HEPATITIS C ONLINE

Ledipasvir-Sofosbuvir (*Harvoni*)

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Ledipasvir-Sofosbuvir (*Harvoni*)

Background and Dosing

Ledipasvir-Sofosbuvir (*Harvoni*) Indications and Usage

Genotype	Patient Populations	Regimen & Duration*
GT 1	Treatment naïve without cirrhosis or with compensated cirrhosis (Child-Pugh A)	LDV-SOF x 12 weeks*
	Treatment experienced** without cirrhosis	LDV-SOF x 12 weeks
	Treatment experienced** with compensated cirrhosis (Child-Pugh A)	LDV-SOF x 24 weeks[+]
	Treatment naïve and treatment experienced** with decompensated cirrhosis (Child-Pugh B or C)	LDV-SOF + RBV[§] x 12 weeks
GT 1, 4	Treatment naïve and treatment experienced** liver transplant recipients without cirrhosis, or with compensated cirrhosis (Child-Pugh A)	LDV-SOF + RBV[§] x 12 weeks
GT 4, 5, or 6	Treatment naïve and treatment experienced**, without cirrhosis or with compensated cirrhosis (Child-Pugh A)	LDV-SOF x 12 weeks

*LDV-SOF for 8 weeks can be considered in treatment-naïve genotype 1 patients without cirrhosis who have a pretreatment HCV RNA less than 6 million IU/mL
**Treatment-experienced adult and pediatric patients who failed a peginterferon alfa + ribavirin based regimen +/- an HCV protease inhibitor
[+]LDV-SOF for 12 weeks can be considered in treatment-experienced genotype 1 patients with cirrhosis who are eligible for ribavirin.
[§]Weight-based ribavirin dosing per package insert

Source: *Harvoni* Prescribing Information. Gilead Sciences

Ledipasvir-Sofosbuvir (*Harvoni*)

- **Approval Status**
  - Initial approval by United States FDA October 10, 2014
  - Expanded indications approved by FDA in 2015 and 2019
- **Indications and Usage**
  - Indicated for the treatment of chronic HCV genotypes 1, 4, 5, and 6
  - Indicated for the treatment of chronic HCV in patients coinfected with HIV
- **Class & Mechanism**
  - Ledipasvir: NS5A inhibitor
  - Sofosbuvir: Nucleotide analog NS5B polymerase inhibitor
- **Dosing**
  - Ledipasvir-Sofosbuvir (fixed dose 90 mg/400 mg): 1 tablet orally once daily with or without food
- **Common Adverse Effects (AE)**
  - Fatigue, headache

Source: *Harvoni* Prescribing Information. Gilead Sciences

Ledipasvir-Sofosbuvir (*Harvoni*): Indications and Usage

Genotype Patient Populations	Treatment Duration*
Genotype 1	
Treatment naïve with or without cirrhosis	12 weeks
Treatment experienced** without cirrhosis	12 weeks
Treatment experienced** with cirrhosis	24 weeks
Genotype 4, 5, or 6	
Treatment naïve with or without cirrhosis	12 weeks
Treatment experienced** with or without cirrhosis	12 weeks

*Consider treatment duration of 8 weeks in treatment-naïve patients without cirrhosis who have a pretreatment HCV RNA less than 6 million IU/mL

**Treatment-experienced patients who have failed treatment with a peginterferon alfa plus ribavirin-based regimen, with or without an HCV protease inhibitor

Source: *Harvoni* Prescribing Information. Gilead Sciences

Ledipasvir-Sofosbuvir (*Harvoni*): Adverse Effects

Adverse Effects with Ledipasvir-Sofosbuvir Reported in ≥5% of Subjects			
	Ledipasvir-Sofosbuvir		
	8 Weeks (n = 215)	12 Weeks (n = 539)	24 Weeks (n = 326)
Fatigue	16%	13%	18%
Headache	11%	14%	17%
Nausea	6%	7%	9%
Diarrhea	4%	3%	7%
Insomnia	3%	5%	6%

Source: *Harvoni* Prescribing Information. Gilead Sciences

Ledipasvir-Sofosbuvir (LDV-SOF): Summary of Key Studies

- Treatment Naïve
  - ION-1: GT-1 / LDV-SOF +/- RBV x 12 or 24 weeks
  - ION-3: GT-1 / LDV-SOF +/- RBV x 8 weeks vs LDV/SOF x 12 weeks
- Treatment Experienced
  - ION-2: GT-1 / LDV-SOF +/- RBV x 12 or 24 weeks
  - SIRIUS: GT-1 / LDV-SOF + RBV x 12 weeks or LSV-SOF x 24 weeks
- HIV Coinfection
  - ION-4: GT 1 or 4 / LDV-SOF x 12 weeks +/- HIV antiretrovirals
- Advanced Liver Disease: Pre and Post Transplant
  - SOLAR-1: GT 1,4 / LDV-SOF + RBV x 12 or 24 weeks
  - SOLAR-2: GT 1,4 / LDV-SOF + RBV x 12 or 24 weeks

Abbreviations: TN = treatment-naïve; GT = genotype; TE = treatment experienced; RBV = ribavirin

Ledipasvir-Sofosbuvir in Treatment-Naïve Patients

Ledipasvir-Sofosbuvir +/- Ribavirin in HCV Genotype 1

ION-1

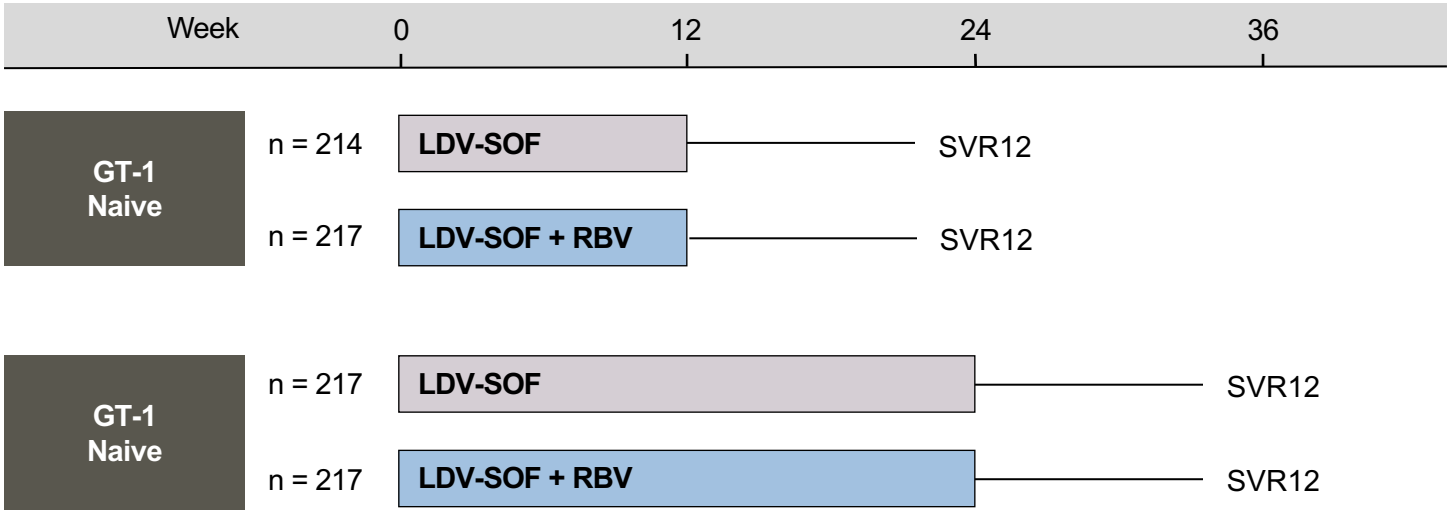
Source: Afdhal N, et al. N Engl J Med. 2014;370:1889-98.

Ledipasvir-Sofosbuvir +/- Ribavirin in Treatment-Naïve HCV GT 1
ION-1 Study: Features

- **Design**: Open-label, randomized, phase 3 trial using fixed-dose combination of ledipasvir-sofosbuvir +/- ribavirin for 12 or 24 weeks in treatment-naïve patients with GT1 HCV
- **Setting**: 99 sites in United States and Europe
- **Entry Criteria**
  - Chronic HCV genotype 1 (n = 865)
  - 18 years or older
  - No prior HCV treatment
  - Patients with compensated cirrhosis accepted (up to 20% of patients)
- **Primary End Point**: SVR12

Source: Afdhal N, et al. N Engl J Med. 2014;370:1889-98.

Ledipasvir-Sofosbuvir +/- Ribavirin in Treatment-Naïve HCV GT 1 ION-1 Study: Study Design



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

Drug Dosing: Ledipasvir-sofosbuvir (90/400 mg): fixed dose combination; one pill once daily *or* Ribavirin (weight-based and divided bid): 1000 mg/day if < 75 kg or 1200 mg/day if ≥ 75 kg

Source: Afdhal N, et al. N Engl J Med. 2014;370:1889-98.

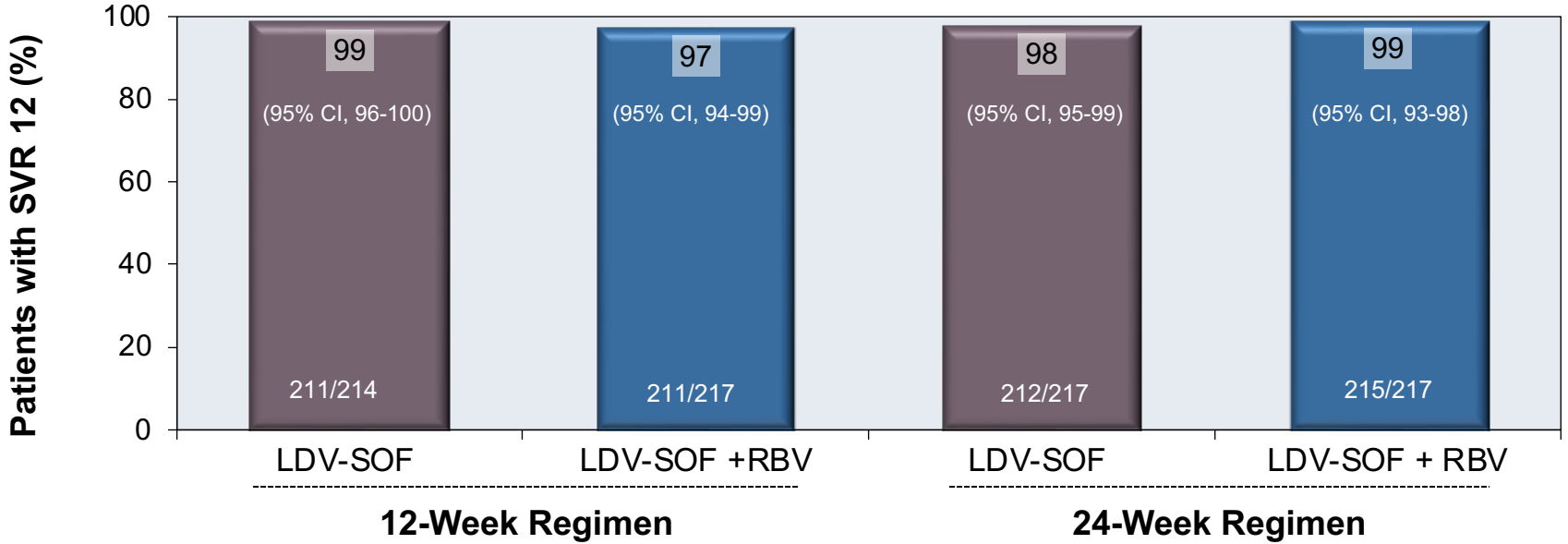
Ledipasvir-Sofosbuvir +/- Ribavirin in Treatment-Naïve HCV GT 1 ION-1 Study: Baseline Characteristics

Baseline Characteristic	12-Week Treatment		24-Week Treatment	
	LDV-SOF (n = 214)	LDV-SOF + RBV (n = 217)	LDV-SOF (n = 217)	LDV-SOF + RBV (n = 217)
Mean age, y (range)	52 (18–75)	52 (18–78)	53 (22–80)	53 (24–77)
BMI, kg/m^2 mean (range)	27 (18–41)	27 (18–42)	27 (18–48)	26 (18–48)
Male sex, n (%)	127 (59)	128 (59)	139 (64)	119 (55)
Race				
White, n (%)	187 (87)	188 (87)	177 (82)	183 (84)
Black, n (%)	24 (11)	26 (12)	32 (15)	26 (12)
Hispanic ethnic group, n (%)	26 (12)	20 (9)	29 (13)	26 (12)
HCV Genotype				
1a, n (%)	144 (67)	148 (68)	146 (67)	143 (66)
1b, n (%)	66 (31)	68 (31)	68 (31)	71 (33)
IL28B non CC, n (%)	175 (76)	141 (65)	165 (76)	144 (66)
Cirrhosis, n (%)	34 (16)	33 (15)	33 (15)	36 (17)
HCV RNA, $\log_{10}$ IU/mL (mean)	6.4	6.4	6.3	6.3

Source: Afdhal N, et al. N Engl J Med. 2014;370:1889-98.

