

Improvement of sustained virologic response (SVR) in the treatment of chronic hepatitis C genotype 1 with PEG-IFN alfa-2b by ribavirin dose adjustments: evidence obtained from the German PEG-IFN alfa-2b observational study

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1. Background

- ▶ Treatment options for hepatitis C have developed rapidly in the past decade.
- ▶ A combination of pegylated interferon-alfa (PEG-IFN-alfa) plus ribavirin (RBV) is the current standard of care for treatment of chronic hepatitis C.
- ▶ The EMEA approved weight-based dosing of PEG-IFN alfa-2b (PegIntron®) 1.5 µg/kg/week and ribavirin (REBETOL®) 800–1,200 mg/day on March 26, 2001.

2. Objectives

- ▶ Recently two peginterferon regimens (weight-based PEG-IFN alfa-2b and fixed-dose PEG-IFN alfa-2a) and ribavirin (RBV) approved for HCV treatment were compared in the IDEAL study.
- ▶ While overall SVR rates of patients infected with G1 were similar in both regimens, a 10% difference was observed for patients weighing 75–85 kg.
- ▶ The latter were treated either with PEG-IFN alfa-2b (1.5 µg/kg/wk) plus 1,000 mg RBV/d or with PEG-IFN alfa-2a (180 µg/wk) plus 1,200 mg RBV/d suggesting RBV under dosage in the PEG 2b regimen.
- ▶ Therefore the SVR rates of G1 patients treated in the German PEG-IFN alfa-2b/ribavirin observational cohort study within different body weight classes were re-evaluated.

3. Methods

- ▶ Between 9/2003 and 5/2007, 279 sites enrolled a total of 4061 patients.
- ▶ For the treatment of G1 patients PEG-IFN alfa-2b 1.5 µg/kg/wk plus weight-based RBV (800–1,200 mg/day) for up to 48 wks was recommended.
- ▶ Due to the character of this study, physicians treated patients with PEG-IFN alfa-2b and RBV according to their discretion.

