

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; 149:649-59.

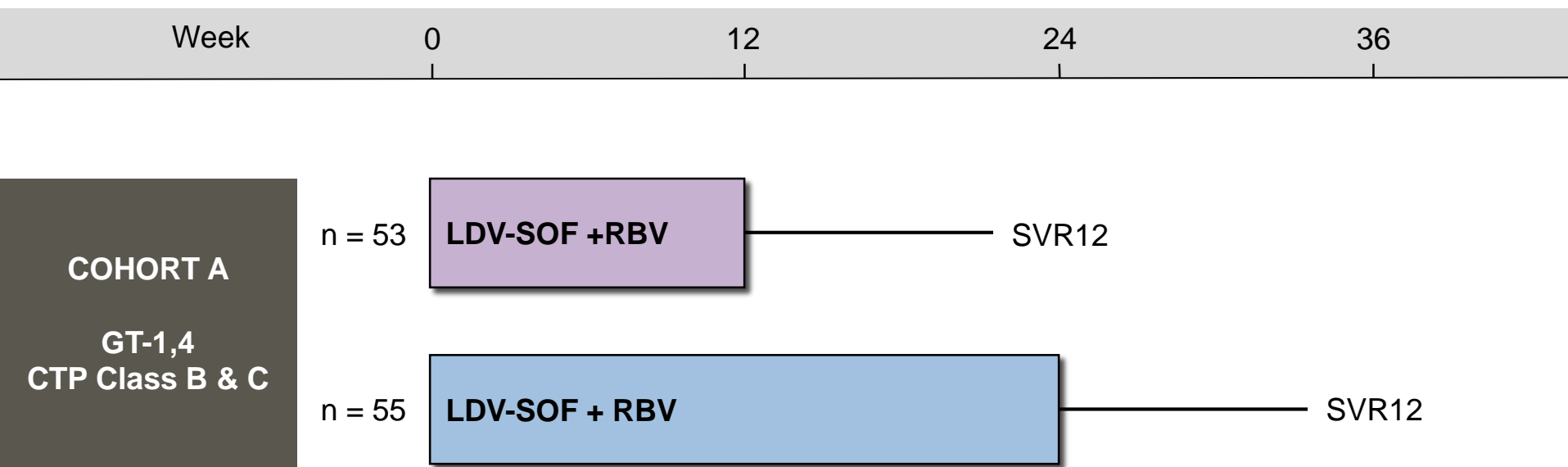
Ledipasvir-Sofosbuvir + Ribavirin in Advanced Liver Disease

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 GT 1 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 \leq 10 mg/dL; Creatinine clearance \geq 40 mL/min
 - Hemoglobin \geq 10 g/dL; Platelet count $>$ 30,000/mm³
 - Exclusion: hepatitis B or HIV coinfection or prior receipt of NS5a inhibitor
- **Primary End-Point:** SVR12

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

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

Cohort A 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, n (%)	22 (73)	18 (62)	14 (61)	18 (69)
White, n (%)	29 (97)	26 (90)	21 (91)	24 (92)
HCV RNA, log ₁₀ IU/mL	5.9	5.8	5.6	5.8
<i>IL28B</i> 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 (66)	11 (48)	18 (69)

Abbreviations: CTP=Child-Turcotte-Pugh

Source: Charlton M, et al. *Gastroenterology*. 2015; 149:649-59.

