Treatment Experienced

Elbasvir + Grazoprevir + Ribavirin in PI-experienced HCV GT1

C-SALVAGE

Source: (1) Buti M, et al. Clin Infect Dis. 2016;62:32-6. (2) Forns X, et al. J Hepatol. 2015;63:564-72.

Elbasvir + Grazoprevir + Ribavirin in PI-experienced HCV GT1 C-SALVAGE Study: Features

C-SALVAGE Trial

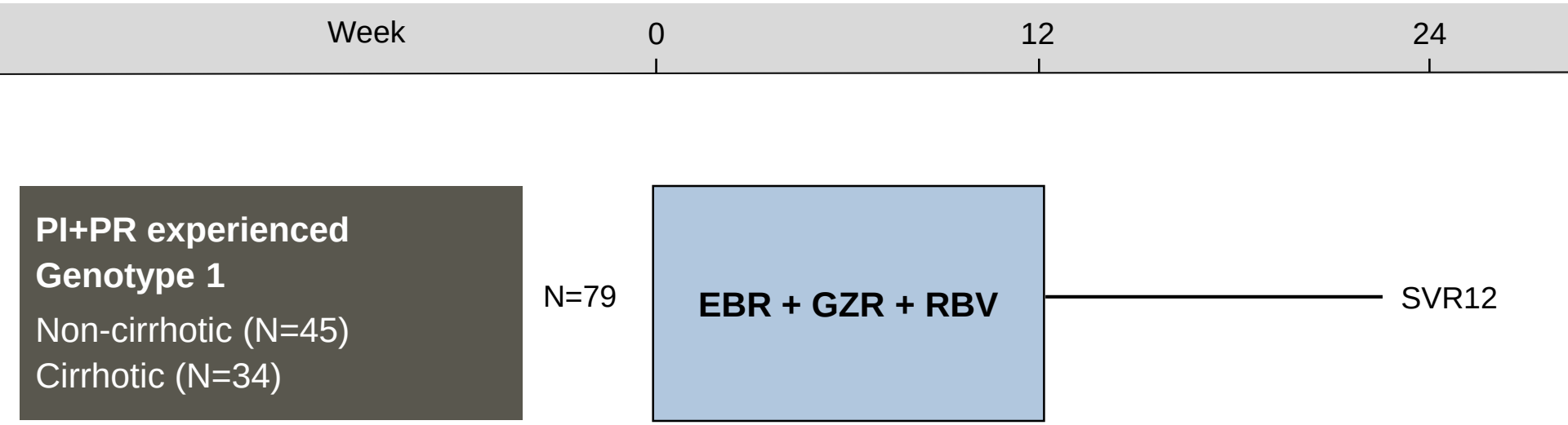
- **Design**: Prospective, open-label, single-arm, phase 2 trial of elbasvir plus grazoprevir plus ribavirin for 12 weeks in treatment-experienced patients with HCV GT1, with or without cirrhosis, and previous failure of peginterferon and ribavirin plus an early-generation HCV protease inhibitor (boceprevir, simeprevir, or telaprevir)

- **Entry Criteria**
  - Chronic HCV genotype 1
  - Age 18 years or older
  - HCV RNA ≥10,000 IU/mL
  - Prior treatment failure with ≥4 weeks of peginterferon + ribavirin + PI
  - Patients with compensated cirrhosis accepted

- **Primary End-Points**:
  SVR12 data analysis: Buti M, et al. Clin Infect Dis. 2016;62:32-6.
  SVR24 data analysis: Forns X, et al. J Hepatol. 2015;63:564-72.

Source: (1) Buti M, et al. Clin Infect Dis. 2016;62:32-6. (2) Forns X, et al. J Hepatol. 2015;63:564-72.

Elbasvir + Grazoprevir + Ribavirin in PI-experienced HCV GT1 C-SALVAGE Study: Design



Abbreviations:
EBR = elbasvir; GZR = grazoprevir; RBV = ribavirin; PI = protease inhibitor; PR = peginterferon+ribavirin

Drug Dosing:
Elbasvir: 50 mg once daily
Grazoprevir: 100 mg once daily
Ribavirin (weight-based and divided bid): 800 to 1400 mg/day

Source: Buti M, et al. Clin Infect Dis. 2016;62:32-6.

Elbasvir + Grazoprevir + Ribavirin in PI-experienced HCV GT1 C-SALVAGE Study: Participants

Baseline Characteristic	All Patients (n = 79)	Baseline NS3 RAVs* (n = 34)	No Baseline NS3 RAVs* (n = 44)
Mean age, years	54.4	53.9	54.6
Male/Female, %	58.2/41.8	61.8/38.2	54.5/45.5
HCV genotype, % 1a 1b	 38.0 62.0	 67.6 32.4	 15.9 84.1
Cirrhosis, %	43.0	44.1	43.2
Previous PI, % Boceprevir Telaprevir Simeprevir	 35.4 54.4 10.1	 29.4 55.9 14.7	 38.6 54.5 6.8
Non-virologic failure⁺, %	16.5	5.9	25.0

