

Ledipasvir-Sofosbuvir + RBV in Decompensated Cirrhosis or Post-Liver Transplantation
SOLAR-2

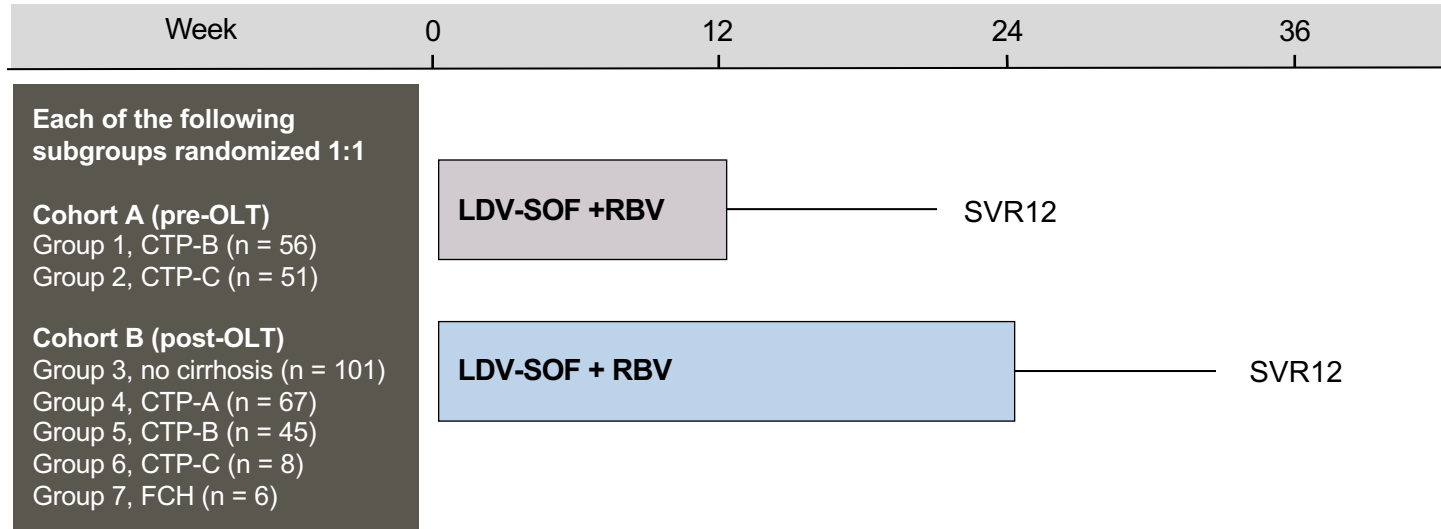
Ledipasvir-Sofosbuvir + Ribavirin in Advanced Liver Disease

SOLAR-2: Features

- **Design:** Phase 2, open label, randomized trial evaluating the fixed-dose combination of ledipasvir-sofosbuvir plus ribavirin for 12 or 24 weeks in patients with decompensated cirrhosis or after liver transplantation.
- **Cohorts**
 - Cohort A = Child-Turcotte-Pugh (CTP) class B or C cirrhosis before liver transplantation
 - Cohort B = post liver transplantation
- **Setting:** 34 sites in Europe, Canada, Australia, and New Zealand
- **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
 - Platelet count $> 30,000/\text{mm}^3$
 - Exclusion: CTP score 13-15 or prior receipt of NS5a inhibitor
- **Primary End Point:** SVR12

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SOLAR-2: Design



Abbreviations: OLT= orthotopic liver transplantation; 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: started at 600 mg/day and then escalated as tolerated up to maximum of 1200 mg/day

Ledipasvir-Sofosbuvir + Ribavirin in Advanced Liver Disease SOLAR-2 (Cohort A = Pre-transplantation): Baseline Characteristics

Cohort A Characteristics	CTP B		CTP C	
	12 Weeks (n = 28)	24 Weeks (n = 28)	12 Weeks (n = 25)	24 Weeks (n = 26)
Median age, years	57	57	58	50
Male, n (%)	23 (82)	19 (68)	15 (60)	20 (77)
White, n (%)	25 (89)	28 (100)	23 (92)	25 (96)
HCV RNA, log ₁₀ IU/mL	6.0	5.9	5.6	5.7
<i>IL28B</i> genotype CC, n (%)	6 (21)	9 (32)	7 (28)	4 (15)
HCV Genotype				
1a, n (%)	13 (46)	12 (43)	13 (52)	12 (46)
1b, n (%)	12 (43)	13 (46)	11 (44)	11 (42)
4, n (%)	3 (11)	3 (11)	1 (4)	3 (12)
Prior Treatment, n (%)	25 (89)	24 (86)	13 (52)	18 (69)

