Treatment Naïve and Treatment Experienced

Simeprevir + Sofosbuvir +/- Ribavirin in Genotype 1 COSMOS Trial

Lawitz E, et al. Lancet. 2014;384;1756-65.

Simeprevir + Sofosbuvir +/- Ribavirin for HCV GT 1
COSMOS Trial: Study Features

COSMOS Trial: Features

- **Design**: Randomized, phase 2a, open-label, using sofosbuvir + simeprevir +/- ribavirin in treatment naive or experienced, chronic HCV GT 1
- **Setting**: 23 centers in United States
- **Entry Criteria**
  - Chronic HCV Genotype 1
  - Age ≥18
  - HCV RNA greater than 10,000 IU/mL
  - Cohort 1: prior nonresponders; Metavir F0-F2
  - Cohort 2: treatment naïve & prior nonresponders; Metavir F3-F4
- **Patient Characteristics (range in different treatment arms)**
  - N = 167 (n = 80 in Cohort 1 and n = 87 in Cohort 2)
  - Baseline GT1a with Q80K: Cohort 1 = 50%; Cohort 2 = 40%
  - Non-CC IL28b Genotype: Cohort 1 = 94%; Cohort 2 = 79%
- **End-Points**: Primary = SVR12

Source: Lawitz E, et al. Lancet. 2014;384;1756-65.

Simeprevir + Sofosbuvir +/- Ribavirin for HCV GT 1
COSMOS Trial: Baseline Characteristic

Baseline Characteristic (n = 167)	Cohorts 1 and 2
Median Age, years (range)	57 (27-70)
Male, %	64
White, %	81
Median Body Mass Index (BMI)	28
HCV genotype	1a= 78%; 1b = 22%
IL28B non-CC genotype, (%)	86%
Mean baseline HCV RNA, $\log_{10}$ IU/ml	6.6
Metavir Score	F01= 20%; F2=28%; F3 = 28%; F4=25%
Previous HCV treatment No response (%) Treatment-naïve (%)	 76% 24%

Source: Lawitz E, et al. Lancet. 2014;384;1756-65.

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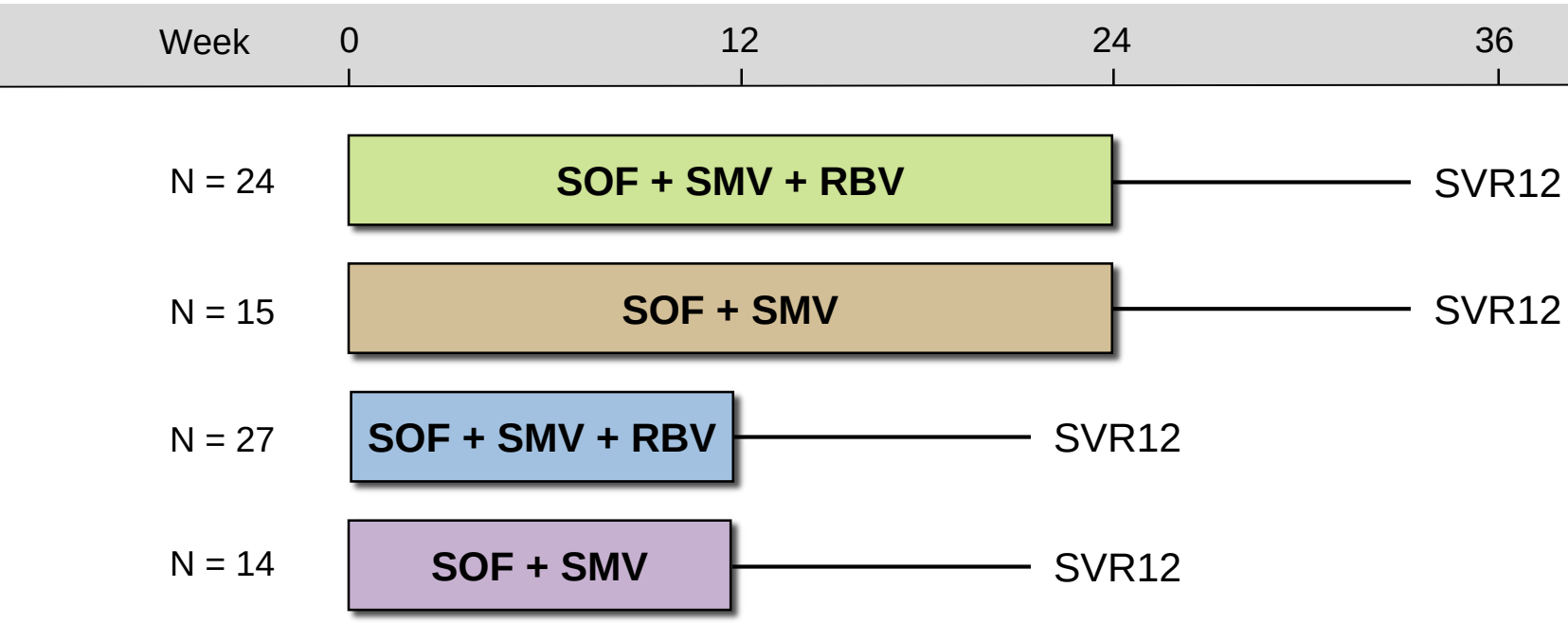
Simeprevir + Sofosbuvir +/- Ribavirin for HCV GT 1
COSMOS Trial: Design for Cohort 1

