

Treatment Naïve

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

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

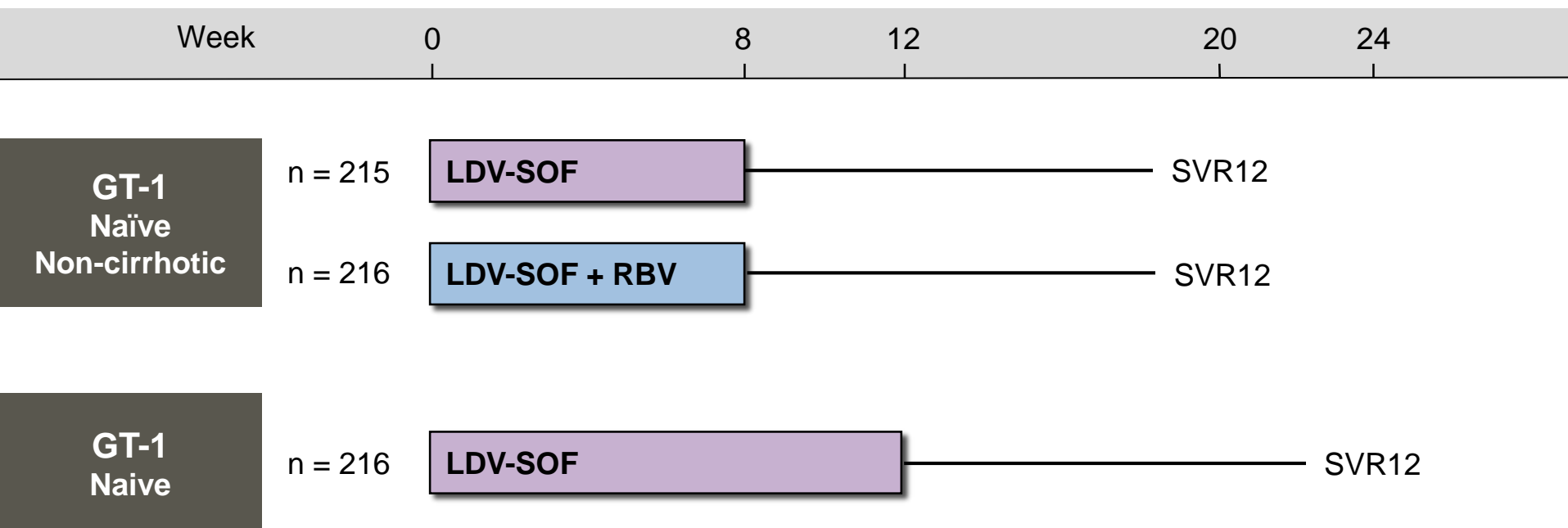
# Ledipasvir-Sofosbuvir for 8 or 12 Weeks in Treatment-Naïve HCV GT 1

## ION-3 Study: Features

### ION-3 Trial

- **Design:** Open-label, randomized, phase 3, comparing ledipasvir-sofosbuvir with or without ribavirin for 8 weeks and ledipasvir-sofosbuvir for 12 weeks in treatment-naïve, non-cirrhotic 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  $\geq$  10,000 IU/ml
  - No limits on BMI
- **Primary End-Point:** SVR12