Abbreviations: CTP=Child-Turcotte-Pugh

Ledipasvir-Sofosbuvir + Ribavirin in Advanced Liver Disease SOLAR-2 (Cohort B = Post-transplantation): Baseline Characteristics

Cohort B Characteristics	No Cirrhosis		CTP A	
	12 Weeks (n = 52)	24 Weeks (n = 49)	12 Weeks (n = 34)	24 Weeks (n = 33)
Median age, years	58	60	58	62
Male, n (%)	41 (79)	39 (80)	28 (82)	26 (79)
White, n (%)	50 (96)	47 (96)	33 (97)	30 (91)
HCV RNA, log ₁₀ IU/mL	6.4	6.5	6.3	6.5
<i>IL28B</i> genotype CC, n (%)	9 (17)	10 (20)	3 (9)	7 (21)
HCV Genotype				
1a, n (%)	27 (52)	29 (59)	14 (41)	13 (39)
1b, n (%)	18 (35)	15 (31)	16 (47)	15 (45)
4, n (%)	7 (13)	5 (10)	4 (12)	5 (15)
Prior Treatment, n (%)	41 (79)	36 (73)	31 (91)	29 (88)

Abbreviations: CTP = Child-Turcotte-Pugh

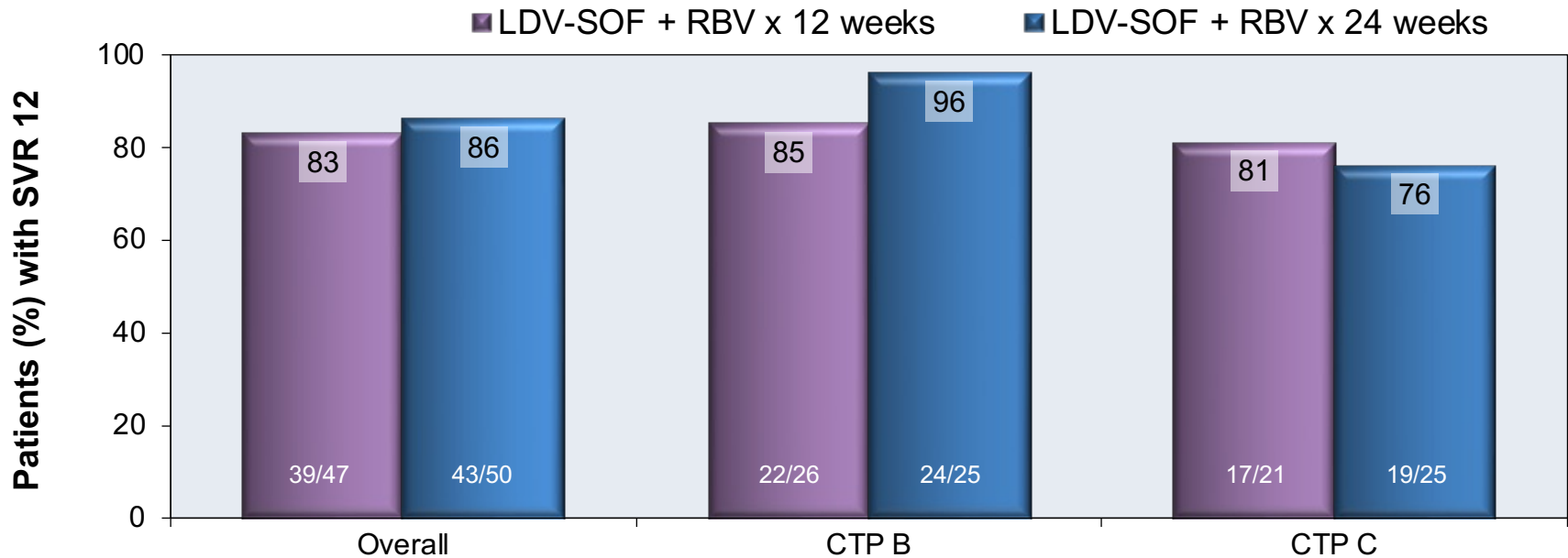
Ledipasvir-Sofosbuvir + Ribavirin in Advanced Liver Disease SOLAR-2 (Cohort B = Post-transplantation): Baseline Characteristics

