eligibility criteria: creatinine clearance (CL_{cr}) >50 mL/min, platelets >30,000/mm^3; no hepatocellular carcinoma or liver transplant

SVR12, sustained virologic response 12 weeks after treatment end.

Charlton M, et al. 66th AASLD; San Francisco, CA; November 13-17, 2015; Abst. LB-13.

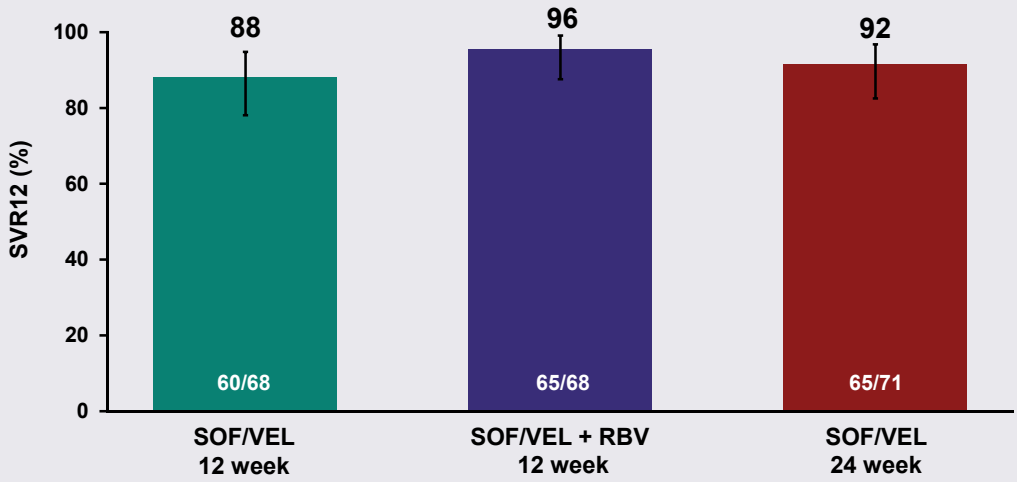
ASTRAL-4: Results - Overall SVR12

- P-value < 0.001 for comparison of SVR12 rate to 1% for each treatment group



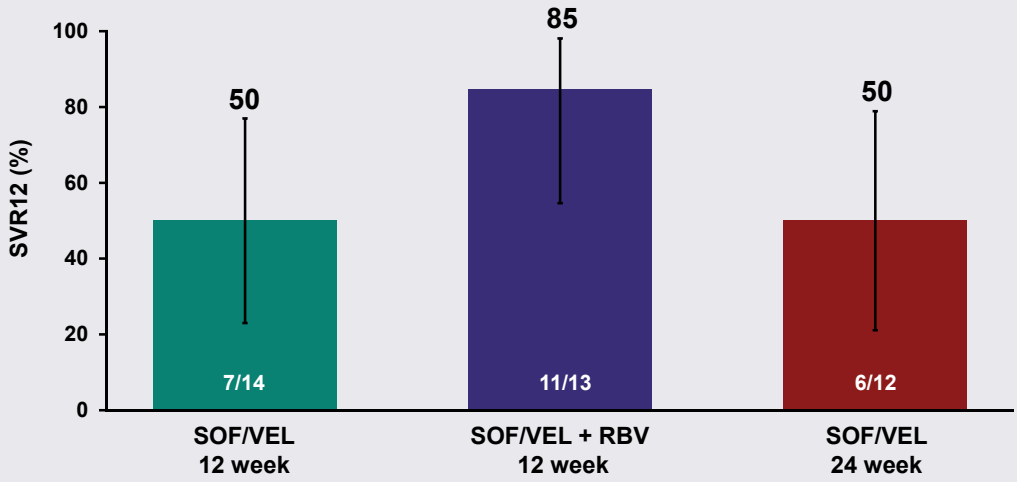
Charlton M, et al. 66th AASLD; San Francisco, CA; November 13-17, 2015; Abst. LB-13.

ASTRAL-4: Results - SVR12 in GT 1 Patients



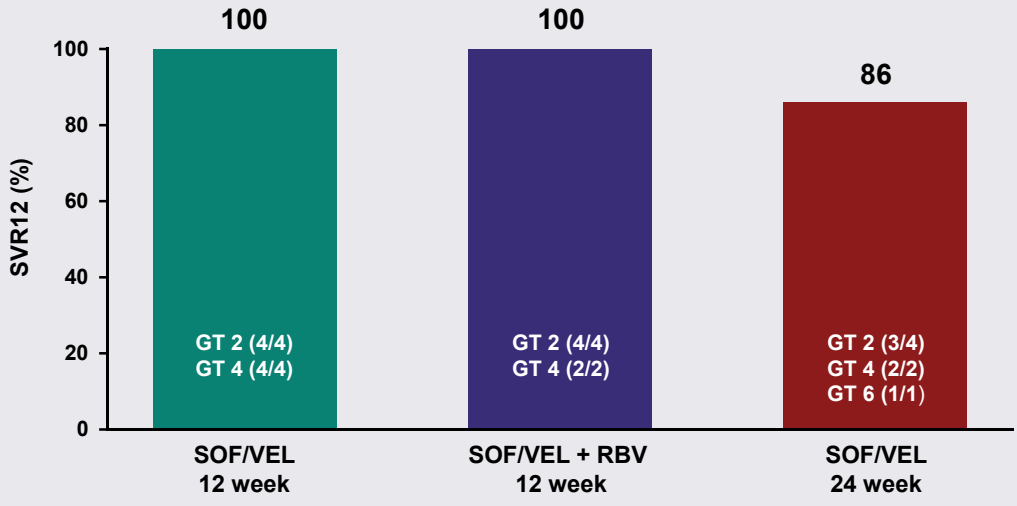
Charlton M, et al. 66th AASLD; San Francisco, CA; November 13-17, 2015; Abst. LB-13.