# 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

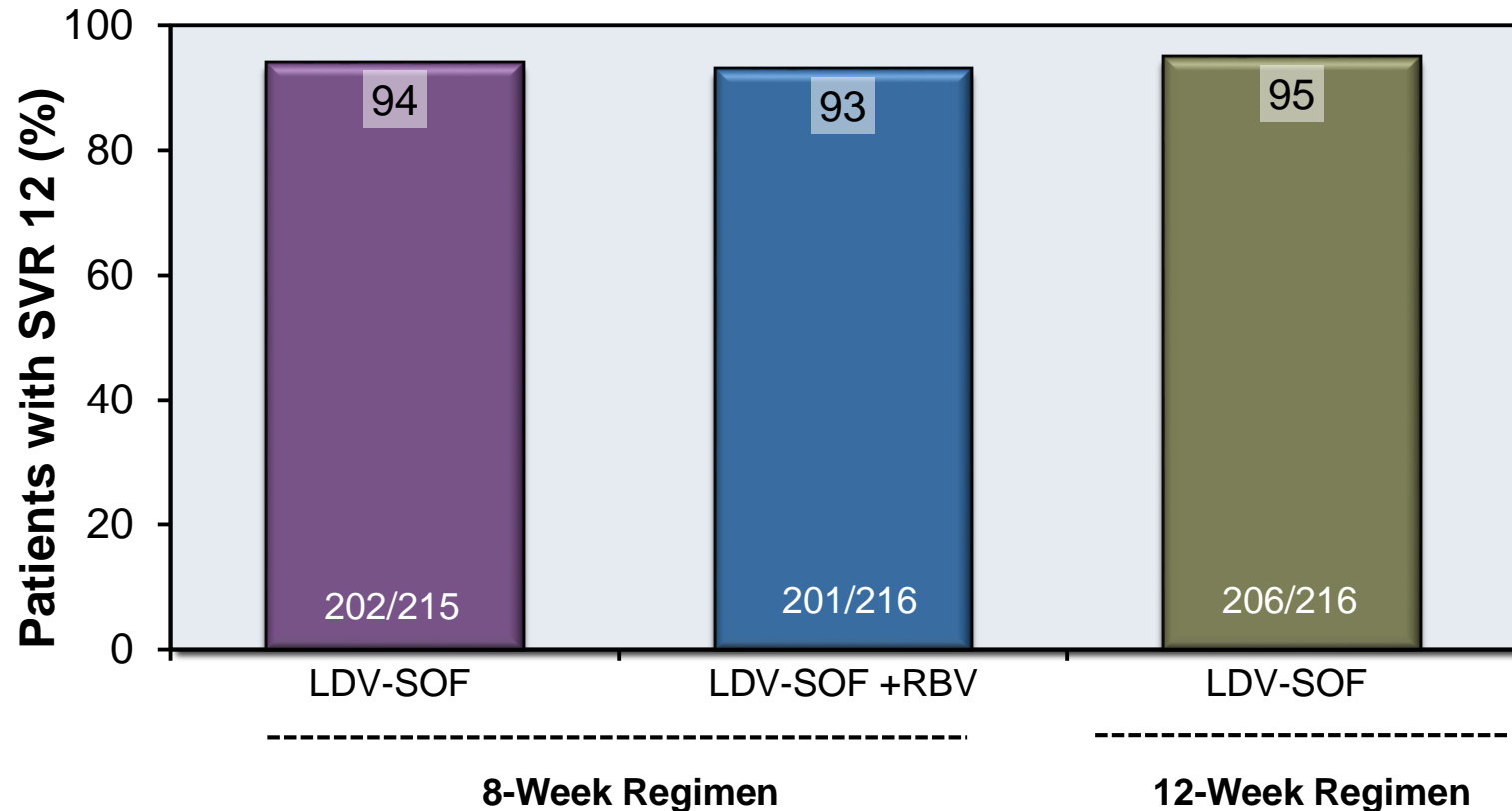
# Ledipasvir-Sofosbuvir for 8 or 12 Weeks in Treatment-Naïve HCV GT 1 ION-3 Study: Baseline Characteristics

Baseline Characteristics	8 Weeks		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 <sup>2</sup> 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 <sub>10</sub> 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 Weeks	12 Weeks
	N=215	N=216
Number of Responders at End of Treatment	100% (215/215)	100% (216/216)
SVR	94% (202/215)	96% (206/216)
Relapse	5% (11/215)	1% (3/216)
Relapse According to Baseline HCV RNA		
HCV RNA $\leq$ 6 million IU/mL	2% (2/123)	2% (2/131)
HCV RNA $\geq$ 6 million IU/mL	10% (9/92)	1% (1/85)

# 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 who had viral relapse, 15 (65%) had NS5A-resistant variants at time of relapse

# 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.”



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](http://www.hepatitisc.uw.edu)

Hepatitis Web Study

<http://depts.washington.edu/hepstudy/>

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