

Treatment Naïve and Treatment Experienced

Elbasvir + Grazoprevir +/- RBV in GT 1 Cirrhotics & Null Responders C-WORTHY

Source: Lawitz E, et al. Lancet 2015;385:1075-86.

Elbasvir + Grazoprevir +/- Ribavirin in HCV GT1 C-WORTHY Study: Features

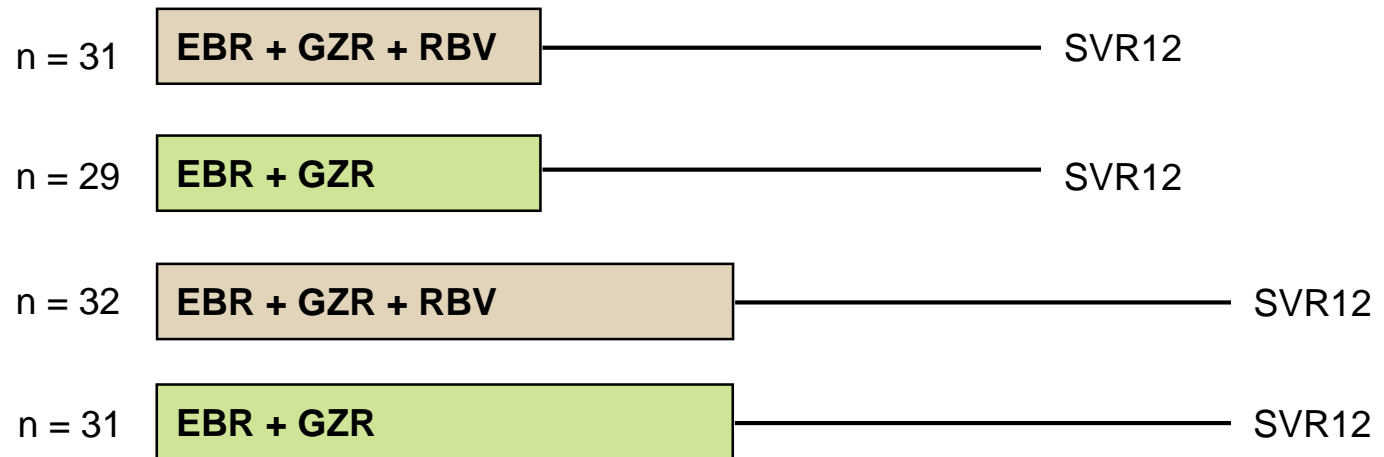
C-WORTHY (Protocol 035) Trial

- **Design:** Randomized, open label phase 2 trial examining the safety and efficacy of elbasvir plus grazoprevir, with or without ribavirin, for 12 or 18 weeks in treatment-naïve patients with cirrhosis (cohort 1) or patients with a previous null response to peginterferon/ribavirin (PR) (cohort 2)
- **Entry Criteria**
 - Chronic HCV Genotype 1
 - Age 18 years or older
 - HCV RNA $\geq 10,000$ IU/mL
 - ALT and AST < 350 IU/L
 - Cohort 1: compensated cirrhosis (Child-Pugh class A)
 - Cohort 2: prior PR null response ($< 2 \log_{10}$ HCV RNA decline at week 12)
- **Primary End-Point:** SVR12

Elbasvir + Grazoprevir +/- Ribavirin in HCV GT1 C-WORTHY: Study Design Cohort 1 (Cirrhosis)