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

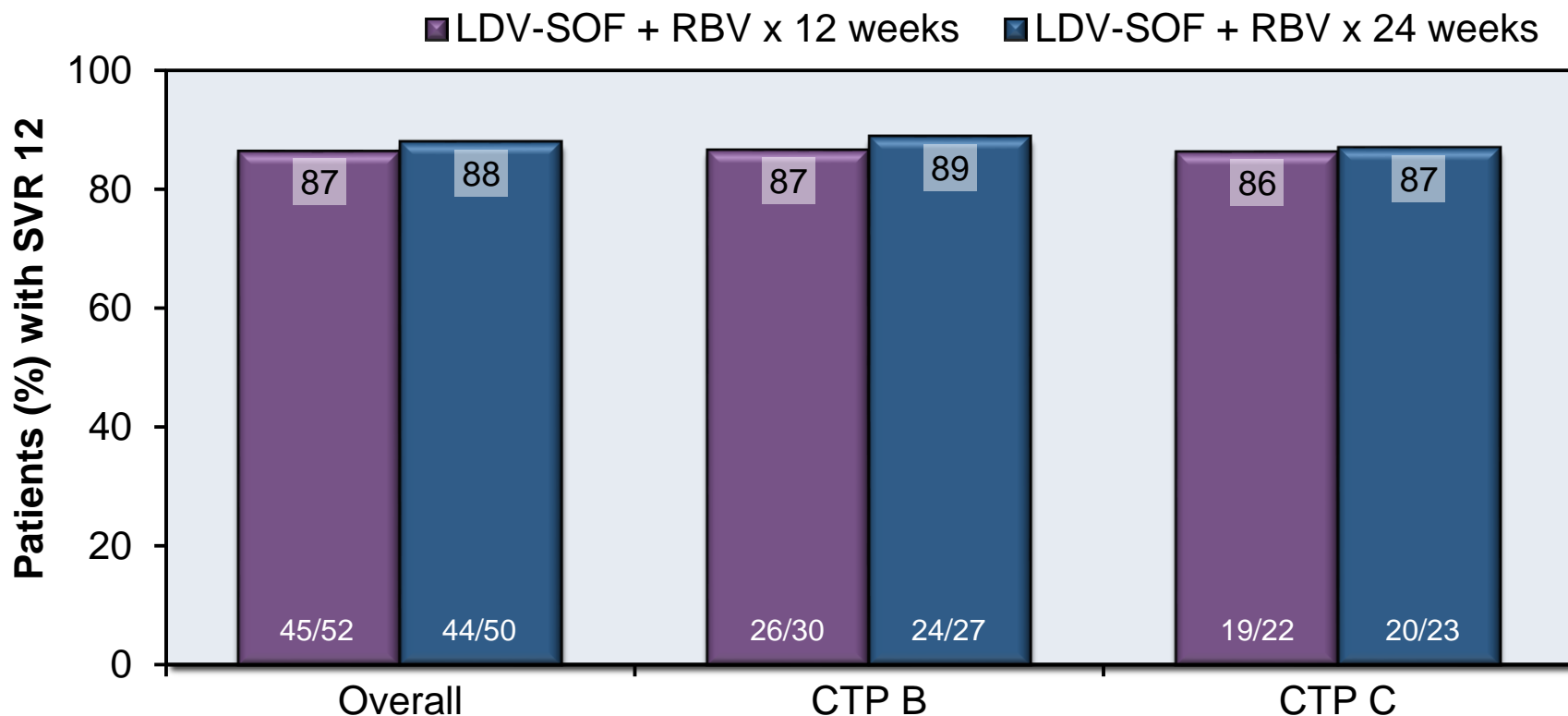
Cohort A Characteristic	CTP B		CTP C	
	12-Weeks n=30	24-Weeks n=29	12-Weeks n=23	24-Weeks n=26
Child-Turcotte-Pugh				
Class A (5-6)	0	1 (3)	0	0
Class B (7-9)	27 (90)	27 (93)	7 (30)	4 (15)
Class C (10-12)	3 (10)	1 (3)	16 (70)	22 (85)
MELD Score, n (%)				
<10	6 (20)	8 (28)	0	0
10-15	21 (70)	16 (55)	16 (70)	13 (50)
16-20	3 (10)	5 (17)	7 (30)	12 (46)
21-25	0	0	0	1 (4)
Median eGFR, mL/min	98	81	77	78
Median platelets, x 10 ³ μ L	88	73	81	71

Abbreviations: CTP=Child-Turcotte-Pugh

Source: Charlton M, et al. *Gastroenterology*. 2015; 149:649-59.

