Phase 3

Treatment Naïve & Experienced

Sofosbuvir-Velpatasvir in Decompensated HCV Cirrhosis
ASTRAL-4

Curry MP, et al. N Engl J Med. 2015;373:2618-28.

Hepatitis web study

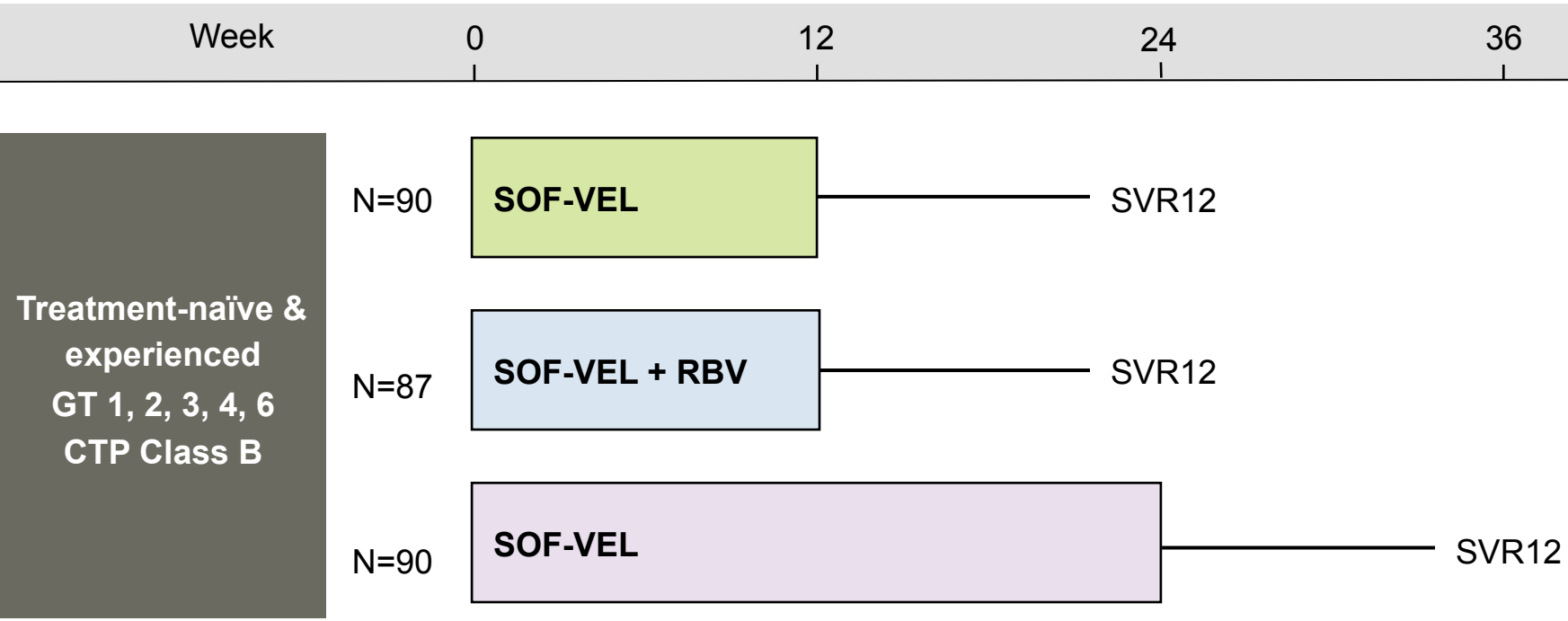
Sofosbuvir-Velpatasvir in Decompensated HCV Cirrhosis
ASTRAL-4: Study Features

ASTRAL-4 Trial

- **Design**: Randomized, phase 3 trial to examine the safety and efficacy of a fixed-dose combination of sofosbuvir-velpatasvir for 12 weeks +/- ribavirin or for 24 weeks in patients with GT 1-6 chronic HCV with decompensated cirrhosis
- **Setting**: 47 sites in United States
- **Entry Criteria**
  - Chronic HCV GT 1, 2, 3, 4, 6
  - Child-Pugh-Turcotte class B
  - Prior treatment failure (except for prior NS5A or NS5B) allowed
- **Exclusion Criteria**
  - Prior or impending (within 12 weeks of study entry) liver transplantation
  - Platelet count <30,000 or CrCl <50 ml/min
- **Primary End-Point**: SVR12

Source: Curry MP, et al. N Engl J Med. 2015;373:2618-28.

