Treatment Experienced

Ledipasvir-Sofosbuvir +/- Ribavirin in HCV Genotype 1

ION-2

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

ION-2 Trial

- **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 achieved 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.

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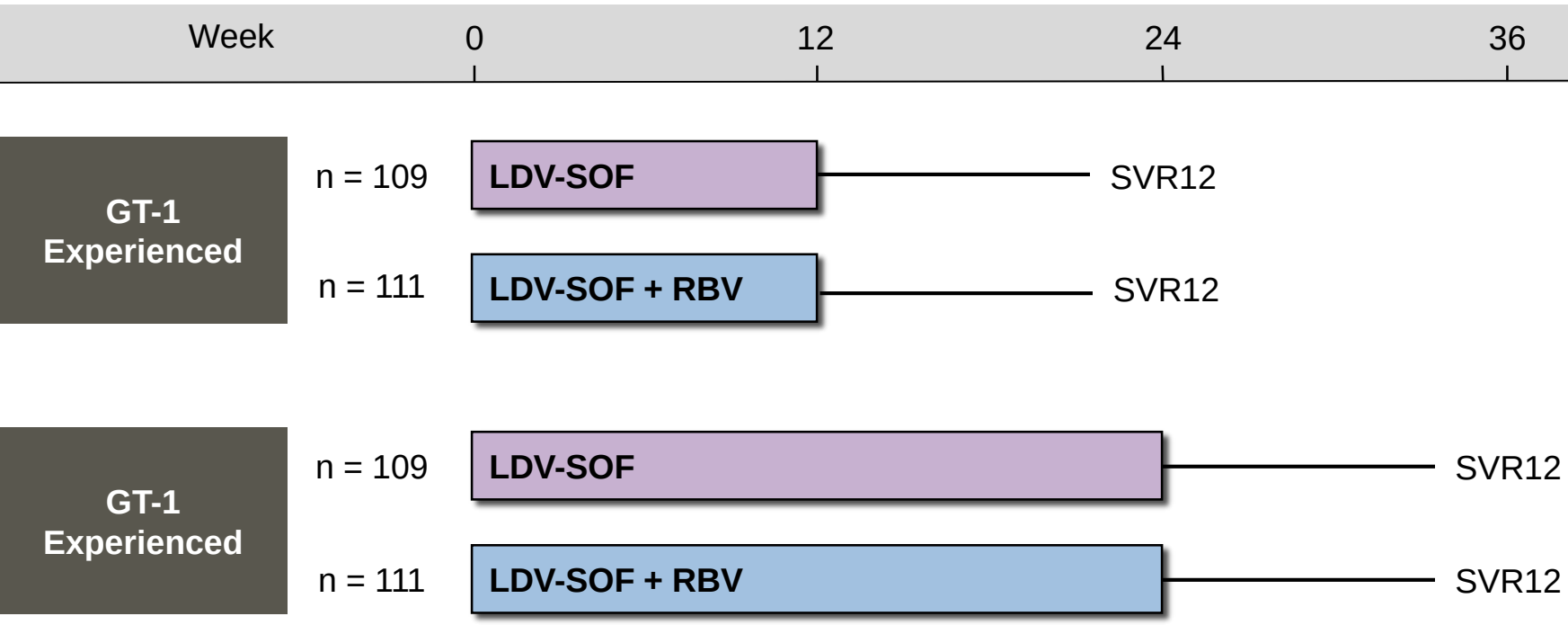
ION-2 Study: Study Design



