Treatment Experienced

Ledipasvir-Sofosbuvir + RBV in Sofosbuvir-Experienced HCV GT1

Retreatment of Sofosbuvir Failures

Wyles D, et al. Hepatology. 2015;61:1793-7.

LDV-SOF + RBV in Sofosbuvir-Experienced GT 1 HCV
Study Features

- **Design**: Open-label, phase 2 retreatment study examining the efficacy of ledipasvir-sofosbuvir plus ribavirin in patients who did not achieve SVR with sofosbuvir-based therapy in one of 5 clinical trials.
- **Setting**: 24 study locations in United States
- **Entry Criteria**
  - Chronic HCV Genotype 1
  - Failed prior combination therapy with sofosbuvir in phase 2/3 clinical trials
  - Compensated cirrhosis allowed
  - Cirrhosis defined as FibroTest >0.75 and APRI > 2
- **Primary End-Point**: SVR12
- **Secondary End-Points**: Treatment discontinuation, adverse events, laboratory abnormalities

Source: Wyles D, et al. Hepatology. 2015;61:1793-7.

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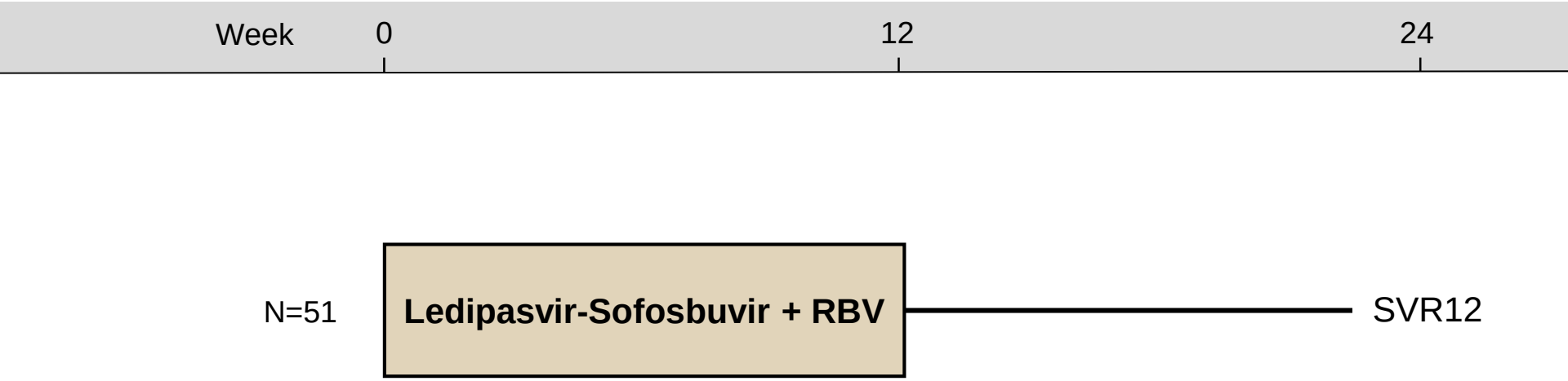
Study Features



Abbreviations: LDV = ledipasvir; SOF = sofosbuvir; PEG = peginterferon; 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: Wyles D, et al. Hepatology. 2015;61:1793-7.

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Baseline Characteristics

Patient Characteristics	Ledipasvir-Sofosbuvir + RBV x 12 wks N = 51
Mean age, years (SD)	54 (8.7)
Male sex, n (%)	31 (61)
Race, n (%) White Black	 43 (84) 8 (16)
Mean body mass index, kg/m^2 (SD)	30.4 (5.4)
Cirrhosis	14 (27)
Genotype, n (%) 1a 1b 3a	 30 (59) 20 (39) 1 (2)
IL28b, n (%) CC CT TT	 4 (8) 33 (65) 14 (27)

Abbreviation: SD, standard deviation

Source: Wyles D, et al. Hepatology. 2015;61:1793-7.

Hepatitis web study

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Baseline Characteristics

Patient Characteristics	Ledipasvir-Sofosbuvir + RBV x 12 wks N = 51
Previous HCV treatment regimen (by Sofosbuvir exposure in weeks), n (%)	
Sofosbuvir + Peginterferon + Ribavirin	
For 4 weeks	1 (2)
For 12 weeks	22 (43)
For 24 weeks	2 (4)
Sofosbuvir + Ribavirin	
For 12 weeks	6 (12)
For 24 weeks	14 (27)
Without Sofosbuvir	6 (12)
Outcome with previous treatment	
Virologic Failure	47 (92)
Discontinuation from Adverse Events	2 (4)
Study terminated by sponsor	2 (4)

Source: Wyles D, et al. Hepatology. 2015;61:1793-7.