Cohort 1: Prior Nonresponders; Metavir Scores F0-F2



Drug Dosing

SOF= Sofosbuvir: 400 mg once daily

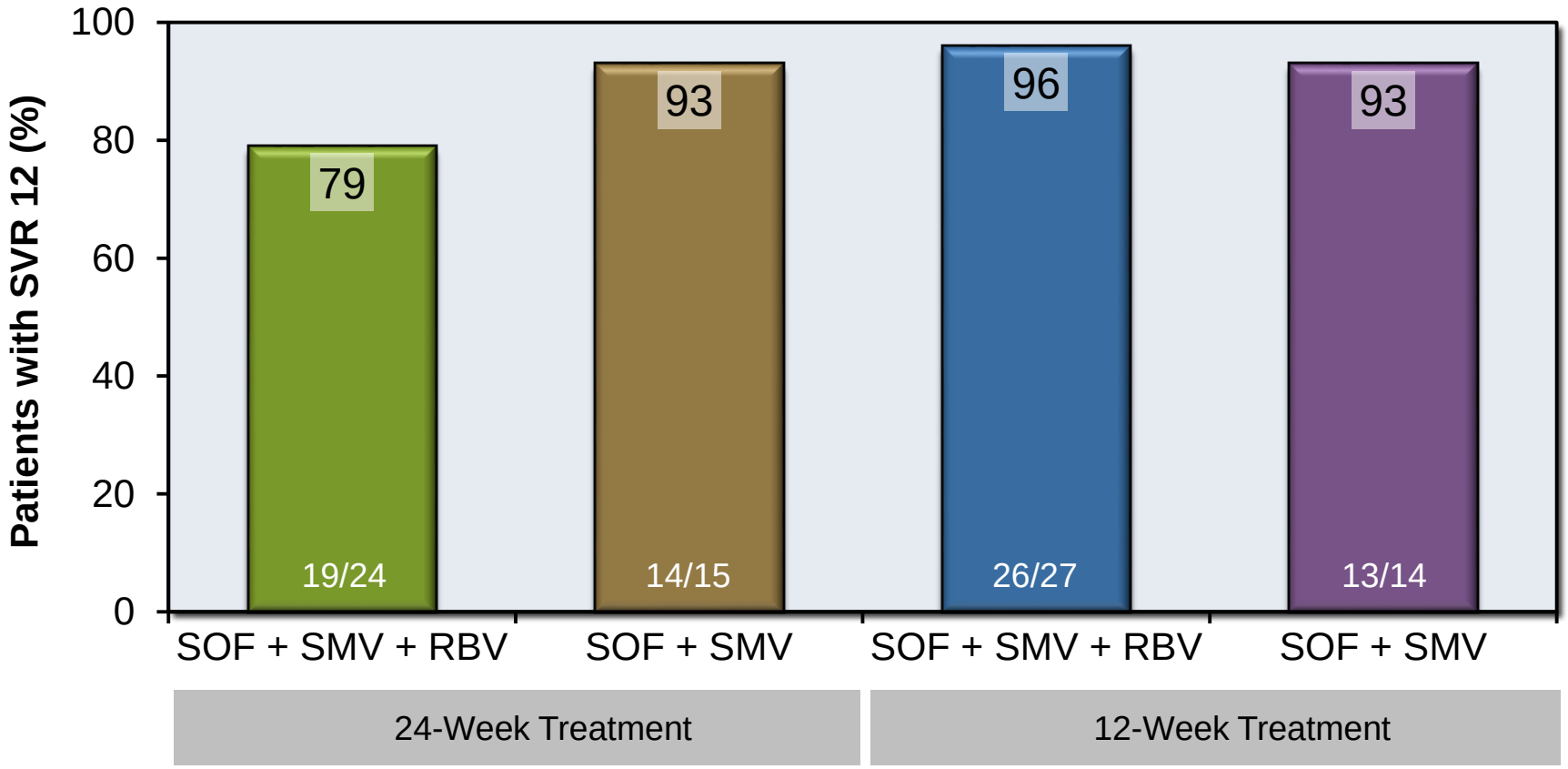
SMP =Simeprevir: 150 mg once daily

RBV = Ribavirin (weight-based and divided bid): 1000 mg/day if < 75 kg or 1200 mg/day if ≥ 75 kg