4. Study Design

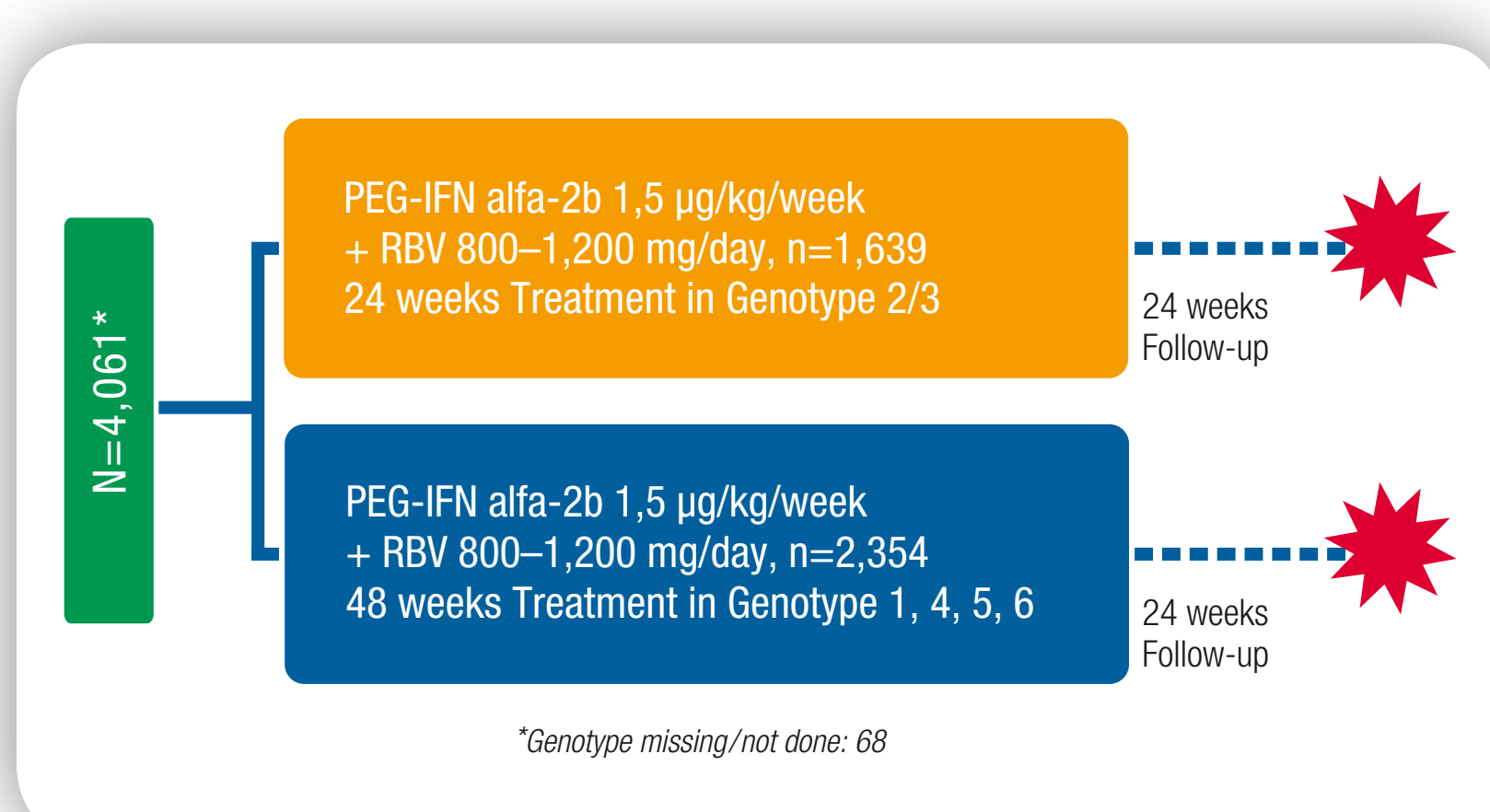


Figure 1. Study Design.

5. Patient Characteristics

	Patients with G1 Infection
Patients - no.	1,387
Age - yr	43.4 ± 12.6
Male - no. (%)	757 / 1,387 (54.6)
Female - no. (%)	606 / 1,387 (43.7)
Weight - kg	73.6 ± 12.8
BMI	24.8 ± 3.6
HCV RNA	
≥ 600,000 IU/ml - no. (%)	725 / 1,387 (52.3)
< 600,000 IU/ml - no. (%)	622 / 1,387 (44.8)
Hemoglobin - mg/dl	14.3 ± 1.9
Platelet count - n/ul	227,134 ± 72,294

Table 1. Patient characteristics of treatment-naïve G1 patients. (Statistical Testing: χ^2 -Test)

6. Results

- ▶ Data of 1,387 treatment-naïve patients with G1 infection and without HIV-coinfection were analysed.
- ▶ 287 patients weighing 40–65 kg received the recommended RBV dose of 800 mg/d while 136 patients were treated with 1,000 mg/d. SVR was not enhanced by the higher RBV dose (see Table 2 and Figure 2).
- ▶ A trend towards higher SVR rates was obtained for patients weighing > 65–< 75 kg of whom 278 patients received the recommended RBV dose of 1,000 mg/d and 28 patients were treated with 1,200 mg/d (Figure 3).
- ▶ A small decline in SVR rates was observed in the 75–85 kg group, most prominently in the 80–85 kg subgroup treated with the approved RBV dose (38.3%) in contrast to 54.0% of patients treated with 1,200 mg RBV/d (Figure 4).
- ▶ SVR rates decreased within the > 85–105 kg group with lower SVR rates in patients weighing > 95–105 kg, possibly due to RBV underdosage (Figure 5).