Ledipasvir-Sofosbuvir +/- Ribavirin in Treatment-Naïve HCV GT 1 ION-1 Study: Results

ION-1: SVR 12* by Treatment Duration and Regimen

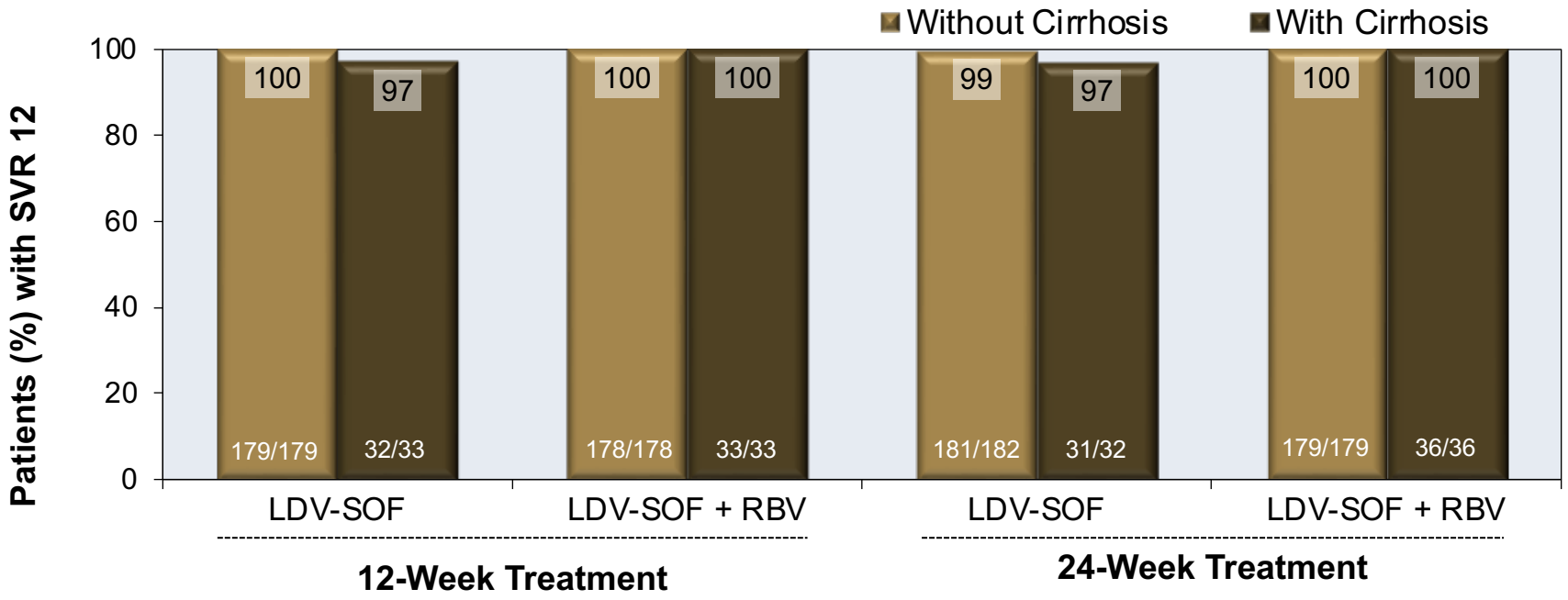


Abbreviations: LDV-SOF=Ledipasvir-sofosbuvir; RBV=ribavirin
* Primary end-point by intention-to-treat analysis

Source: Afdhal N, et al. N Engl J Med. 2014;370:1889-98.

Ledipasvir-Sofosbuvir +/- Ribavirin in Treatment-Naïve HCV GT 1
ION-1 Study: Results

ION-1: SVR12 by Treatment Regimen and Liver Disease

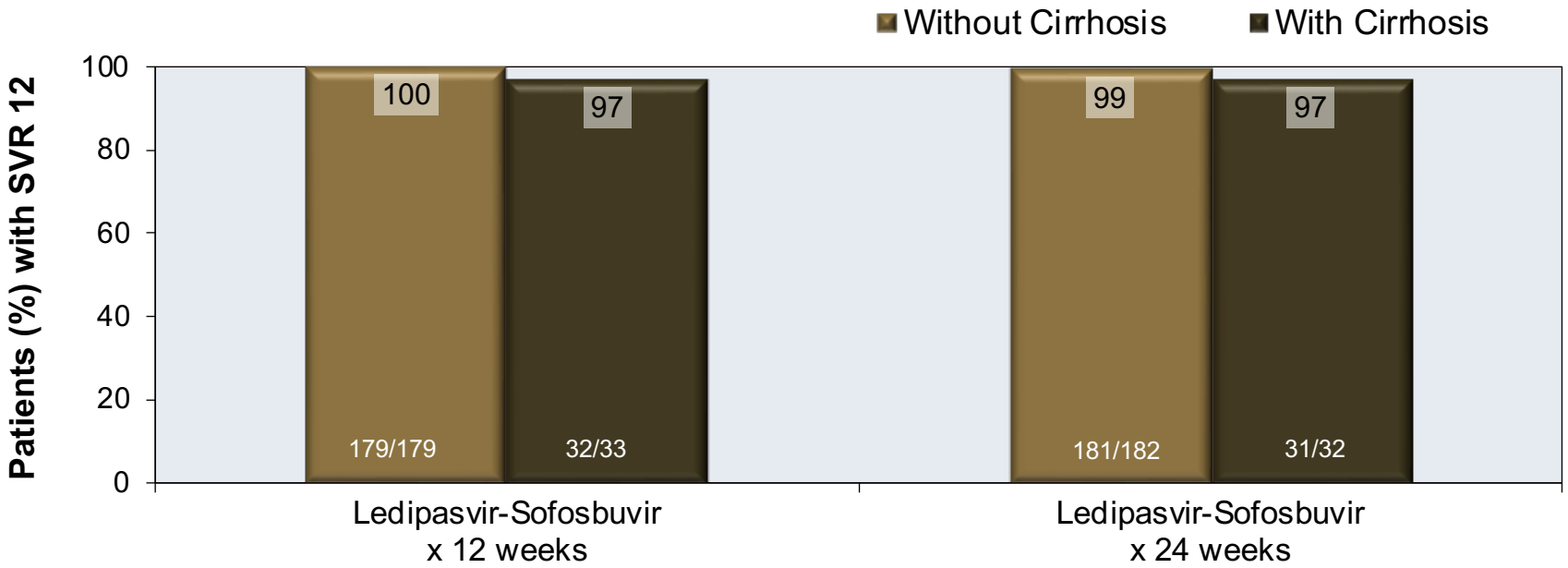


Note: subgroup results do not include patients who withdrew consent or were lost to follow-up

Source: Afdhal N, et al. N Engl J Med. 2014;370:1889-98.

Ledipasvir-Sofosbuvir +/- Ribavirin in Treatment-Naïve HCV GT 1
ION-1 Study: Results for Ledipasvir-Sofosbuvir

ION-1: SVR12 by Treatment Duration and Liver Disease



Source: Afdhal N, et al. N Engl J Med. 2014;370:1889-98.

Ledipasvir-Sofosbuvir +/- Ribavirin in Treatment-Naïve HCV GT 1 ION-1 Study: Resistance Data

- **NS5A resistant variants**
  - Baseline resistance in 140 (16%) of 861 patients tested
  - SVR12 in 135 (96%) of 140 patients with NS5A resistance
  - 2 of the 3 patients with virologic failure had baseline NS5A resistance

Source: Afdhal N, et al. N Engl J Med. 2014;370:1889-98.

Ledipasvir-Sofosbuvir +/- Ribavirin in Treatment-Naïve HCV GT 1
ION-1 Study: Conclusions

Conclusions: “Once-daily ledipasvir–sofosbuvir with or without ribavirin for 12 or 24 weeks was highly effective in previously untreated patients with HCV genotype 1 infection.”

Source: Afdhal N, et al. N Engl J Med. 2014;370:1889-98.

Ledipasvir-Sofosbuvir for 8 or 12 weeks in HCV GT1
ION-3

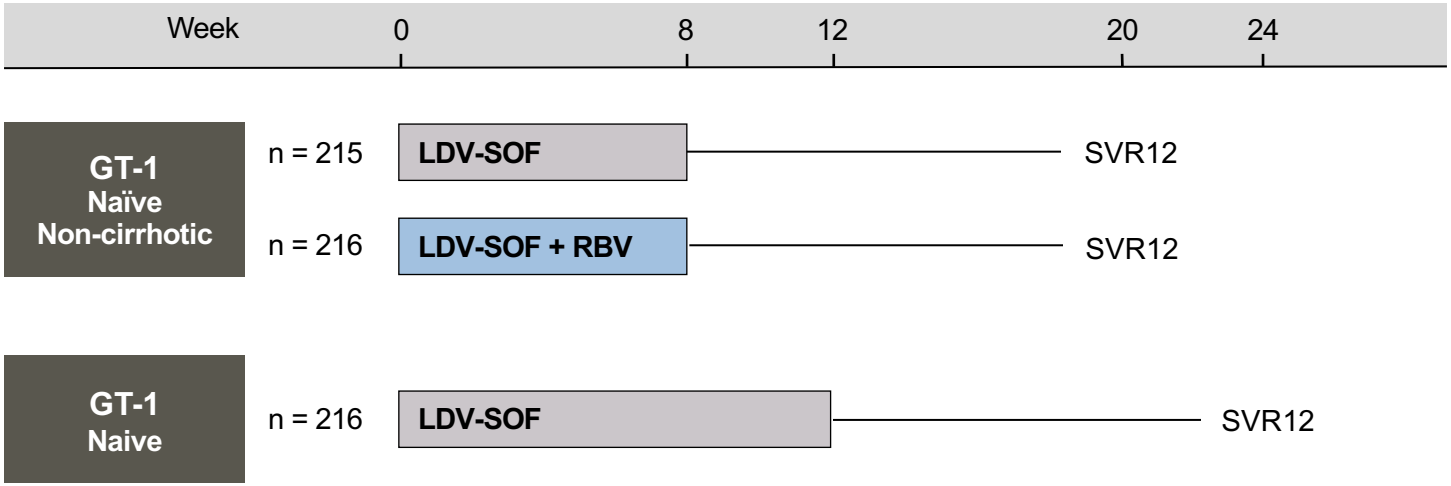
Source: Kowdley K, et al. N Engl J Med. 2014;370:1879-88.

Ledipasvir-Sofosbuvir for 8 or 12 Weeks in Treatment-Naïve HCV GT 1 ION-3 Study: Features

- **Design**: Open-label, randomized, phase 3 trial comparing ledipasvir-sofosbuvir with or without ribavirin for 8 weeks and ledipasvir-sofosbuvir for 12 weeks in treatment-naïve, noncirrhotic patients with GT1 HCV
- **Setting**: 58 sites in United States
- **Entry Criteria**
  - Chronic HCV Genotype 1 (n = 647)
  - 18 years or older
  - No prior HCV treatment
  - Patients with cirrhosis were excluded
  - HCV RNA ≥10,000 IU/mL
  - No limits on body mass index
- **Primary End Point**: SVR12

Source: Kowdley, K, et al. N Engl J Med. 2014;370:1879-88.

Ledipasvir-Sofosbuvir for 8 or 12 Weeks in Treatment-Naïve HCV GT 1 ION-3 Study: Study Design



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

Drug Dosing:
Ledipasvir-sofosbuvir (90/400 mg): fixed dose combination; one pill once daily
Ribavirin (weight-based and divided bid): 1000 mg/day if <75 kg or 1200 mg/day if ≥75 kg

Source: Kowdley, K, et al. N Engl J Med. 2014;370:1879-88.