Source: Lawitz E, et al. Lancet. 2014;384;1756-65.

Simeprevir + Sofosbuvir +/- Ribavirin for HCV GT 1
COSMOS Trial: Results for Cohort 1

COSMOS (Cohort 1): SVR 12 by Regimen

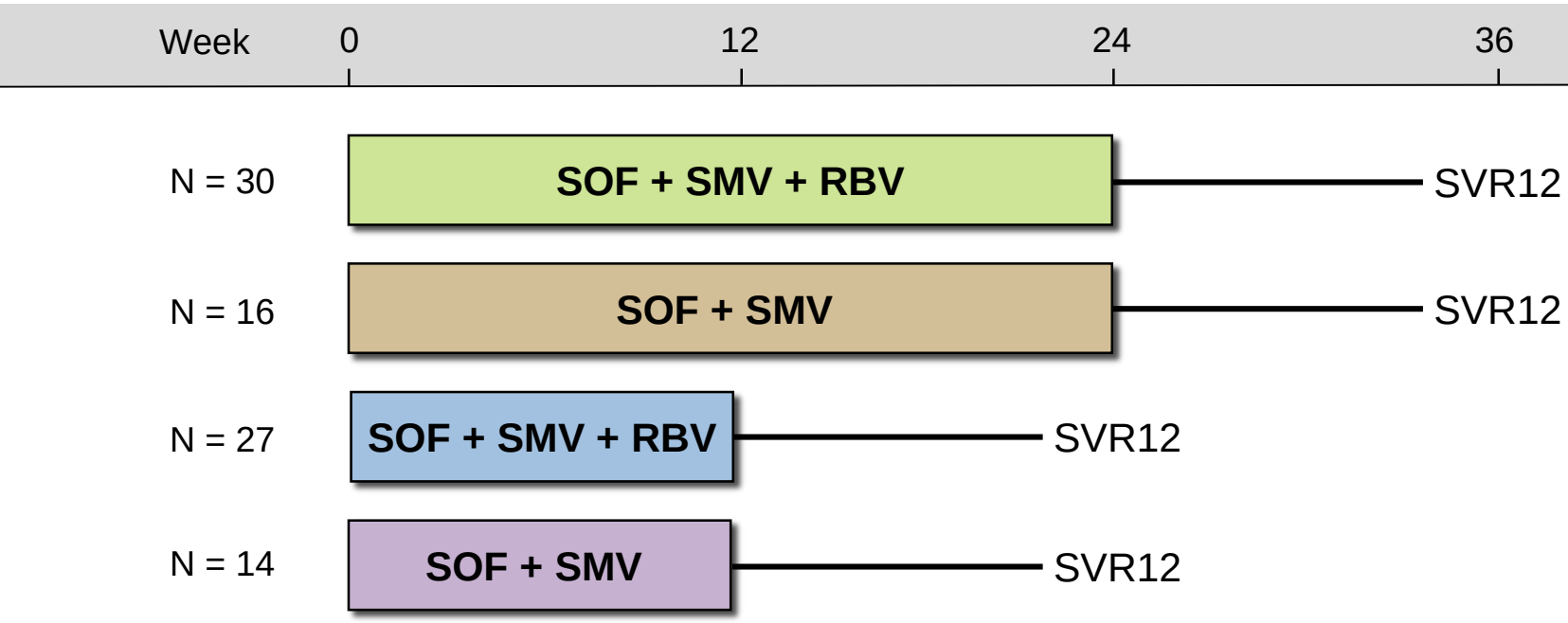


SOF = sofosbuvir; SMV = simeprevir; RBV = ribavirin

Source: Lawitz E, et al. Lancet. 2014;384;1756-65.

