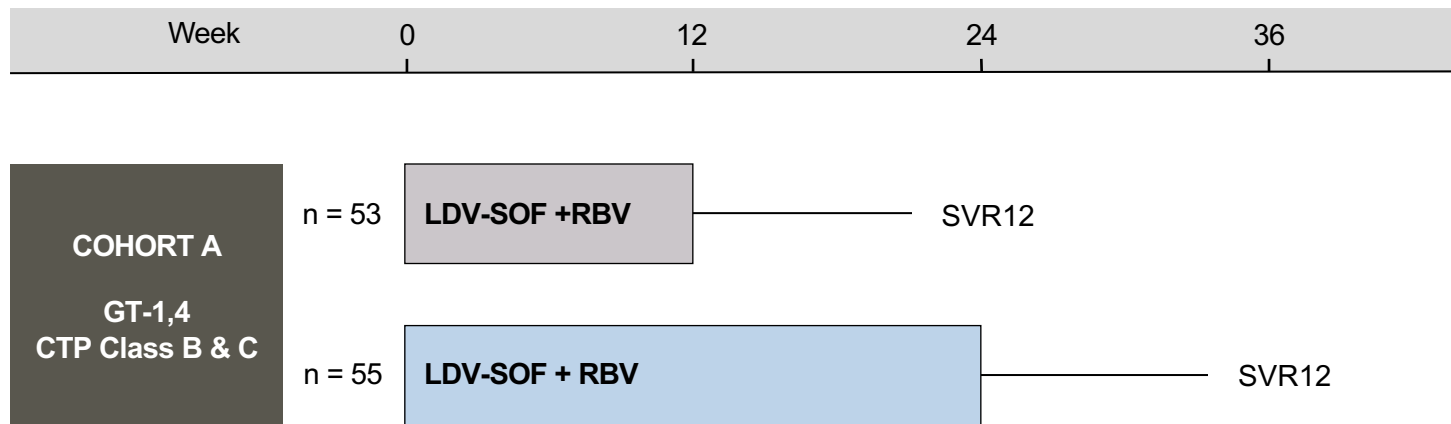


Ledipasvir-Sofosbuvir + RBV in HCV GT 1,4 and Advanced Liver Disease  
**SOLAR-1 (Cohorts A and B)**

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

- **Design:** Phase 2, open label, randomized, multicenter, prospective trial, using fixed-dose combination of ledipasvir-sofosbuvir plus ribavirin for 12 or 24 weeks in treatment-naïve and treatment-experienced participants with HCV GT 1 or 4 in United States.
- **Cohorts**
  - Cohort A = cirrhosis and moderate to severe hepatic impairment who had not undergone liver transplantation
  - Cohort B = post liver transplantation
- **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  $>30,000/\text{mm}^3$
  - 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 *or* 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 Characteristics	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)
Black, n (%)	1 (3)	3 (10)	2 (9)	1 (4)
HCV RNA, log <sub>10</sub> 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

