

Treatment Experienced

# Elbasvir + Grazoprevir + Ribavirin in PI-experienced HCV GT1 C-SALVAGE

(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 examining the safety and efficacy of elbasvir plus grazoprevir plus ribavirin for 12 weeks in treatment-experienced patients with GT 1 HCV, 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
  - 18 years or older
  - HCV RNA  $\geq 10,000$  IU/mL
  - Prior treatment failure with  $\geq 4$  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.

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

Week

0

12

24

**PI+PR experienced  
Genotype 1**

Non-cirrhotic (N=45)

Cirrhotic (N=34)

N=79

**EBR + GZR + RBV**

SVR12

## 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

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

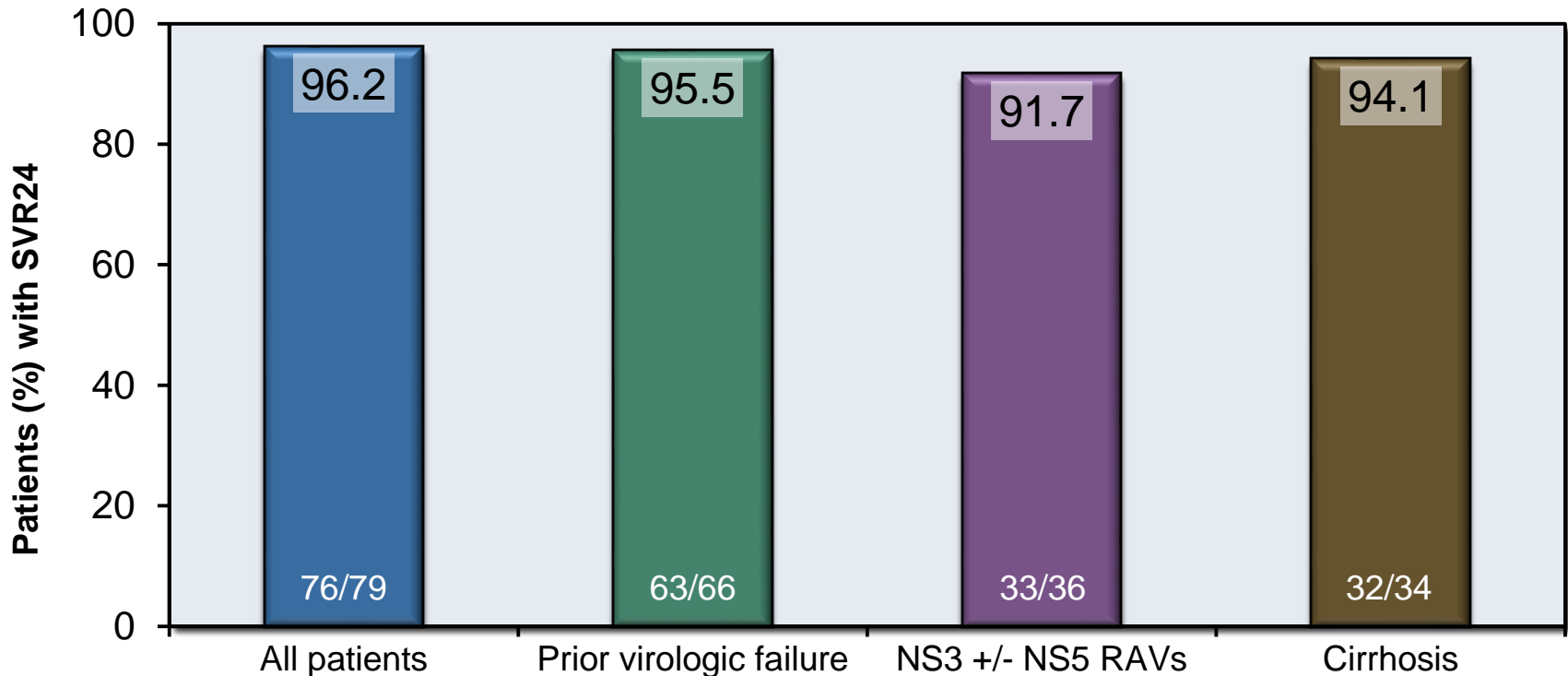
Baseline Characteristic	All Patients (N=79)	Baseline NS3 RAVs* (N=34)	No Baseline NS3 RAVs* (N=44)
Mean age, years	54.4	53.9	54.6
Male/Female, %	58.2/41.8	61.8/38.2	54.5/45.5
HCV genotype, %			
1a	38.0	67.6	15.9
1b	62.0	32.4	84.1
Cirrhosis, %	43.0	44.1	43.2
Previous PI, %			
Boceprevir	35.4	29.4	38.6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

\* Among evaluable patients

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

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

## C-SALVAGE: SVR 24\* by Baseline Factors



\* Analysis per protocol: excluding patients who dropped out due to reasons other than virologic failure  
RAVs = resistance-associated variants (at baseline)

# 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

# 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 $\geq 10\%$ of patients		
Fatigue	22 (28%)	
Headache	15 (19%)	
Asthenia	12 (15%)	
Nausea	9 (12%)	
Grade 3 or 4 laboratory abnormality		
Total bilirubin	<u>Grade 3</u> 4 (5.1%)	<u>Grade 4</u> 1 (1.3%)
Direct bilirubin	2 (2.5%)	0
AST or ALT	0	0
Lipase	4 (5.1%)	0
Hemoglobin	2 (2.5%)	0

# 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.”