Simeprevir + Sofosbuvir +/- Ribavirin for HCV GT 1
COSMOS Trial: Design for Cohort 2

Cohort 2: Treatment Naïve & Prior Nonresponders; Metavir Scores F3-F4



Drug Dosing

Sofosbuvir: 400 mg once daily

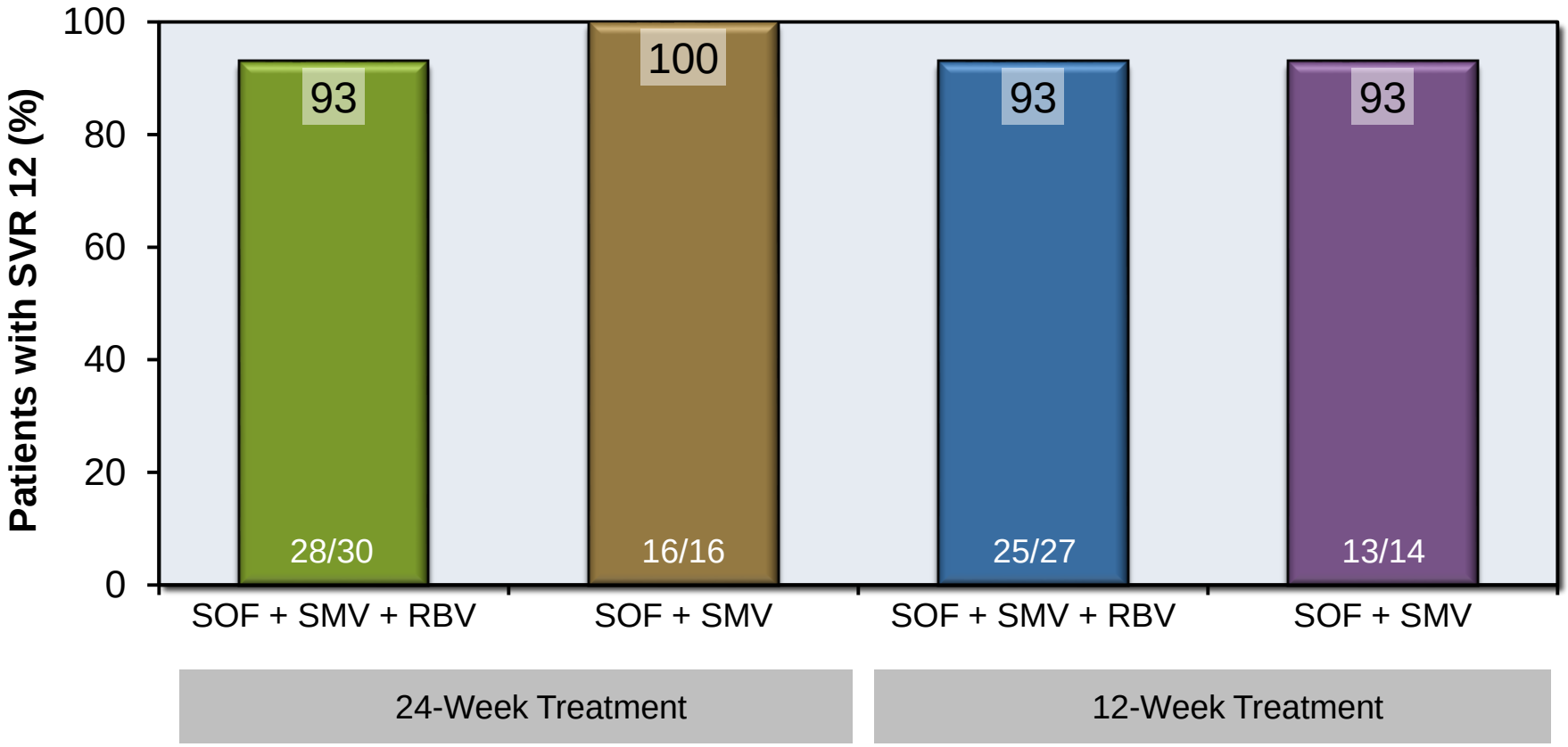
Simeprevir: 150 mg once daily

Ribavirin (weight-based and divided bid): 1000 mg/day if < 75 kg or 1200 mg/day if ≥ 75 kg

Source: Lawitz E, et al. Lancet. 2014;384;1756-65.

