Treatment Naïve (unfavorable baseline treatment characteristics)

Ledipasvir-Sofosbuvir +/- 3rd DAA in HCV Genotype 1

NIAID SYNERGY: Genotype 1

Source: Kohli A, et al. Lancet. 2015:385:1107-13.

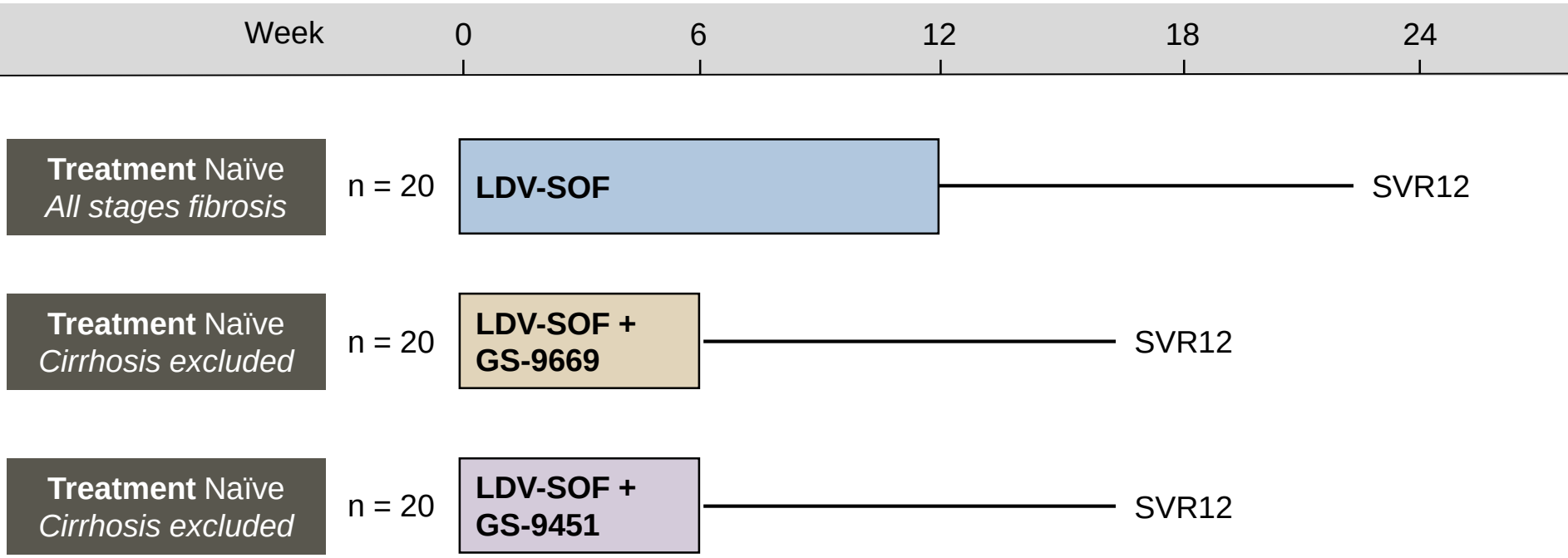
Ledipasvir-Sofosbuvir +/- [GS-9669 or GS-9451] in Naïve GT1
NIAID SYNERGY GT-1 Trial: Features

NIAID SYNERGY Trial

- **Design**: Open-label, phase 2a, using fixed dose ledipasvir-sofosbuvir alone or in combination with either GS-9669 (non-nucleoside NS5B inhibitor) or GS-9451 (NS3/4A protease inhibitor) in treatment-naïve GT 1
- **Setting**: single site, United States
- **Entry Criteria**
  - 18 years of age or older
  - Chronic HCV genotype 1
  - Treatment naive
  - HCV RNA ≥2,000 IU/mL
  - Patients in 6 week group excluded if cirrhotic
- **Primary End-Point**: SVR12

Source: Kohli A, et al. Lancet. 2015:385:1107-13.

Ledipasvir-Sofosbuvir +/- [GS-9669 or GS-9451] in Naïve GT1 NIAID SYNERGY GT-1 Trial: Features



