Treatment Experienced

Simeprevir in Genotype 1 (Viral Relapsers)
PROMISE Trial

Forns X, et al. Gastroenterology. 2014;146:1669-79.e3.

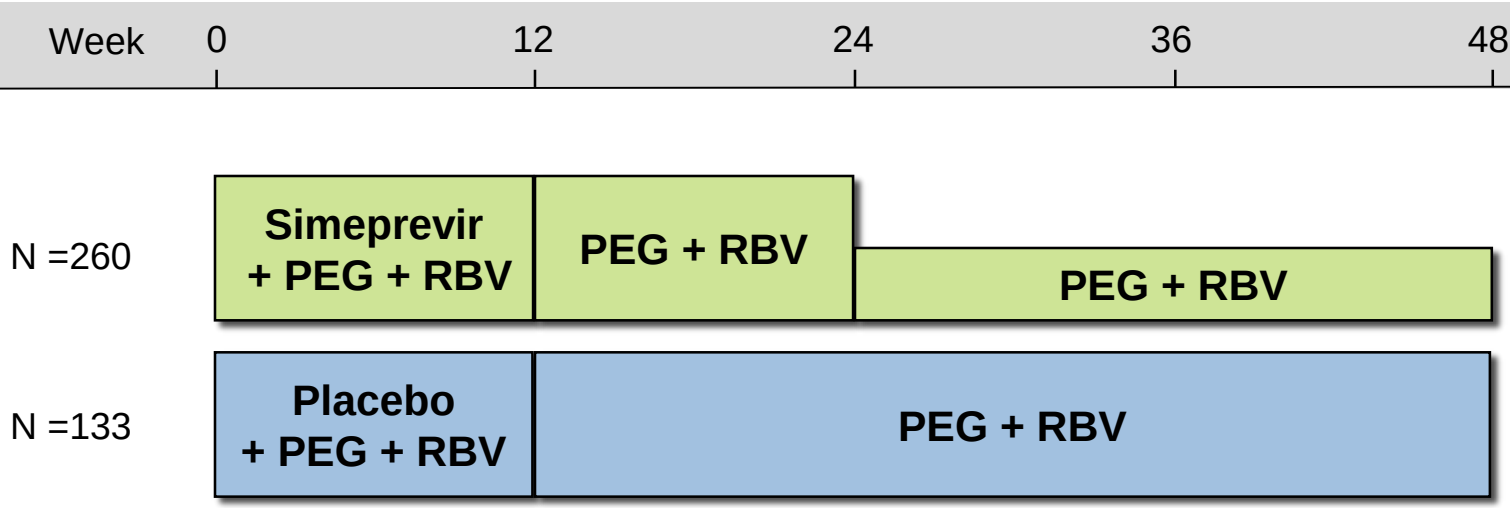
Simeprevir + PEG + Ribavirin for Chronic HCV
PROMISE Trial

PROMISE Trial: Study Features

- **Design**: Randomized, double-blind, placebo-controlled phase 3 trial of triple therapy with simeprevir, peginterferon alfa-2a, and ribavirin
- **Entry Criteria**
  - Treatment-experienced, chronic HCV monoinfection
  - Viral relapse with prior (≥ 24 weeks) of peginterferon-based therapy
  - HCV Genotype 1
- **Patient Characteristics**
  - N = 393
  - HCV Genotype: 1a (42%); 1b (58%)
  - IL28B Genotype: 76% non-CC
  - Age and Sex: median age 52; 66% male
  - Race: 94% white
  - Liver disease: 15% had METAVIR F3; 15% F4
- **Primary end-points**: Efficacy (SVR12)

Source: Forns X, et al. Gastroenterology. 2014;146:1669-79.e3.