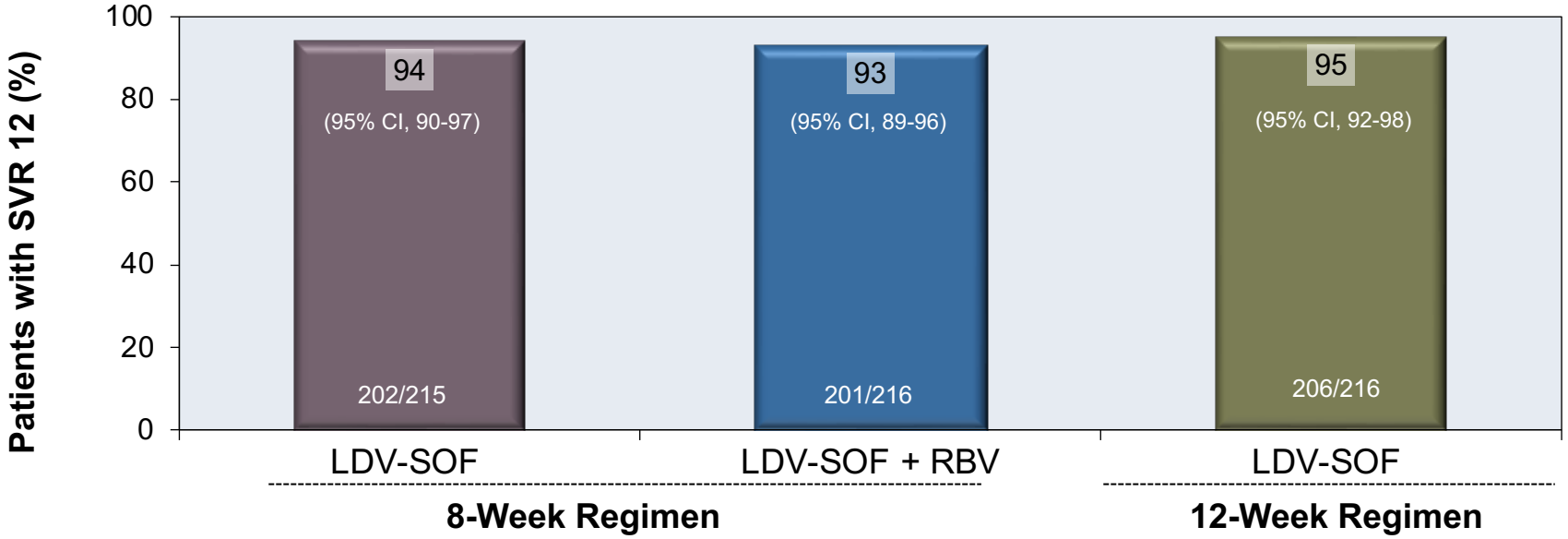
Ledipasvir-Sofosbuvir for 8 or 12 Weeks in Treatment-Naïve HCV GT 1 ION-3 Study: Baseline Characteristics

Baseline Characteristics	8-Week Treatment		12-Week Treatment
	LDV-SOF (n = 215)	LDV-SOF + RBV (n = 216)	LDV-SOF (n = 216)
Mean age, y (range)	53 (22–75)	51 (21–71)	53 (20–71)
BMI, kg/m^2 mean (range)	28 (18–43)	28 (18–56)	28 (19–45)
Male sex, n (%)	130 (60)	117 (54)	128 (59)
Race			
White, n (%)	164 (76)	176 (81)	177 (82)
Black, n (%)	45 (21)	36 (17)	42 (19)
Other, n (%)	6 (3)	4 (2)	7 (3)
HCV Genotype			
1a, n (%)	171 (80)	172(68)	172 (80)
1b, n (%)	43 (20)	44 (20)	44 (20)
IL28B non CC, n (%)	159 (74)	156 (72)	160 (74)
F3 fibrosis, n (%)	29 (13)	28 (13)	29 (13)
HCV RNA, $\log_{10}$ IU/mL, mean	6.5	6.4	6.4

Source: Kowdley, K, et al. N Engl J Med. 2014;370:1879-88.

Ledipasvir-Sofosbuvir for 8 or 12 Weeks in Treatment-Naïve HCV GT 1 ION-3 Study: Results

ION-3: SVR 12* by Treatment Duration and Regimen



Abbreviations: LDV-SOF=ledipasvir-sofosbuvir; RBV=ribavirin
*Primary end point by intention-to-treat analysis

Source: Kowdley, K, et al. N Engl J Med. 2014;370:1879-88.

Ledipasvir-Sofosbuvir for 8 or 12 Weeks in Treatment-Naïve HCV GT 1 ION-3 Study: Results

Response to Ledipasvir-Sofosbuvir Based on 8 or 12 Weeks of Therapy		
	8-Week Treatment (n = 215)	**12-Week Treatment** (n = 216)
Number of Responders at End of Treatment	100% (215/215)	100% (216/216)
SVR	94% (202/215)	96% (202/216)
Relapse	5% (11/215)	1% (3/216)
Relapse According to Baseline HCV RNA		
HCV RNA ≤6 million IU/mL	2% (2/123)	2% (2/131)
HCV RNA ≥6 million IU/mL	10% (9/92)	1% (1/85)

Source: *Harvoni* Prescribing Information. Gilead Sciences

Ledipasvir-Sofosbuvir for 8 or 12 Weeks in Treatment-Naïve HCV GT 1 ION-3 Study: Resistance Data

- **NS5B S282T variant (reduces susceptibility to sofosbuvir)**
  - Not observed in any patients at baseline or after treatment by deep sequencing
- **NS5A resistant variants**
  - Baseline resistance in 116 (18%) of 647 patients
  - SVR12 in 104 (90%) of 116 patients with NS5A resistance
  - Of the 23 patients with viral relapse, 15 (65%) had NS5A-resistant variants at time of relapse

Source: Kowdley, K, et al. N Engl J Med. 2014;370:1879-88.

Ledipasvir-Sofosbuvir for 8 or 12 Weeks in Treatment-Naïve HCV GT 1 ION-3 Study: Conclusions

Conclusions: “Ledipasvir-sofosbuvir for 8 weeks was associated with a high rate of sustained virologic response among previously untreated patients with HCV genotype 1 infection without cirrhosis. No additional benefit was associated with the inclusion of ribavirin in the regimen or with extension of the duration of treatment to 12 weeks.”

Source: Kowdley, K, et al. N Engl J Med. 2014;370:1879-88.

Ledipasvir-Sofosbuvir in Treatment-Experienced Patients

Ledipasvir-Sofosbuvir +/- Ribavirin in HCV Genotype 1

ION-2

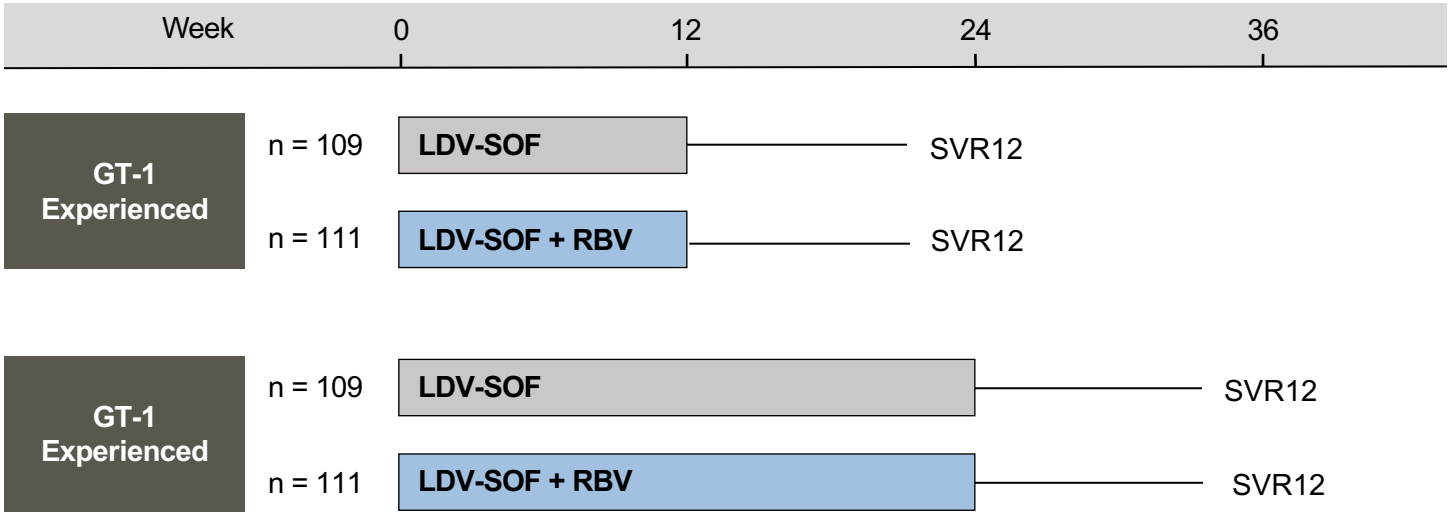
Source: Afdhal N, et al. N Engl J Med. 2014;370:1483-93.

Ledipasvir-Sofosbuvir +/- Ribavirin in Treatment-Experienced HCV GT 1 ION-2 Study: Features

- **Design**: Open-label, randomized, phase 3, using fixed-dose combination of ledipasvir-sofosbuvir with or without ribavirin for 12 or 24 weeks in treatment-experienced patients with GT1 HCV
- **Setting**: 64 sites in United States
- **Entry Criteria**
  - Chronic HCV Genotype 1 (n = 440) 18 years or older
  - Treatment experienced
  - Did not achieve SVR with prior dual therapy (peginterferon + ribavirin), or triple therapy (NS3/4A protease inhibitor plus peginterferon + ribavirin)
  - Patients with cirrhosis accepted (up to 20% of patients)
- **Primary End Point**: SVR12

Source: Afdhal N, et al. N Engl J Med. 2014;370:1483-93.

Ledipasvir-Sofosbuvir +/- Ribavirin in Treatment-Experienced HCV GT 1 ION-2 Study: Study Design



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

Drug Dosing
Ledipasvir-sofosbuvir (90/400 mg): fixed dose combination; one pill once daily
Ribavirin (weight-based and divided bid): 1000 mg/day if <75 kg or 1200 mg/day if ≥75 kg

Source: Afdhal N, et al. N Engl J Med. 2014;370:1483-93.

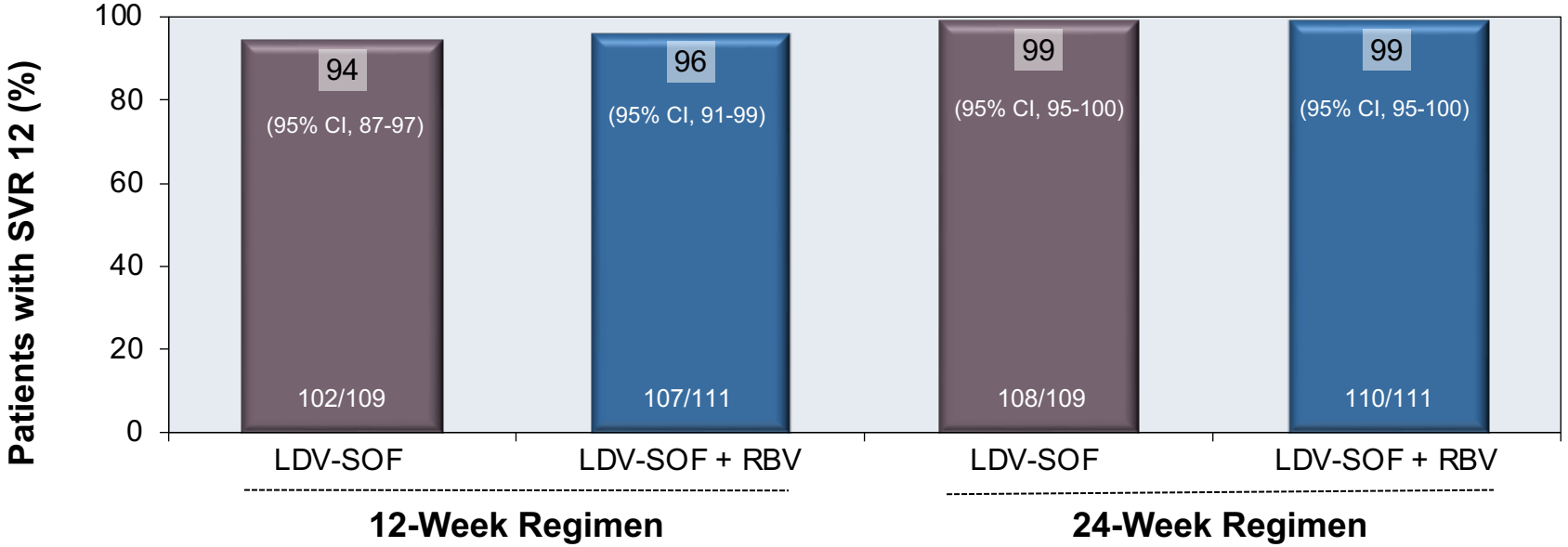
Ledipasvir-Sofosbuvir +/- Ribavirin in Treatment-Experienced HCV GT 1 ION-2 Study: Baseline Characteristics

Baseline Characteristic	12-Week Treatment		24-Week Treatment	
	LDV-SOF (n = 109)	LDV-SOF + RBV (n = 111)	LDV-SOF (n = 109)	LDV-SOF + RBV (n = 111)
Mean age, y (range)	56 (24–67)	57 (27–75)	56 (25–68)	55 (28–70)
BMI, kg/m^2 mean (range)	29 (19–47)	28 (19–45)	28 (19–41)	28 (19–50)
Male sex, n (%)	74 (68)	71 (64)	74 (68)	68 (61)
Race				
White, n (%)	84 (77)	94 (85)	91 (83)	89 (80)
Black, n (%)	24 (22)	16 (14)	17 (16)	20 (18)
HCV Genotype				
1a, n (%)	86 (79)	88 (79)	85 (78)	88 (79)
1b, n (%)	23 (21)	23 (21)	24 (22)	23 (21)
IL28B non CC, n (%)	99 (91)	100 (90)	93 (85)	93 (84)
Cirrhosis, n (%)	22 (20)	22 (20)	22 (20)	22 (20)
Prior nonresponse	49 (45)	46 (41)	49 (45)	51 (46)
HCV RNA, $\log_{10}$ IU/ml (mean)	6.5	6.4	6.4	6.5

Source: Afdhal N, et al. N Engl J Med. 2014;370:1483-93.

