

Pegylated Interferon alfa-2b Plus Ribavirin in Patients With Genotype 1 Chronic Hepatitis C With a Slow Virologic Response: A Preliminary Report of the SUCCESS Study

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Background

- Pegylated interferon (PEG-IFN) alfa plus ribavirin is standard treatment for patients with chronic hepatitis C, and the duration of treatment varies according to hepatitis C virus (HCV) genotype (G1, 48 weeks; G2/3, 24 weeks).
- Despite a longer duration of therapy, G1 patients have lower sustained virologic response (SVR) rates than G2/3 patients.^{1,3}
- Patients who have an early virologic response (EVR; $\geq 2 \log_{10}$ reduction in HCV RNA levels or undetectable HCV RNA at week 12) have a higher likelihood of attaining an SVR than those with a $< 2 \log_{10}$ reduction in HCV RNA levels at week 12.^{4,6}
- Extending duration of therapy from 48 weeks to 72 weeks has been shown to significantly increase SVR rates and reduce relapse rates in G1 patients who have detectable HCV RNA at week 12 (29% vs 17%, $P = .04$).⁷
 - Although these data are encouraging, more than 70% of G1 patients who have detectable HCV RNA at week 12 and receive 72 weeks of treatment still do not achieve a successful treatment outcome.⁷
- To improve treatment outcomes in G1 patients, we are seeking to better identify or predict those who will most likely benefit from 72 weeks of antiviral therapy.
- The Study to Assess Treatment with PegIntron® and Rebetol® in Treatment-Naive Patients with Genotype 1 Chronic hepatitis C and Slow Virologic rESponse (SUCCESS) was designed to compare virologic response after 48 and 72 weeks' treatment with PEG-IFN alfa-2b (PegIntron®) plus ribavirin in patients with G1 chronic hepatitis C who had a $\geq 2 \log_{10}$ reduction in HCV RNA levels at week 12 and undetectable HCV RNA at week 24.

Aim

- This preliminary report of the SUCCESS study evaluates response in G1 patients, including those with a $\geq 2 \log_{10}$ reduction in HCV RNA levels at week 12 and undetectable HCV RNA at week 24 ("slow responders").

Methods

Study Design

- This was an open-label, multicenter study conducted at 133 centers in Europe, Canada, and Israel.

Patients

- Treatment-naive patients 18 to 70 years of age were eligible for study participation if they had liver biopsy-confirmed G1 chronic hepatitis C and compensated liver disease.
- Exclusion criteria included pregnancy/lactation, coinfection with HIV or hepatitis B virus, and any cause of liver disease other than chronic hepatitis C.

Treatment

- All patients received PEG-IFN alfa-2b 1.5 $\mu\text{g}/\text{kg}/\text{wk}$ plus ribavirin 800-1400 mg/d (Figure 1; Table 1).
- At week 12, treatment was stopped in patients who had detectable HCV RNA but a $< 2 \log_{10}$ decrease in HCV RNA from baseline.
- Patients who had undetectable HCV RNA (< 100 copies/mL; ≤ 29 IU/mL) at week 12 continued treatment for an additional 36 weeks.
- Patients who had detectable HCV RNA at week 12 and had a $\geq 2 \log_{10}$ decrease in HCV RNA from baseline received treatment for an additional 12 weeks.
 - Treatment was stopped in patients who had detectable HCV RNA after 24 weeks of therapy.
 - Patients who had undetectable HCV RNA after 24 weeks of therapy were randomly assigned to an additional 24 or 48 weeks of treatment (total duration of treatment of 48 weeks and 72 weeks, respectively).
- Patients will be followed up for 24 weeks after treatment cessation to determine SVR rates.