Simeprevir and Peginterferon plus Ribavirin for Chronic HCV PROMISE Trial: Design



Study Notes

- Randomized 2:1, stratified on IL28B and HCV subtype
- Response-guided therapy (RGT): In simeprevir study arm, patients with HCV RNA<25 IU/ml at week 4 (undetectable or detectable) and <25 IU/ml at week 12 (undetectable) stopped treatment after 24 weeks

Drug Dosing

Simeprevir: 150 mg once daily

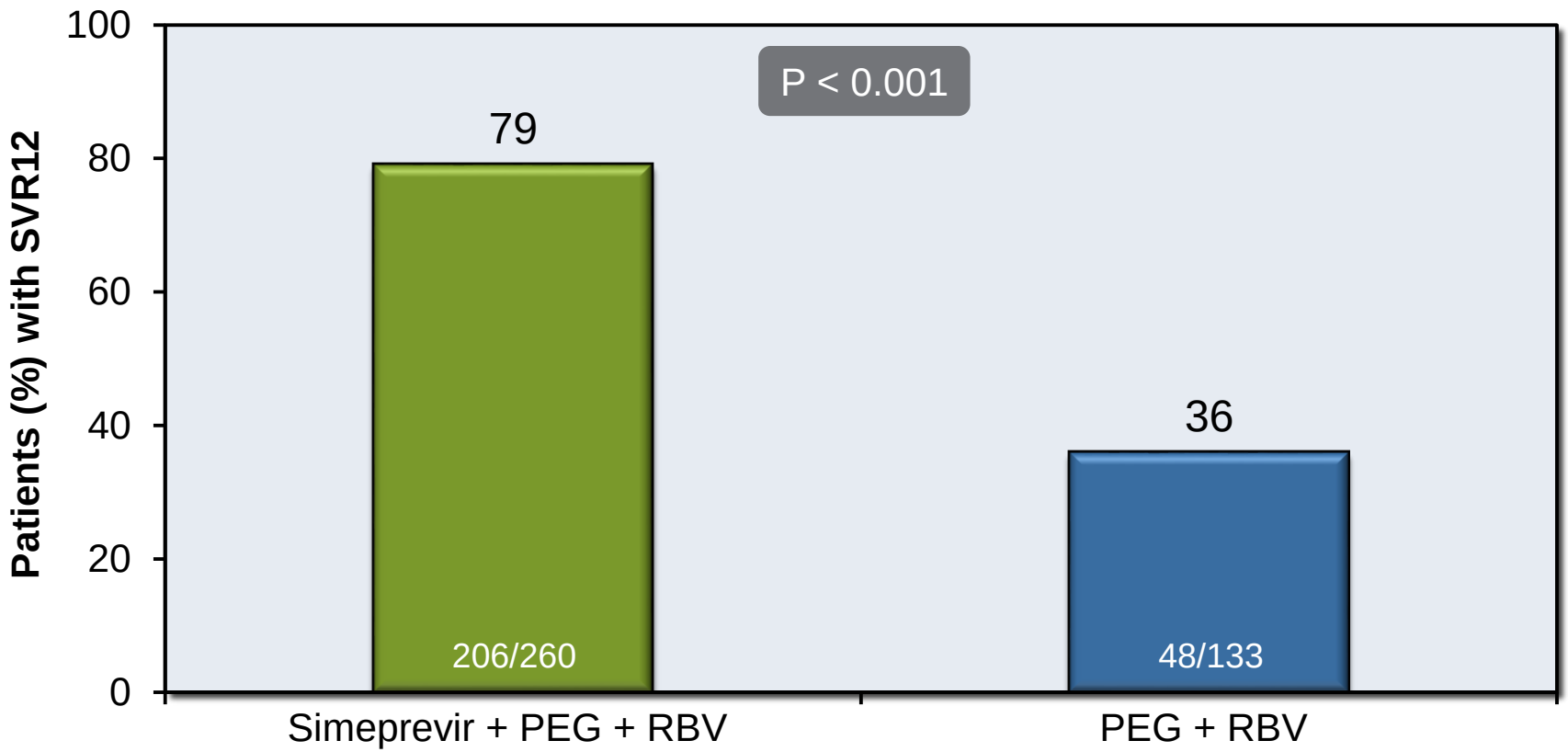
Peginterferon alfa-2a (PEG): 180 mcg/week

Ribavirin (RBV) weight-based (in 2 divided doses): 1000 mg if < 75kg or 1200 mg/day if ≥ 75kg

Source: Forns X, et al. Gastroenterology. 2014;146:1669-79.e3.