Week 0 12 18 24 30

**Cohort 1
Treatment-Naive
Cirrhosis
(n = 123)**



Abbreviations: EBR = elbasvir; GZR = grazoprevir; RBV = ribavirin

Drug Dosing

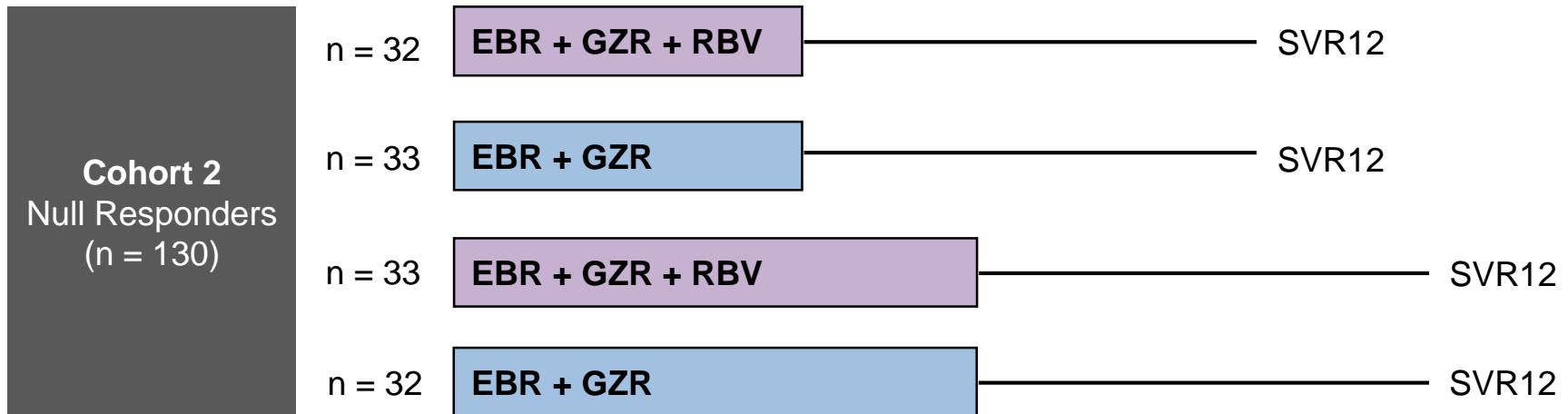
Elbasvir: 50 mg once daily

Grazoprevir: 100 mg once daily

Ribavirin (weight-based and divided bid): 800 to 1400 mg/day

Elbasvir + Grazoprevir +/- Ribavirin in HCV GT1 C-WORTHY: Study Design Cohort 2 (Null Responders)

Week 0 12 18 24 30



Abbreviations: EBR = elbasvir; GZR = grazoprevir; RBV = ribavirin

Drug Dosing

Elbasvir: 50 mg once daily

Grazoprevir: 100 mg once daily

Ribavirin (weight-based and divided bid): 800 to 1400 mg/day

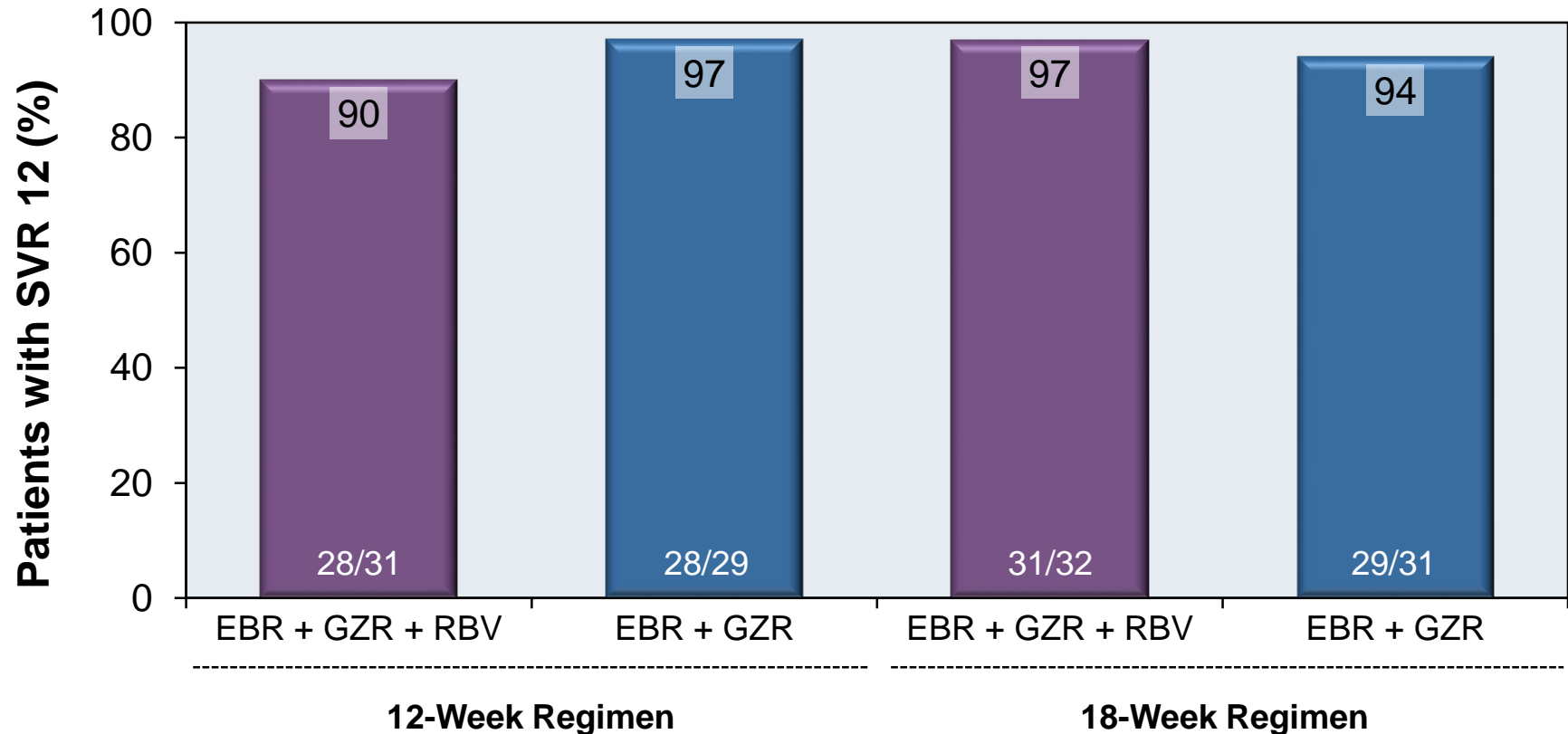
Elbasvir + Grazoprevir +/- Ribavirin in HCV GT1 C-WORTHY: Baseline Characteristics