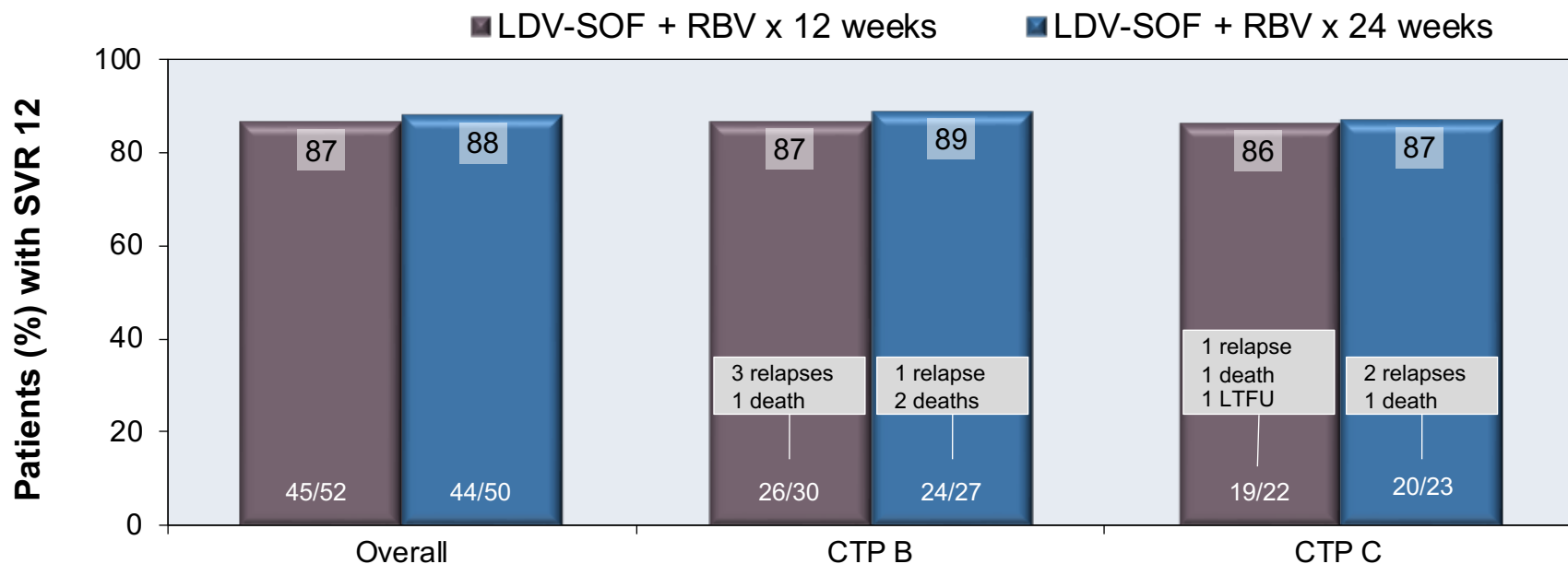
Source: Charlton M, et al. *Gastroenterology*. 2015;149:649-59.

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

Cohort A Characteristics	CTP B		CTP C	
	12 Weeks (n = 30)	24 Weeks (n = 29)	12 Weeks (n = 23)	24 Weeks (n = 26)
Child-Turcotte-Pugh Score				
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 <sup>3</sup> $\mu$ L	88	73	81	71
<b>Abbreviations:</b> CTP = Child-Turcotte-Pugh				

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

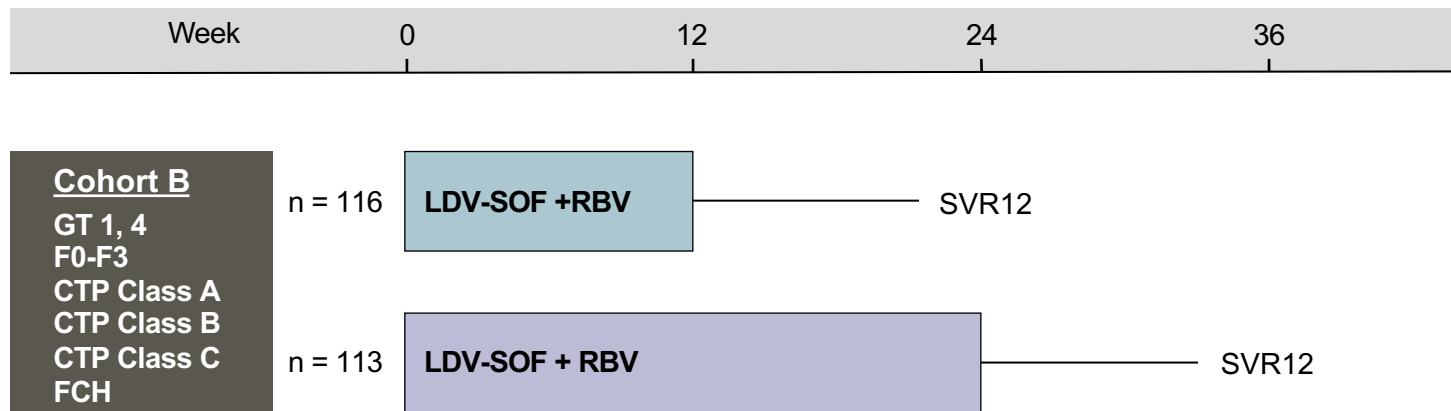
## SOLAR-1 Cohort A (Pre-Transplantation): SVR12 Results