Simeprevir and Peginterferon plus Ribavirin for Chronic HCV
PROMISE Trial: Results

PROMISE Trial: Proportion of Patients with SVR12

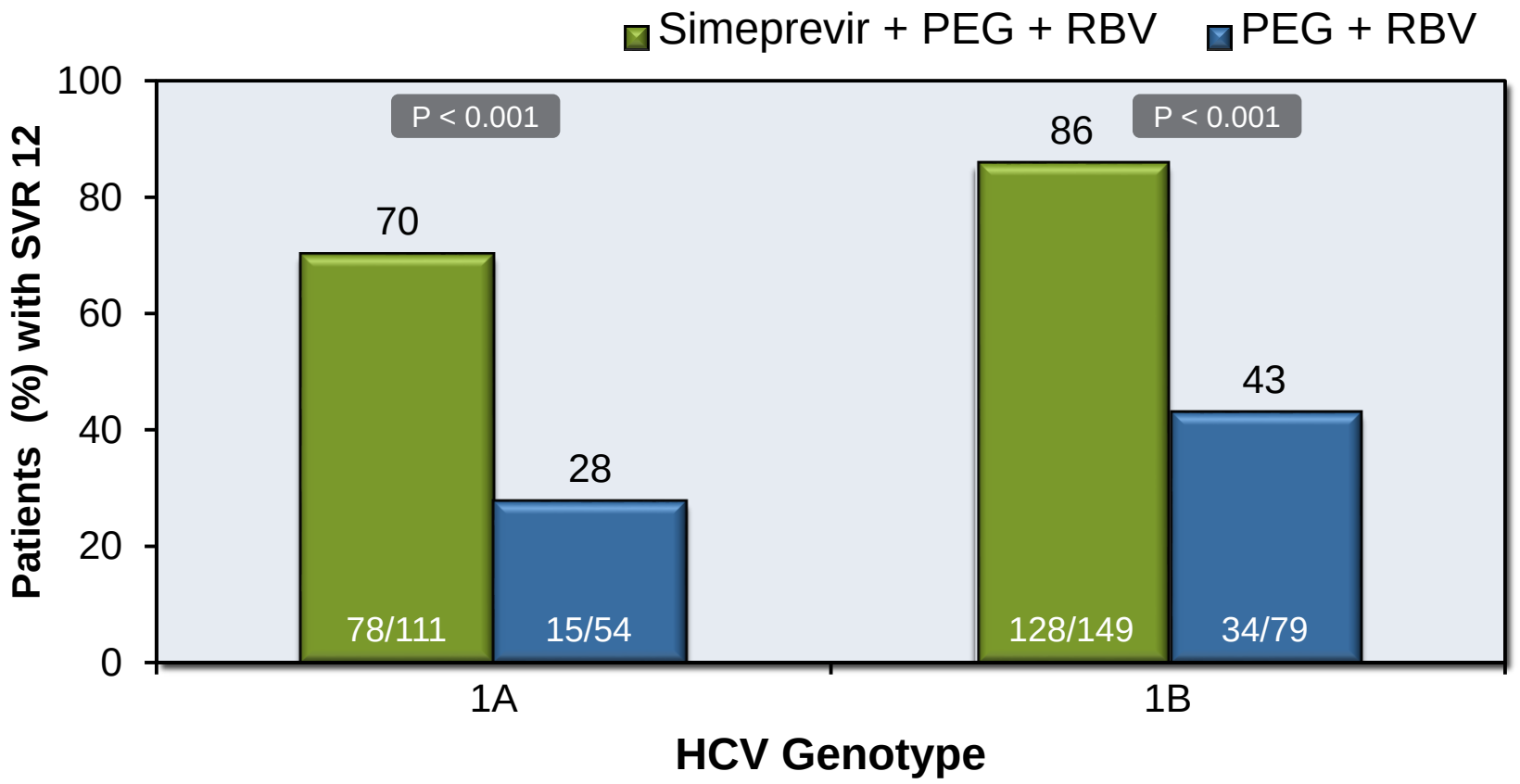


Abbreviations: SVR12 = sustained virologic response at 12 weeks; PEG = peginterferon; RBV = ribavirin

Source: Forns X, et al. Gastroenterology. 2014;146:1669-79.e3.