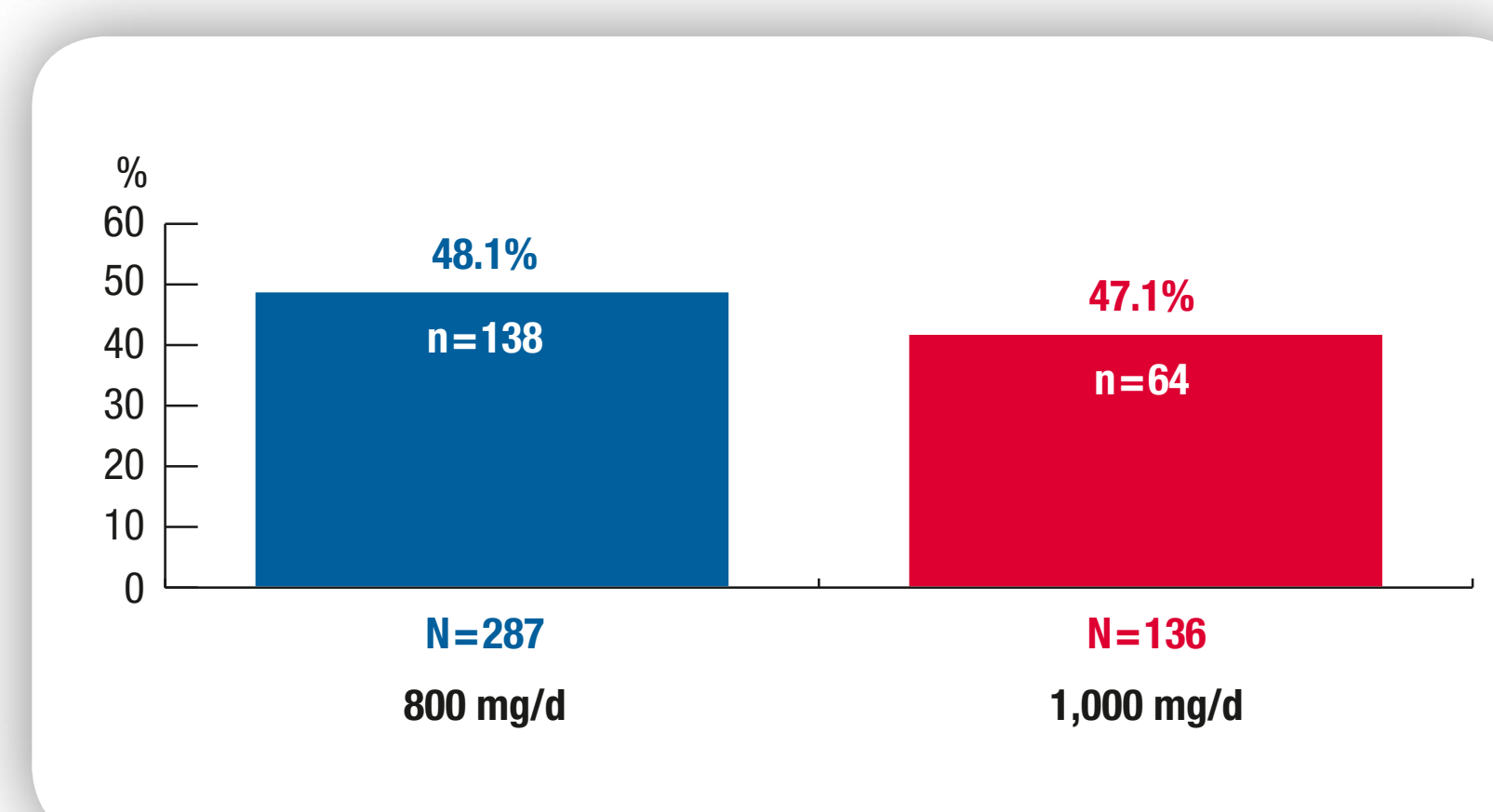


Figure 2. SVR (%) by RBV dose for patients with body weight 40–65 kg (recommended RBV dose: 800 mg/d).

