Ledipasvir/Sofosbuvir With Ribavirin for the Treatment of HCV in Patients With Decompensated Cirrhosis: Preliminary Results of a Prospective, Multicenter Study

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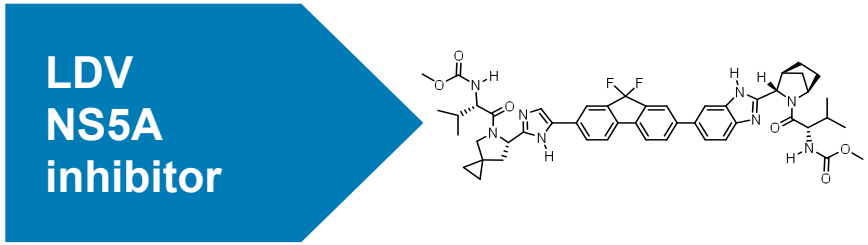
Disclosures

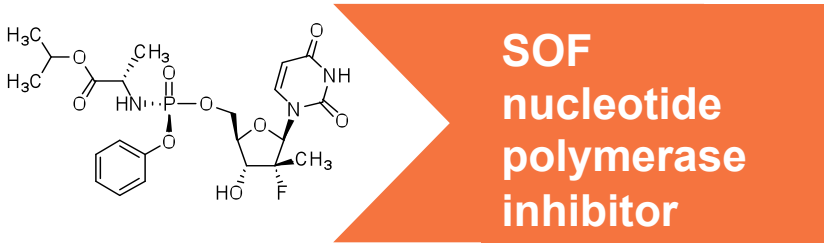
[AASLD prepares a disclosure slide — based on the information you submitted with your abstract — for your approval upon check-in at the Speaker Ready Room. It will be the first slide in your PowerPoint presentation and will pause for three seconds at the beginning of your talk.]

Background

- **Ledipasvir**
  - Once-daily, oral, 90-mg NS5A inhibitor



- **Sofosbuvir**
  - Once-daily, oral, 400-mg NS5B inhibitor



- **Ledipasvir/Sofosbuvir FDC**
  - Once-daily, oral, fixed-dose (90/400 mg) combination tablet
  - Single-tablet regimen for hepatitis C

FDC, fixed-dose combination.

Background and Aims

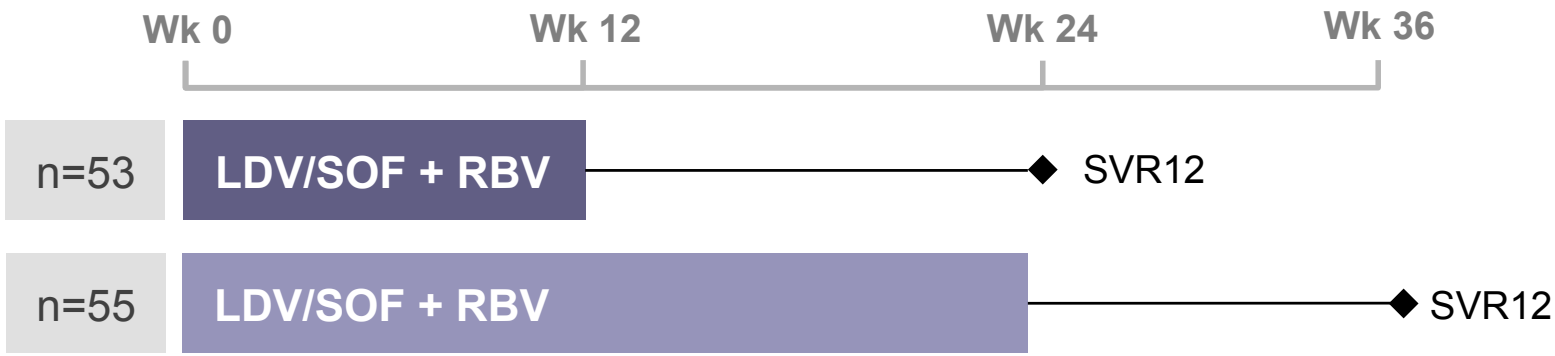
GT 1 and 4, CPT Class B and C

- The number of patients with advanced liver disease and the proportion listed for liver transplantation is steadily increasing[1,2]
- There are no approved treatment options for patients with decompensated cirrhosis due to HCV infection
- The aim of this study is to evaluate the safety and efficacy of LDV/SOF + ribavirin (RBV) for 12 or 24 weeks in HCV patients with GT 1 or 4 infection and decompensated cirrhosis