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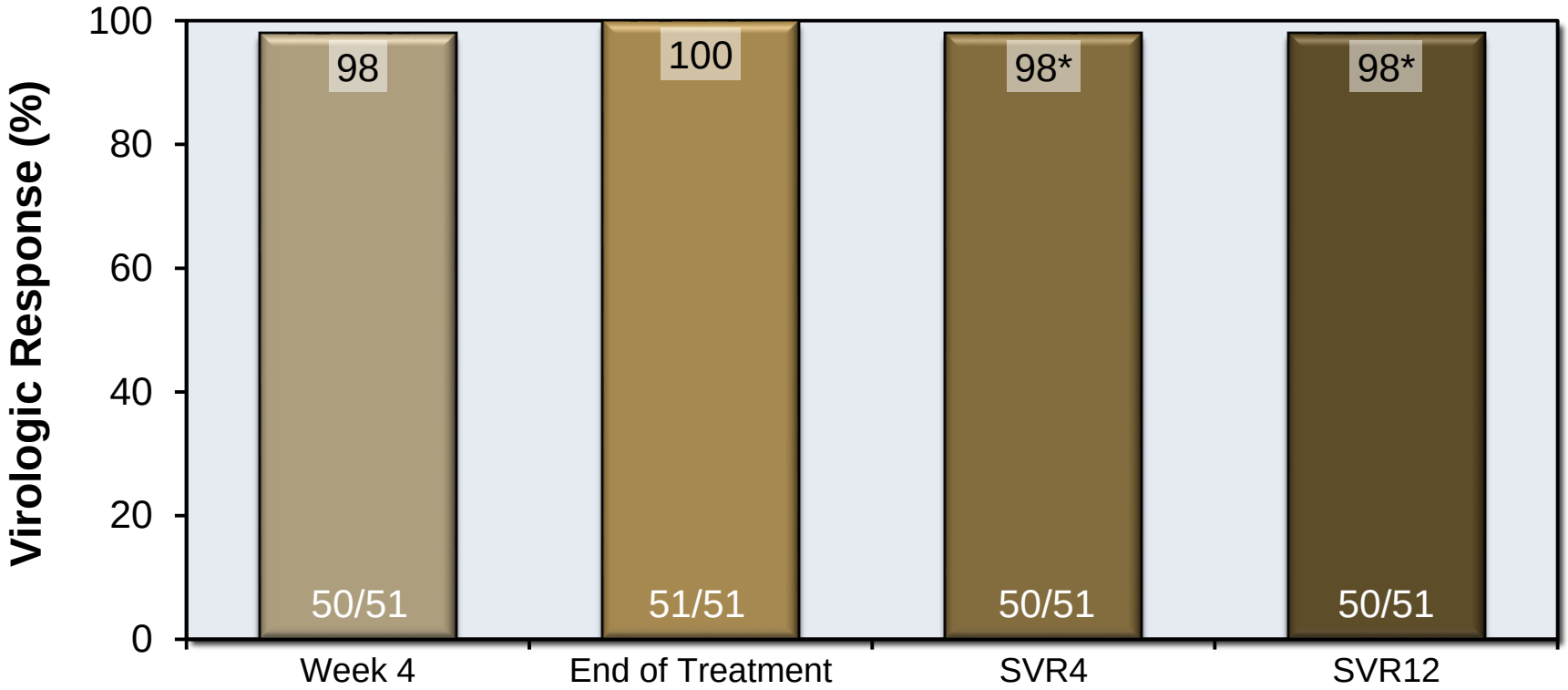
Study Results

Virologic Response at Week 4, End-of-Treatment and SVR12, 24



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* The one patient who relapsed found to have genotype 3a infection and was enrolled erroneously.

Source: Wyles D, et al. Hepatology. 2015;61:1793-7.

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Adverse Events

Event	Ledipasvir-Sofosbuvir + Ribavirin (n=51)
Discontinuation due to adverse event	1 (2%)
Serious adverse event	2 (4%)
Fatigue	13 (25%)
Headache	11 (22%)
Diarrhea	7 (14%)
Rash	6 (12%)
Insomnia	6 (12%)
Nausea	5 (10%)
Constipation	4 (8%)

Source: Wyles D, et al. Hepatology. 2015;61:1793-7.

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Conclusions

Conclusions: “Twelve weeks of ledipasvir-sofosbuvir plus ribavirin was an effective and safe treatment for patients who have not achieved SVR with earlier regimens that included sofosbuvir.”

Source: Wyles D, et al. Hepatology. 2015;61:1793-7.

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/

Funded by a grant from the Centers for Disease Control and Prevention.

Hepatitis web study