Simeprevir + Sofosbuvir +/- Ribavirin for HCV GT 1
COSMOS Trial: Results

COSMOS (Cohort 2 with F3-F4 Fibrosis): SVR12 by Regimen



SOF = sofosbuvir; SMV = simeprevir; RBV = ribavirin

Source: Lawitz E, et al. Lancet. 2014;384;1756-65.

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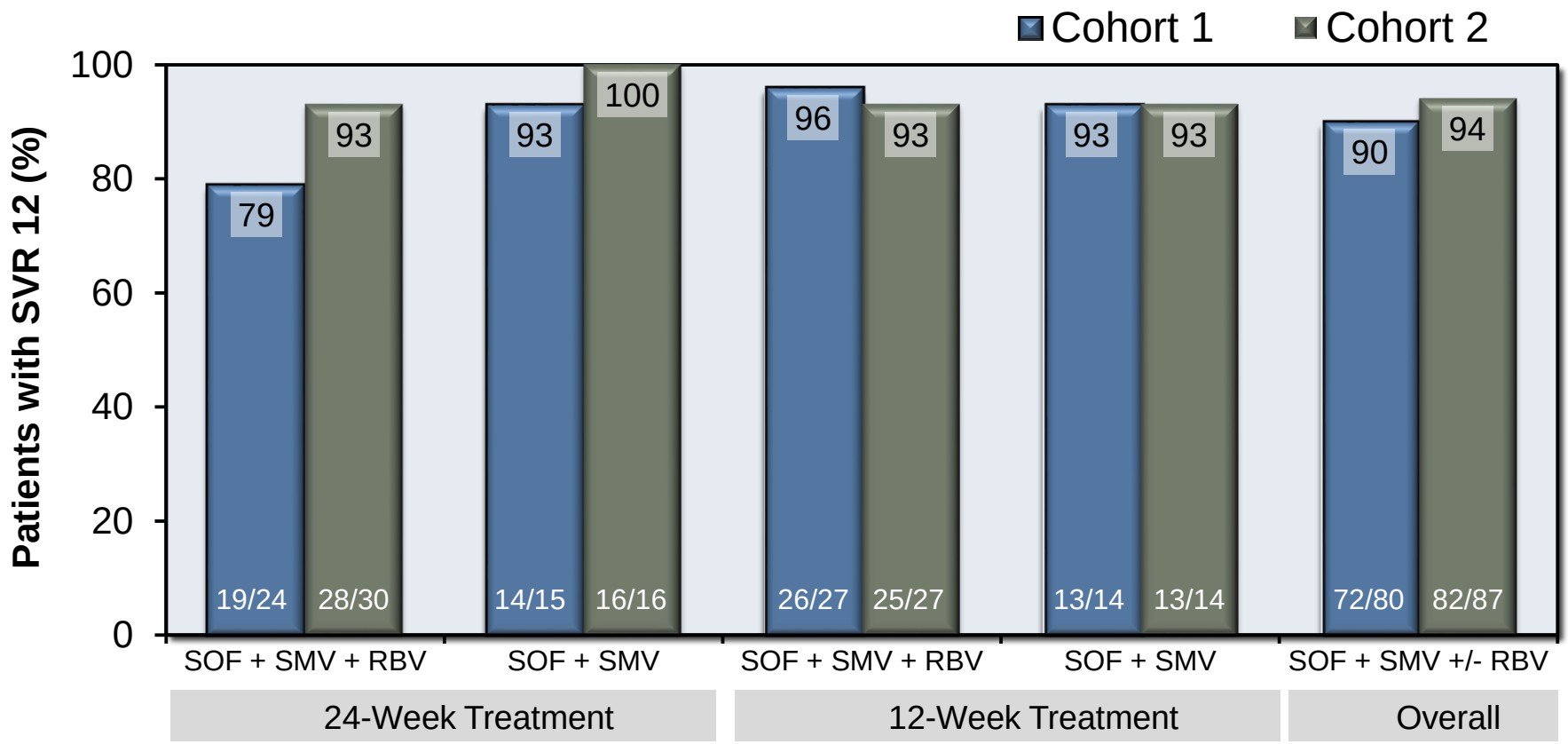
Simeprevir + Sofosbuvir +/- Ribavirin for HCV GT 1
COSMOS Trial: Results for Cohort 1 & 2

Cohort 1 & 2: SVR12



Source: Lawitz E, et al. Lancet. 2014;384;1756-65.