Cohort B Characteristics	CTP B		CTP C		FCH	
	12 Weeks (n = 22)	24 Weeks (n = 23)	12 Weeks (n = 3)	24 Weeks (n = 5)	12 Weeks (n = 3)	24 weeks (n = 2)
Median age, years	58	60	63	62	57	56
Male, n (%)	15 (68)	15 (65)	2 (67)	5 (100)	2 (67)	1 (50)
White, n (%)	21 (95)	21 (91)	3 (100)	5 (100)	2 (67)	1 (50)
HCV RNA, log ₁₀ IU/mL	6.1	6.2	6.0	6.5	7.3	6.0
<i>IL28B</i> genotype CC, n (%)	3 (14)	5 (22)	0	3 (60)	0	1 (50)
HCV Genotype						
1a, n (%)	11 (5)	13 (57)	1 (33)	1 (20)	2 (67)	2 (100)
1b, n (%)	9 (41)	7 (30)	1 (33)	4 (80)	1 (33)	0
4, n (%)	2 (9)	3 (13)	1 (33)	0	0	0
Prior Treatment	18 (82)	19 (83)	2 (67)	5 (100)	2 (67)	2 (100)

Abbreviations: CTP=Child-Turcotte-Pugh, FCH=Fibrosing cholestatic hepatitis

Ledipasvir-Sofosbuvir + Ribavirin in Advanced Liver Disease SOLAR-2 (Cohort A= Pre-transplantation): Results

SOLAR-2 Cohort A (Pre-Transplantation): SVR12 Results

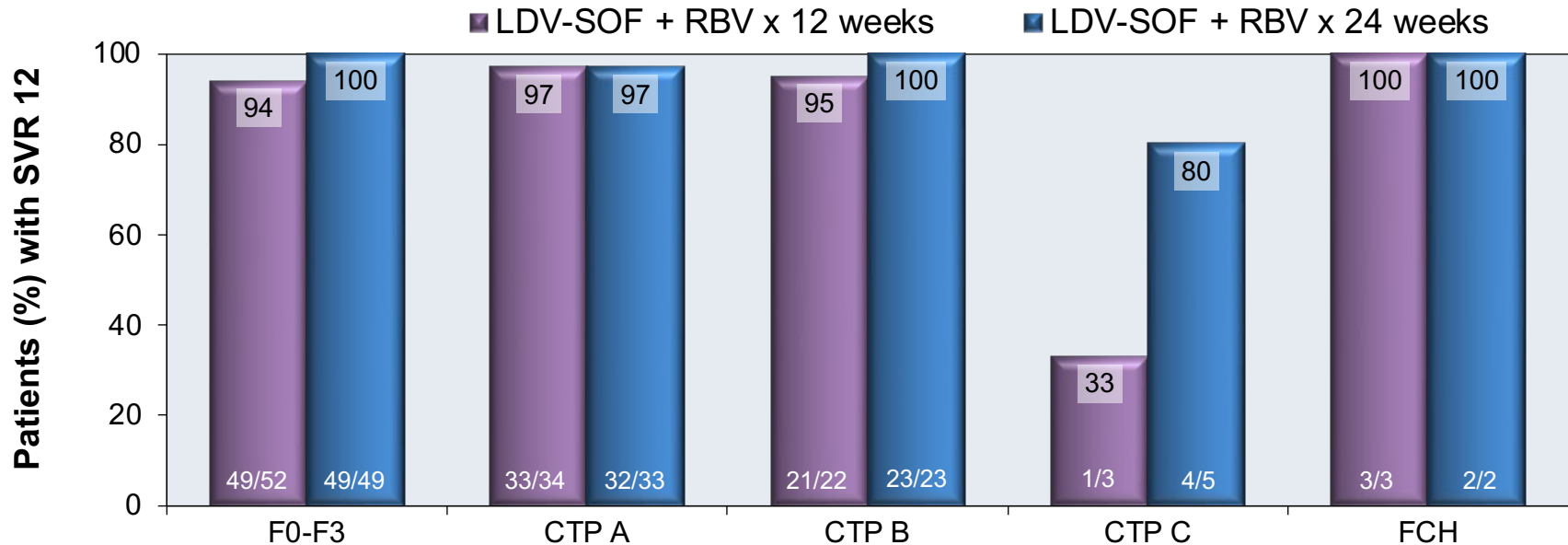


Abbreviations: CTP=Child-Turcotte-Pugh

Notes: 6 subjects excluded because received transplant before SVR12 could be assessed; SVR12 estimates reflect combination of GT1 and GT4 outcomes together, and differ from stratified SVR12 estimates presented in the published manuscript.

Ledipasvir-Sofosbuvir + Ribavirin in Advanced Liver Disease SOLAR-2 (Cohort B = Post-transplantation): Results

SOLAR-2 Cohort B (Post-Transplantation): SVR12 Results



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

Note: SVR12 estimates reflect combination of GT1 and GT4 outcomes together, and differ from stratified SVR12 estimates presented in the published manuscript.

Ledipasvir-Sofosbuvir + Ribavirin in Advanced Liver Disease SOLAR-2 (Cohort B = Post-transplantation): Conclusion

Interpretation: “Ledipasvir-sofosbuvir and ribavirin provided high rates of SVR12 for patients with advanced liver disease, including those with decompensated cirrhosis before or after liver transplantation.”

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