1. Everson G. J Hepatol 2005;42:S65-S74. 2. Chen S. Int J Med Sci 2006;3:47-52.

Study Design

GT 1 and 4, CPT Class B and C



- 108 patients randomized 1:1 to 12 or 24 weeks of treatment
- GT 1 or 4 treatment-naïve or -experienced patients with decompensated cirrhosis (CPT class B [score 7-9] or C [score 10–12]*)
- Broad inclusion criteria
  - No history of major organ transplant, including liver
  - No hepatocellular carcinoma (HCC)
  - Total bilirubin ≤10 mg/dL, hemoglobin ≥ 10 g/dL
  - CL_{cr} ≥40 mL/min, platelets >30,000 x 10^3/μL
- Stratified by CPT class B or C

*Patients with CPT scores 13-15 excluded.

Endpoints

GT 1 and 4, CPT Class B and C

- Primary efficacy endpoint: SVR12 (intent to treat)
  - HCV RNA <LLOQ (<15 IU/mL) by COBAS® Ampliprep® HCV Test
- Safety
  - AEs leading to discontinuation of study treatment
  - SAEs, including death

Results: Demographics

GT 1 and 4, CPT Class B and C

	CPT B		CPT C	
	12 Weeks n=30	24 Weeks n=29	12 Weeks n=23	24 Weeks n=26
Median age, y (range)	60 (28-69)	58 (35-69)	58 (41-71)	59 (48-68)
Male, n (%)	22 (73)	18 (62)	14 (61)	18 (69)
White, n (%)	29 (97)	26 (90)	21 (91)	24 (92)
BMI ≥30 kg/m^2, n (%)	10 (33)	10 (34)	13 (57)	9 (35)
Median HCV RNA, $\log_{10}$ IU/mL (range)	5.9 (4.3-6.7)	5.8 (3.2-7.1)	5.6 (4.1-6.5)	5.8 (3.7-6.9)
GT, n (%)				
1a	19 (63)	22 (76)	15 (65)	18 (69)
4	1 (3)	0	2 (9)	0
IL28B non-CC, n (%)	26 (87)	23/28 (82)	17 (74)	19 (73)
Prior HCV treatment, n (%)	22 (73)	19 (66)	11 (48)	18 (69)

Results: Baseline Characteristics

GT 1 and 4, CPT Class B and C

	CPT B		CPT C	
	12 Weeks n=30	24 Weeks n=29	12 Weeks n=23	24 Weeks n=26
MELD score, n (%)				
<10	6 (20)	8 (28)	0	0
10–15	21 (70)	16 (55)	16 (70)	13 (50)
16-20	3 (10)	5 (17)	7 (30)	12 (46)
21-25	0	0	0	1 (4)
Ascites, n (%)	17 (57)	17 (59)	22 (96)	25 (96)
Encephalopathy, n (%)	20 (67)	16 (55)	21 (91)	23 (88)
Median bilirubin, mg/dL (range)	2.0 (0.6-5.5)	1.4 (0.8-4.5)	2.9 (1.2-14.5)	3.8 (1.1-5.7)
Median albumin, g/dL (range)	2.9 (2.1-3.7)	3.0 (2.2-3.4)	2.6 (1.6-3.5)	2.6 (2.0-3.3)
Median INR (range)	1.3 (1.0-1.5)	1.3 (1.0-2.6)	1.4 (1.2-1.9)	1.4 (1.1-2.2)
Median platelets, x 10^3 µL (range)	88 (36-212)	73 (30-154)	81 (39-177)	71 (32-179)
Median hemoglobin, g/dL (range)	13.1 (9.7-16.3)	13 (9.9-15.4)	12.3 (10.6-14.9)	12.6 (7.5-15.8)
Median CL_{Cr}, mL/min (range)	98 (34-166)	81 (45-148)	77 (36-114)	78 (54-150)