Abbreviations: LDV-SOF= ledipasvir-sofosbuvir

Drug Dosing

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

GS-9669: 500 mg once daily

GS-9451: 80 mg once daily

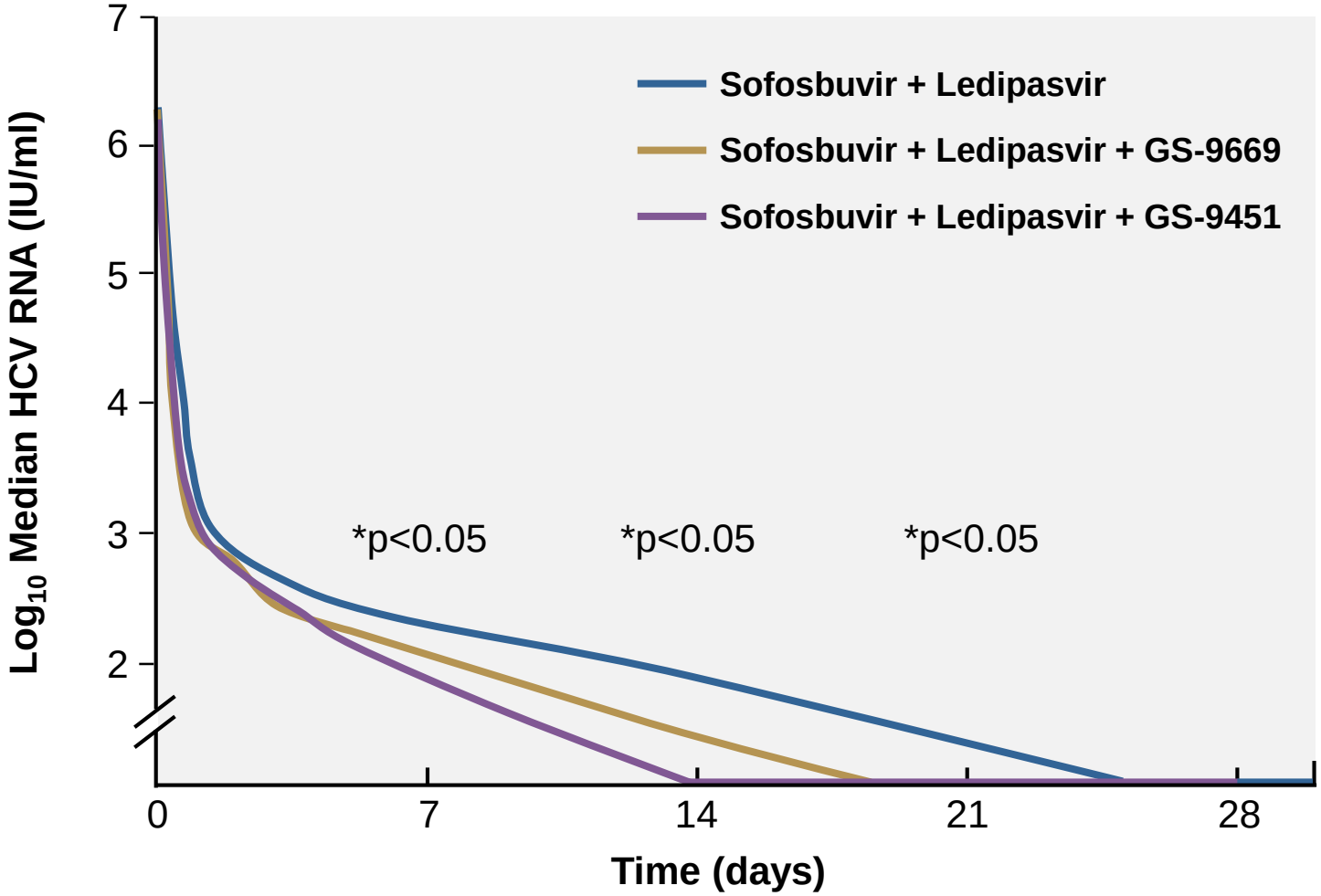
Source: Kohli A, et al. Lancet. 2015:385:1107-13.

Ledipasvir-Sofosbuvir +/- [GS-9669 or GS-9451] in Naïve GT1 NIAID SYNERGY GT-1 Trial: Participants

Baseline Characteristic	LDV-SOF x 12 weeks (n = 20)	LDV-SOF + GS-9669 x 6 weeks (n = 20)	LDV-SOF + GS-9451 x 6 weeks (n = 20)
Age, mean	57	54	54
Male, %	70	65	80
Black, %	80	95	90
White, %	20	5	10
HCV genotype, %			
1A	55	70	85
1B	45	30	15
HCV RNA >800,000 IU/mL, %	75	65	70
IL28B CT/TT, %	75	90	75
Advanced fibrosis, %			
Knodell score 3	25	25	25
Knodell score 4	15	0	0

Source: Kohli A, et al. Lancet. 2015:385:1107-13.