Simeprevir and Peginterferon plus Ribavirin for Chronic HCV
PROMISE Results

PROMISE Trial: SVR12 by HCV Genotype 1 Subtype



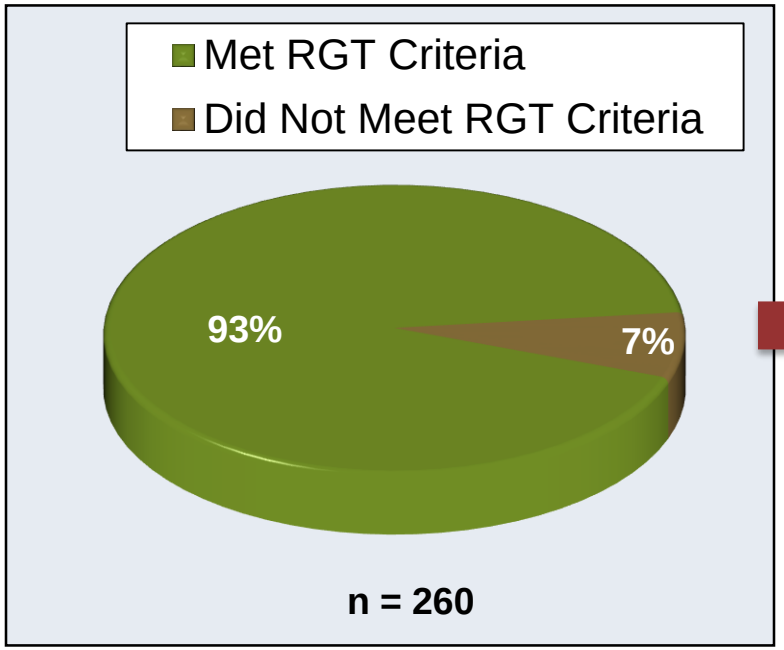
Abbreviations: SVR12 = sustained virologic response at 12 weeks; PEG = peginterferon; RBV = ribavirin

Source: Forns X, et al. Gastroenterology. 2014;146:1669-79.e3.

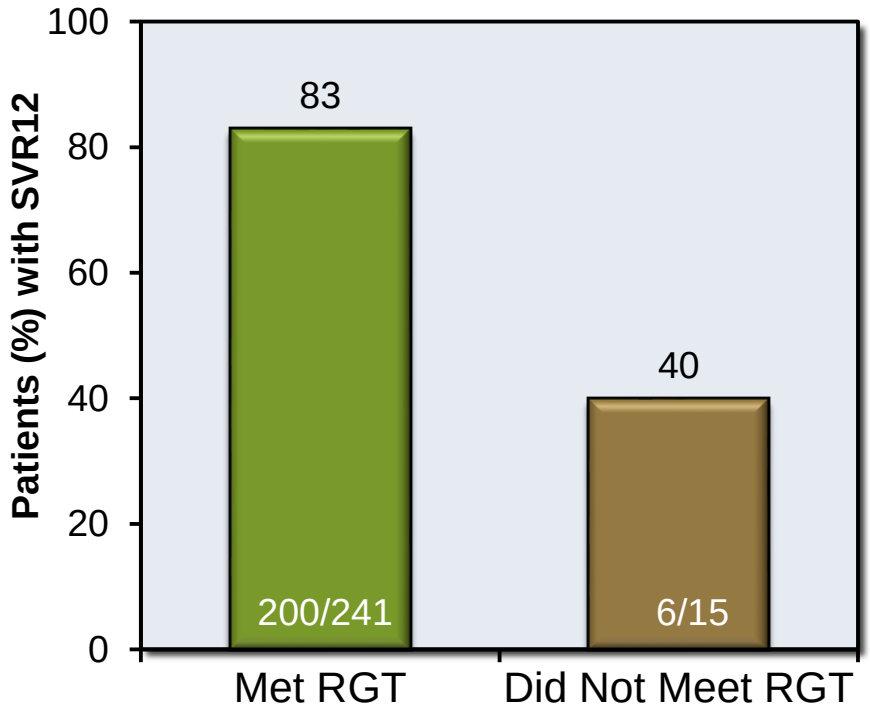
Simeprevir and Peginterferon plus Ribavirin for Chronic HCV PROMISE Results