Baseline Characteristic	Treatment-naïve + cirrhosis		Null responders	
	EBR + GZR + RBV (n = 63)	EBR + GZR (n = 60)	EBR + GZR + RBV (n = 65)	EBR + GZR (n = 65)
Mean age, y (range)	58 (41-79)	59 (42-82)	54 (24-76)	54 (18-77)
Male, %	54	67	55	58
Race				
White	90	92	92	94
Non-white	10	8	8	6
Hispanic/Latino, %	11	7	0	2
HCV Genotype, %				
1a	70	72	57	60
1b	29	25	43	40
Unclassified	2	3	0	0
IL28B CC, %	27	35	0	3
Cirrhosis, %	100	98	35	38
HCV RNA >2 million IU/mL, %	65	73	78	86

Source: Lawitz E, et al. Lancet 2015;385:1075-86.

Elbasvir + Grazoprevir +/- Ribavirin in HCV GT1 C-WORTHY: Results for Naïve Cirrhotics (Cohort 1)

C-WORTHY: SVR 12* by Treatment Duration and Regimen



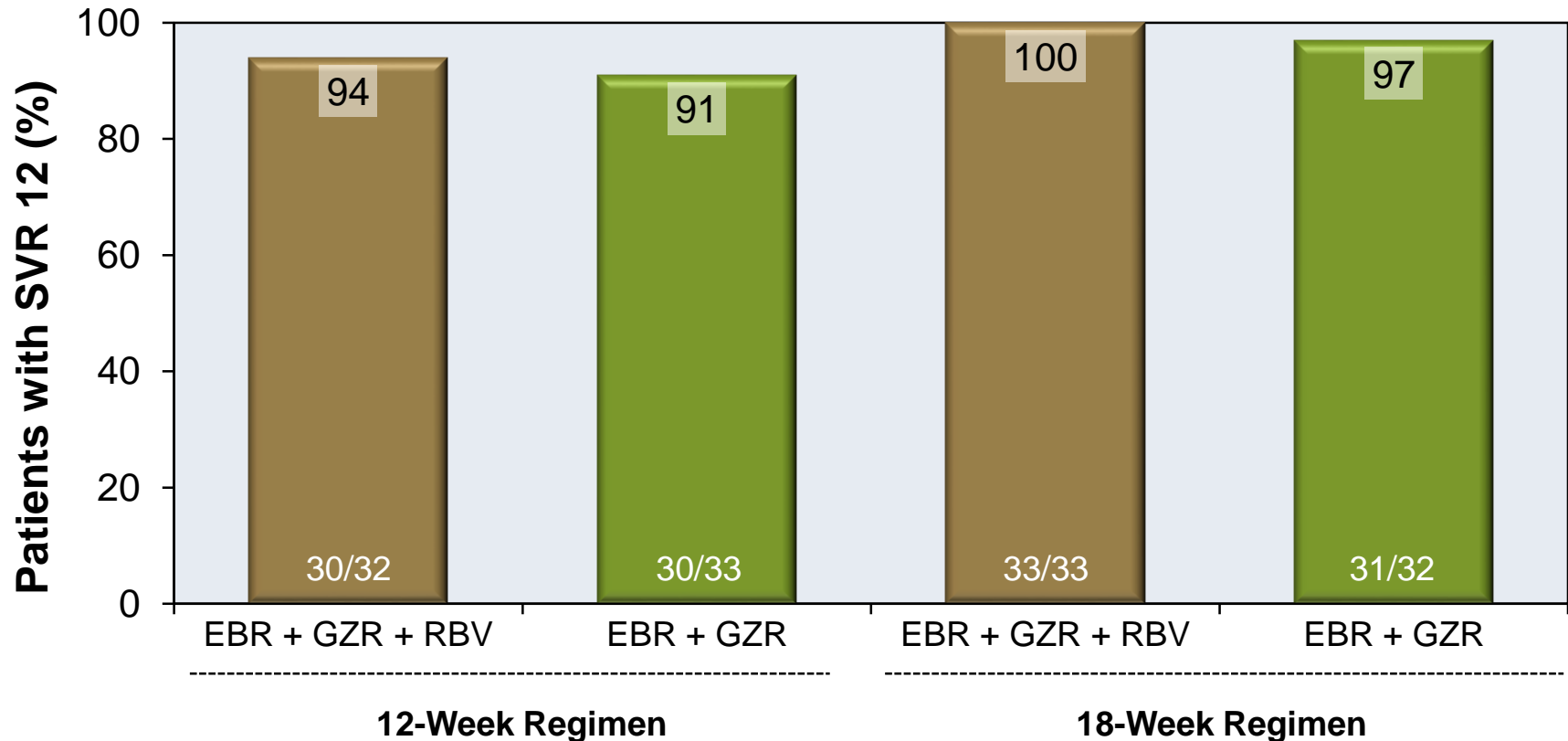
Abbreviations: EBR = elbasvir; GZR = grazoprevir; RBV = ribavirin

*Analysis per intent to treat

Source: Lawitz E, et al. *Lancet* 2015;385:1075-86.

Elbasvir + Grazoprevir +/- Ribavirin in HCV GT1 C-WORTHY: Results for Null Responders (Cohort 2)

C-WORTHY: SVR 12* by Treatment Duration and Regimen



Abbreviations: EBR = elbasvir; GZR = grazoprevir; RBV = ribavirin