Ledipasvir-Sofosbuvir +/- Ribavirin in Treatment-experienced HCV GT 1 ION-2 Study: Results

ION-2: SVR 12* by Treatment Duration and Regimen

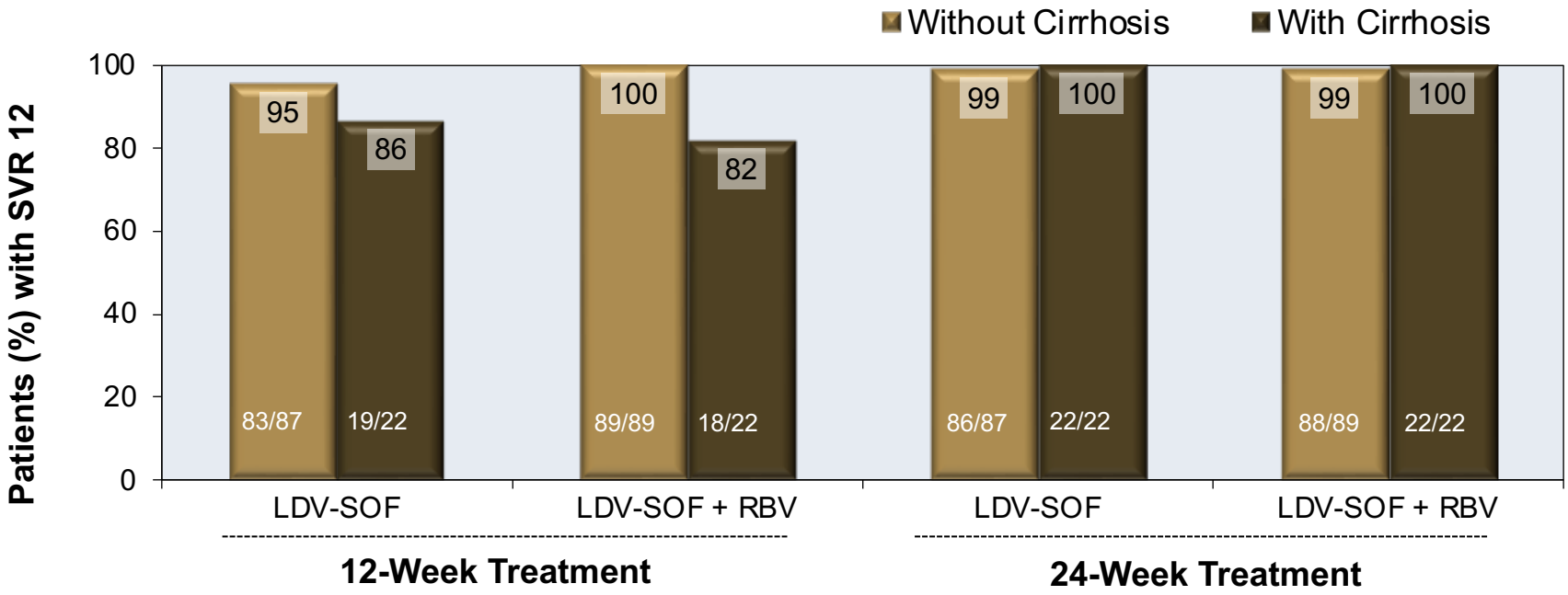


Abbreviations: LDV-SOF=ledipasvir-sofosbuvir; RBV=ribavirin
* Primary end point by intention-to-treat analysis

Source: Afdhal N, et al. N Engl J Med. 2014;370:1483-93.

Ledipasvir-Sofosbuvir +/- Ribavirin in Treatment-experienced HCV GT 1 ION-2 Study: Results

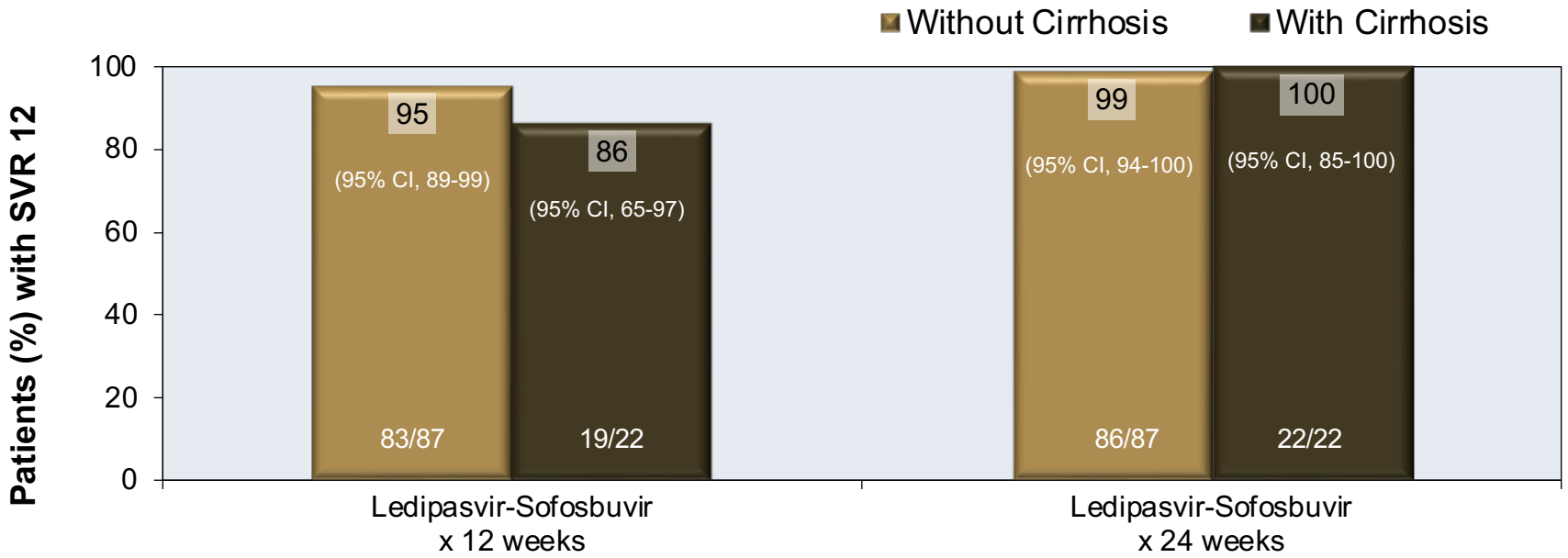
ION-2: SVR12 by Treatment Regimen and Liver Disease



Source: Afdhal N, et al. N Engl J Med. 2014;370:1483-93.

Ledipasvir-Sofosbuvir +/- Ribavirin in Treatment-experienced HCV GT 1
ION-2 Study: Results for Ledipasvir-Sofosbuvir

ION-2: SVR12 by Treatment Regimen and Liver Disease

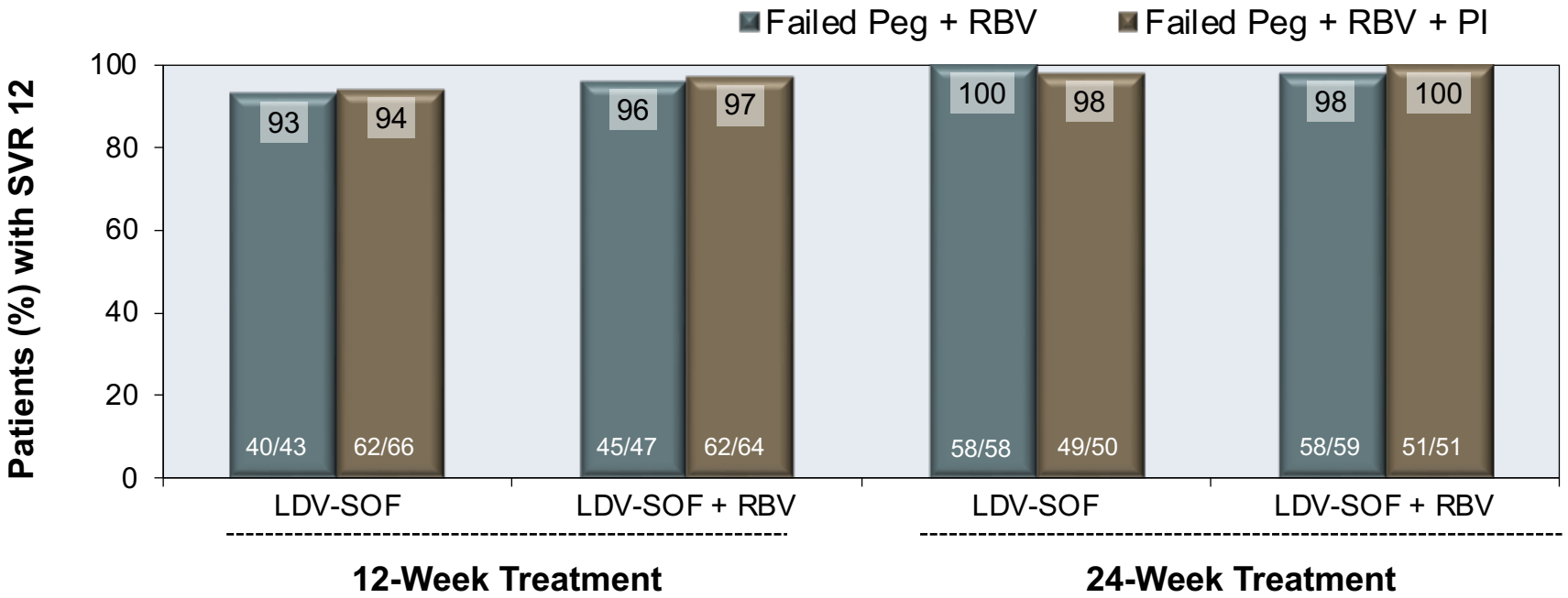


Note: subgroup results do not include patients who withdrew consent or were lost to follow-up

Source: Afdhal N, et al. N Engl J Med. 2014;370:1483-93.

Ledipasvir-Sofosbuvir +/- Ribavirin in Treatment-experienced HCV GT 1 ION-2 Study: Results

ION-2: SVR12 by Prior Treatment Regimen



Source: Afdhal N, et al. N Engl J Med. 2014;370:1483-93.

Ledipasvir-Sofosbuvir +/- Ribavirin in Treatment-experienced HCV GT 1 ION-2 Study: Resistance Data

- **NS5B S282T variant (reduces susceptibility to sofosbuvir)**
  - Not observed in any patients at baseline or after treatment
- **NS5A resistant variants**
  - Baseline resistance in 62 (14%) of 439 patients tested
  - SVR12 in 55 (89%) of 62 patients with NS5A resistance
  - All 11 patients with viral relapse had detectable NS5A resistant variants at relapse
- **NS3/4A resistant variants**
  - Baseline resistance in 163 (71%) of 228 patients tested
  - SVR12 in 159 (98%) of 163 patients with resistance

Source: Afdhal N, et al. N Engl J Med. 2014;370:1483-93.

Ledipasvir-Sofosbuvir +/- Ribavirin in Treatment-Experienced HCV GT 1 ION-2 Study: Conclusions

Conclusions: “Treatment with a once-daily, single-tablet regimen of ledipasvir and sofosbuvir resulted in high rates of sustained virologic response among patients with HCV genotype 1 infection who had not had a sustained virologic response to prior interferon-based treatment.”

Source: Afdhal N, et al. N Engl J Med. 2014;370:1483-93.

