Treatment Experienced

Prior Sofosbuvir Failure

Ledipasvir-Sofosbuvir Retreatment with HCV Genotype 1

NIAID Retreatment

Source: Osinusi A, et al. Ann Intern Med. 2014;161:634-8.

Ledipasvir-Sofosbuvir Retreatment of SOF + RBV Failure in HCV GT 1

NIAID Retreatment Study: Features

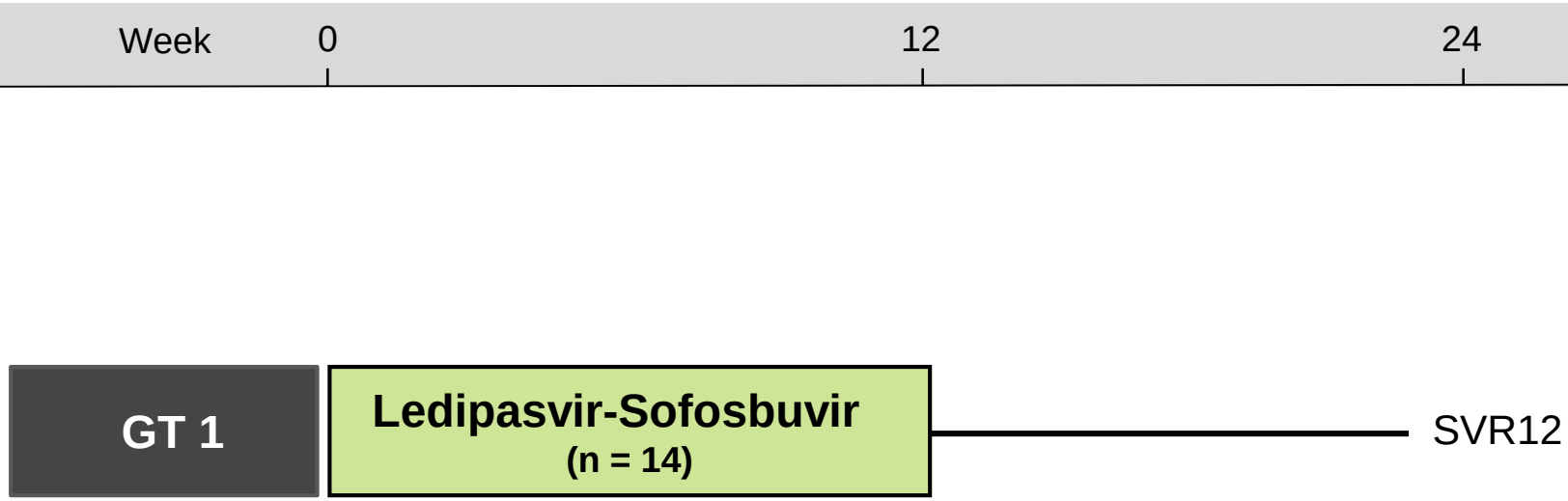
NIAID Retreatment Trial

- **Design**: Open-label, phase 2a, using fixed-dose combination of ledipasvir-sofosbuvir for 12 weeks in patients with GT1 HCV who previously had failed a 24-week treatment course of sofosbuvir plus ribavirin
- **Setting**: single site in United States (NIH and community clinics in DC)
- **Entry Criteria**
  - Chronic HCV genotype 1 (n = 14)
  - Age 18 years or older
  - Prior relapse after a 24-week treatment course of sofosbuvir plus ribavirin
- **Primary End-Point**: SVR12

Source: Osinusi A, et al. Ann Intern Med. 2014;161:634-8.

Ledipasvir-Sofosbuvir Retreatment of SOF + RBV Failure in HCV GT 1

NIAID Retreatment Study: Design



Drug Dosing

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

Source: Osinusi A, et al. Ann Intern Med. 2014;161:634-8.