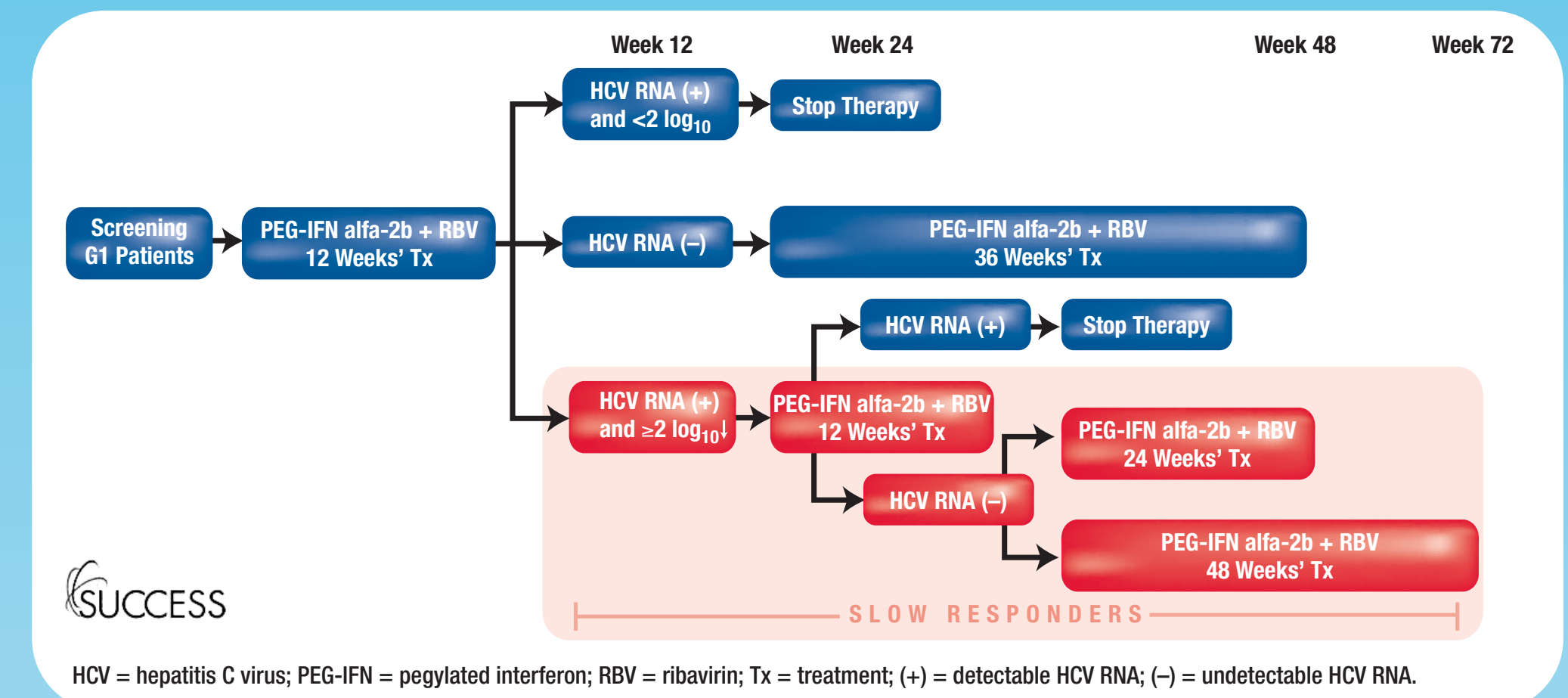


Figure 1. Study flow diagram

Table 1. Weight-Based PEG-IFN alfa-2b and Ribavirin Dosing

Weight, kg	PEG-IFN alfa-2b, $\mu\text{g}/\text{kg}/\text{wk}$	Ribavirin, mg/d
40-50	80	800
51-64	80	800
65-75	100	1000
76-85	120	1000
86-105	150	1200
106-125	150	1400

PEG-IFN = pegylated interferon.

Efficacy Assessments

- Primary end point of the SUCCESS trial: To compare the proportion of G1 patients who attained SVR 24 weeks after completing treatment for 48 or 72 weeks.
- The proportion of slow responder patients and rapid and early virologic responders were also evaluated.
- In this preliminary report, rapid virologic responders, early virologic responders, and slow responders (Figure 2) were identified using data available as of May 2006 or September 2006.
 - Rapid virologic response (RVR), data available as of May 2006.
 - EVR, data available as of May 2006 and September 2006.
 - Slow responder, data available as of May 2006 and September 2006.
- HCV RNA levels in the SUCCESS trial are measured using TaqMan® (Applied Biosystems, Foster City, CA) assay (lower limit of quantification [LLQ], < 100 copies/mL or ≤ 29 IU/mL) at screening, baseline, weeks 4, 12, 24, 48, 72, and follow-up.