Ledipasvir-Sofosbuvir in Treatment-Experienced GT1 with Cirrhosis

SIRIUS

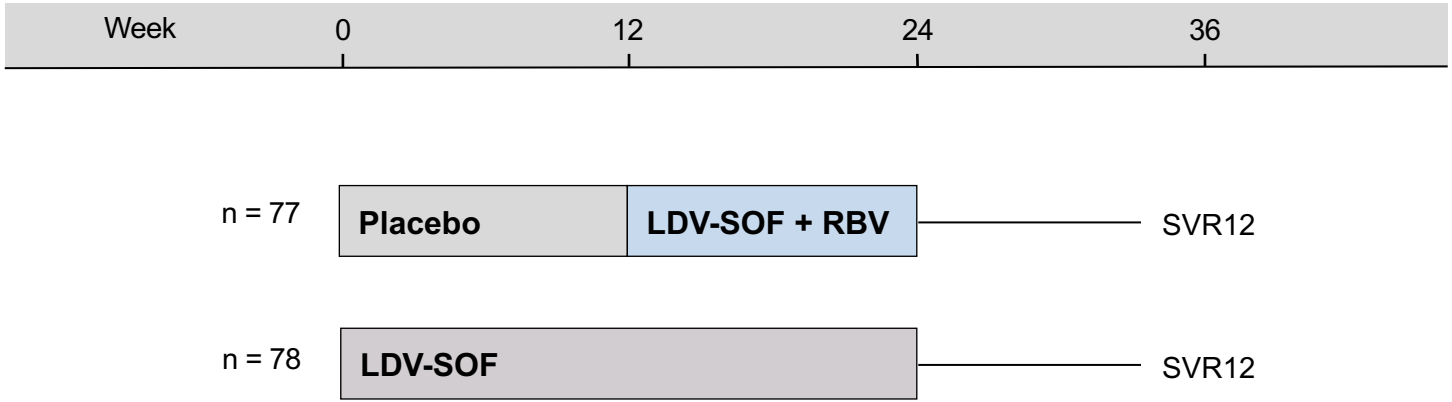
Source: Bourliere M, et al. Lancet Infect Dis. 2015;15:397-404.

Ledipasvir-Sofosbuvir in Treatment-Experienced GT1 with Cirrhosis SIRIUS Trial: Features

- **Design**: Phase 2, double-blind, randomized, trial that evaluated ledipasvir-sofosbuvir x 24 weeks or ledipasvir-sofosbuvir plus ribavirin for 12 weeks in treatment-experienced patients with GT1 HCV and compensated cirrhosis
- **Setting**: Multiple sites in France
- **Entry Criteria**
  - Chronic HCV Genotype 1 (n = 155 randomized)
  - Age 18 years or older
  - Failed prior therapy with sequential PEG + RBV and PEG + RBV + PI
  - Compensated cirrhosis by: (1) biopsy, (2) FibroScan >12.5 kPa, or (3) FibroTest (FibroSURE) >0.75 and APRI >2
  - Excluded if evidence of hepatic decompensation or HCC
- **Primary End Point**: SVR12

Source: Bourliere M, et al. Lancet Infect Dis. 2015;15:397-404.

Ledipasvir-Sofosbuvir in Treatment-Experienced GT1 with Cirrhosis
SIRIUS Trial: 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 (weight-based and divided bid): 1000 mg/day if < 75 kg or 1200 mg/day if ≥ 75 kg

Source: Bourliere M, et al. Lancet Infect Dis. 2015;15:397-404.

Ledipasvir-Sofosbuvir in Treatment-Experienced GT1 with Cirrhosis SIRIUS Trial: Baseline Characteristics

	LDV-SOF + RBV 12 wks (n = 77)	LDV-SOF x 24 wks (n = 78)
Age (years)	56	57
BMI, kg/m^2 mean	27.9	26.3
Male sex, n (%)	58 (75)	56 (72)
White Race, n (%)	76 (99)	75 (96)
IL28B CC, n (%)	4 (5)	6 (8)
HCV RNA (log_{10} IU/mL)	6.5	6.5
Mean MELD (range)	7 (6-16)	7 (6-12)
Varices, n (%)	16 (21)	25 (32)
Platelets <100 x 10^9/L, n (%)	14 (18)	13 (17)
Albumin < 35 g/L, n (%)	6 (8)	14 (18)

Source: Bourliere M, et al. Lancet Infect Dis. 2015;15:397-404.

Ledipasvir-Sofosbuvir in Treatment-Experienced GT1 with Cirrhosis SIRIUS Trial: Baseline Characteristics (continued)

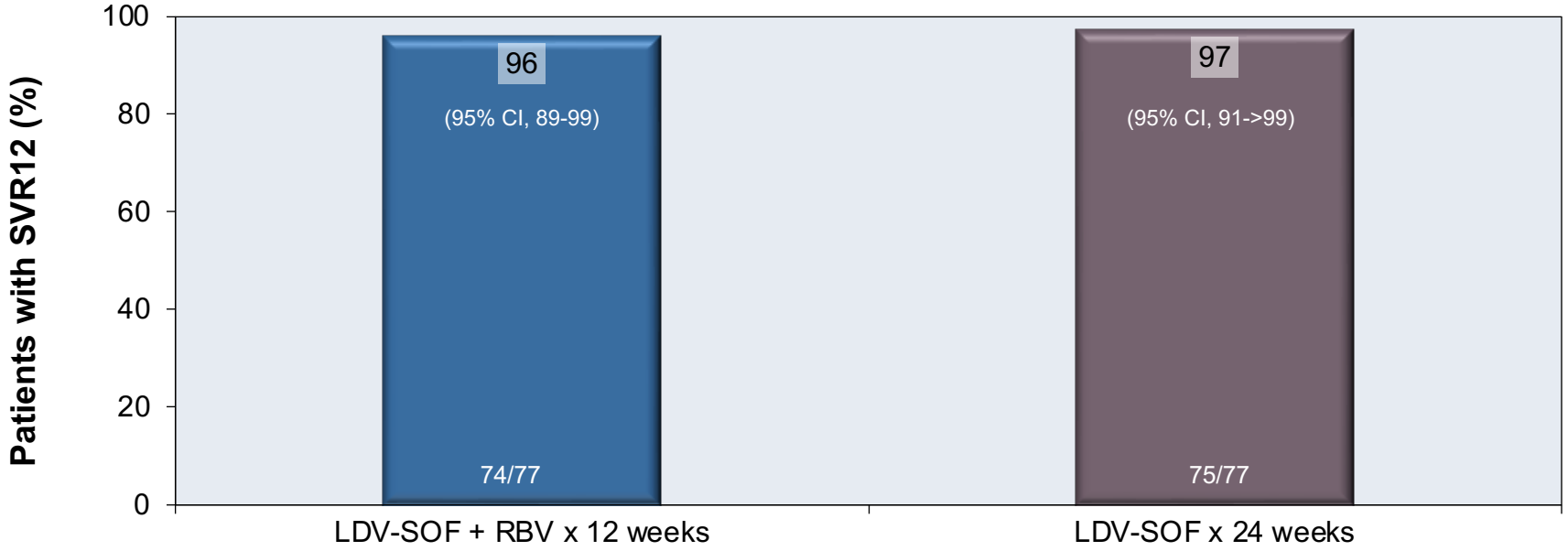
	LDV-SOF + RBV 12 wks (n = 77)	LDV-SOF x 24 wks (n = 78)
HCV Genotype		
1a	48 (62%)	50 (64)
1b	28 (36%)	27 (35%)
1 (no confirmed subtype)	1 (1%)	1 (1%)
Prior Protease Inhibitor		
Telaprevir	43 (56%)	49 (63%)
Boceprevir	30 (39%)	27 (35%)
Telaprevir and Boceprevir	1 (1%)	1 (1%)
Simeprevir	1 (1%)	2 (3%)
Faldaprevir	2 (3%)	0
Patients with NS3A RAVs	44 (57%)	39 (50%)
Patients with NS5A RAVs	12 (16%)	12 (15%)

Abbreviations: RAVs = Resistant Associated Variants

Source: Bourliere M, et al. Lancet Infect Dis. 2015;15:397-404.

Ledipasvir-Sofosbuvir in Treatment-Experienced GT1 with Cirrhosis SIRIUS Trial: Results

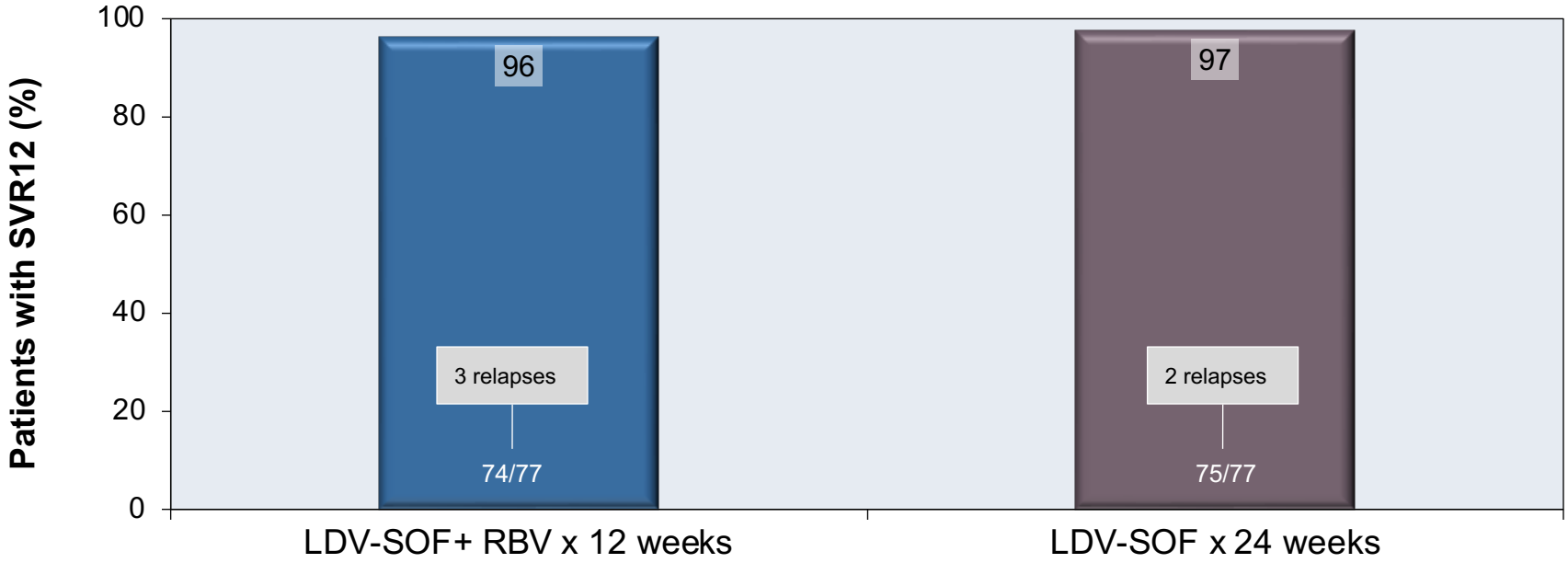
SIRIUS: SVR 12 by Treatment Duration and Regimen



Source: Bourliere M, et al. Lancet Infect Dis. 2015;15:397-404.

Ledipasvir-Sofosbuvir in Treatment-Experienced GT1 with Cirrhosis SIRIUS Trial: Results

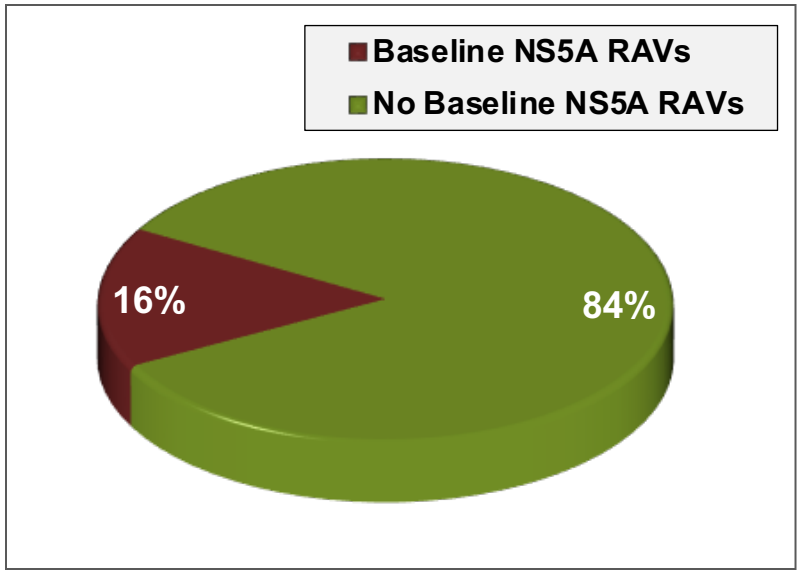
SIRIUS: SVR 12 by Treatment Duration and Regimen

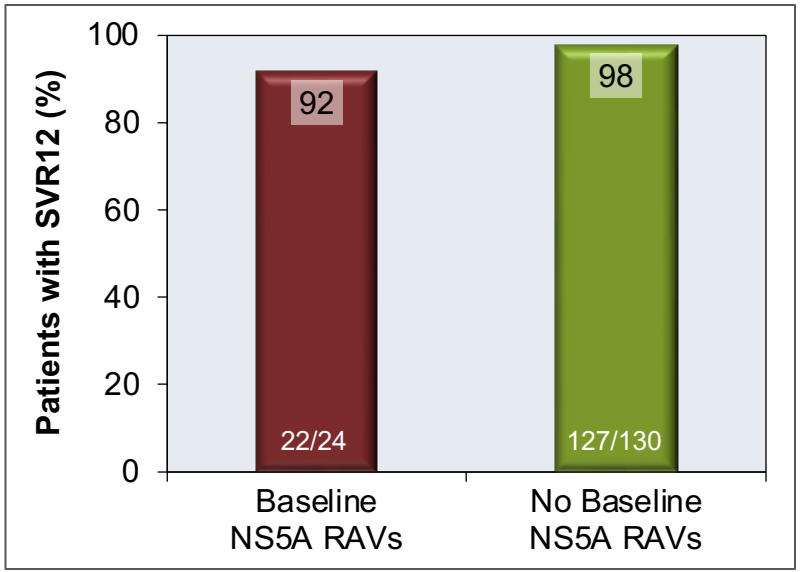


Source: Bourliere M, et al. Lancet Infect Dis. 2015;15:397-404.