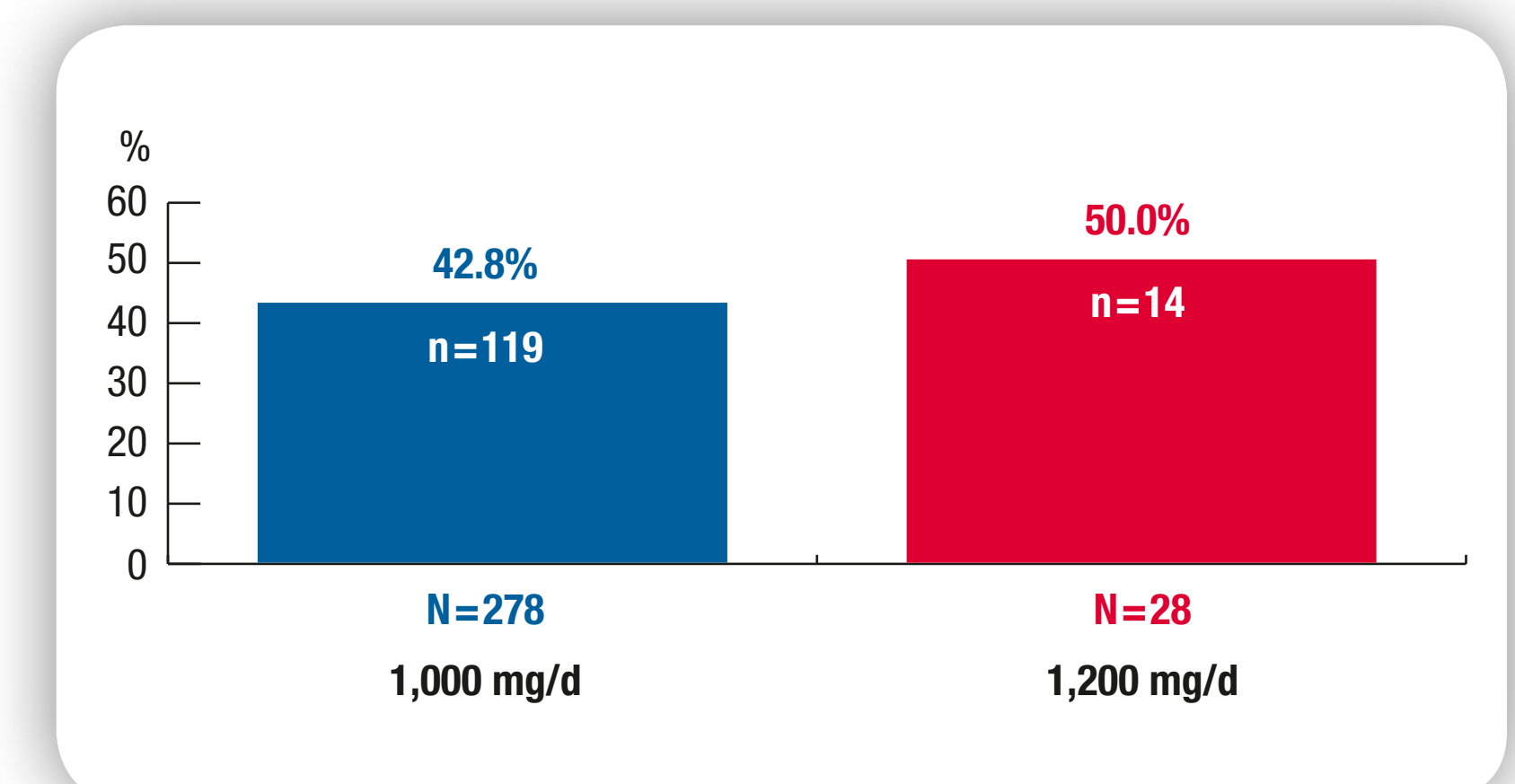


Figure 3. SVR (%) by RBV dose or patients with body weight > 65–< 75 kg (recommended RBV dose: 1,000 mg/d).