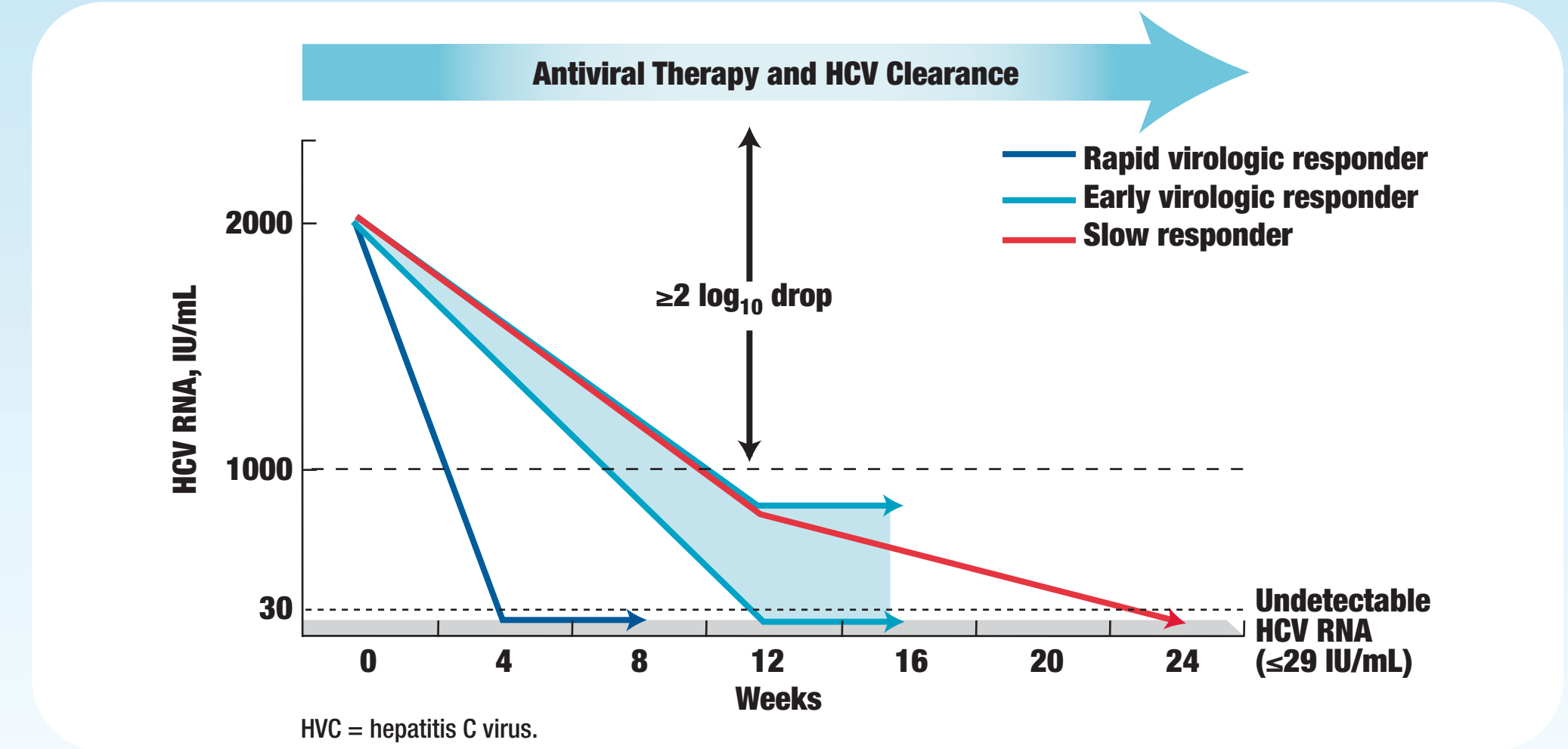


Figure 2. Virologic responders

Results

- Data from this current status report of the SUCCESS trial are preliminary; final study results will be presented on completion of the trial.