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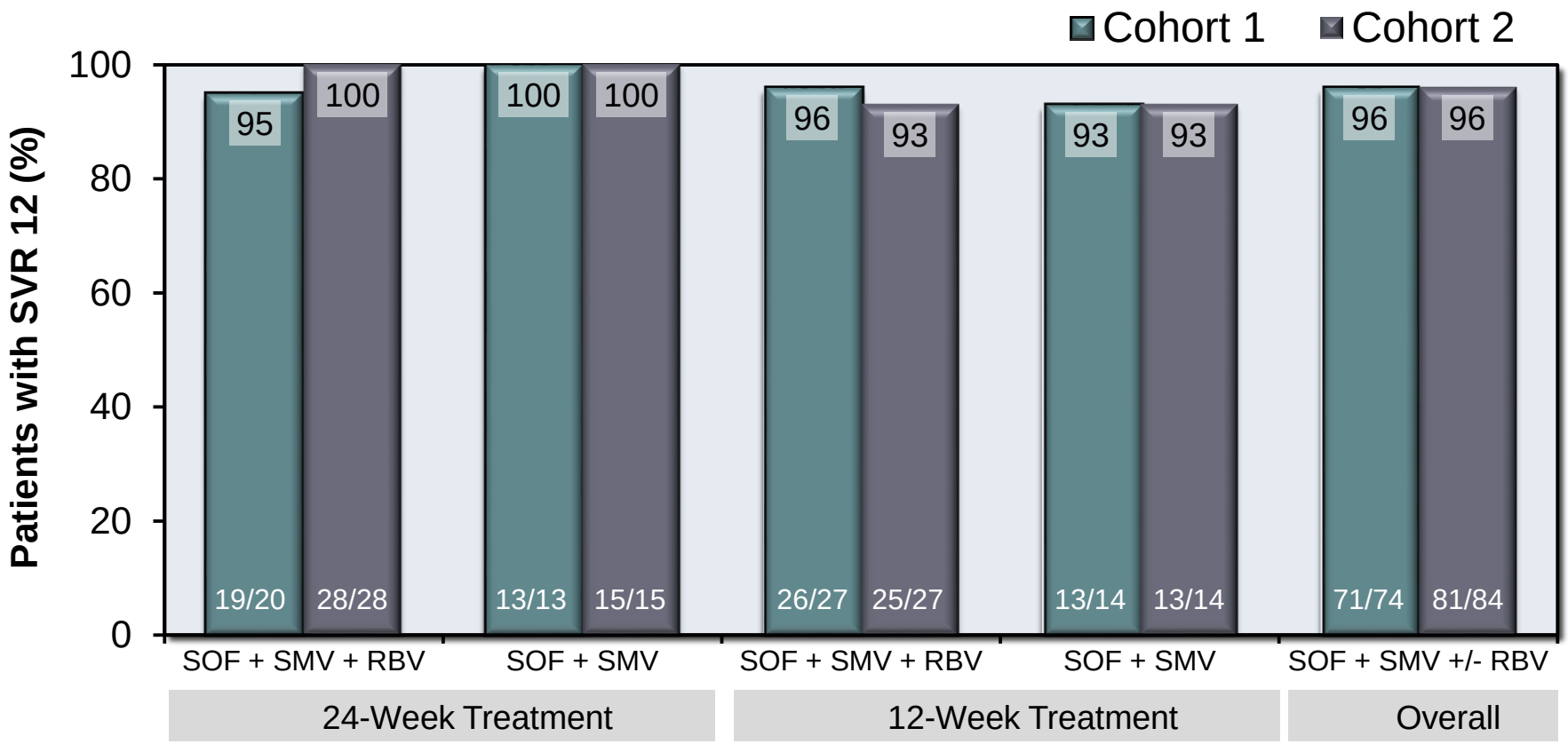
Simeprevir + Sofosbuvir +/- Ribavirin for HCV GT 1
COSMOS Trial: Results for Cohort 1 & 2

Cohort 1 & 2: SVR12 (Non-VR excluded analysis*)



*Non-VR excluded analysis = SVR12 excludes early discontinuation due to non-virologic reasons or missing data at SVR12 time point

Source: Lawitz E, et al. Lancet. 2014;384;1756-65.

