Treatment Naïve and Treatment Experienced

Ledipasvir-Sofosbuvir + RBV in HCV GT 1,4 and Advanced Liver Disease

SOLAR-1 (Cohorts A and B)

Charlton M, al. Gastroenterology. 2015; [Epub ahead of print]

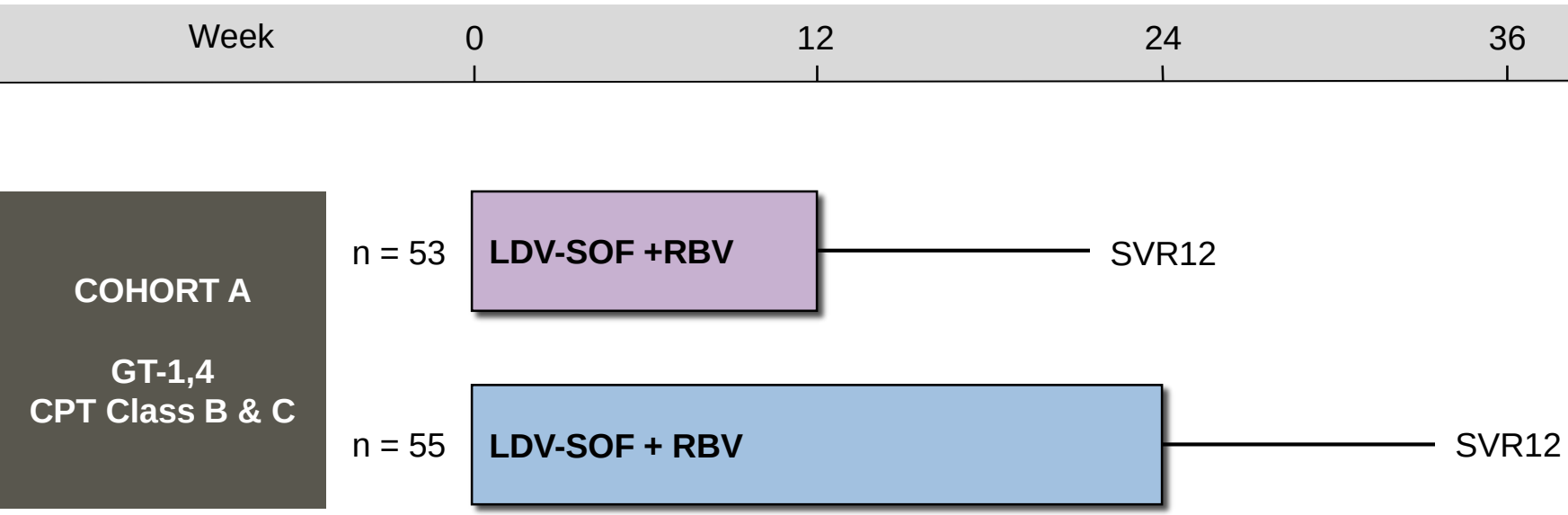
Ledipasvir-Sofosbuvir + Ribavirin in Advanced Liver Disease
SOLAR-1 (Cohorts A and B): Features

SOLAR-1 (Cohorts A and B): Design

- **Design**: Phase 2, open label, randomized prospective, trial, using fixed-dose combination of ledipasvir-sofosbuvir plus ribavirin for 12 or 24 weeks in treatment-naïve and treatment-experienced patients with HCV GT1 or 4.
- **Cohorts**
  Cohort A = cirrhosis and moderate to severe hepatic impairment who had not undergone liver transplantation
  Cohort B = post liver transplantation
- **Setting**: multicenter study in United States
- **Entry Criteria**
  - Adults with Chronic HCV Genotype 1 or 4
  - Treatment-naïve or treatment experienced
  - Total bilirubin ≤ 10 mg/dL; Creatinine clearance ≥ 40 mL/min
  - Hemoglobin ≥ 10 g/dL; Platelet count > 30,000/mm^3
  - Exclusion: hepatitis B or HIV coinfection or prior receipt of NS5a inhibitor
- **Primary End-Point**: SVR12

Source: Charlton M, al. Gastroenterology. 2015; [Epub ahead of print]

Ledipasvir-Sofosbuvir + Ribavirin in HCV GT 1,4
SOLAR-1 (Cohort A = Pre-transplantation): Study Design



Abbreviations: LDV= ledipasvir; SOF = sofosbuvir; RBV = ribavirin

Drug Dosing
Ledipasvir-sofosbuvir (90/400 mg): fixed dose combination; one pill once daily
Ribavirin: started at 600 mg/day and then escalated as tolerated up to maximum of 1200 mg/day

Source: Charlton M, al. Gastroenterology. 2015; [Epub ahead of print]