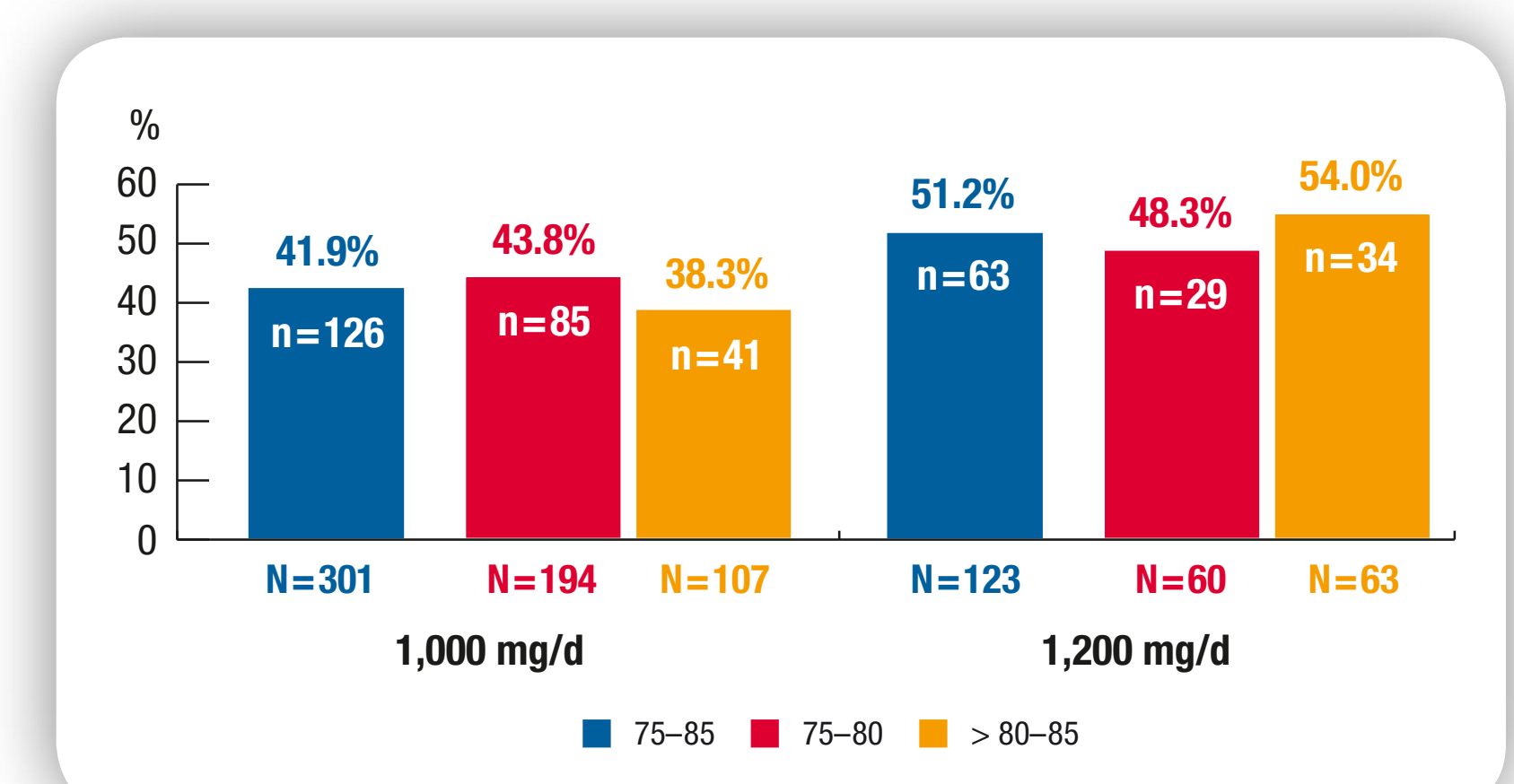


Figure 4. SVR (%) by RBV dose or patients with body weight 75–85 kg (recommended RBV dose: 1,000 mg/d).

