Ombitasvir-Paritaprevir-Ritonavir + Dasabuvir + RBV in GT1

TURQUOISE-I

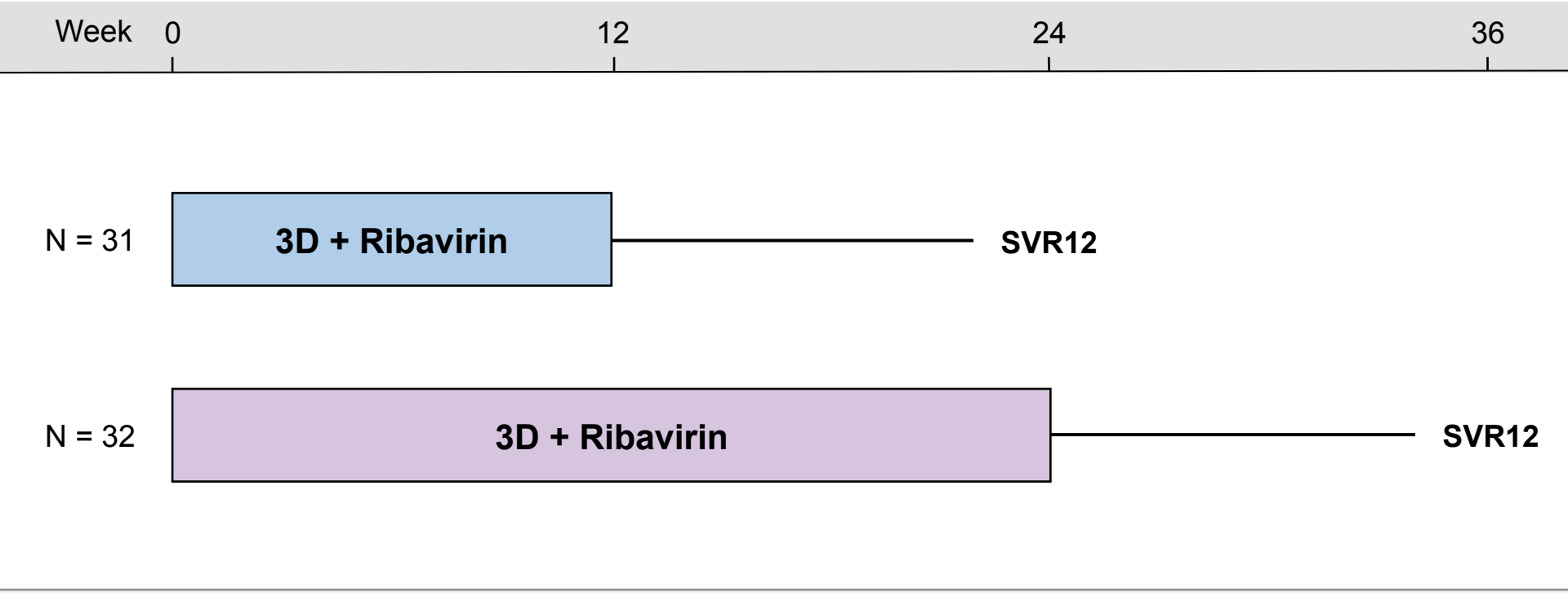
3D + Ribavirin for HCV-HIV Coinfection and GT1
TURQUOISE-I: Part 1a Study Design

TURQUOISE-I: Features

- **Design**: Multipart, phase 2/3, randomized, open-label trial evaluating safety and efficacy of 3D (ombitasvir-paritaprevir-ritonavir and dasabuvir) plus ribavirin for 12 or 24 weeks in treatment-naïve and experienced patients with chronic HCV GT 1 and HIV coinfection, including patients with cirrhosis
- **Setting:** Multicenter study in United States and Puerto Rico
- **Entry Criteria**
  - Chronic HCV infection with genotype 1 and HIV coinfection
  - Treatment-naïve or previously treated with peginterferon + ribavirin
  - Age 18-70
  - Plasma HCV RNA greater than 10,000 IU/mL
  - Child-Pugh A cirrhosis permitted
  - CD4 count ≥200 cells/mm^3 (or CD4% ≥14) and HIV RNA level <40 copies/ml
  - Receiving atazanavir- or raltegravir-based regimen
- **Primary End-Point**: SVR12

Source: Sulkowski MS, et al. JAMA. 2015:313:1223-31.

3D + Ribavirin for HCV-HIV Coinfection and GT1
TURQUOISE-I: Part 1a Study Regimens



3D = Ombitasvir-Paritaprevir-Ritonavir and Dasabuvir

Drug Dosing

Ombitasvir-Paritaprevir-Ritonavir (25/150/100 mg once daily) and Dasabuvir: 250 mg twice daily

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

Source: Sulkowski MS, et al. JAMA. 2015:313:1223-31.

3D + Ribavirin for HCV-HIV Coinfection and GT 1
TURQUOISE-I: Patient Population

Baseline Characteristic	12-Week Arm (n=31)	24-Week Arm (n=32)
Age (years), Mean	50.9	50.9
Male sex %	94	91
Black Race (%)	23	25
Cirrhosis (%)	19	19
HCV genotype (%) 1a 1b	 87 13	 91 9
HCV RNA, $\log_{10}$ IU/ml (mean)	6.54	6.60
IL28B non-CC genotype, (%)	84	78
Previous Response to PEG + RBV Naïve Relapse Partial response Null response	 65 3 16 16	 69 9 6 16
CD4 Count, cells/mm^3 (mean)	633	625

Source: Sulkowski MS, et al. JAMA. 2015:313:1223-31.