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

SOLAR-1 Cohort A (Pre-Transplantation): SVR12 Results



Abbreviations: CTP=Child-Turcotte-Pugh

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

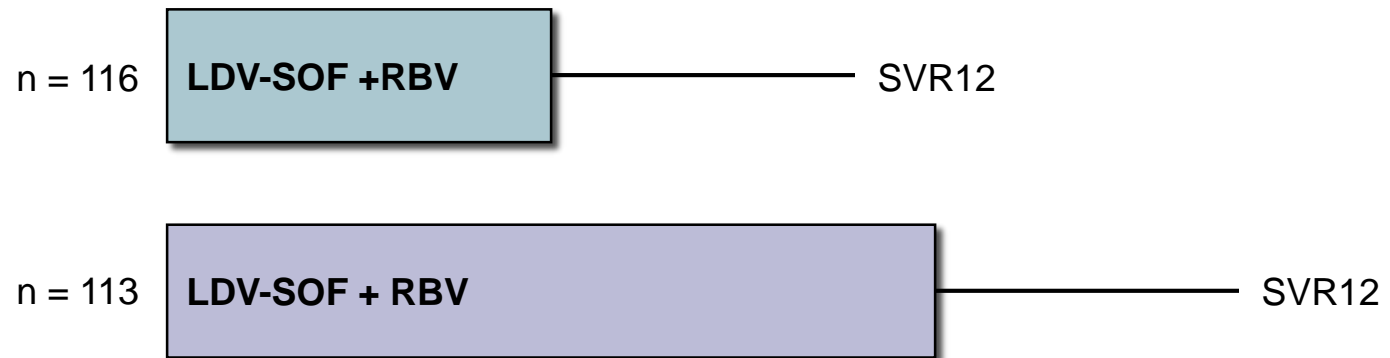
Source: Charlton M, et al. *Gastroenterology*. 2015; 149:649-59.

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

Week 0 12 24 36

Cohort B

GT 1, 4
F0-F3
CTP Class A
CTP Class B
CTP Class C
FCH



Abbreviations: CTP=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

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

Cohort B Characteristic	No Cirrhosis		CTP A		CTP B		CTP C		FCH	
	12w n=55	24w n=56	12w n=26	24w n=25	12w n=26	24w n=26	12w n=5	24w n=4	12w n=4	24w n=2
Median age, years	59	58	60	61	61	61	58	61	62	58
Male, n (%)	45 (82)	46 (82)	19 (73)	22 (88)	22 (85)	23 (88)	5 (100)	4 (100)	4 (100)	2 (100)
White, n (%)	50 (91)	49 (88)	21 (81)	20 (80)	21 (81)	24 (92)	4 (80)	4 (100)	4 (100)	2 (100)
HCV RNA, log ₁₀ IU/mL	6.5	6.4	6.2	6.7	6.3	6.2	6.4	6.3	6.5	7.1
<i>IL28B</i> GT CC, n (%)	11 (20)	10 (18)	7 (27)	1 (4)	3 (12)	5 (19)	12 (40)	1 (25)	0	0
HCV Genotype										
1a, n (%)	40 (73)	40 (71)	17 (65)	17 (68)	20 (77)	18 (69)	4 (80)	3 (75)	3 (75)	2 (100)
1b, n (%)	14 (25)	16 (29)	9 (35)	8 (32)	6 (23)	7 (27)	1 (20)	1 (25)	1 (25)	0
4, n (%)	1 (2)	0	0	0	0	1 (4)	0	0	2 (9)	0
Prior Treatment	39 (71)	48 (86)	22 (85)	24 (96)	22 (85)	22 (85)	4 (80)	4 (100)	4 (100)	1 (50)

Abbreviations: CTP=Child-Turcotte-Pugh

Source: Charlton M, et al. *Gastroenterology*. 2015; 149:649-59.