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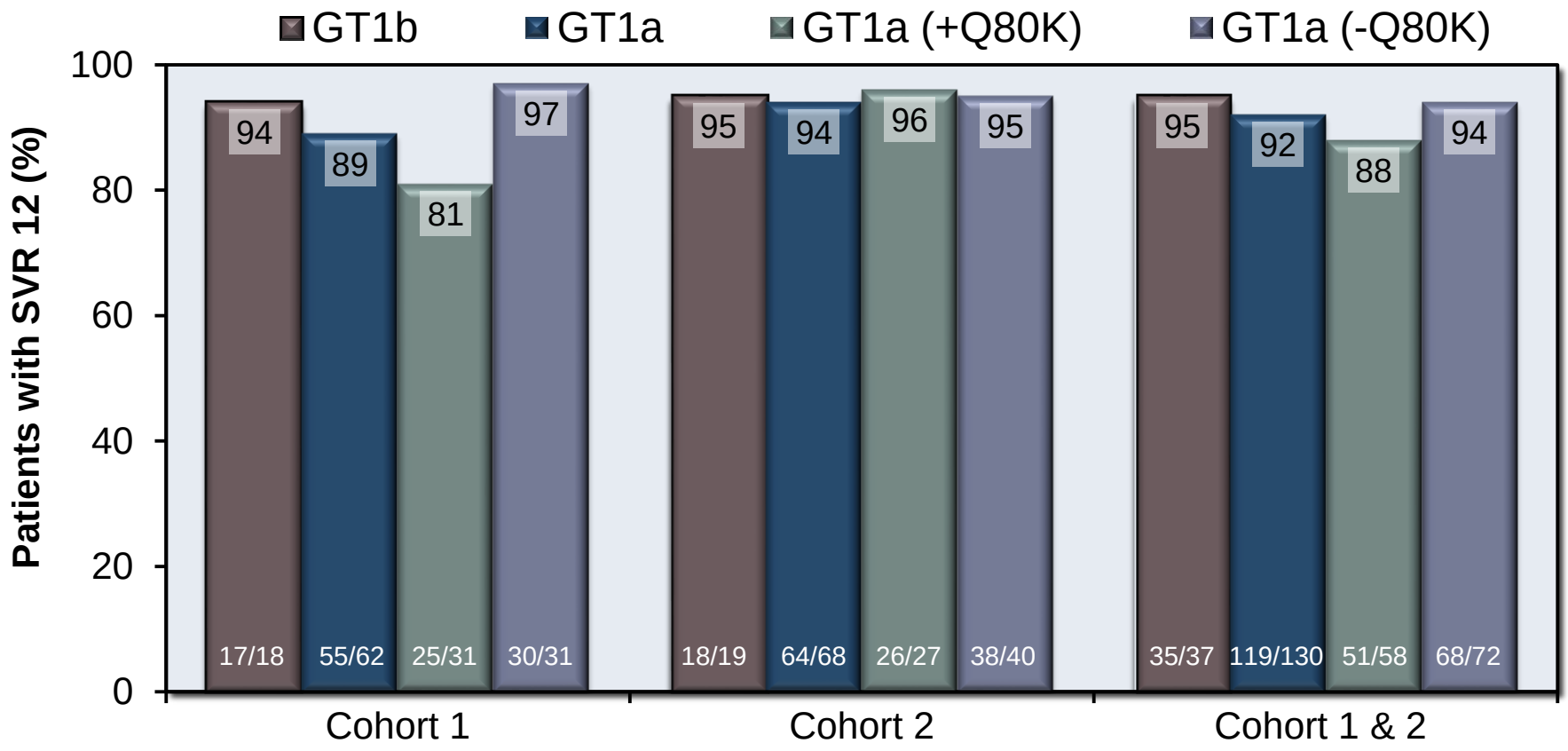
Simeprevir + Sofosbuvir +/- Ribavirin for HCV GT 1
COSMOS Trial: Results for Cohort 1 & 2

Impact of Q80K on SVR in Patients with GT1



*Q80K = Gln80Lys

Source: Lawitz E, et al. Lancet. 2014;384;1756-65.

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Simeprevir + Sofosbuvir +/- Ribavirin for HCV GT 1
COSMOS Trial: Interpretation

Interpretation: “Combined simeprevir and sofosbuvir was efficacious and well tolerated.”

Source: Lawitz E, et al. Lancet. 2014;384;1756-65.

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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/

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