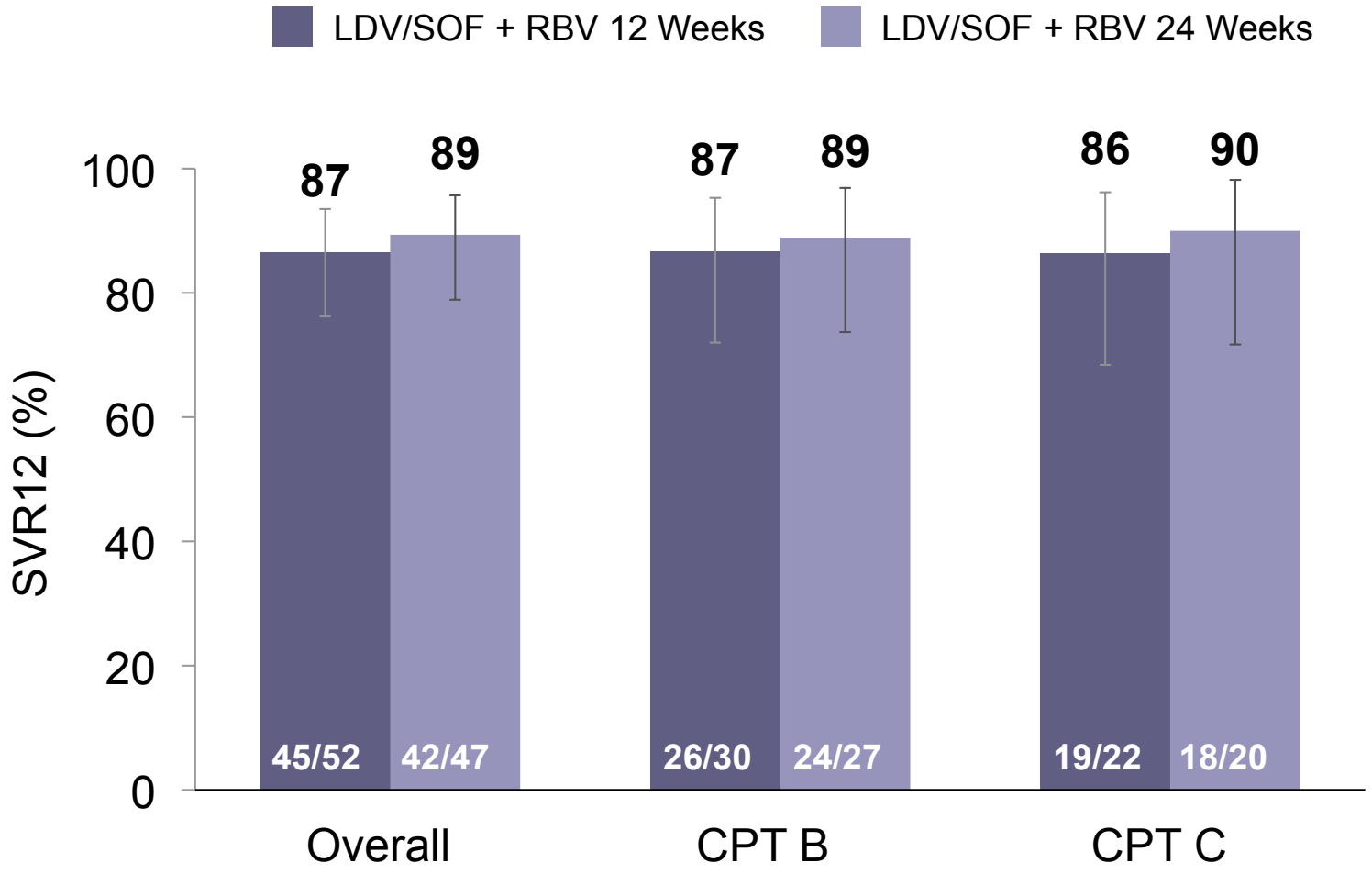
Results: Disposition

GT 1 and 4, CPT Class B and C

Patients, n (%)	CPT B		CPT C	
	12 Weeks n=30	24 Weeks n=29	12 Weeks n=23	24 Weeks n=26
Completed Treatment	30 (100)	25 (86)	21 (91)	22 (85)
Reasons for DC Treatment				
Liver Transplant	0	2 (7)	1 (4)	1 (4)
Adverse Event	0	1 (3)	0	2 (8)
Death	0	1 (3)	1 (4)	1 (4)