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

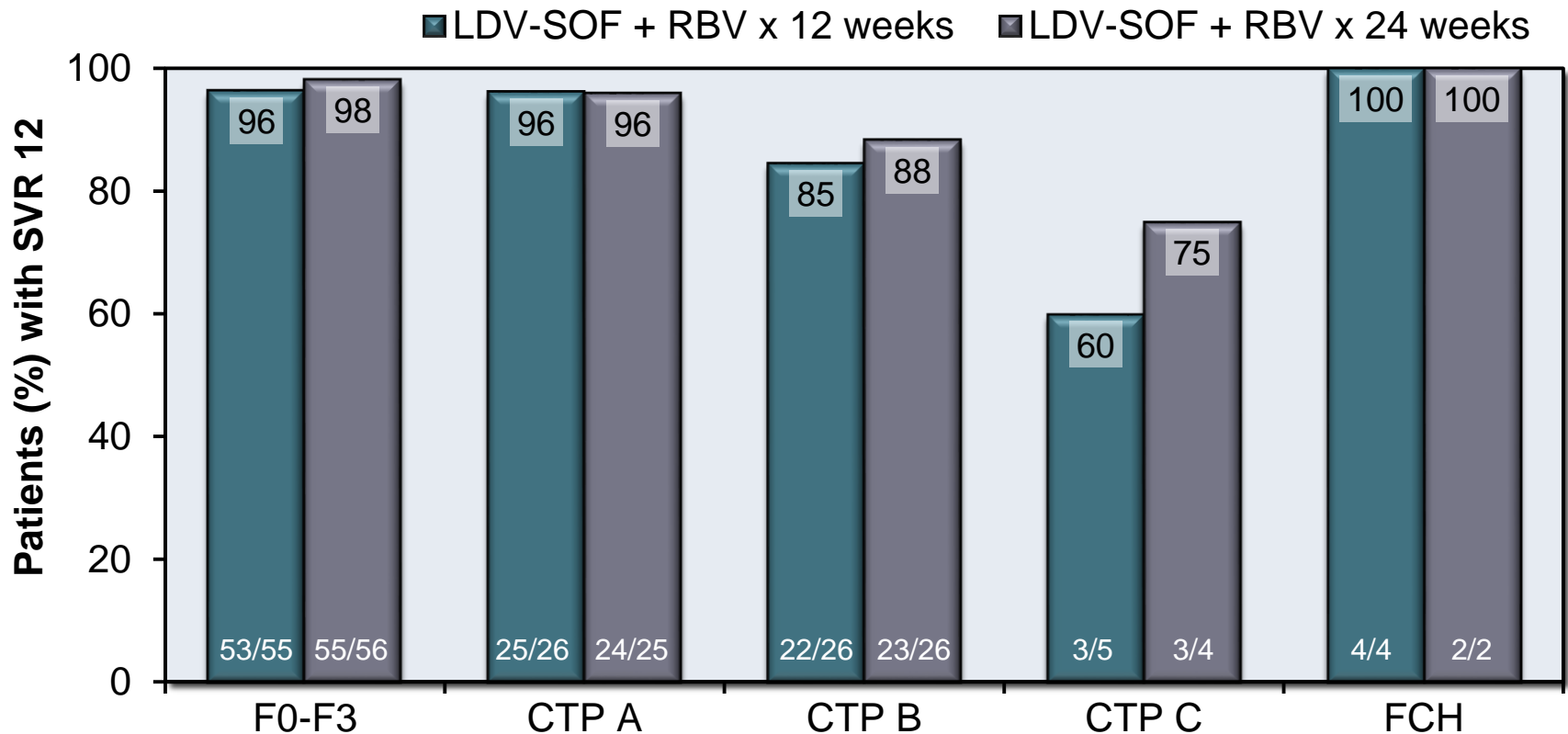
Cohort B Characteristic	F0-F3		CTP A		CTP B		CTP C		FCH	
	12w n=55	24w n=56	12w n=26	24w n=25	12w n=26	24w n=26	12w n=5	24w n=4	12w n=4	24w n=2
Median yrs post transplant	2.9	2.8	8.8	6.6	5.1	6.3	5.2	5.7	1.1	0.3
Child-Turcotte-Pugh										
Class A (5-6)	-	-	25 (96)	22 (88)	0	2 (8)	0	0	-	-
Class B (7-9)	-	-	1 (4)	3 (12)	24 (92)	24 (92)	2 (40)	1 (25)	-	-
Class C (10-12)	-	-	0	0	2 (8)	0	3 (60)	3 (75)	-	-
Meld Score, n (%)										
<10	-	-	15 (58)	13 (52)	8 (31)	5 (19)	1 (20)	0	-	-
10-15	-	-	10 (38)	10 (40)	14 (54)	19 (73)	3 (60)	2 (50)	-	-
16-20	-	-	1 (4)	2 (8)	2 (8)	2 (8)	1 (20)	1 (25)	-	-
21-25	-	-	0	0	2 (8)	0	0	1 (25)	-	-
Median eGFR, mL/min	61	71	59	68	68	56	67	62	90	69
Median platelets x 10 ³ µL	143	152	106	112	93	97	106	65	45	196

Abbreviations: CTP=Child-Turcotte-Pugh

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

SOLAR-1 Cohort B (Post-Transplantation): SVR12 Results



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

Source: Charlton M, et al. *Gastroenterology*. 2015; 149:649-59.

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.”

Ledipasvir-Sofosbuvir in Prior Failure with Sofosbuvir-Based Regimen