Patient Flow and Demographics

- As of September 2006, a total of 1933 patients from 133 sites in Europe, Canada, and Israel were screened, and 1428 patients are enrolled in the SUCCESS study (Figure 3).
- Patient demographics for those included in this preliminary report are presented in Table 2.
 - Most patients are men (63%) and white (96%).
 - Mean age of patients is 43 years (range, 18-100).
 - Mean body weight is 76 kg (range, 45-124).

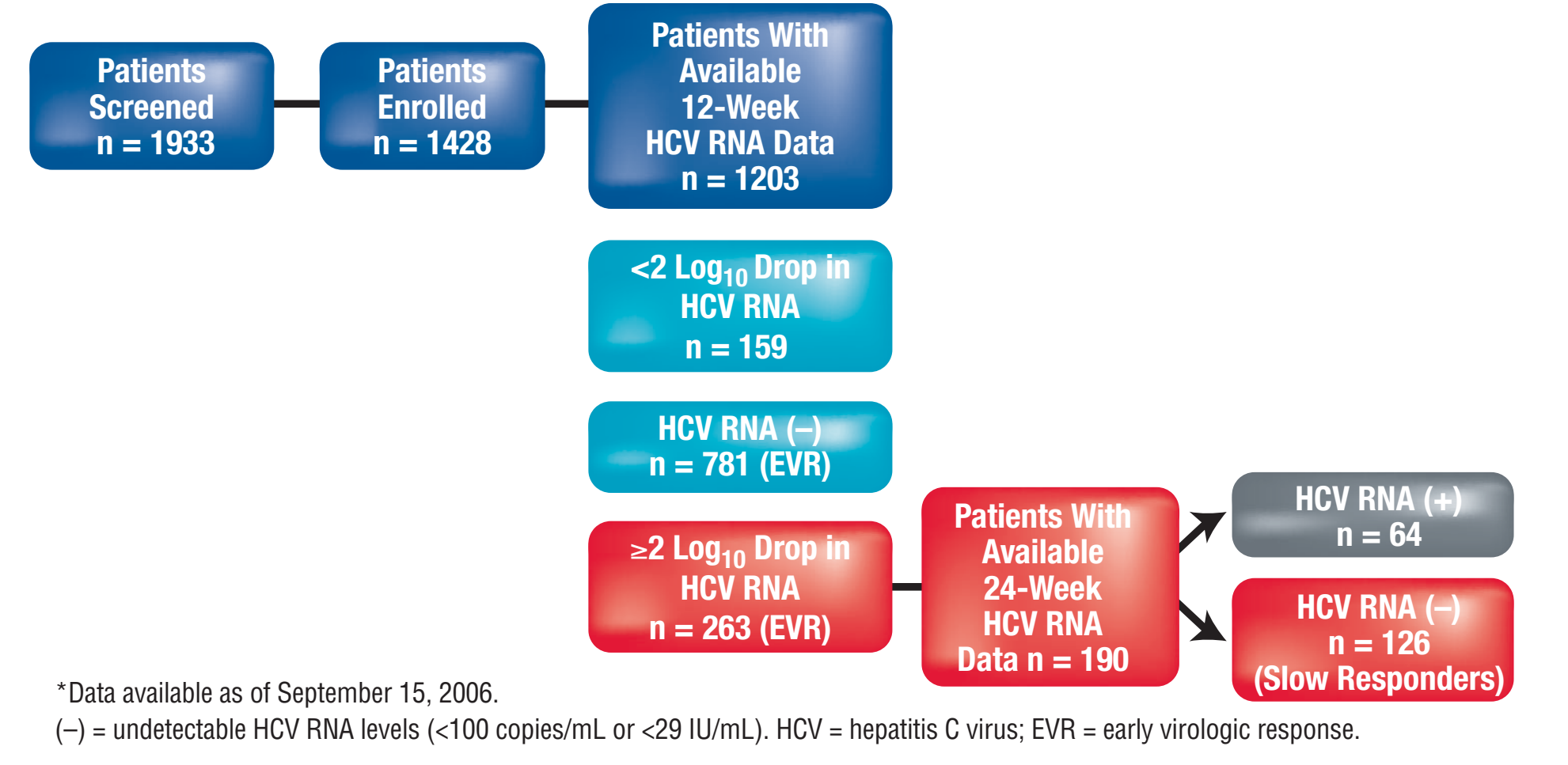


Figure 3. Patient flow*

Table 2. Patient Demographics

	Patients (n = 1262*)
Sex (n = 1209)	
Male, n (%)	765 (63.3)
Female, n (%)	444 (36.7)
Mean age, y (n = 1214)	43
18-65, n (%)	1176 (96.9)
>65, n (%)	38 (3.1)
Ethnicity, n (%) (n = 1209)	
White	1163 (96.2)
Black	8 (0.7)
Asian	23 (1.9)
Other	15 (1.2)
Mean disease duration (range), y (n = 1195)	10 (0.05-52.05)
Mean weight (range), kg (n = 1214)	76 (45.0-124.0)