Results: SVR12

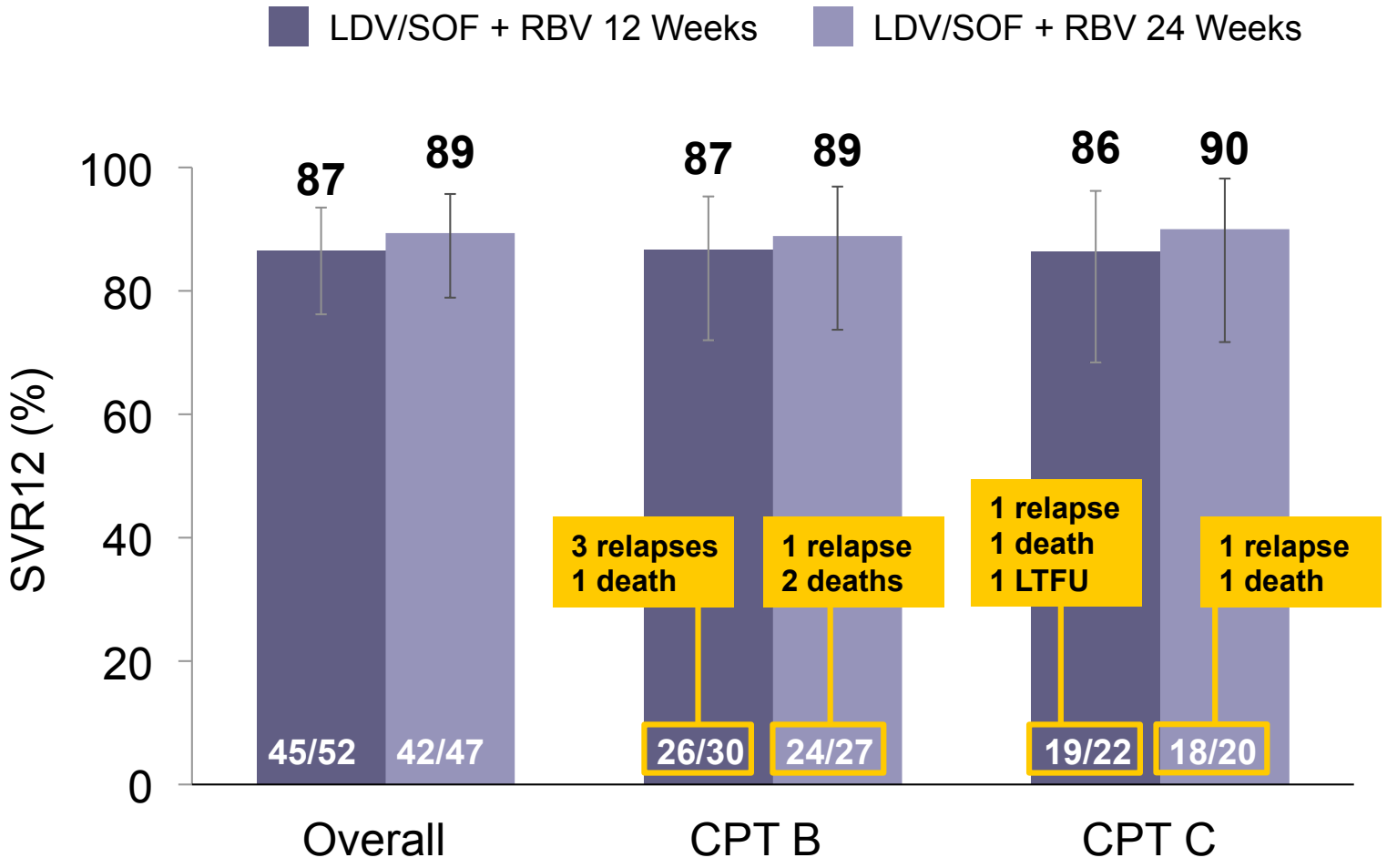
GT 1 and 4, CPT Class B and C



6 subjects (2 CPT B/24 Wk, 1 CPT C/12 Wk and 3 CPT C/24 Wk) excluded (transplant on study);
3 subjects CPT C/24 Wk have not reached SVR12.
Error bars represent 90% confidence intervals.