Sofosbuvir-Velpatasvir in Decompensated HCV Cirrhosis
ASTRAL-4: Study Design



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

Source: Curry MP, et al. N Engl J Med. 2015;373:2618-28.

Sofosbuvir-Velpatasvir in Decompensated HCV Cirrhosis
ASTRAL-4: Participants

Baseline Characteristic	SOF-VEL 12 weeks n=90	SOF-VEL + RBV 12 weeks n=87	SOF-VEL 24 weeks n=90
Mean age, years (range)	58 (42-73)	58 (40-71)	58 (46-72)
Male sex, %	63	76	70
Race, %			
White	88	91	90
Black	7	6	7
Asian	3	0	2
HCV Genotype, %			
1a	56	62	61
1b	20	16	18
2	4	5	4
3	16	15	13
4	4	2	2
6	0	0	1
HCV RNA ≥800,000 IU/mL, %	66	52	50
IL28B genotype, non-CC, %	78	75	78
Mean eGFR, ml/min (range)	89 (15-169)	90 (50-167)	90 (43-198)

Source: Curry MP, et al. N Engl J Med. 2015;373:2618-28.

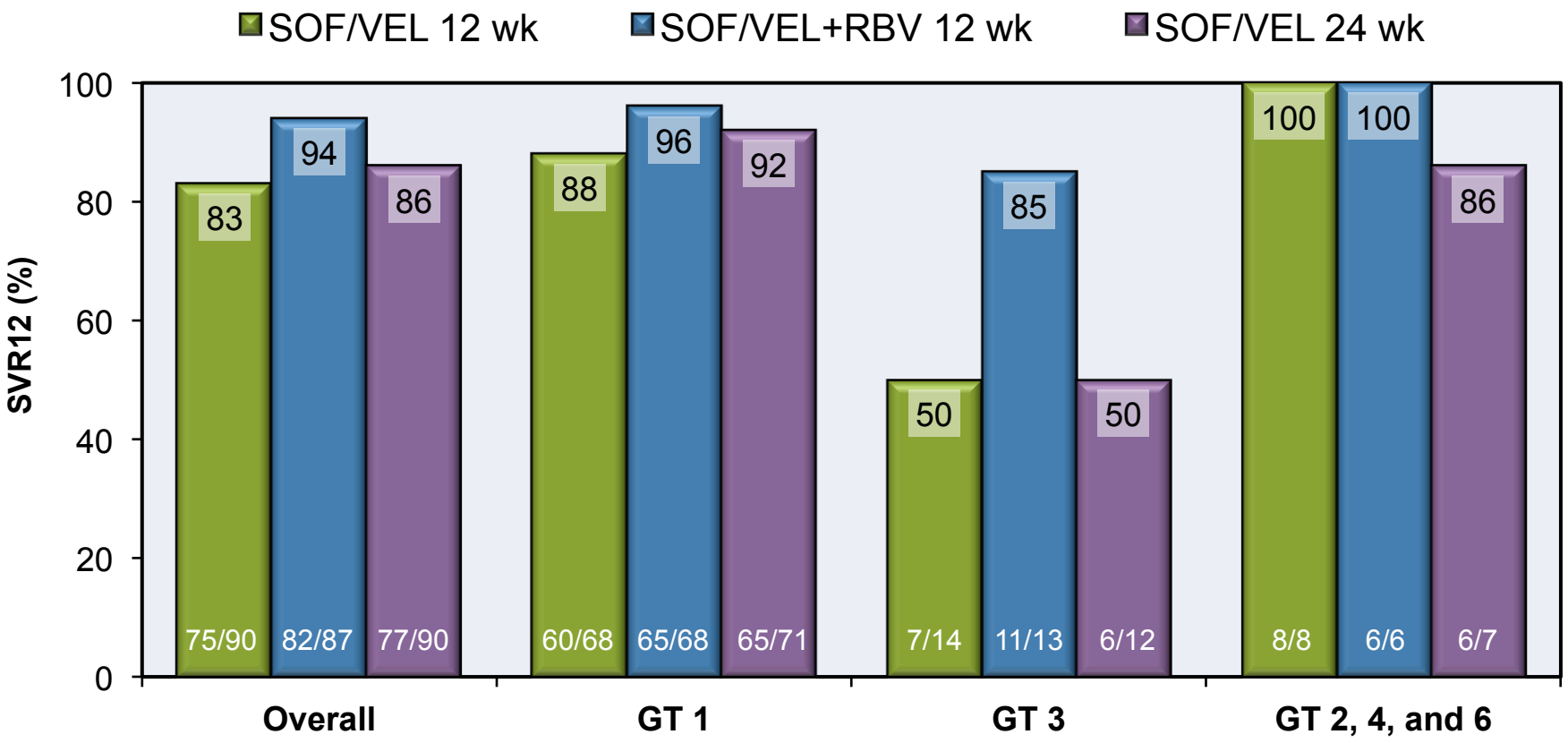
Sofosbuvir-Velpatasvir in Decompensated HCV Cirrhosis
ASTRAL-4: Participants