ASRAL-4: Results - SVR12 in GT 3 Patients



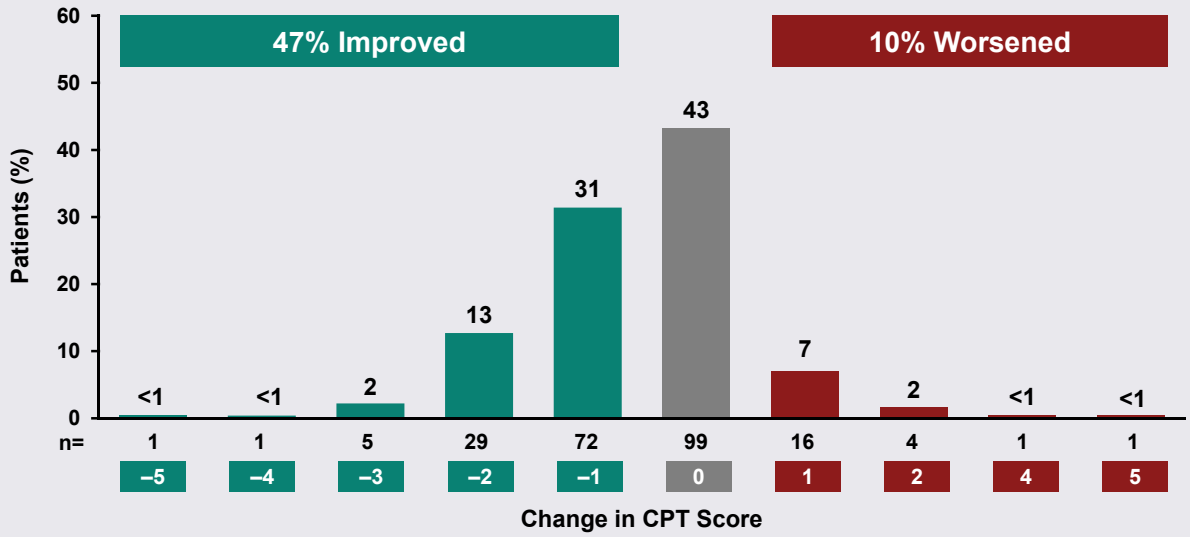
Charlton M, et al. 66th AASLD; San Francisco, CA; November 13-17, 2015; Abst. LB-13.

ASTRAL-4: Results - SVR12 in GT 2, 4, 6 Patients



Charlton M, et al. 66th AASLD; San Francisco, CA; November 13-17, 2015; Abst. LB-13.

ASTRAL-4: Results - CPT Score Change From Baseline



Total n=234; 5 patients had no follow-up Week 12 assessment.

Charlton M, et al. 66th AASLD; San Francisco, CA; November 13-17, 2015; Abst. LB-13.

ASTRAL-4: Results - Overall Safety Summary

Patients, n (%)	SOF/VEL 12 Weeks n=90	SOF/VEL + RBV 12 Weeks n=87	SOF/VEL 24 Weeks n=90
Any AE	73 (81)	79 (91)	73 (81)
Grade 3 or 4 AE	16 (18)	11 (13)	17 (19)
SAE	17 (19)	14 (16)	16 (18)
Treatment-related SAE	0	1 (1)	1 (1)
AE leading to D/C	1 (1)	4 (5)	4 (4)
Transplant	0	0	1 (1)
Death	3 (3)	3 (3)	3 (3)

- SAEs assessed as related included dyspnea (SOF/VEL +RBV 12 Weeks) and hepatorenal syndrome peritonitis, sepsis, hypotension (SOF/VEL 24 weeks)
- Deaths: sepsis/septic shock/MOF (n=4); liver failure (n=2); cardiopulmonary arrest (n=1); respiratory failure (n=1); myocardial infarction (n=1)
  - None considered treatment related

Charlton M, et al. 66th AASLD; San Francisco, CA; November 13-17, 2015; Abst. LB-13.

ASTRAL-4: Results - RBV Tolerance

Patients, n (%)	SOF/VEL + RBV 12 Weeks n=87
Hemoglobin <10 g/dL, n (%)	20 (23)
Hemoglobin <8.5 g/dL, n (%)	6 (7)
Max median hemoglobin decline, mg/dL (range)	-1.5 (-5.1, 1.6)
RBV dosing	
Median average daily dose, mg (range)	1124 (486-1200)
Median days on RBV, n (range)	84 (4-89)
Discontinued, n (%)	15 (17)
Dose interruption ≥3 days, n (%)	4 (5)
Dose reduction, n (%)	32 (37)
Concomitant blood products or epoetin, n (%)	
Anti anemia therapy	1 (1)
Blood substitutes	2 (2)

Charlton M, et al. 66th AASLD; San Francisco, CA; November 13-17, 2015; Abst. LB-13.