PROMISE Trial: SVR12 Response in Simeprevir Arm Based on RGT Criteria

Patients (%) who Met RGT Criteria



Patient (%) with SVR 12 Response

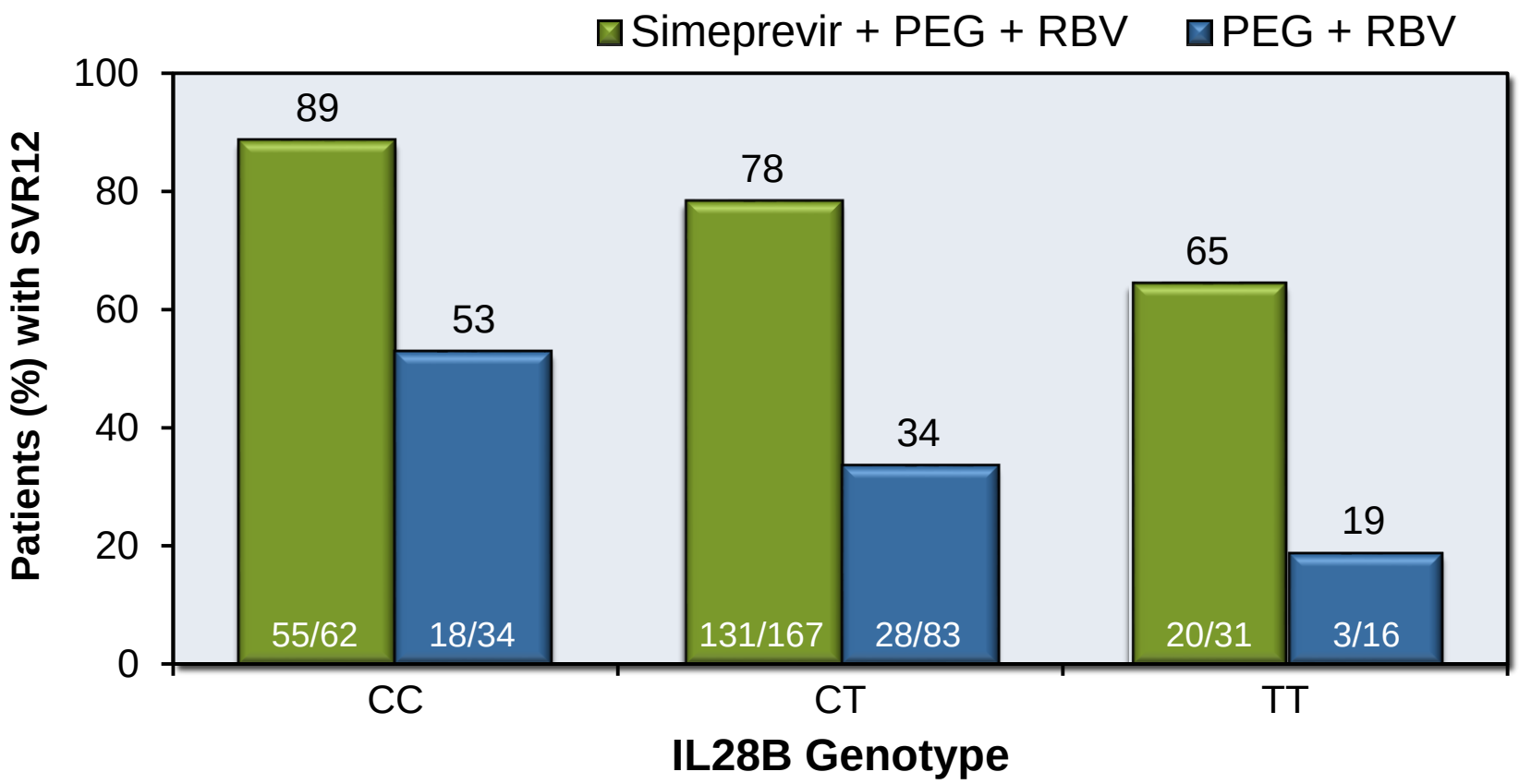


RGT= response-guided therapy: in simeprevir study arm, patients with HCV RNA<25 IU/ml at week 4 (undetectable or detectable) and <25 IU/ml at week 12 (undetectable) stopped treatment after 24 weeks

Source: Forns X, et al. Gastroenterology. 2014;146:1669-79.e3.

Simeprevir and Peginterferon plus Ribavirin for Chronic HCV
PROMISE Trial: Results