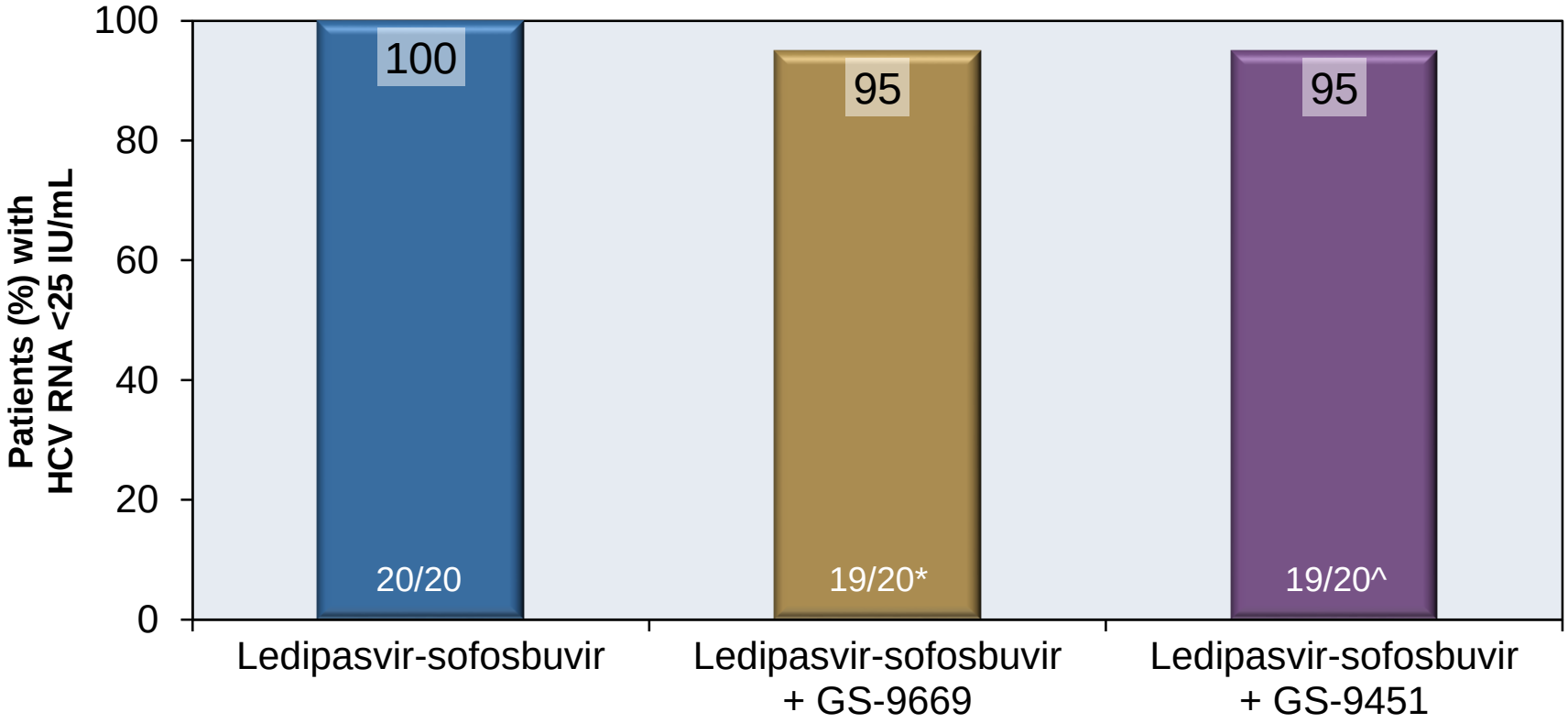
Ledipasvir-Sofosbuvir +/- [GS-9669 or GS-9451] in Naïve GT1
NIAID SYNERGY GT-1 Trial: Viral Kinetics



Source: Kohli A, et al. Lancet. 2015:385:1107-13.

Ledipasvir-Sofosbuvir +/- [GS-9669 or GS-9451] in Naïve GT1 NIAID SYNERGY GT-1 Trial: Results

NIH SYNERGY: SVR 12 by Treatment Regimen



*1 patient relapsed 2 weeks after completion of treatment

^1 patient lost to follow-up after reaching SVR at 4 weeks

Source: Kohli A, et al. Lancet. 2015:385:1107-13.

Ledipasvir-Sofosbuvir +/- [GS-9669 or GS-9451] in Naïve GT1

NIAID SYNERGY GT-1 Trial: Interpretation

Interpretation: “In this small proof-of-concept study, two different three-drug regimens that were given for 6 weeks resulted in high cure rates for HCV infection with excellent tolerability. Addition of a third potent direct-acting antiviral drug can reduce the duration of treatment required to achieve sustained viral response in patients with chronic HCV genotype 1 infection without cirrhosis.”

Source: Kohli A, et al. Lancet. 2015:385:1107-13.