Ledipasvir-Sofosbuvir in Treatment-Experienced GT1 with Cirrhosis SIRIUS Trial: Results HCV Sequence Analysis

Correlation of Baseline NS5A RAVs and SVR12 Responses





No statistically significant difference in SVR12 based on baseline NS5A mutations

Abbreviations: RAVs = Resistant Associated Variants

Source: Bourliere M, et al. Lancet Infect Dis. 2015;15:397-404.

Ledipasvir-Sofosbuvir in Treatment-Experienced GT1 with Cirrhosis SIRIUS Trial: Safety Summary

Patients, n (%)	LDV-SOF + RBV x 12 Weeks			LDV-SOF x 24 Weeks	
	Placebo 12 Wks (n = 78)	LDV/SOF + RBV 12 Wks (n = 77)	Overall Period (n = 78)	First 12 Wks (n = 77)	Overall Period (n = 77)
Any adverse event	63 (81%)	66 (86%)	75 (96%)	65 (84%)	67 (87%)
Treatment D/C due to AEs	1 (1%)	0	1 (1%)	0	0
Serious adverse event	1 (1%)	3 (4%)	4 (5%)	3 (4%)	8 (10%)
Grade 3-4 lab abnormalities	18 (23%)	8 (10%)	24 (31%)	15 (19%)	11 (14%)
Hemoglobin <100 g/L	1 (1%)	1 (1%)	2 (3%)	0	1 (1%)
Hemoglobin <85 g/L	1 (1%)	1 (1%)	2 (3%)	0	0

Abbreviations: LDV-SOF=ledipasvir-sofosbuvir; AE=adverse event; D/C=discontinued

Source: Bourliere M, et al. Lancet Infect Dis. 2015;15:397-404.

Ledipasvir-Sofosbuvir in Treatment-Experienced GT1 with Cirrhosis SIRIUS Trial: Adverse Events ≥10%

	LDV-SOF + RBV x 12 Weeks			LDV-SOF x 24 Weeks	
	Placebo 12 Wks (n = 78)	LDV/SOF + RBV 12 Wks (n = 77)	Overall Period (n = 78)	First 12 Wks (n = 77)	Overall Period (n = 77)
Asthenia	24 (31%)	29 (38%)	45 (58%)	28 (36%)	35 (45%)
Headache	16 (21%)	13 (17%)	21 (27%)	27 (35%)	31 (40%)
Pruritus	14 (18%)	11 (14%)	22 (28%)	4 (5%)	7 (9%)
Insomnia	9 (12%)	7 (9%)	17 (22%)	11 (14%)	13 (17%)
Nausea	8 (10%)	8 (10%)	14 (18%)	7 (9%)	8 (10%)
Fatigue	3 (4%)	5 (6%)	7 (9%)	13 (17%)	15 (19%)
Dry skin	6 (8%)	4 (5%)	11 (14%)	4 (5%)	4 (5%)
Arthralgia	5 (6%)	0	6 (8%)	6 (8%)	12 (16%)
Bronchitis	1 (1%)	4 (5%)	4 (5%)	4 (5%)	13 (17%)

Abbreviations: LDV-SOF = ledipasvir-sofosbuvir; AE = adverse event; D/C = discontinued

Source: Bourliere M, et al. Lancet Infect Dis. 2015;15:397-404.

Ledipasvir-Sofosbuvir in Treatment-Experienced GT1 with Cirrhosis SIRIUS Trial: Interpretation

Interpretation: “Ledipasvir-sofosbuvir plus ribavirin for 12 weeks and ledipasvir-sofosbuvir for 24 weeks provided similarly high SVR12 rates in previous non-responders with HCV genotype 1 and compensated cirrhosis. The shorter regimen, when given with ribavirin, might, therefore, be useful to treat treatment-experienced patients with cirrhosis if longer-term treatment is not possible.”

Source: Bourliere M, et al. Lancet Infect Dis. 2015;15:397-404.

Ledipasvir-Sofosbuvir in HIV Coinfection

Ledipasvir-Sofosbuvir in GT1 or GT4 and HIV Coinfection
ION-4

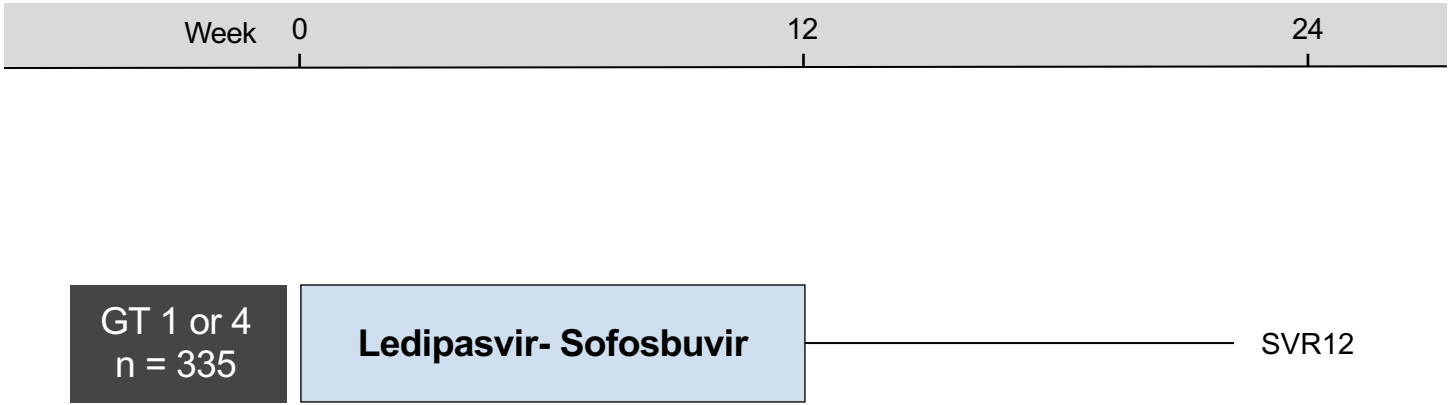
Source: Naggie S, et al. N Engl J Med 2015;378:705-13.

Ledipasvir-Sofosbuvir in GT1 or GT4 with HIV Coinfection
ION-4 Trial: Features

- **Design**: Open-label, single group, phase 3 trial, using ledipasvir-sofosbuvir for 12 weeks in treatment-naïve or treatment-experienced patients with GT 1 or 4 and HIV coinfection
- **Setting**: multicenter in United States, Canada, New Zealand
- **Entry Criteria**
  - Chronic HCV Genotype 1 or 4
  - Treatment-naïve or treatment-experienced
  - Noncirrhotic or compensated cirrhosis
  - Platelet count >50,000/mm^3, hemoglobin ≥10 mg/dL, CrCl ≥60 mL/min
  - Stable ARV with HIV RNA <50 mL and CD4 count >100 cells/mm^3
  - ARV Regimens: tenofovir DF-emtricitabine + [efavirenz, rilpivirine, or raltegravir]
- **Primary End Point**: SVR12

Source: Naggie S, et al. N Engl J Med 2015;378:705-13.

Ledipasvir-Sofosbuvir in GT1 or GT4 with HIV Coinfection
ION-4 Trial: Study Design



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

Antiretrovirals allowed: tenofovir DF-emtricitabine plus either efavirenz, rilpivirine, or raltegravir

Source: Naggie S, et al. N Engl J Med 2015;378:705-13.

Ledipasvir-Sofosbuvir in GT1 or GT4 with HIV Coinfection
ION-4 Trial: Baseline Characteristics

Baseline Characteristic	Ledipasvir-Sofosbuvir (n = 335)
Mean age, years	52
Male, n (%)	276 (82)
African American, n (%)	115 (34)
Hispanic or Latino, n (%)	56 (17)
Mean BMI, kg/m^2	26
IL28B CC, n (%)	81 (24)
GT 1 (%)	327 (98)
HCV treatment experienced, n (%)	185 (55)
Cirrhosis, n (%)	67 (20)
Mean HCV RNA, log_{10} IU/mL	6.7 ± 0.6
Median CD4 Count, cells/mm^3 (range)	628 (100-2069)

Source: Naggie S, et al. N Engl J Med 2015;378:705-13.

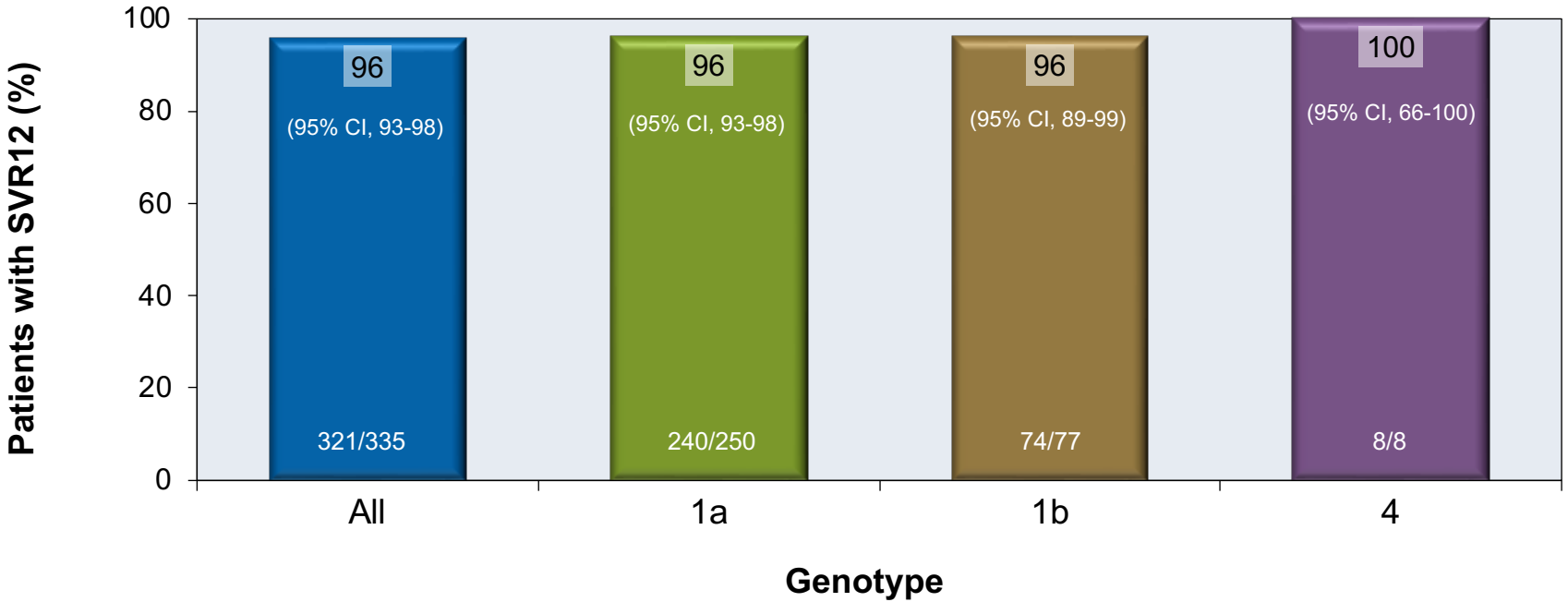
Ledipasvir-Sofosbuvir in GT1 or GT4 with HIV Coinfection
ION-4 Trial: Antiretroviral Regimens

ION-4: HIV Antiretroviral Regimen	
Antiretroviral Agent	**Antiretroviral Received** (n = 335)
Tenofovir DF-emtricitabine-efavirenz	160 (48)
Tenofovir DF-emtricitabine-rilpivirine	29 (9)
Tenofovir DF-emtricitabine + Raltegravir	146 (44)

Source: Naggie S, et al. N Engl J Med 2015;378:705-13.