*Demographic data available as of September 7, 2006.

Virologic Response

- RVR was observed in 188 (17%) of 1129 patients with available data for week 4 and EVR was observed in 726 (78%) of 934 patients with available data for week 12 as of May 2006 (Figure 4).

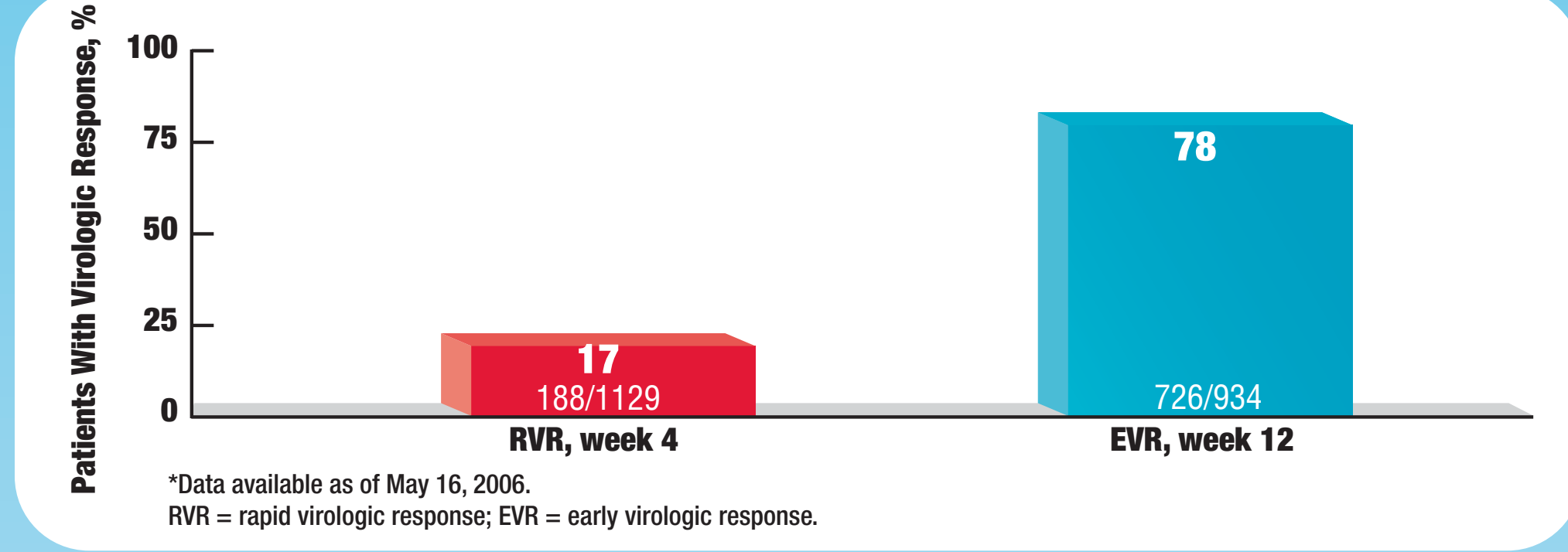


Figure 4. RVR and EVR rates for patients with 4- and 12-week data as of May 2006*

- EVR was observed in 1044 (87%) of 1203 of patients with available week 12 HCV RNA data as of September 2006 (Figure 5).
 - 781 (75%) of 1044 had undetectable levels of HCV RNA.
 - 263 (25%) of 1044 had a $\geq 2 \log_{10}$ decrease from baseline in HCV RNA levels.
- Of those with available 12- and 24-week HCV RNA data as of September 2006, 126 (66%) of 190 had a $\geq 2 \log_{10}$ decrease from baseline in HCV RNA levels at week 12 and undetectable HCV RNA at week 24 and were classified as slow responders (Figure 5).