Baseline Characteristic	SOF-VEL 12 weeks n=90	SOF-VEL + RBV 12 weeks n=87	SOF-VEL 24 weeks n=90
CPT score, %			
≤6	3	7	8
7	40	26	23
8	34	47	38
9	21	15	24
10	1	5	7
MELD score, %			
<10	40	33	29
10-15	56	62	66
≥16	4	5	6
Ascites, %			
None	18	25	17
Mild or moderate	80	70	82
Severe	2	5	1
Prior HCV treatment, %			
No	36	46	53
Yes	64	54	47
Protease inhibitor regimen	16	26	17
Peginterferon + Ribavirin	83	74	83

Source: Curry MP, et al. N Engl J Med. 2015;373:2618-28.

Sofosbuvir-Velpatasvir in Decompensated HCV Cirrhosis
ASTRAL-4: Results

ASTRAL-4: SVR12 Results by Genotype



Source: Curry MP, et al. N Engl J Med. 2015;373:2618-28.

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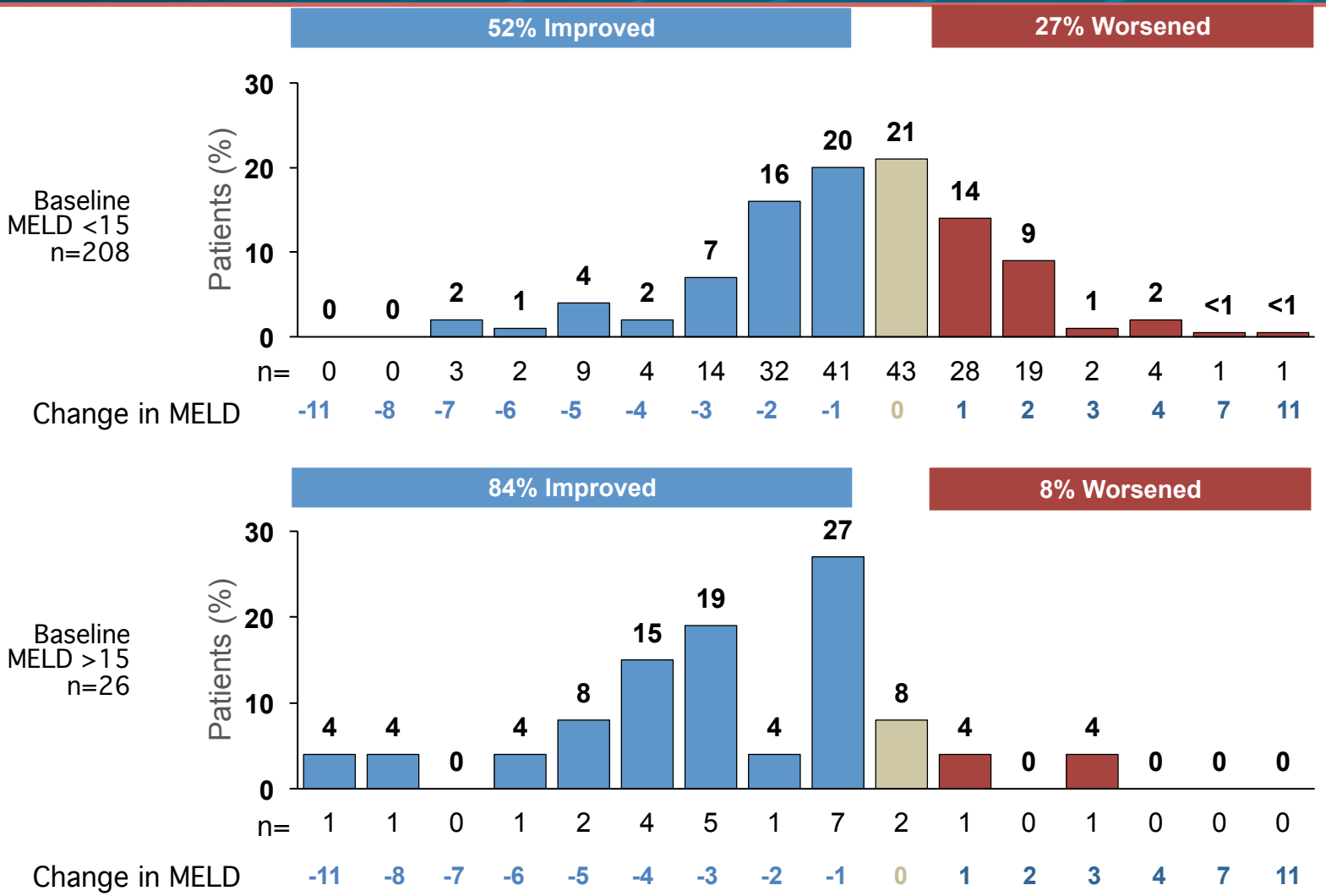
Sofosbuvir-Velpatasvir in Decompensated HCV Cirrhosis
ASTRAL-4: Change in MELD Scores on Treatment



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Sofosbuvir-Velpatasvir in Decompensated HCV Cirrhosis
ASTRAL-4: Adverse Events

Adverse Event (AE), %	SOF-VEL 12 weeks (n=90)	SOF-VEL + RBV 12 weeks (n=87)	SOF-VEL 24 weeks (n=90)
Discontinuation due to AE	1	5	4
Serious AEs	19	16	18
Deaths	3	3	3
Any AE in ≥10% of patients			
Fatigue	26	39	23
Nausea	24	25	20
Headache	26	21	19
Anemia	4	31	3
Diarrhea	7	21	8
Insomnia	10	14	10
Pruritus	11	5	4
Muscle spasm	3	11	2
Dyspnea	4	10	0
Hemoglobin <10 g/dl	8	23	9

Source: Curry MP, et al. N Engl J Med. 2015;373:2618-28.

Sofosbuvir-Velpatasvir in Decompensated HCV Cirrhosis
ASTRAL-4: Conclusions

Conclusions: “Treatment with sofosbuvir–velpatasvir with or without ribavirin for 12 weeks and with sofosbuvir–velpatasvir for 24 weeks resulted in high rates of sustained virologic response in patients with HCV infection and decompensated cirrhosis.”

Source: Curry MP, et al. N Engl J Med. 2015;373:2618-28.