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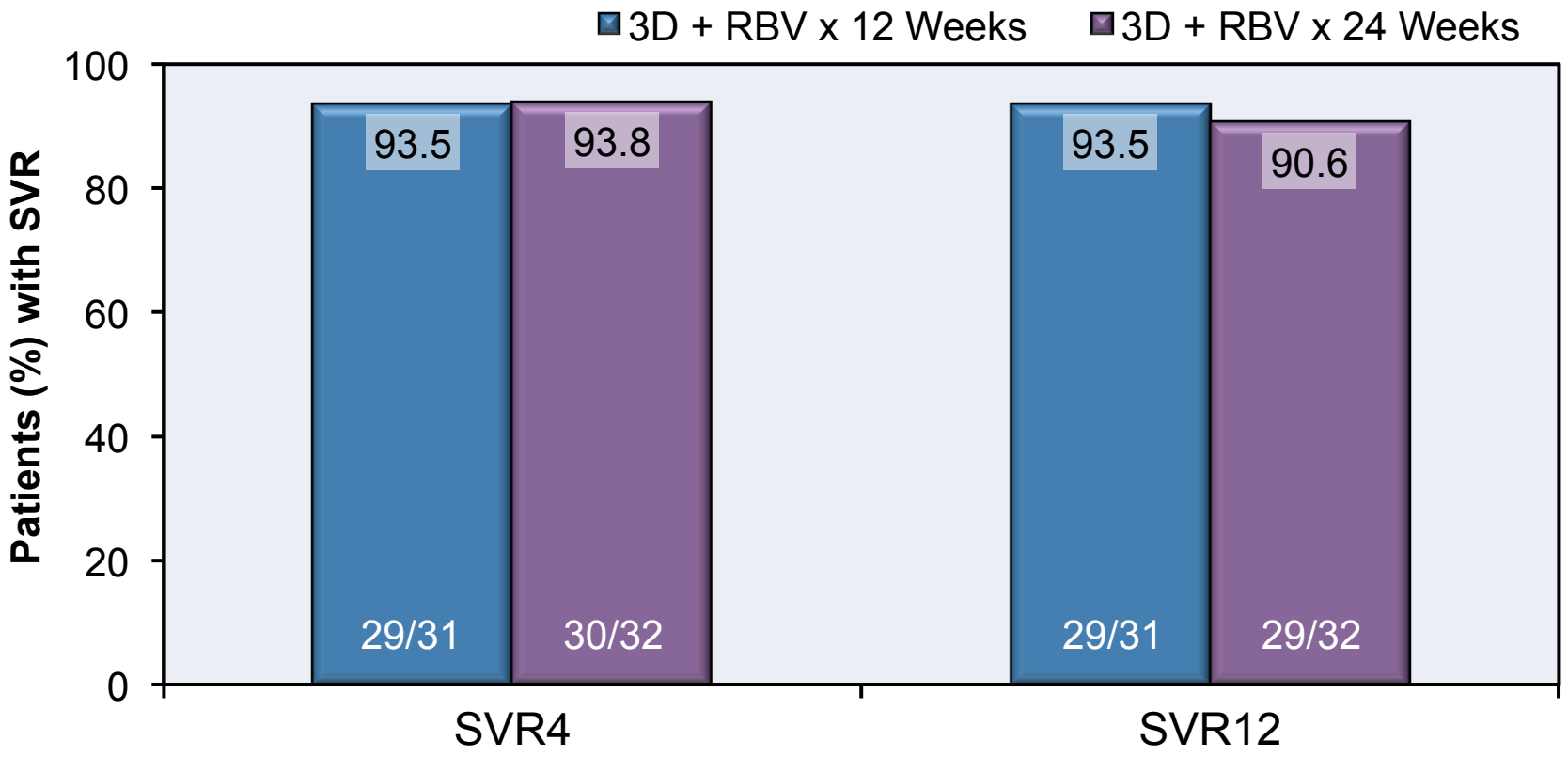
3D + Ribavirin for HCV-HIV Coinfection and GT 1
TURQUOISE-I: Part 1a Results

TURQUOISE-I: SVR Rates (to date)



3D = Ombitasvir-Paritaprevir-Ritonavir and Dasabuvir; **RBV** = Ribavirin

Source: Sulkowski MS, et al. JAMA. 2015:313:1223-31.

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3D + Ribavirin for HCV-HIV Coinfection and GT 1
TURQUOISE-I: Part 1a Results

Details of Five Patients NOT Achieving SVR 12

- One patient in 12-week arm withdrew consent prior to finishing treatment; had undetectable HCV RNA at week 10
- One patient in 12-week arm had virologic relapse at week 4 post treatment; had new resistant HCV variants at 3 viral targets (D168V in NS3/4A, M28T in NS5A, and S556G in NS5B)
- One patient in 24-week arm had virologic breakthrough during treatment; had new resistant HCV variants at 3 viral targets (R155K in NS3/4A, Q30R in NS5A, and S556G in NS5B)
- Two patients in 24-week arm achieved early SVR but appeared to be reinfected with GT1a isolate distinct from baseline HCV isolate; both patients had engaged in high-risk sexual activity post treatment

Source: Sulkowski MS, et al. JAMA. 2015:313:1223-31.

3D + Ribavirin for HCV-HIV Coinfection and GT 1
TURQUOISE-I: Part 1a Conclusions and Relevance

Conclusions and Relevance: “In this open-label, randomized uncontrolled study, treatment with the all-oral, interferon-free 3D-plus-ribavirin regimen resulted in high SVR rates among patients co-infected with HCV genotype 1 and HIV-1 whether treated for 12 or 24 weeks. Further phase 3 studies of this regimen are warranted in patients with co-infection.”

Source: Sulkowski MS, et al. JAMA. 2015:313:1223-31.

Acknowledgment

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