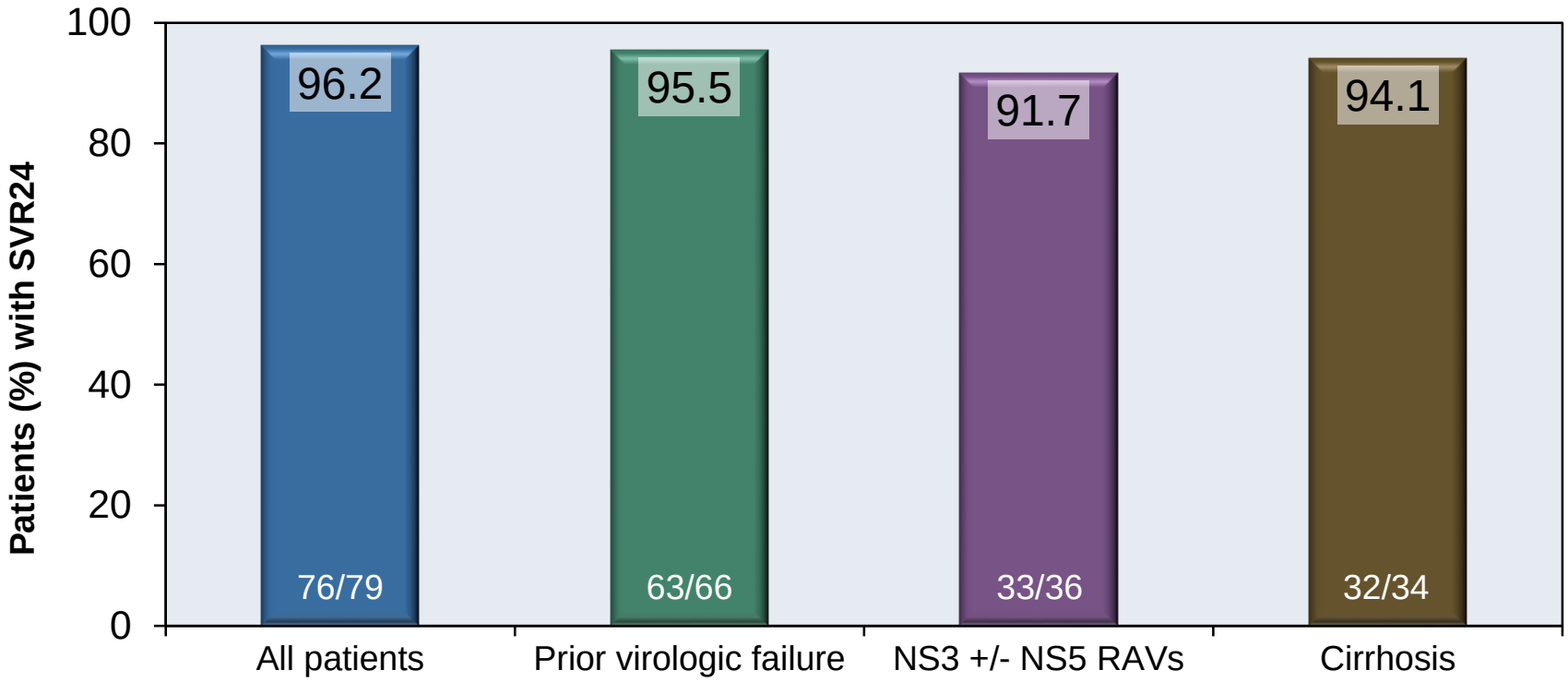
* Among evaluable patients

⁺ Reasons for the 13 non-virologic failure included adverse events/drug intolerance (n=12) and short course regimen in a clinical trial (n=1)

Source: Forns X, et al. J Hepatol. 2015;63:564-72.

Elbasvir + Grazoprevir + Ribavirin in PI-experienced HCV GT1 C-SALVAGE Study: Results

C-SALVAGE: SVR 24* by Baseline Factors



* Analysis per intent to treat

Source: Buti M, et al. Clin Infect Dis. 2016;62:32-6.

Elbasvir + Grazoprevir + Ribavirin in PI-experienced HCV GT1 C-SALVAGE Study: Results

SVR24 Related to Baseline RAVs in 79 Patients with Prior Virologic Failure		
Categories of RAVs	Baseline RAV	SVR24 in Patients with Baseline RAVs
NS3 RAV	34/79 (43%)	31/34 (91%)
NS5A RAV	9/79 (11%)	8/9 (89%)
Total	43/79 (54%)	39/43 (91%)
RAV = Resistance Associated Variants		

Source: Buti M, et al. Clin Infect Dis. 2016;62:32-6.

Elbasvir + Grazoprevir + Ribavirin in PI-experienced HCV GT1 C-SALVAGE Study: Adverse Events

Adverse Event (AE), n (%)	Grazoprevir + Elbasvir + Ribavirin (n = 79)	
Discontinuation due to AE	1 (1.3%)	
Serious AEs	4 (5.1%)	
Deaths	0	
Specific AE in ≥10% of patients		
Fatigue	22 (28%)	
Headache	15 (19%)	
Asthenia	12 (15%)	
Nausea	9 (12%)	
Grade 3 or 4 laboratory abnormality	Grade 3	Grade 4
Total bilirubin	4 (5.1%)	1 (1.3%)
Direct bilirubin	2 (2.5%)	0
AST or ALT	0	0
Lipase	4 (5.1%)	0
Hemoglobin	2 (2.5%)	0

Source: Forns X, et al. J Hepatol. 2015;63:564-72.

Elbasvir + Grazoprevir + Ribavirin in PI-experienced HCV GT1 C-SALVAGE Study: Conclusions

Conclusions: “Grazoprevir and elbasvir with ribavirin for 12 weeks maintained HCV suppression for at least 24 weeks posttherapy without late relapses. Baseline resistance-associated variants (RAVs) stably reappeared at relapse in all 3 patients with virologic failure. NS5A RAVs emerging at relapse persisted for the full 24-week follow-up period. If confirmed, this finding could complicate retreatment of the small number of patients failing regimens containing an NS5A inhibitor.”

Source: Buti M, et al. Clin Infect Dis. 2016;62:32-6.