Results: SVR12

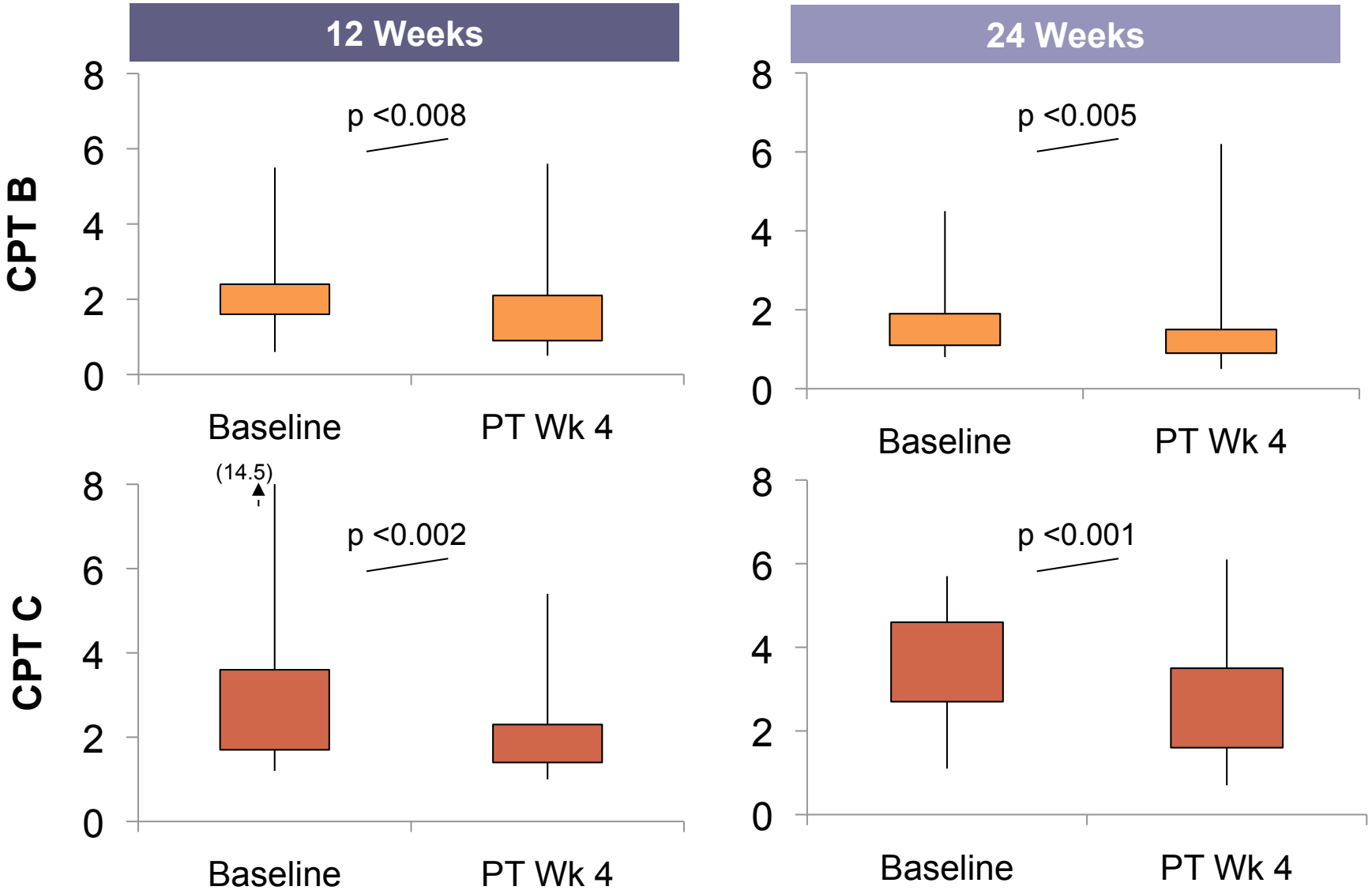
GT 1 and 4, CPT Class B and C



6 subjects (2 CPT B/24 Wk, 1 CPT C/12 Wk and 3 CPT C/24 Wk) excluded (transplant on study);
3 subjects CPT C/24 Wk have not reached SVR12.
Error bars represent 90% confidence intervals.