PROMISE TRIAL: SVR12 by Host *IL28B* Genotype

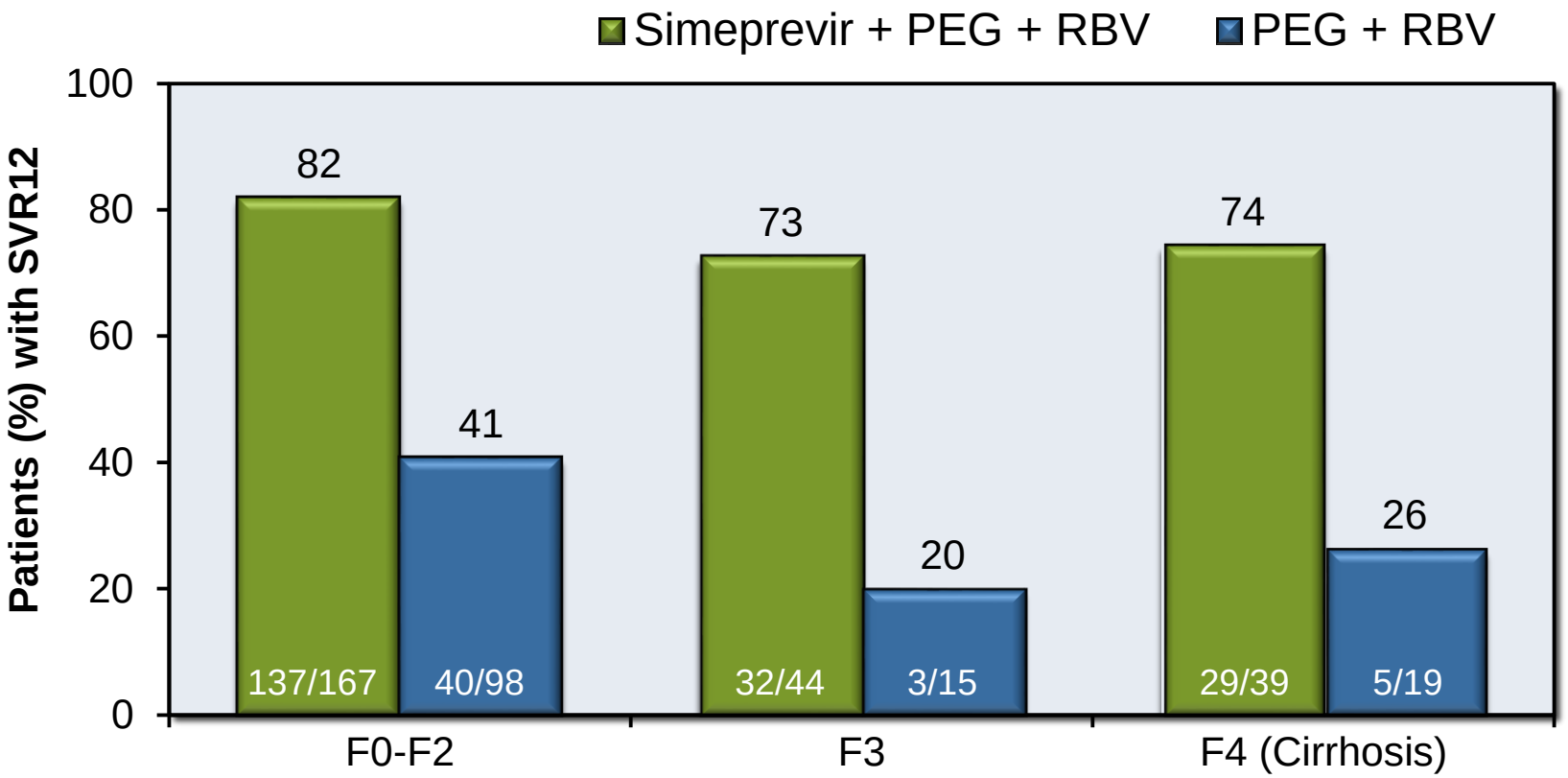


Abbreviations: SVR12 = sustained virologic response at 12 weeks; PEG = peginterferon; RBV = ribavirin

Source: Forns X, et al. Gastroenterology. 2014;146:1669-79.e3.