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

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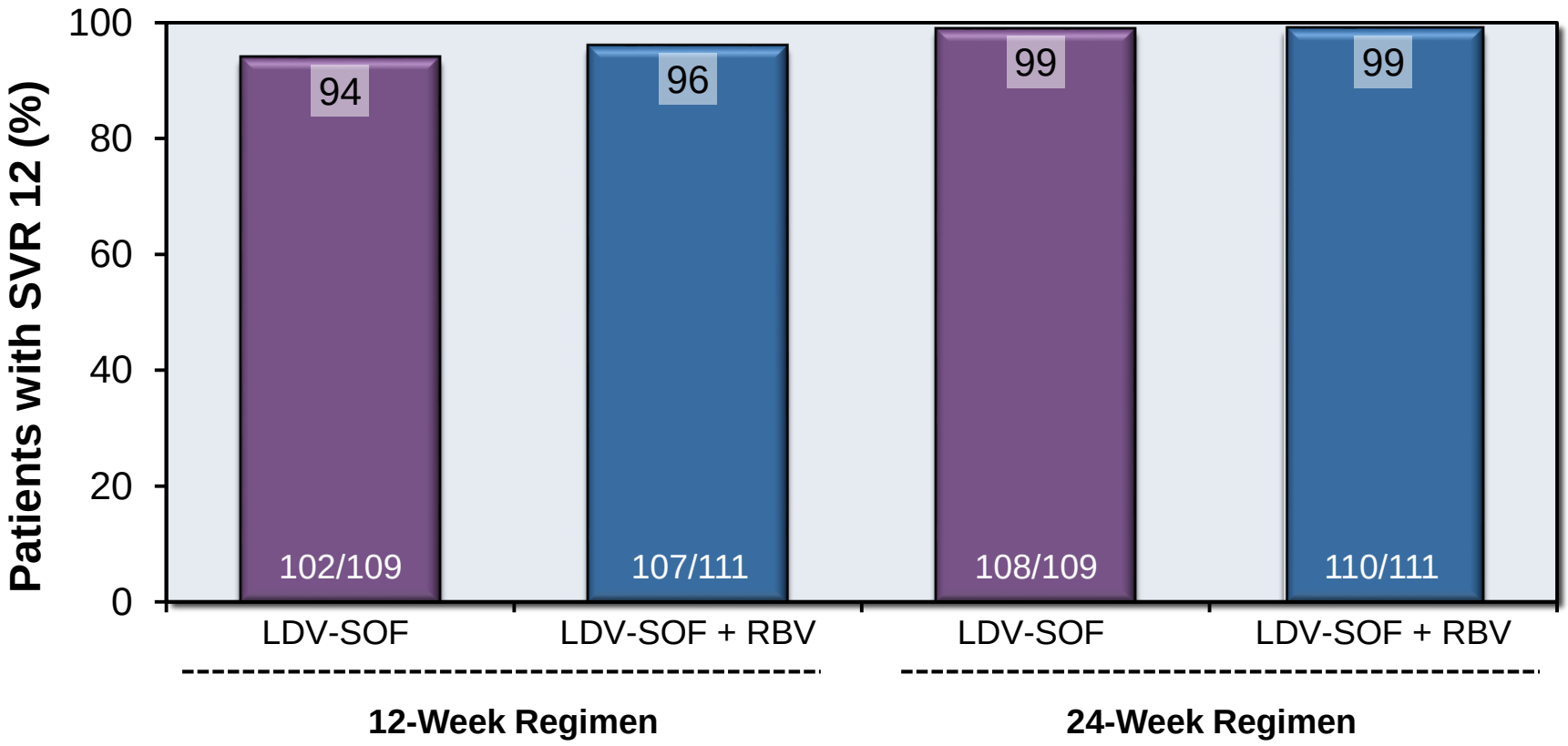
ION-2 Study: Baseline Characteristics