Laboratory Results: Median (IQR) Total Bilirubin

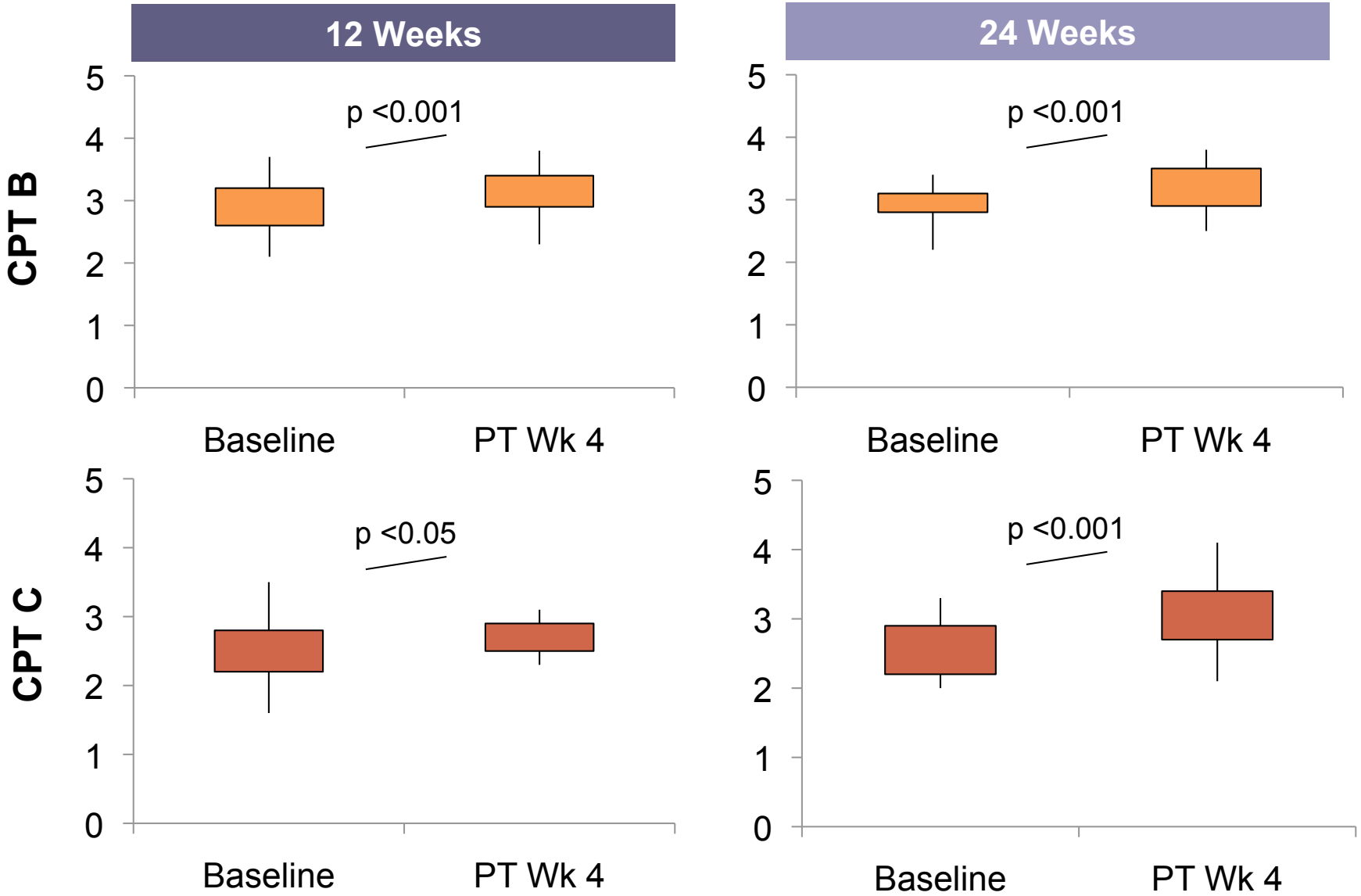
Change From Baseline to Follow-Up Week 4