Ledipasvir-Sofosbuvir + Ribavirin in HCV GT 1,4
SOLAR-1 (Cohort A = Pre-transplantation): Baseline Characteristics

Baseline Characteristic	CTP B		CTP C	
	12-Weeks n=30	24-Weeks n=29	12-Weeks n=23	24-Weeks n=26
Median age, years	60	58	58	59
Male sex, n (%)	22 (73)	18 (62)	14 (61)	18 (69)
White, n (%)	29 (97)	26 (90)	21 (97)	24 (92)
HCV RNA, $\log_{10}$ IU/ml (median)	5.9	5.8	5.6	5.8
IL28B genotype CC, n (%)	4 (13)	5 (17)	6 (26)	7 (27)
HCV Genotype				
1a, n (%)	19 (63)	22 (76)	15 (65)	18 (69)
1b, n (%)	10 (33)	7 (24)	6 (26)	8 (31)
4, n (%)	1 (3)	0	2 (9)	0
Prior Treatment	22 (73)	19 (65)	11 (48)	18 (69)

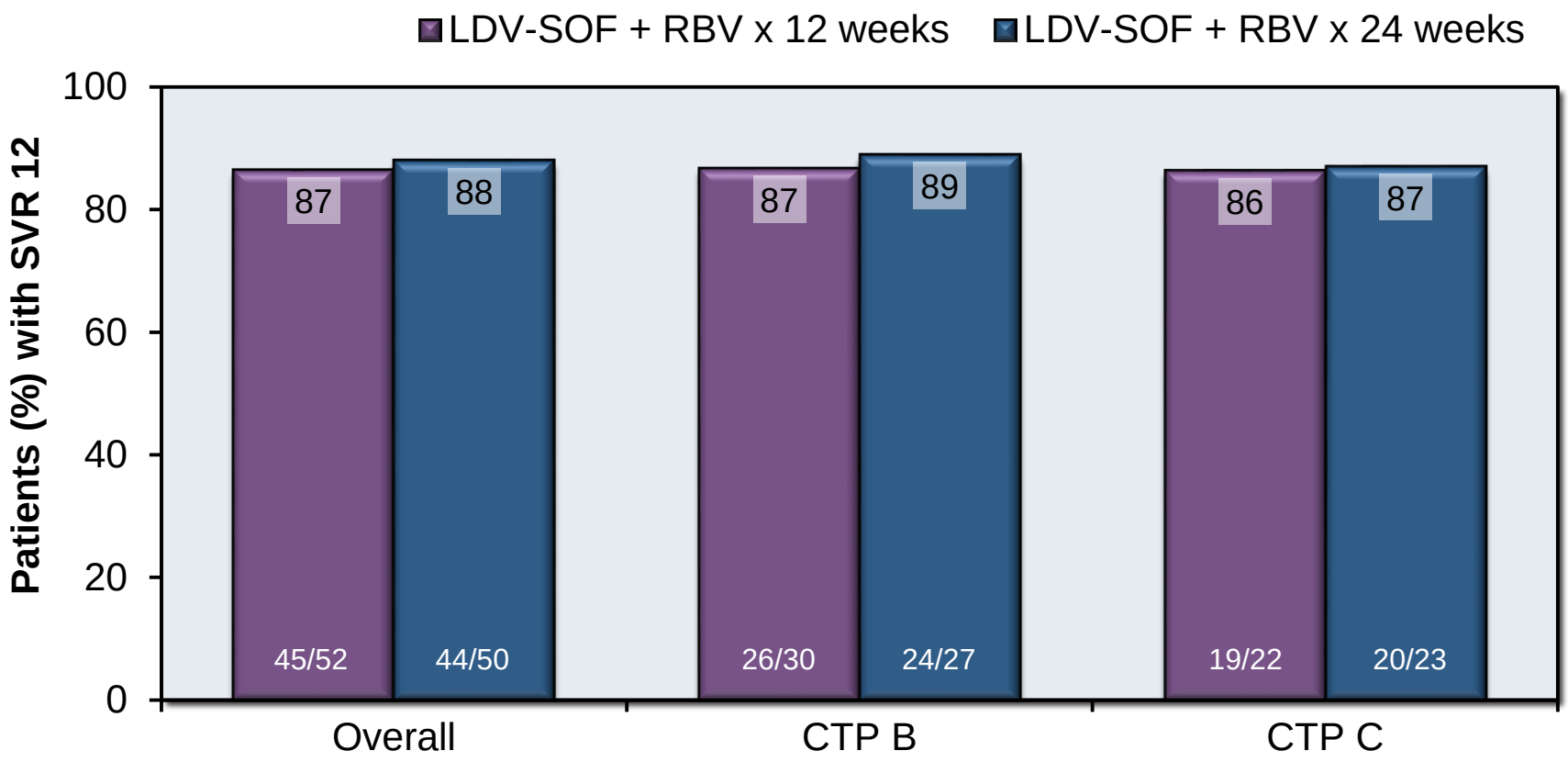
Source: Charlton M, al. Gastroenterology. 2015; [Epub ahead of print]