Simeprevir and Peginterferon plus Ribavirin for Chronic HCV
PROMISE Trial: Results

PROMISE Trial: SVR12 by Liver Fibrosis (METAVIR Fibrosis Score)



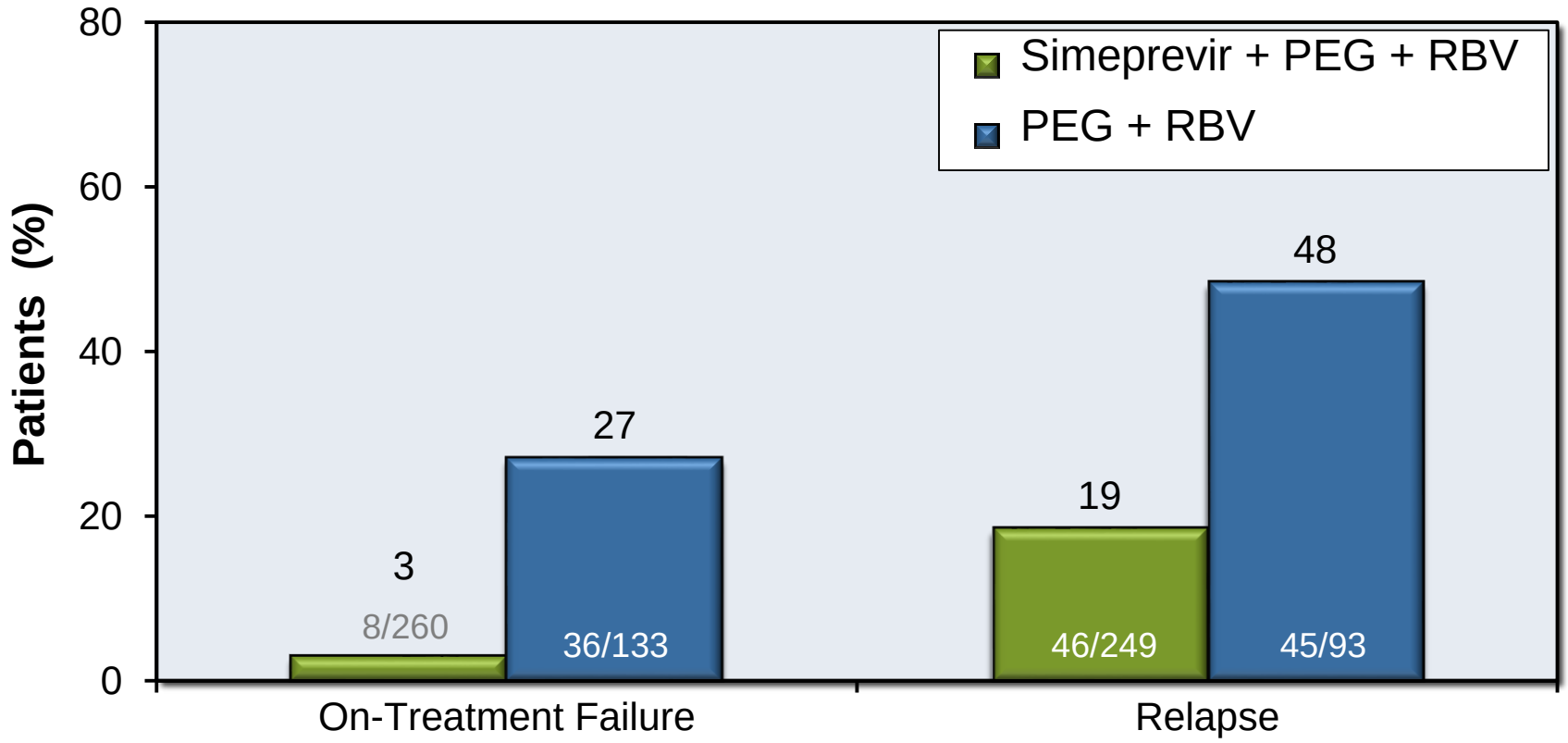
Abbreviations: SVR12 = sustained virologic response at 12 weeks; PEG = peginterferon; RBV = ribavirin