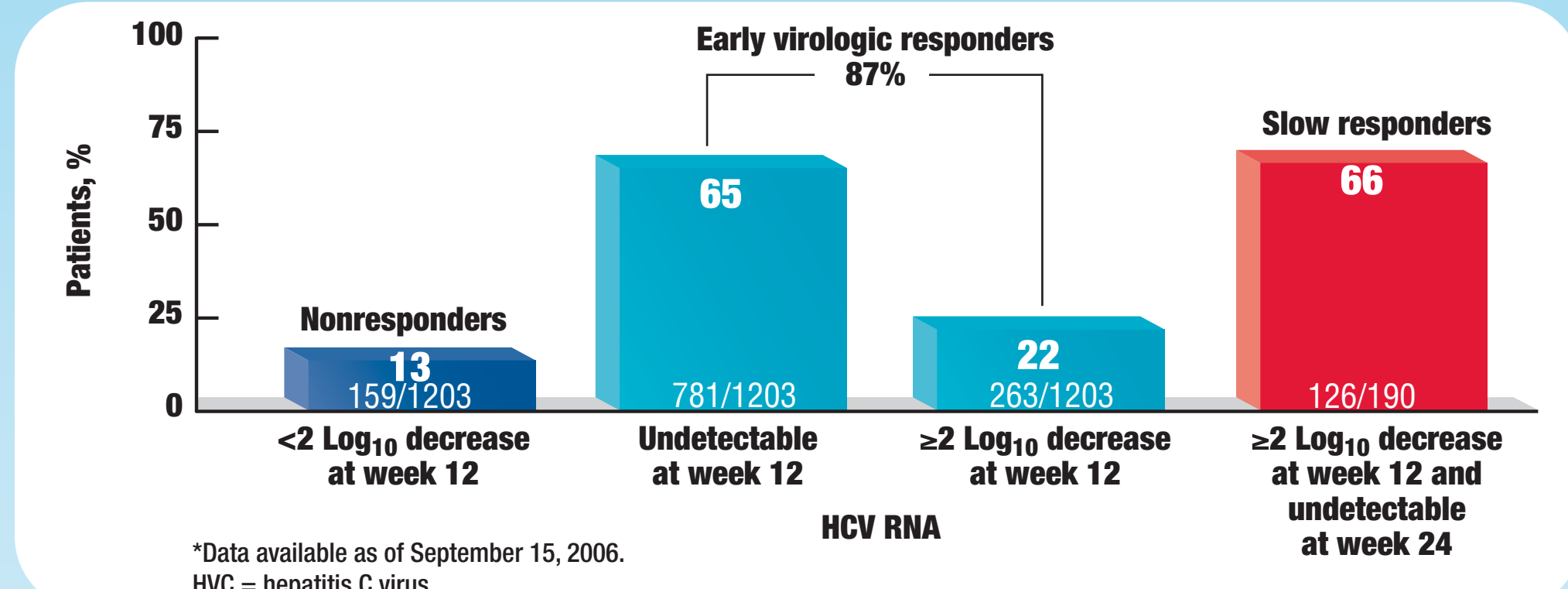


Figure 5. Virologic responses for patients with available 12-week and 12- and 24-week HCV RNA data as of September 2006*

Conclusions

- Preliminary observations from SUCCESS are encouraging and indicate that most (87%) G1 patients treated with PEG-IFN alfa-2b plus ribavirin attain an EVR.
- Upon completion of the study, data from SUCCESS may determine whether extending duration of therapy with PEG-IFN alfa-2b plus ribavirin from 48 weeks to 72 weeks improves SVR in slow responder G1 patients.

References

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