*Analysis per intent to treat

Source: Lawitz E, et al. *Lancet* 2015;385:1075-86.

Elbasvir + Grazoprevir +/- Ribavirin in HCV GT1

C-WORTHY: Adverse Events

Adverse event (AE), %	Treatment-naïve with cirrhosis		Null Responders	
	EBR + GZR + RBV (n = 63)	EBR + GZR (n = 60)	EBR + GZR + RBV (n = 65)	EBR + GZR (n = 65)
Serious AE	2	3	3	3
Discontinuation due to AE	2	0	2	0
Death	0	0	2	0
AEs in ≥10% of patients				
Fatigue	22	23	23	35
Headache	11	35	23	23
Asthenia	5	12	18	20
Laboratory events				
Hemoglobin <10 g/dL	13	0	6	0
Hemoglobin <8.5 g/dL	2	0	0	0
Total bilirubin >5 x baseline	3	0	2	0
ALT or AST >2 to ≤5 x ULN*	0	3	0	5
ALT or AST >5 x ULN*	0	0	2	0

*ULN = upper limit of normal

Elbasvir + Grazoprevir +/- Ribavirin in HCV GT1 C-WORTHY Study: Conclusions

Interpretation: “Treatment with grazoprevir plus elbasvir, both with and without ribavirin and for both 12 and 18 weeks' treatment duration, showed high rates of efficacy in previously untreated patients with cirrhosis and previous PR-null responders with and without cirrhosis. These results support the phase 3 development of grazoprevir plus elbasvir.”