Total Bilirubin Normal Range: 0.2-1.2 mg/dL

Laboratory Results: Median (IQR) Albumin

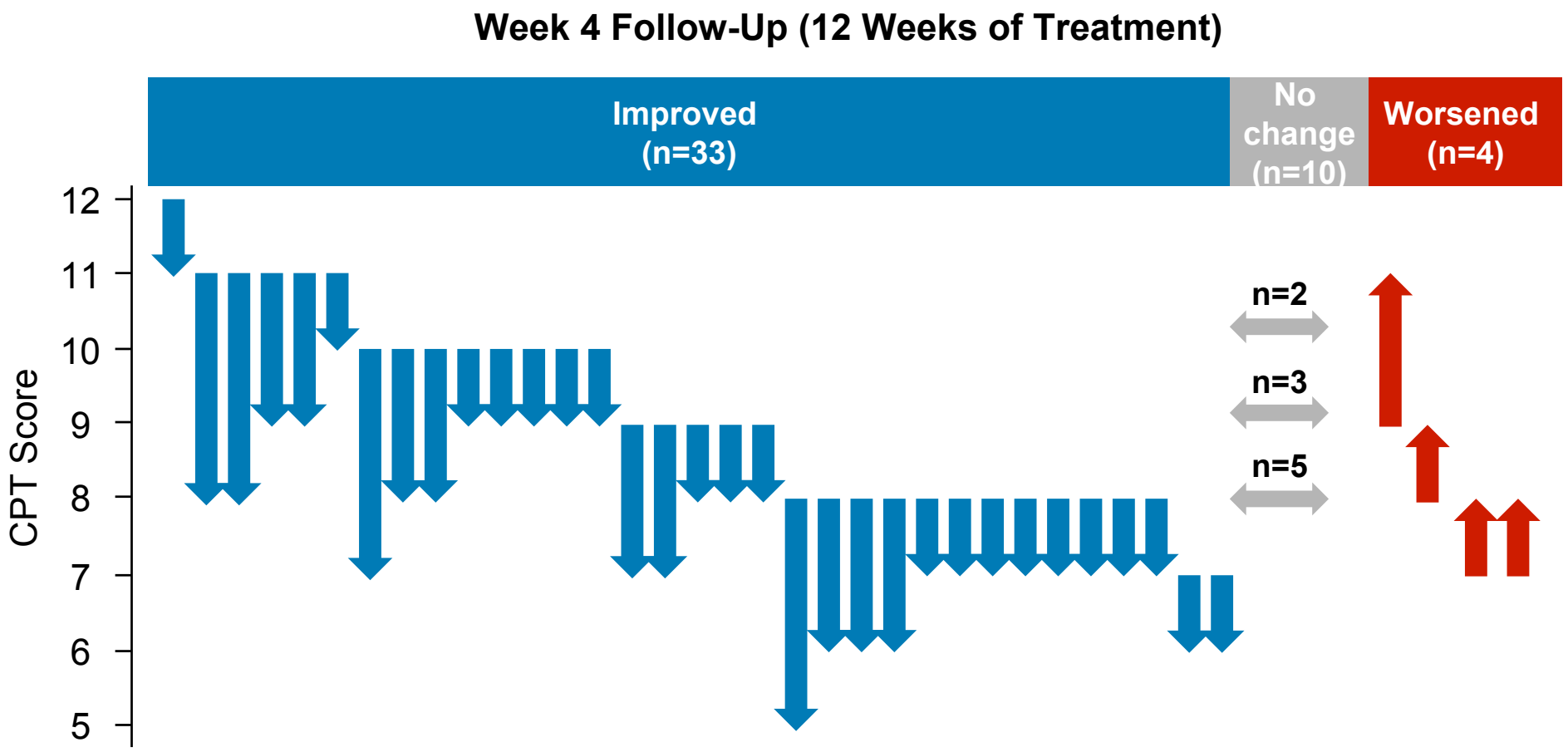
Change From Baseline to Follow-Up Week 4