Ledipasvir-Sofosbuvir in GT1 or GT4 with HIV Coinfection
ION-4 Trial: Results

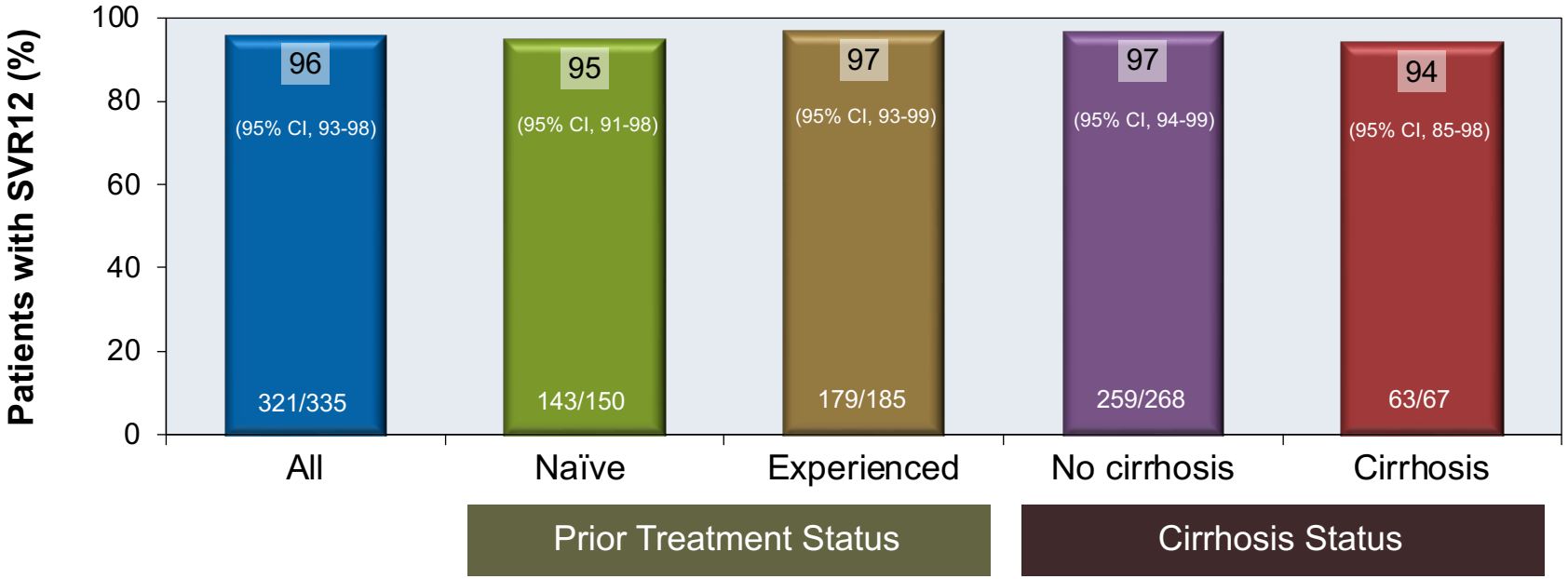
ION-4: SVR12 Results by Genotype



Source: Naggie S, et al. N Engl J Med 2015;378:705-13.

Ledipasvir-Sofosbuvir in GT1 or GT4 with HIV Coinfection
ION-4 Trial: Results

ION-4: SVR12 Results by Prior Treatment Status and Cirrhosis Status



Source: Naggie S, et al. N Engl J Med 2015;378:705-13.

Ledipasvir-Sofosbuvir in GT1 or GT4 with HIV Coinfection
ION-4 Trial: Adverse Effects

Event	Ledipasvir-Sofosbuvir (n = 335)
Discontinuation due to adverse event	0
Grade 3-4 Adverse Event	14 (4%)
Serious Adverse Event	8 (2%)
Headache	83 (25%)
Fatigue	71 (21%)
Diarrhea	36 (11%)
Nausea	33 (10%)
Arthralgia	22 (7%)
Upper respiratory tract infection	18 (5%)
Vomiting	14 (4%)
Muscle spasms	11 (3%)

Source: Naggie S, et al. N Engl J Med 2015;378:705-13.

Ledipasvir-Sofosbuvir in GT1 or GT4 with HIV Coinfection
ION-4 Trial: Conclusions

Conclusions: “Ledipasvir and sofosbuvir for 12 weeks provided high rates of sustained virologic response in patients coinfected with HIV-1 and HCV genotype 1 or 4.”

Source: Naggie S, et al. N Engl J Med 2015;378:705-13.

Sofosbuvir in Patients Pre- and Post-Liver Transplant

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

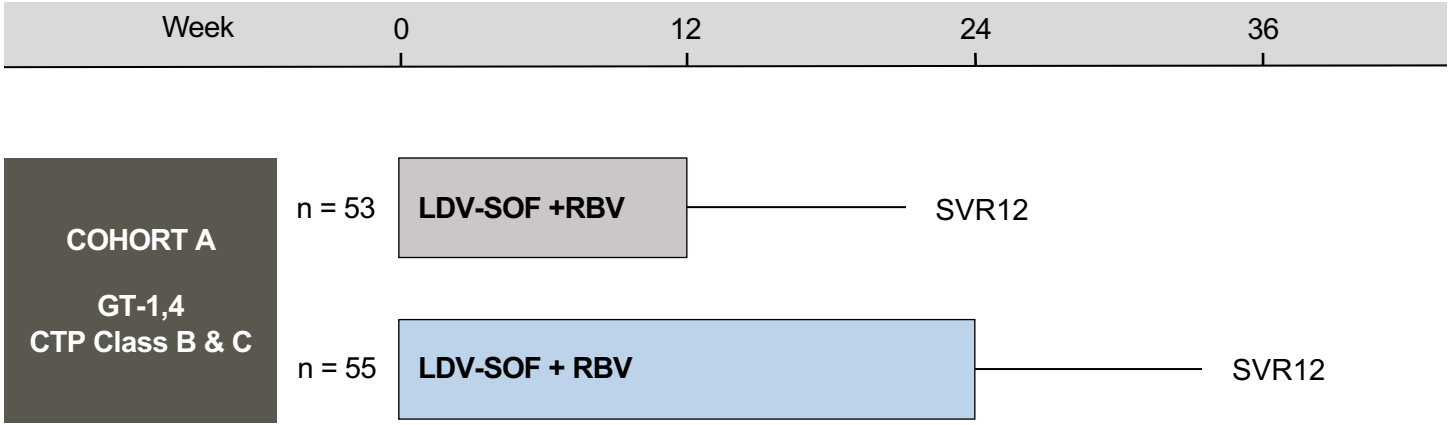
Source: Charlton M, et al. Gastroenterology. 2015;149:649-59.

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 ≤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, et al. Gastroenterology. 2015;149:649-59.

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

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 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, $\log_{10}$ IU/mL	5.9	5.8	5.6	5.8
IL28B genotype CC, n (%)	4 (13)	5 (17)	6 (26)	7 (27)
HCV Genotype 1a, n (%) 1b, n (%) 4, n (%)	 19 (63) 10 (33) 1 (3)	 22 (76) 7 (24) 0	 15 (65) 6 (26) 2 (9)	 18 (69) 8 (31) 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

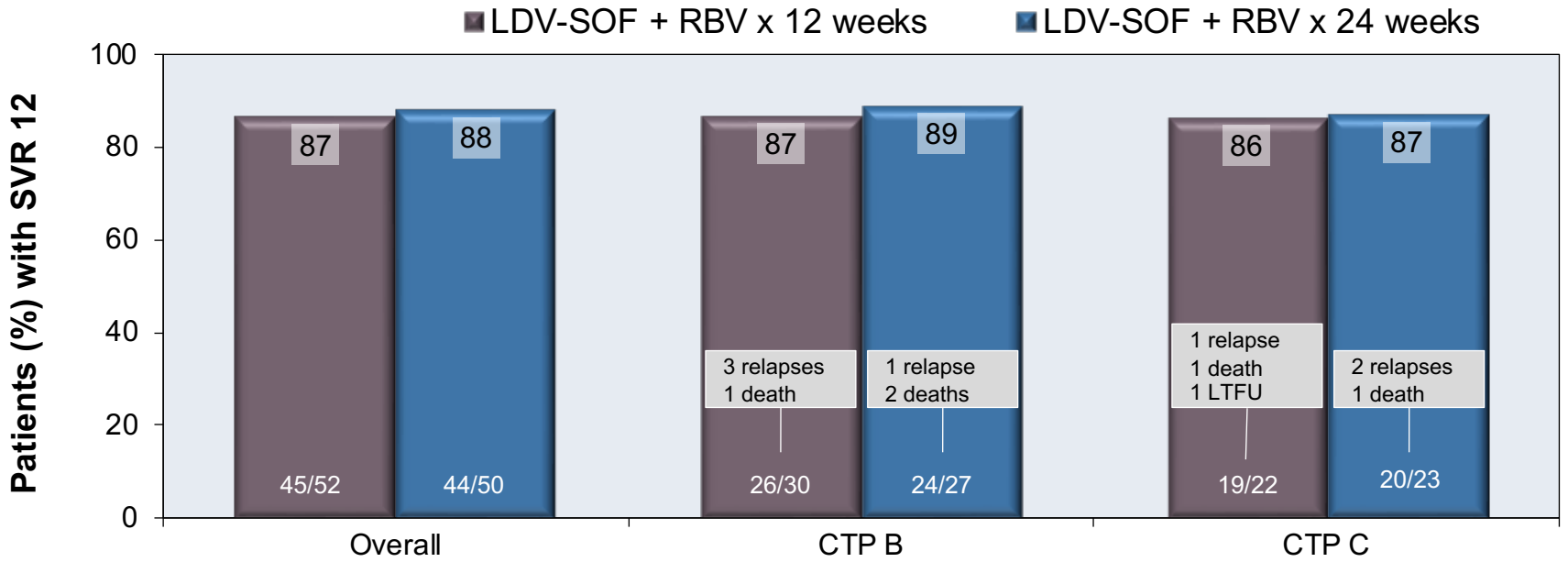
Cohort A **Characteristics**	**CTP B**		**CTP C**	
	12 Weeks (n = 30)	**24 Weeks** (n = 29)	**12 Weeks** (n = 23)	**24 Weeks** (n = 26)
Child-Turcotte-Pugh Score				
Class A (5-6)	0	1 (3)	0	0
Class B (7-9)	27 (90)	27 (93)	7 (30)	4 (15)
Class C (10-12)	3 (10)	1 (3)	16 (70)	22 (85)
MELD Score, n (%)				
<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 10^3 µL	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

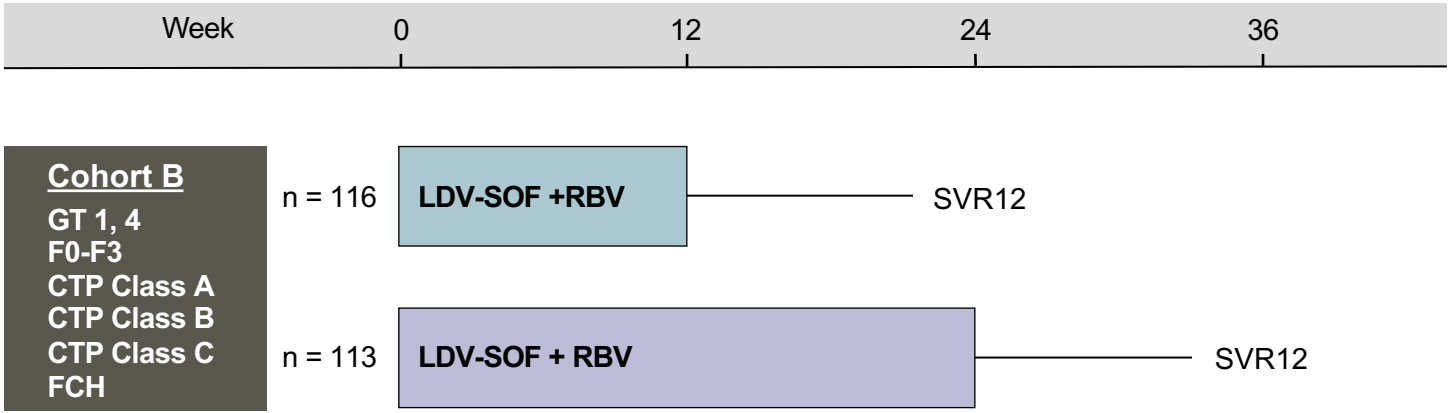


Abbreviations: CTP = Child-Turcotte-Pugh; LTFU = lost to follow-up

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

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



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

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 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, $\log_{10}$ IU/mL	6.5	6.4	6.2	6.7	6.3	6.2	6.4	6.3	6.5	7.1
IL28B 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