Ledipasvir-Sofosbuvir + Ribavirin in HCV GT 1,4
SOLAR-1 (Cohort A = Pre-transplantation): Baseline Liver Status

Baseline Characteristic	CTP B		CTP 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)
Median albumin, g/L (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 platelets, x 10^3 µL	88	73	81	71

Source: Charlton M, al. Gastroenterology. 2015; [Epub ahead of print]

Ledipasvir-Sofosbuvir + Ribavirin in HCV GT 1,4 SOLAR-1 (Cohort A= Pre-transplantation): Results

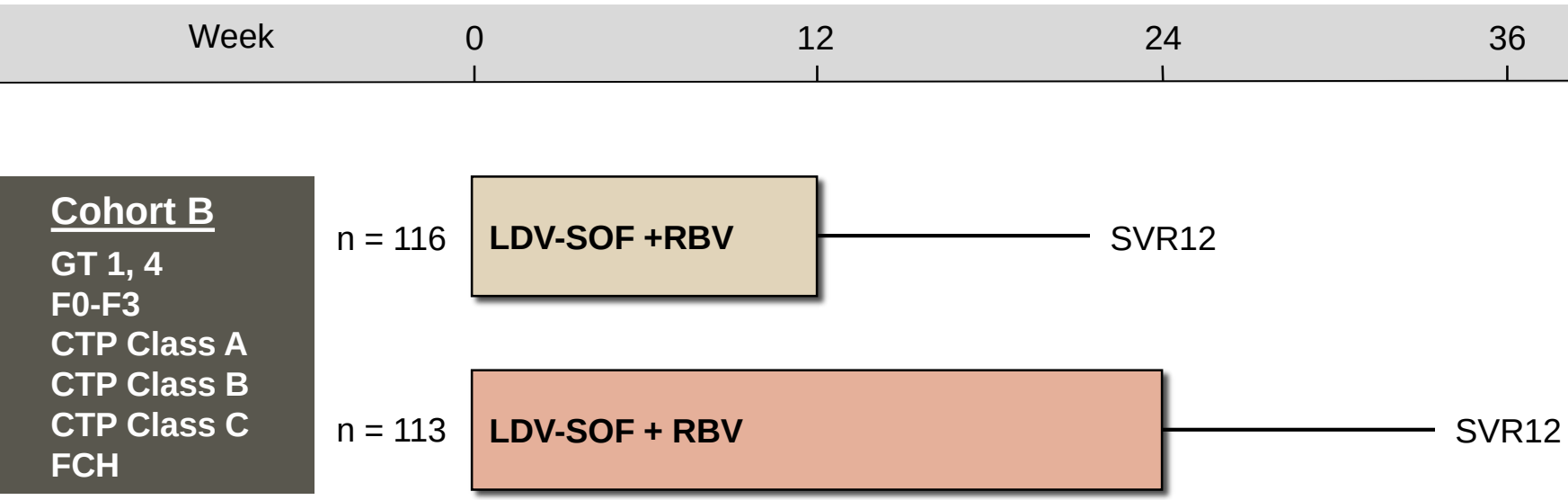


6 subjects excluded because received transplant while on study: (2 CTP B/24 week; 1 CTP 2/12 week; 3 CTP C/24 week

Source: Charlton M, al. Gastroenterology. 2015; [Epub ahead of print]

Hepatitis web study

Ledipasvir-Sofosbuvir + Ribavirin in HCV GT 1,4
SOLAR-1 (Cohort B = Post Transplant): Study Design



Abbreviations: CPT=Child-Turcotte-Pugh; FCH=fibrosing cholestatic hepatitis; LDV=ledipasvir; SOF=sofosbuvir; RBV=ribavirin