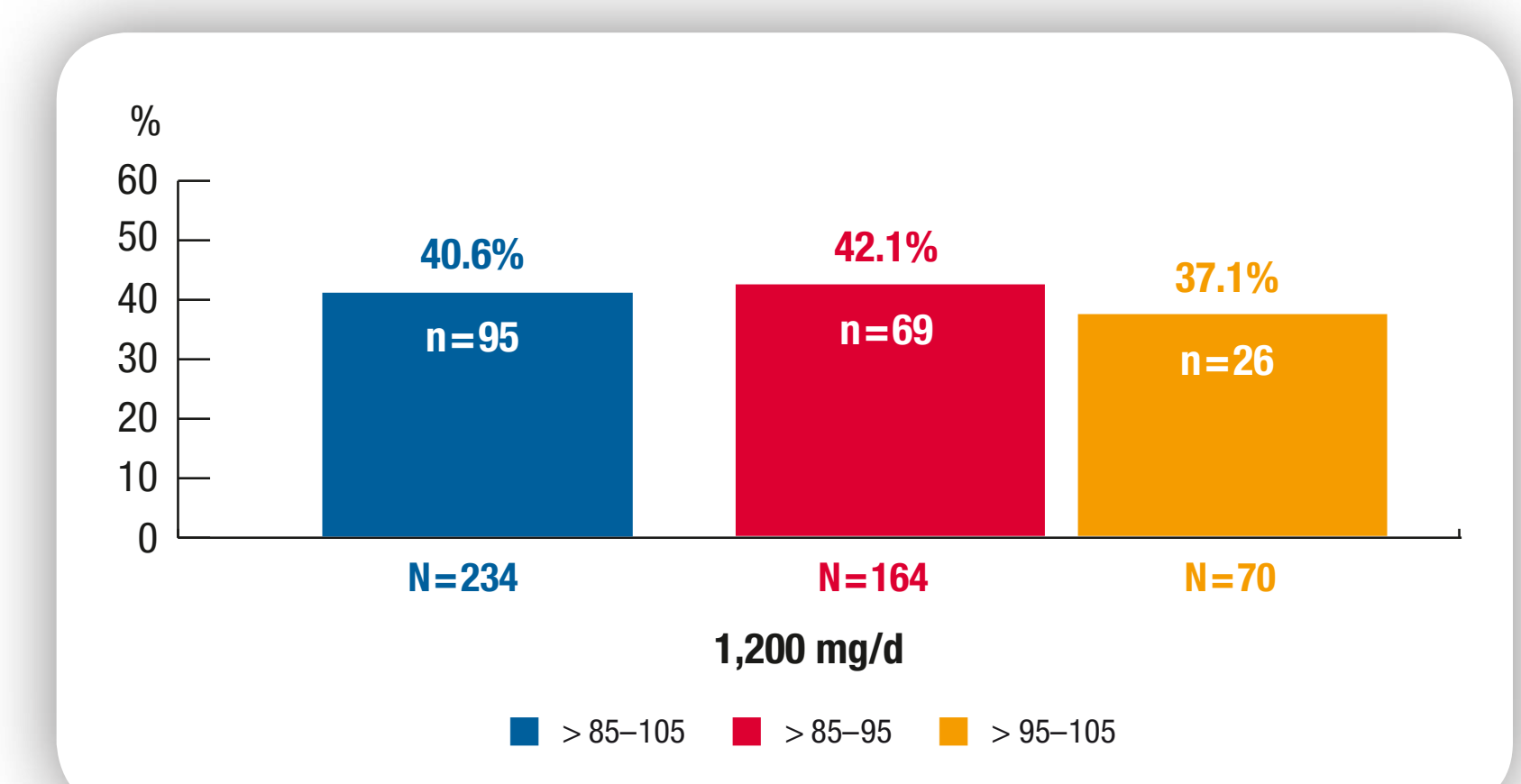


Figure 5. SVR (%) by RBV dose for patients with body weight > 85–105 kg (recommended RBV dose: 1,200 mg/d).

Body Weight (kg)	RBV dose recommended (mg/d)	SVR (%) by RBV dose received			P Value
		800 mg/d	1,000 mg/d	1,200 mg/d	
40–65	800	48.1% (138/287)	47.1% (64/136)		p=0.8438
> 65–< 75	1,000		42.8% (119/278)	50.0% (14/28)	p=0.4642
75–85	1,000		41.9% (126/301)	51.2% (63/123)	p=0.0785
• 75–80			43.8% (85/194)	48.3% (29/60)	p=0.5385
• > 80–85			38.3% (41/107)	54.0% (34/63)	p=0.0472
> 85–105	1,200			40.6% (95/234)	
• > 85–95				42.1% (69/164)	
• > 95–105				37.1% (26/70)	

Table 2. SVR by RBV dose and body weight. (Statistical Testing: χ^2 -Test)

7. Conclusions

- ▶ This study clearly demonstrates that SVR rates of G1 patients weighing 40–75 kg cannot be further improved by increasing the recommended RBV dose.
- ▶ Our results suggest that RBV dose adjustments for the treatment of G1-infected patients weighing 80–85 kg and 95–105 kg may be needed.