Source: Forns X, et al. Gastroenterology. 2014;146:1669-79.e3.

Hepatitis web study

Simeprevir and Peginterferon plus Ribavirin for Chronic HCV
PROMISE Results

Patients Who Had On-Treatment Failure or Relapse



Abbreviations: PEG = Peginterferon; RBV = Ribavirin
On-Treatment Failure: Detectable HCV RNA at end of treatment.

Source: Forns X, et al. Gastroenterology. 2014;146:1669-79.e3.

Simeprevir
Adverse Effects in PROMISE Trial

PROMISE Trial: Event	Simeprevir + PR (n=260)	Placebo + PR (n=133)	Simeprevir + PR (n=260)	Placebo + PR (n=133)
	First 12 Weeks		Entire Treatment Phase	
AE leading to permanent discontinuation of ≥ 1 drug	1.2%	1.5	2.3	5.3
Grade 3 event	18.1%	18.0%	24.2%	25.6%
Grade 4 event	1.9%	3.0%	3.5	4.5
Fatigue	31.9%	42.1%	32.3%	43.6%
Headache	31.9%	36.1%	33.1%	36.1%
Influenza-like illness	29.6%	20.3%	30.0%	20.3%
Rash (any type)	18.5%	14.3%	23.1%	22.6%
Pruritus	23.5%	16.5%	27.7%	27.8%
Neutropenia	14.6%	16.5%	17.7%	21.8%
Photosensitivity	3.5%	0%	3.5%	0%
Anemia	10.8%	6.0%	16.9%	20.3%

Source: Forns X, et al. Gastroenterology. 2014;146:1669-79.e3.

Simeprevir and Peginterferon plus Ribavirin for Chronic HCV PROMISE Results

Emergent Protease Resistance in Patients who Failed to Achieve SVR12

- Most (90.4%) of simeprevir-treated patients who failed to achieve SVR12 developed emerging mutations in the NS3 protease domain
- Genotype 1A: Most common mutation = R155K or D168E, or combination of R155K and mutations at codons 80 and/or 168
- Genotype 1B: Most common mutations = D168V or D168A, E, T or E/V or the combinations Q80R + D168E/V, or Q80R + S122T + D168E

Source: Forns X, et al. Gastroenterology. 2014;146:1669-79.e3.

Simeprevir and Peginterferon plus Ribavirin for Chronic HCV PROMISE Conclusions

Conclusions: “In a Phase 3 trial of patients who had relapsed following interferon-based therapy, addition of simeprevir to PR was generally well tolerated, with an SVR12 rate of 79.2%. Most patients (92.7%) receiving simeprevir were able to shorten therapy to 24 weeks.”

Source: Forns X, et al. Gastroenterology. 2014;146:1669-79.e3.

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/

Funded by a grant from the Centers for Disease Control and Prevention.

Hepatitis web study