Drug Dosing

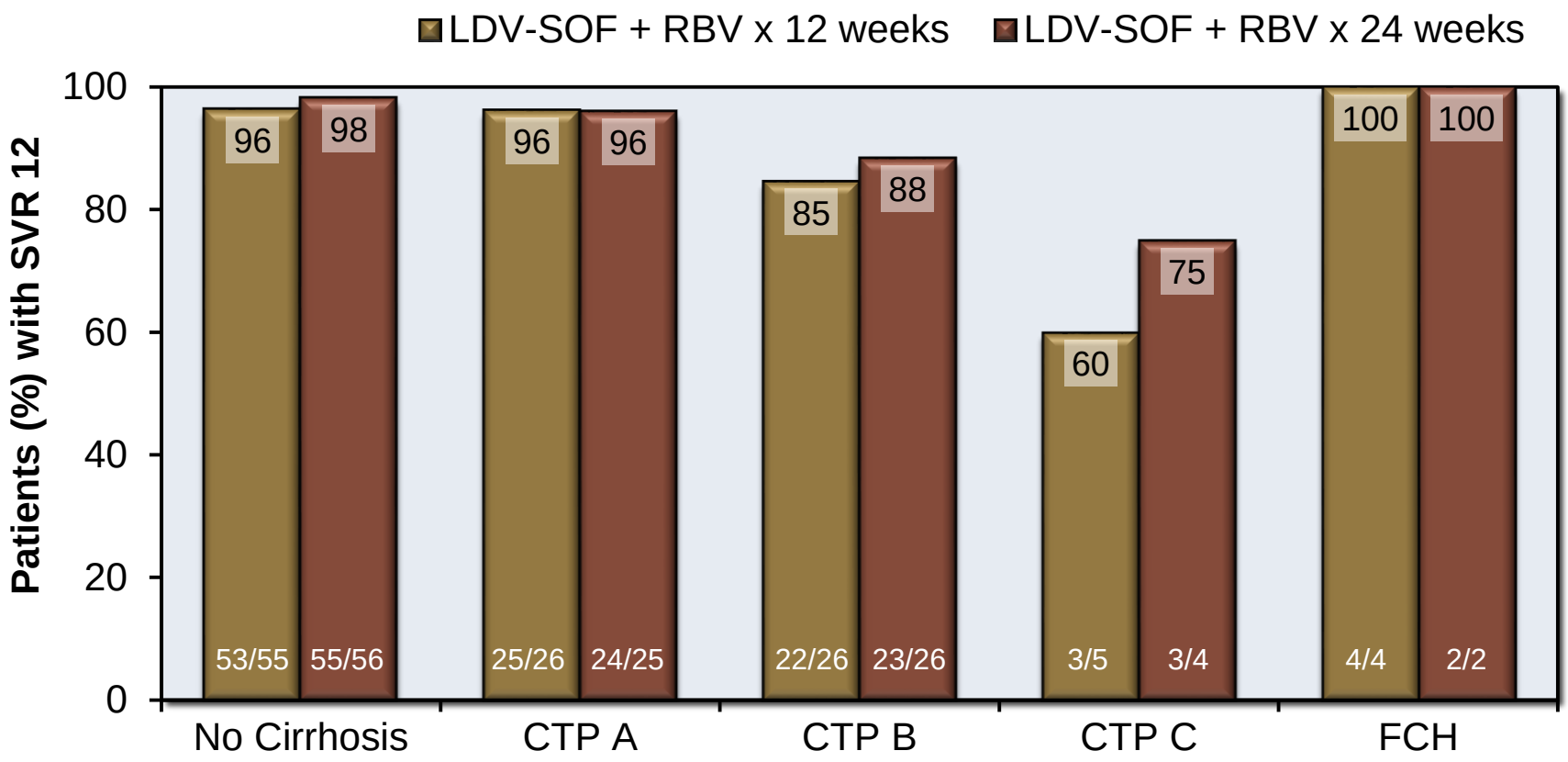
Ledipasvir-sofosbuvir (90/400 mg): fixed dose combination; one pill once daily

Ribavirin Dosing

- No cirrhosis; FCH: weight-based and divided bid (1000 mg/day if < 75 kg or 1200 mg/day if ≥ 75 kg)
- CTP B, C: started at 600 mg/day and escalated up to maximum of 1200 mg/day

Source: Charlton M, al. Gastroenterology. 2015; [Epub ahead of print]

Ledipasvir-Sofosbuvir + Ribavirin in HCV GT 1,4 SOLAR-1 (Cohort B = Post-transplantation): Results



CTP = Child-Turcotte-Pugh; FCH = fibrosing cholestatic hepatitis; 8 subjects CPT B 24 weeks

Source: Charlton M, al. Gastroenterology. 2015; [Epub ahead of print]

Hepatitis web study

Ledipasvir-Sofosbuvir + RBV in Advanced Liver Disease SOLAR-1 (Cohorts A and B): Conclusion

Conclusions: “The combination of ledipasvir, sofosbuvir, and ribavirin for 12 weeks produced high rates of SVR12 in patients with advanced liver disease, including those with decompensated cirrhosis before and after liver transplantation.”

Source: Charlton M, al. Gastroenterology. 2015; [Epub ahead of print]

This slide deck is from the University of Washington's *Hepatitis C Online* and *Hepatitis Web Study* projects.

Hepatitis C Online

www.hepatitisc.uw.edu

Hepatitis Web Study

http://depts.washington.edu/hepstudy/

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Hepatitis web study