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

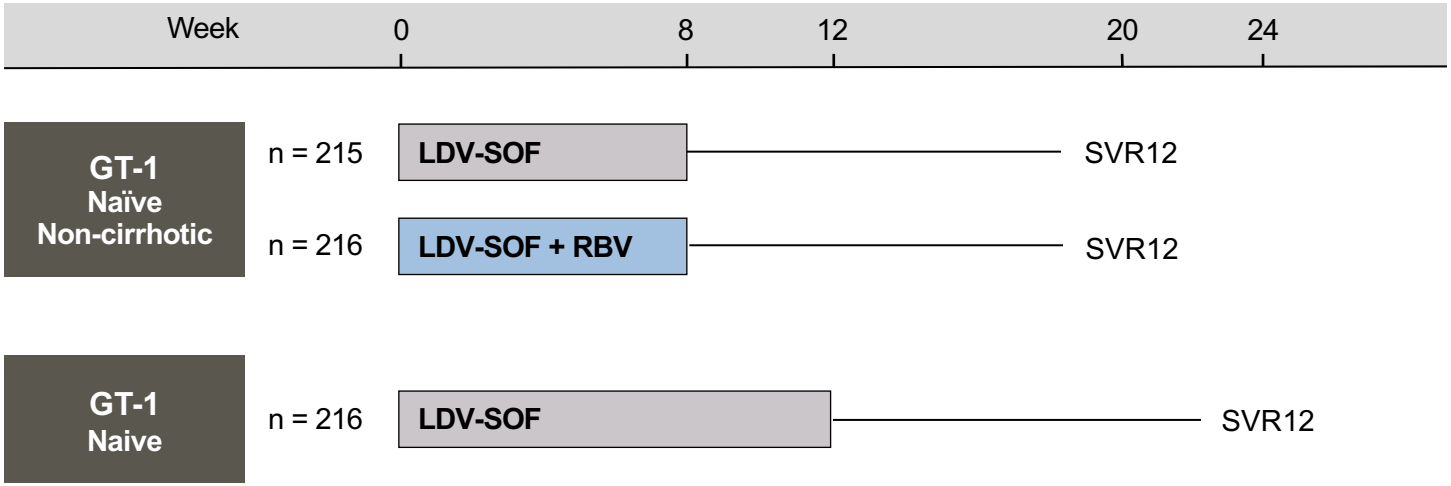
Source: Kowdley K, et al. N Engl J Med. 2014;370:1879-88.

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.

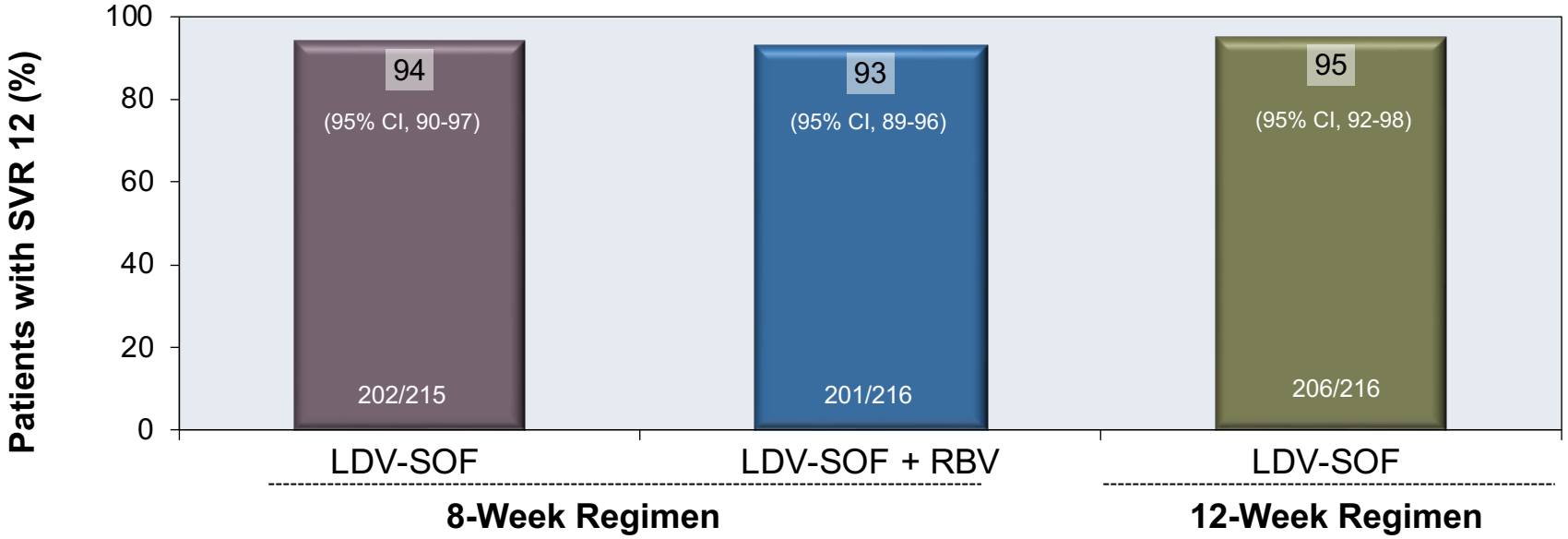
Ledipasvir-Sofosbuvir for 8 or 12 Weeks in Treatment-Naïve HCV GT 1 ION-3 Study: Baseline Characteristics

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.

Acknowledgments

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