**Abbreviations:** CTP = Child-Turcotte-Pugh; LTFU = lost to follow-up

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

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



**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 Characteristics	No Cirrhosis		CTP A		CTP B		CTP C		FCH	
	12wks (n = 55)	24wks (n = 56)	12wks (n = 26)	24wks (n = 25)	12wks (n = 26)	24wks (n = 26)	12wks (n = 5)	24wks (n = 4)	12wks (n = 4)	24wks (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 <sub>10</sub> 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

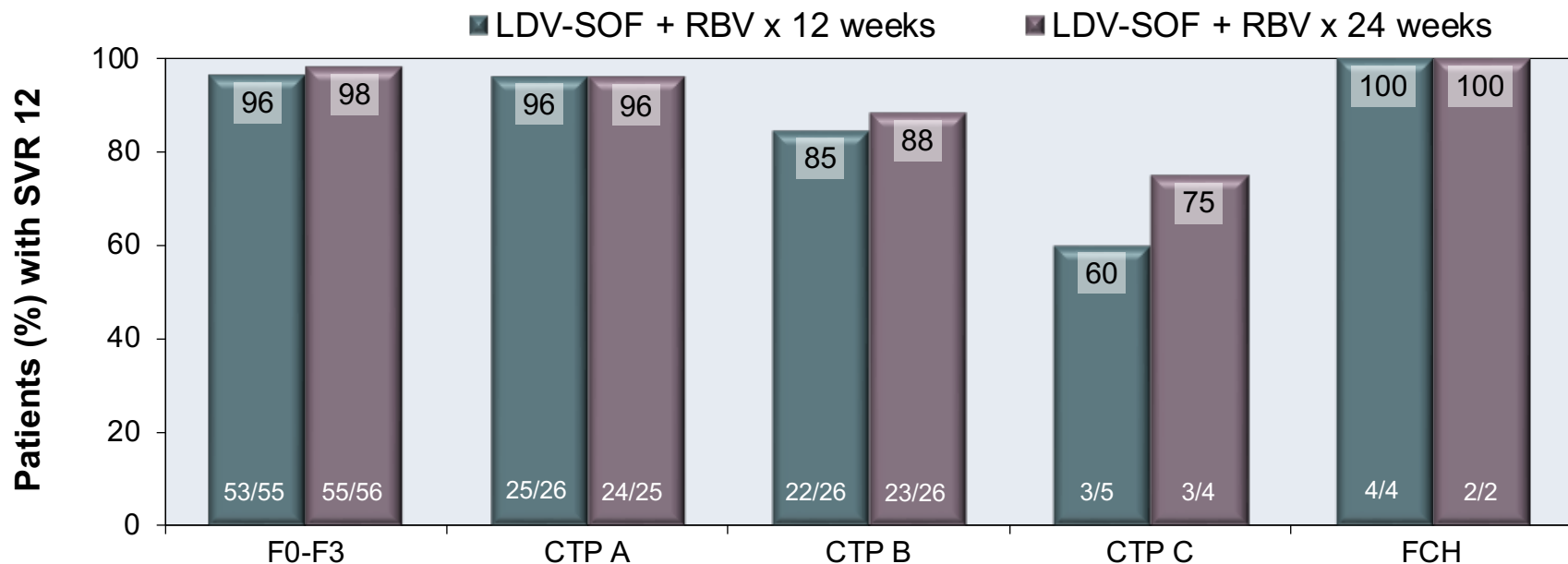


# Ledipasvir-Sofosbuvir + Ribavirin in HCV GT 1,4 SOLAR-1 (Cohort B = Post-transplantation): Baseline Characteristics

Cohort B Characteristics	F0-F3		CTP A		CTP B		CTP C		FCH	
	12wks (n = 55)	24wks (n = 56)	12wks (n = 26)	24wks (n = 25)	12wks (n = 26)	24wks (n = 26)	12wks (n = 5)	24wks (n = 4)	12wks (n = 4)	24wks (n = 2)
Median years 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 <sup>3</sup> µL	143	152	106	112	93	97	106	65	45	196
<b>Abbreviations:</b> CTP = Child-Turcotte-Pugh										

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

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



**Abbreviations:** CTP = Child-Turcotte-Pugh; FCH = fibrosing cholestatic hepatitis

# 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.”

# Acknowledgments

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