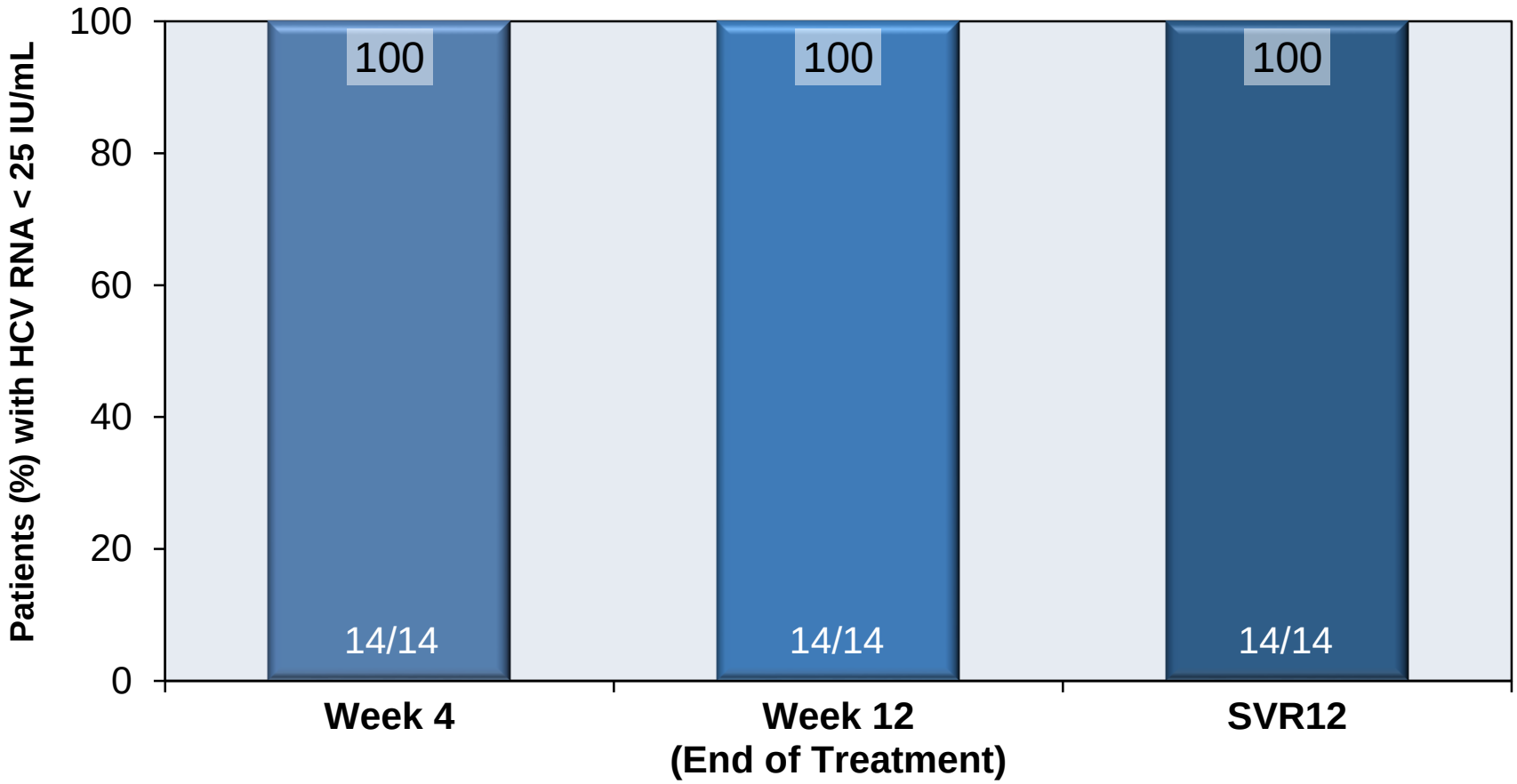
Ledipasvir-Sofosbuvir +/- Ribavirin in Treatment-Experienced HCV GT 1
NIAID Retreatment Study: Baseline Characteristics

Baseline Characteristic	Ledipasvir-Sofosbuvir (n = 14)
Age, median (range)	59 (48-72)
Male, n (%)	13 (93)
Black race, n (%)	13 (93)
Body Mass Index (BMI) ≥30 kg/m^2, n (%)	5 (36)
IL28B genotype CC, n (%)	2 (14)
Knodell Histology Activity Index score, n (%) 0-1 3-4	 7 (50) 7 (50)
HCV GT-1 Subtype 1a 1b	 8 (57) 6 (43)
NS5B S282T Mutation	1 (7)
Median baseline HCV RNA, $\log_{10}$ IU/ml (range)	6.31 (5.50-6.76)

Source: Osinusi A, et al. Ann Intern Med. 2014;161:634-8.

Ledipasvir-Sofosbuvir +/- Ribavirin in Treatment-experienced HCV GT 1
NIAID Retreatment Study: Results

NIAID Retreatment: Virologic Response



Source: Osinusi A, et al. Ann Intern Med. 2014;161:634-8.

Ledipasvir-Sofosbuvir +/- Ribavirin in Treatment-experienced HCV GT 1
NIAID Retreatment Study: Conclusions

Conclusions: “The fixed-dose combination of sofosbuvir plus ledipasvir was efficacious in a small cohort of patients with HCV GT-1 that relapsed after sofosbuvir plus ribavirin therapy, even in the setting of advanced liver disease. Larger studies are needed to confirm these preliminary efficacy results.”

Source: Osinusi A, et al. Ann Intern Med. 2014;161:634-8.