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

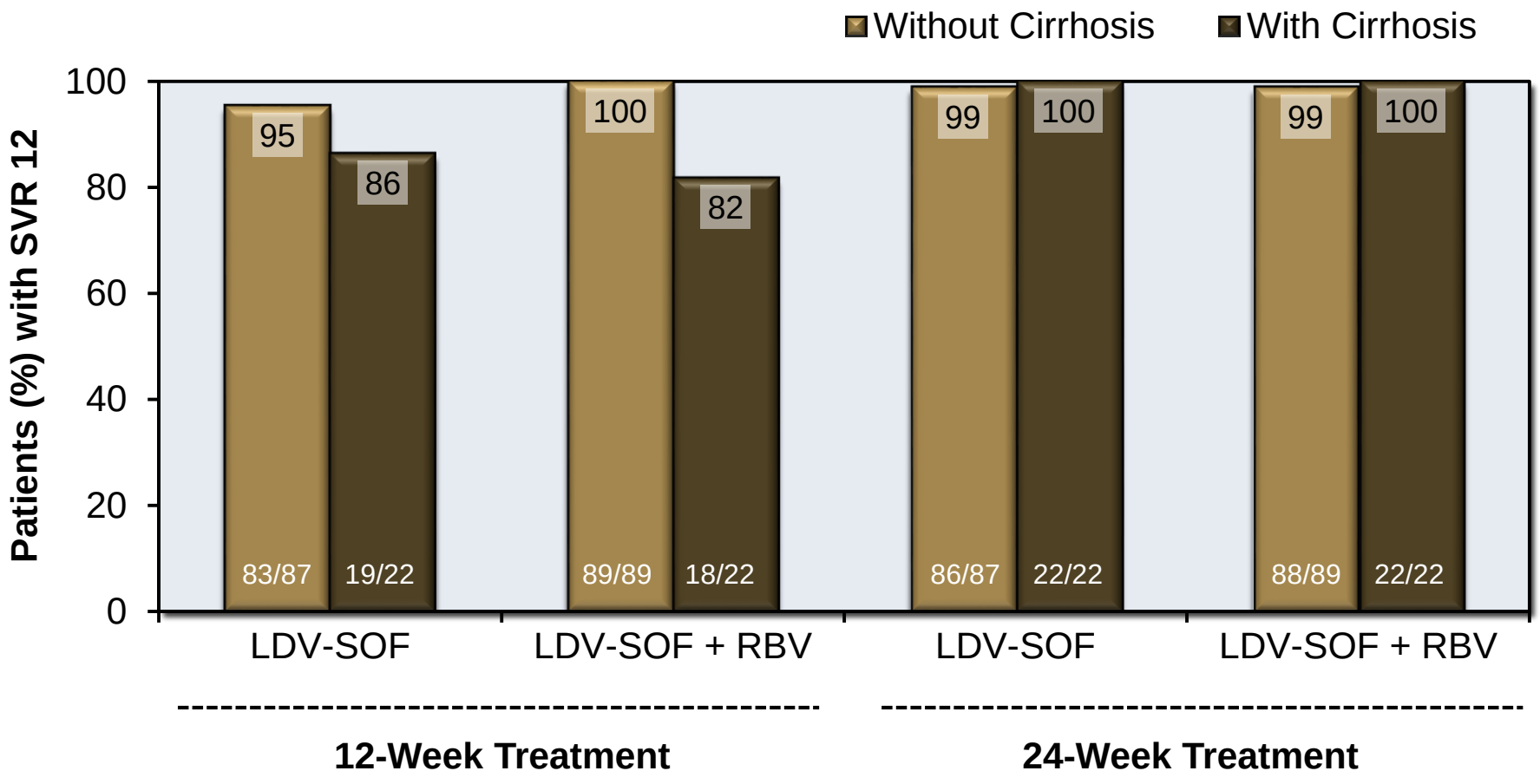


Abbreviations: LDV-SOF= ledipasvir-sofosbuvir; RBV = ribavirin
*Primary end-point by intention-to-treat analysis