Albumin normal range: 3.3-4.9 g/dL

Results: CPT Scores

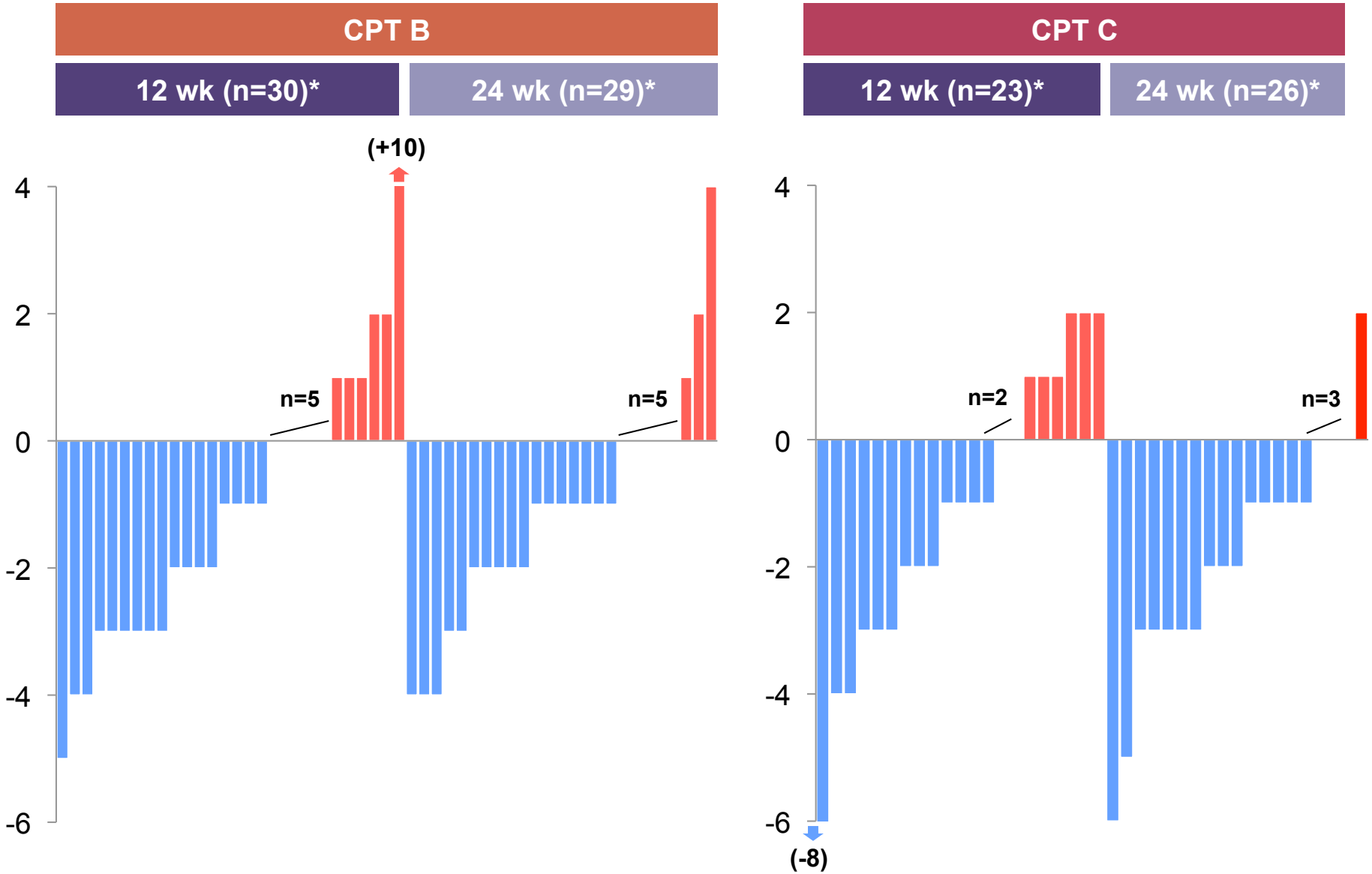
Change From Baseline to Follow-Up Week 4



Arrows represent individual patients.

Laboratory Results: MELD Score

Change From Baseline to Follow-Up Week 4



*Missing FU-4: n=2 CPT B 12 wk; n=4 CPT B 24 wk; n=2 CPT C 12 wk; n=7 CPT C 24 wk.

Results: Overall Safety Summary

GT 1 and 4, CPT Class B and C

	Patients, n (%)	CPT B		CPT C	
		12 Weeks n=30	24 Weeks n=29	12 Weeks n=23	24 Weeks n=26
Overall Safety	AE	29 (97)	27 (93)	23 (100)	26 (100)
	Grade 3–4 AE	2 (7)	8 (28)	6 (26)	11 (42)
	Serious AE	3 (10)	10 (34)	6 (26)	11 (42)
	Treatment-related SAEs	2 (7)	0	0	2 (8)
	Treatment DC due to AE	0	1 (3)	0	2 (8)
	Death	1 (3)	2 (7)	2 (9)	1 (4)

- Related SAEs: Anemia (2), hepatic encephalopathy, peritoneal hemorrhage
- Early discontinuations: Sepsis, hepatic encephalopathy, peritoneal hemorrhage
- Deaths: septic shock (2), multi-organ failure and septic shock (2), oliguric renal failure, cardiac arrest

Conclusions

GT 1 and 4, CPT Class B and C

- LDV/SOF + RBV for 12 weeks resulted in a high SVR12 rate in HCV patients with GT 1 and 4 and advanced liver disease
  - Relapse rates were similar to relapse rates in patients with compensated cirrhosis
  - Extending treatment duration to 24 weeks did not increase the response rate
- Virologic response was associated with improvements in bilirubin, albumin, MELD and CPT scores in both CPT class B and C patients
- LDV/SOF + RBV for 12-24 weeks was generally safe and well tolerated in CPT class B and C patients

Acknowledgments

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