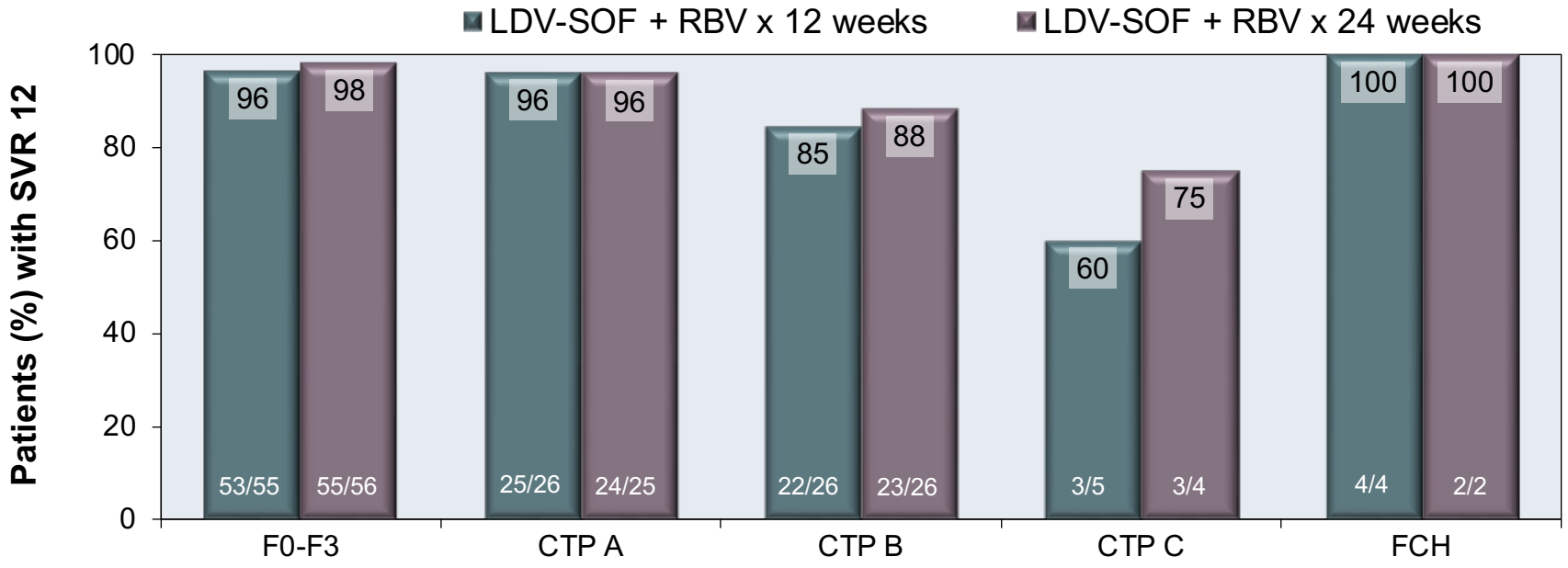
Cohort B Characteristics	F0-F3		CTP A		CTP B		CTP C		FCH	
	12wks (n = 55)	24wks (n = 56)	12wks (n = 26)	24wks (n = 25)	12wks (n = 26)	24wks (n = 26)	12wks (n = 5)	24wks (n = 4)	12wks (n = 4)	24wks (n = 2)
Median years post transplant	2.9	2.8	8.8	6.6	5.1	6.3	5.2	5.7	1.1	0.3
Child-Turcotte-Pugh										
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 10^3 µL	143	152	106	112	93	97	106	65	45	196

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): Results

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



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

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.”

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

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

SOLAR-2

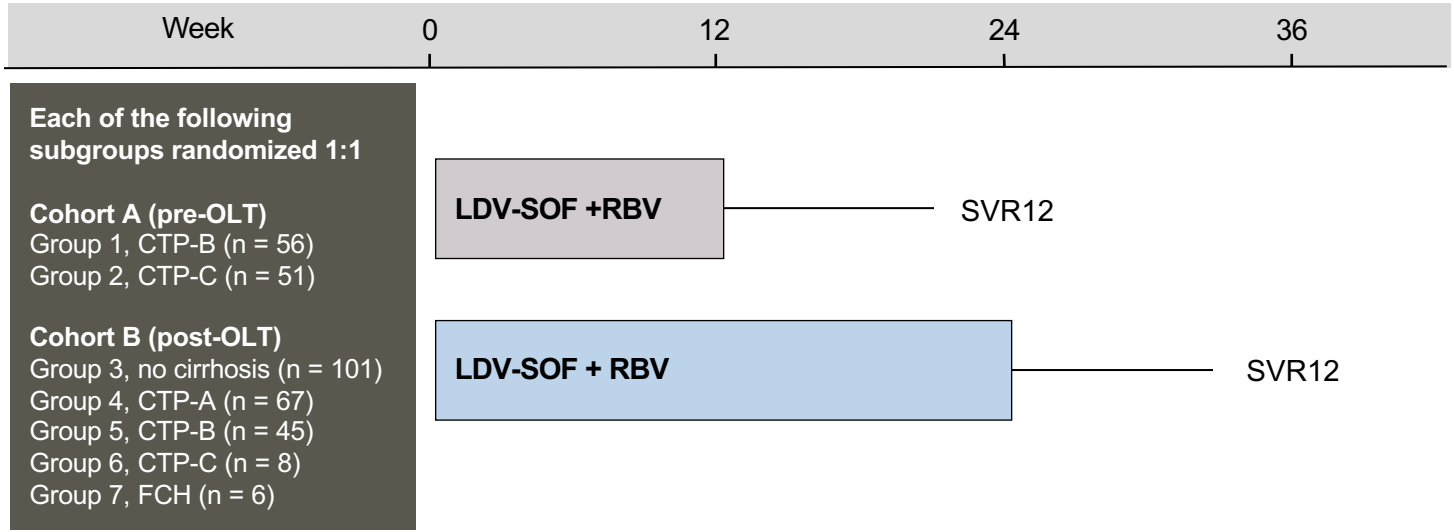
Source: Manns M, et al. Lancet Infect Dis. 2016;16:685-97.

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/mm^3
  - Exclusion: CTP score 13-15 or prior receipt of NS5a inhibitor
- **Primary End Point**: SVR12

Source: Manns M, et al. Lancet Infect Dis. 2016;16:685-97.

Ledipasvir-Sofosbuvir + Ribavirin in Advanced Liver Disease
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

Source: Manns M, et al. Lancet Infect Dis. 2016;16:685-97.

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
IL28B 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

Source: Manns M, et al. Lancet Infect Dis. 2016;16:685-97.

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
IL28B 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

Source: Manns M, et al. Lancet Infect Dis. 2016;16:685-97.

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

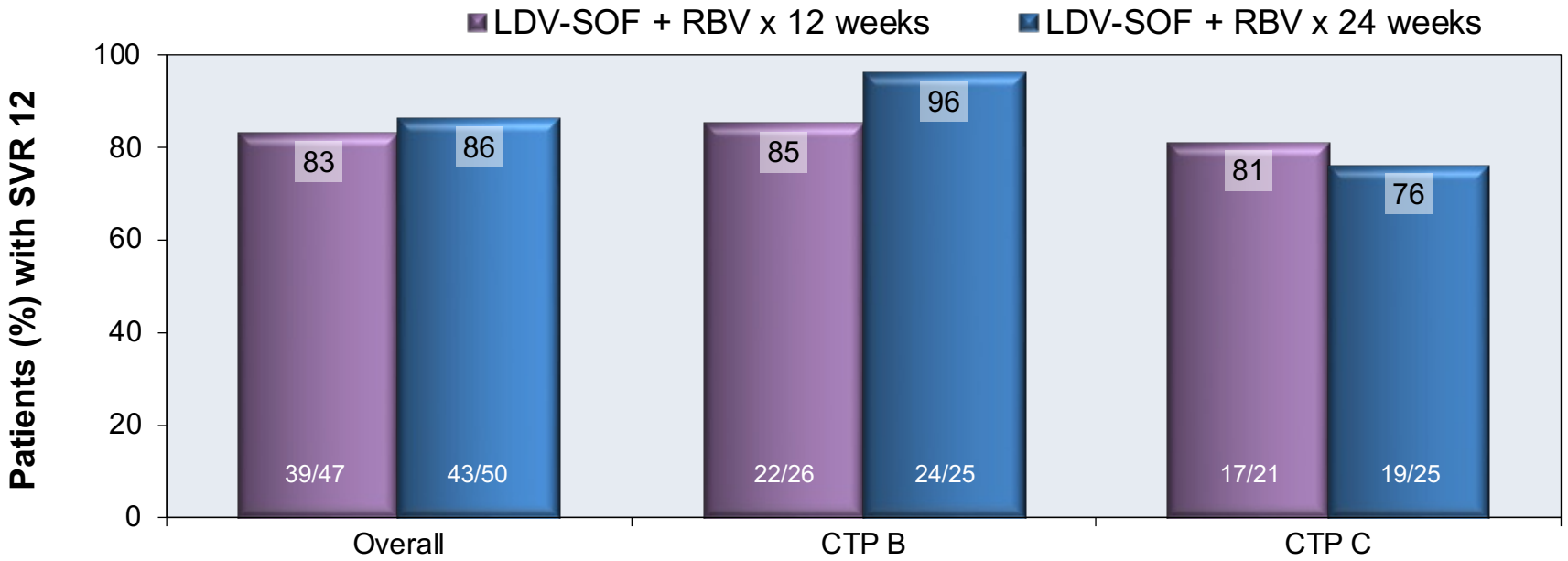
Cohort B Characteristics	CTP B		CTP C		FCH	
	12 Weeks (n = 22)	24 Weeks (n = 23)	12 Weeks (n = 3)	24 Weeks (n = 5)	12 Weeks (n = 3)	24 weeks (n = 2)
Median age, years	58	60	63	62	57	56
Male, n (%)	15 (68)	15 (65)	2 (67)	5 (100)	2 (67)	1 (50)
White, n (%)	21 (95)	21 (91)	3 (100)	5 (100)	2 (67)	1 (50)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

Source: Manns M, et al. Lancet Infect Dis. 2016;16:685-97.

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

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

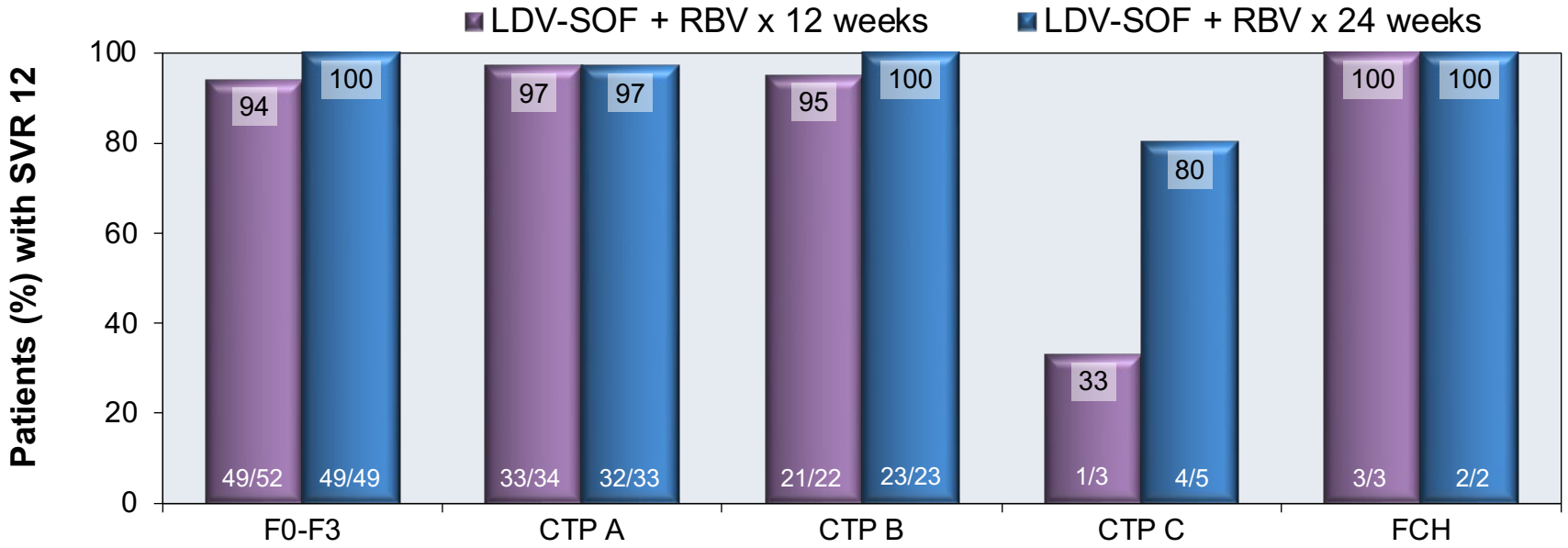


Abbreviations: CTP=Child-Turcotte-Pugh
Notes: 6 subjects excluded because received transplant before SVR12 could be assessed; SVR12 estimates reflect combination of GT1 and GT4 outcomes together, and differ from stratified SVR12 estimates presented in the published manuscript.

Source: Manns M, et al. Lancet Infect Dis. 2016;16:685-97.

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.

Source: Manns M, et al. Lancet Infect Dis. 2016;16:685-97.

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.”

Source: Manns M, et al. Lancet Infect Dis. 2016;16:685-97.

Acknowledgments

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