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

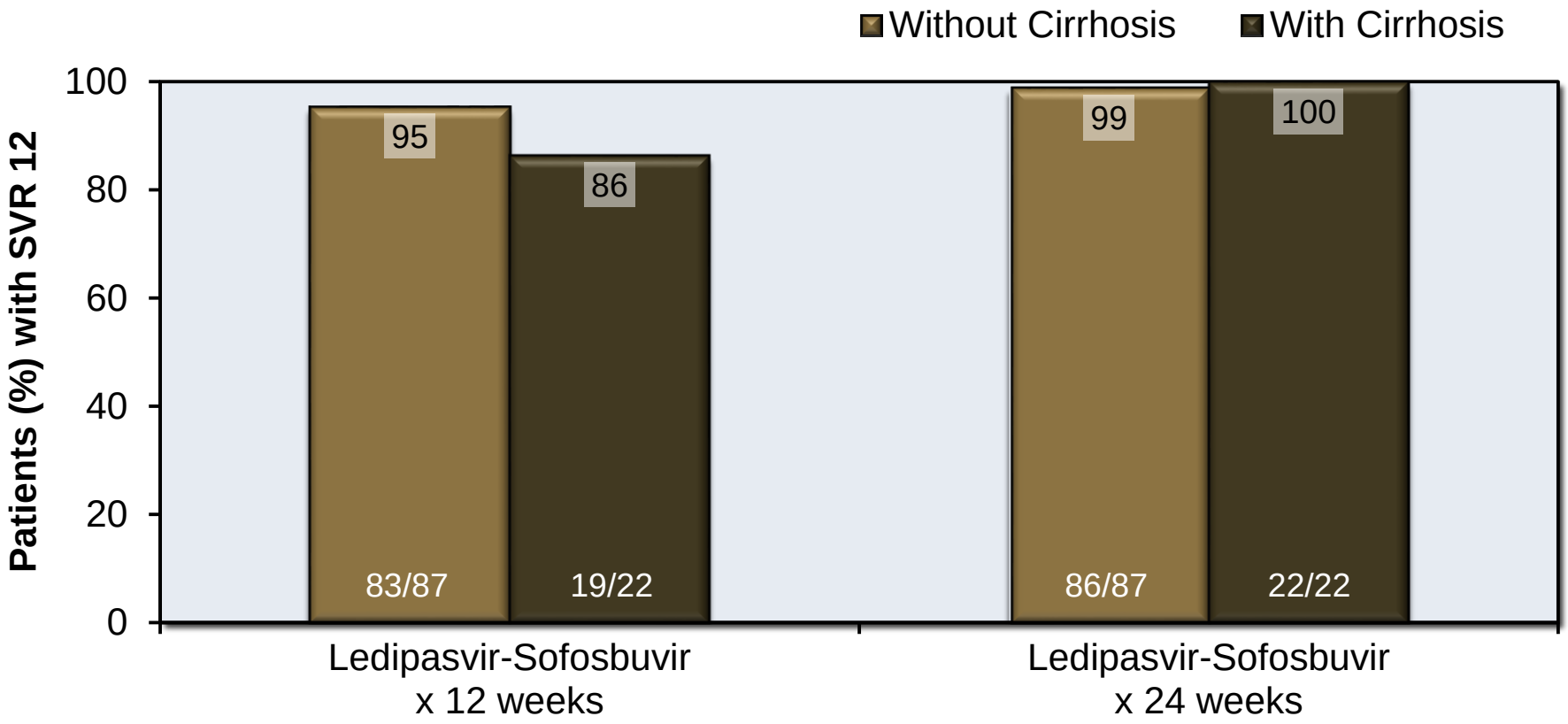


Source: Afdhal N, et al. N Engl J Med. 2014;370:1483-93.

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

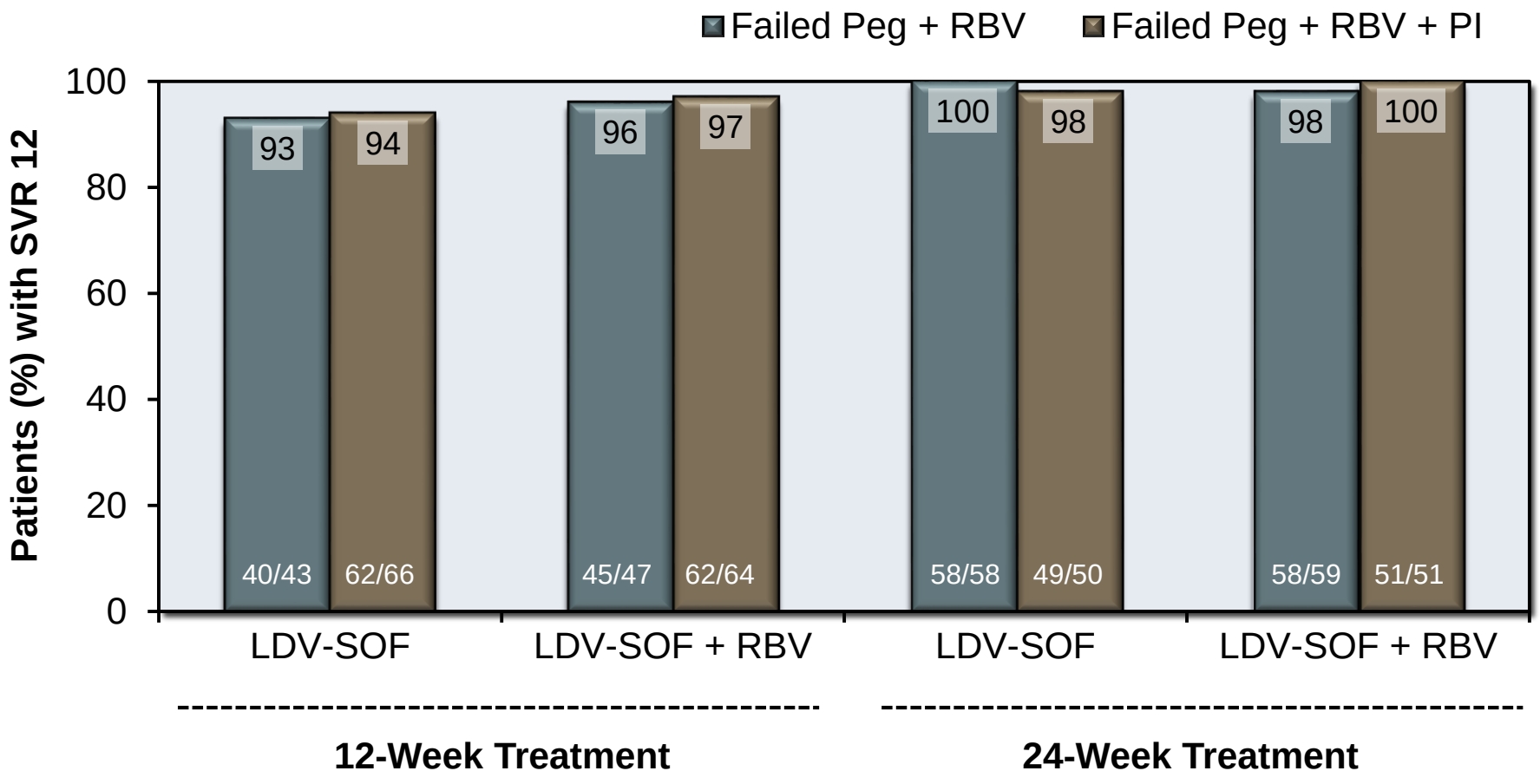
Source: Afdhal N, et al. N Engl J Med. 2014;370:1483-93.

Hepatitis web study

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 who had viral relapse had detectable NS5A resistant variants at the time of 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.

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