Treatment Naïve and Treatment Experienced

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

C-WORTHY

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
  - 18 years or older
  - HCV RNA ≥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

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

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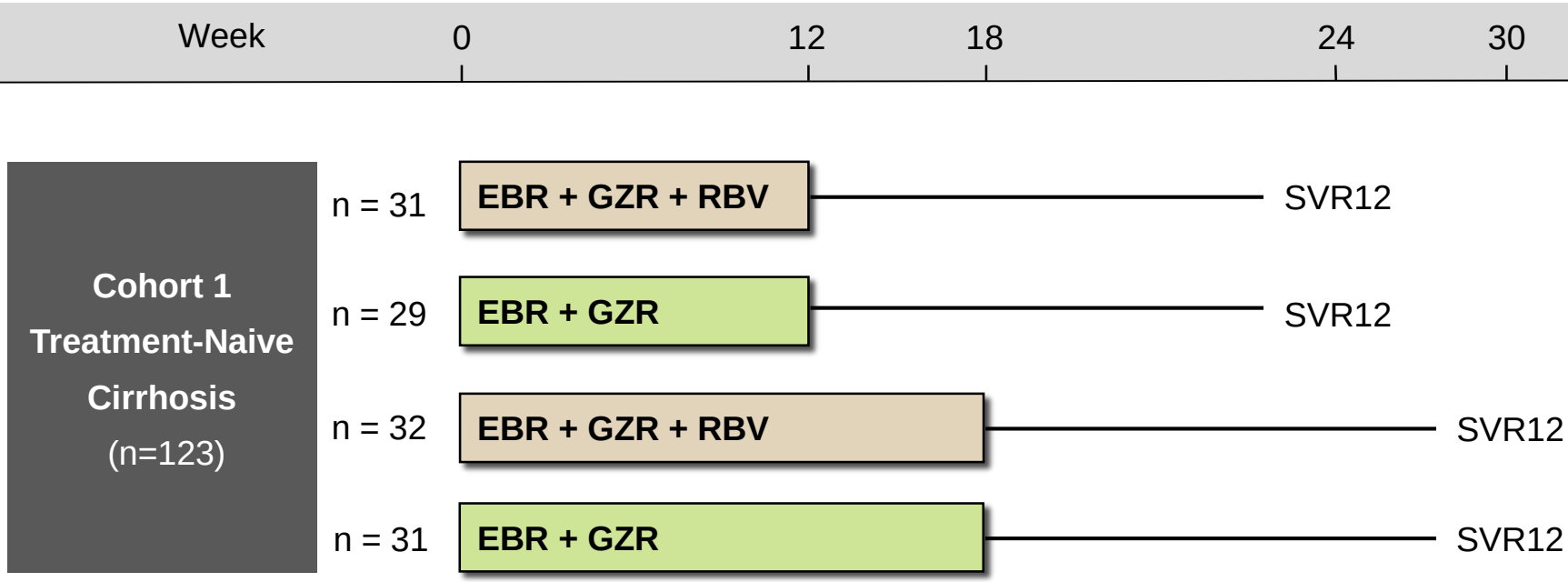
C-WORTHY: Study Design Cohort 1 (Cirrhosis)

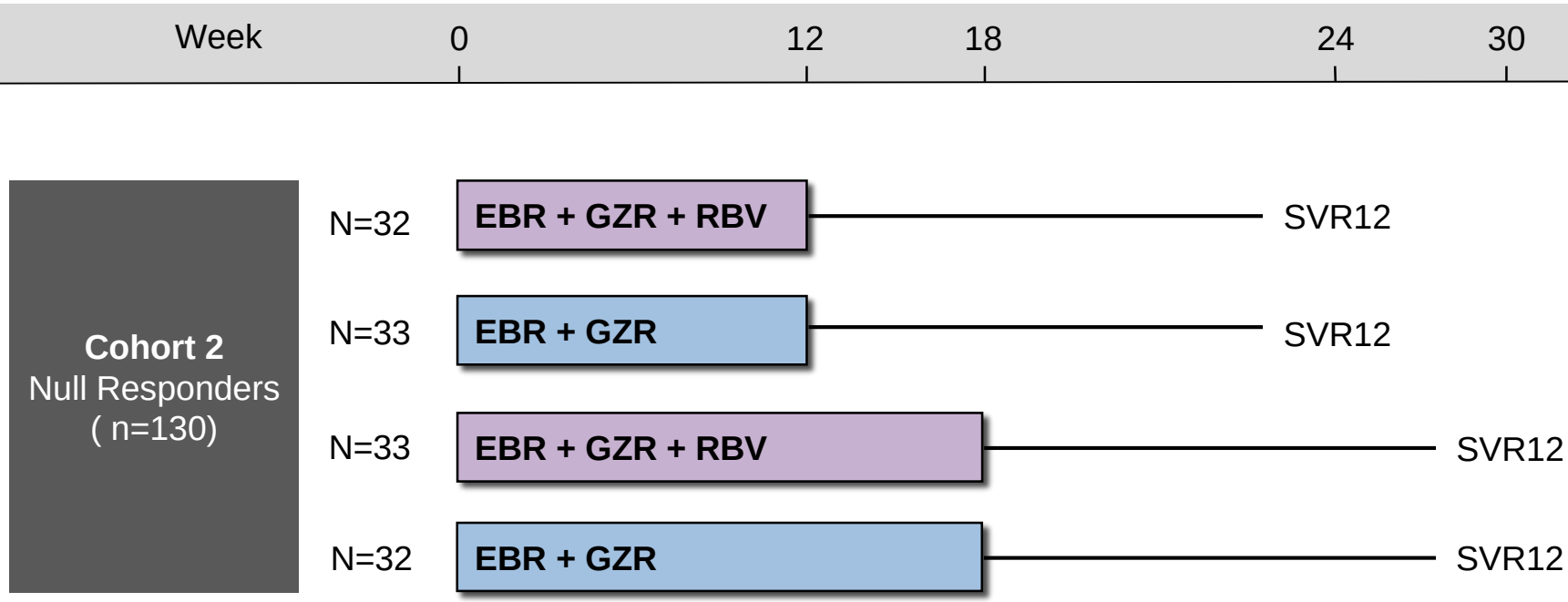


Abbreviations: EBR = elbasvir; GZR = grazoprevir; RBV = ribavirin

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

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

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



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C-WORTHY: Baseline Characteristics

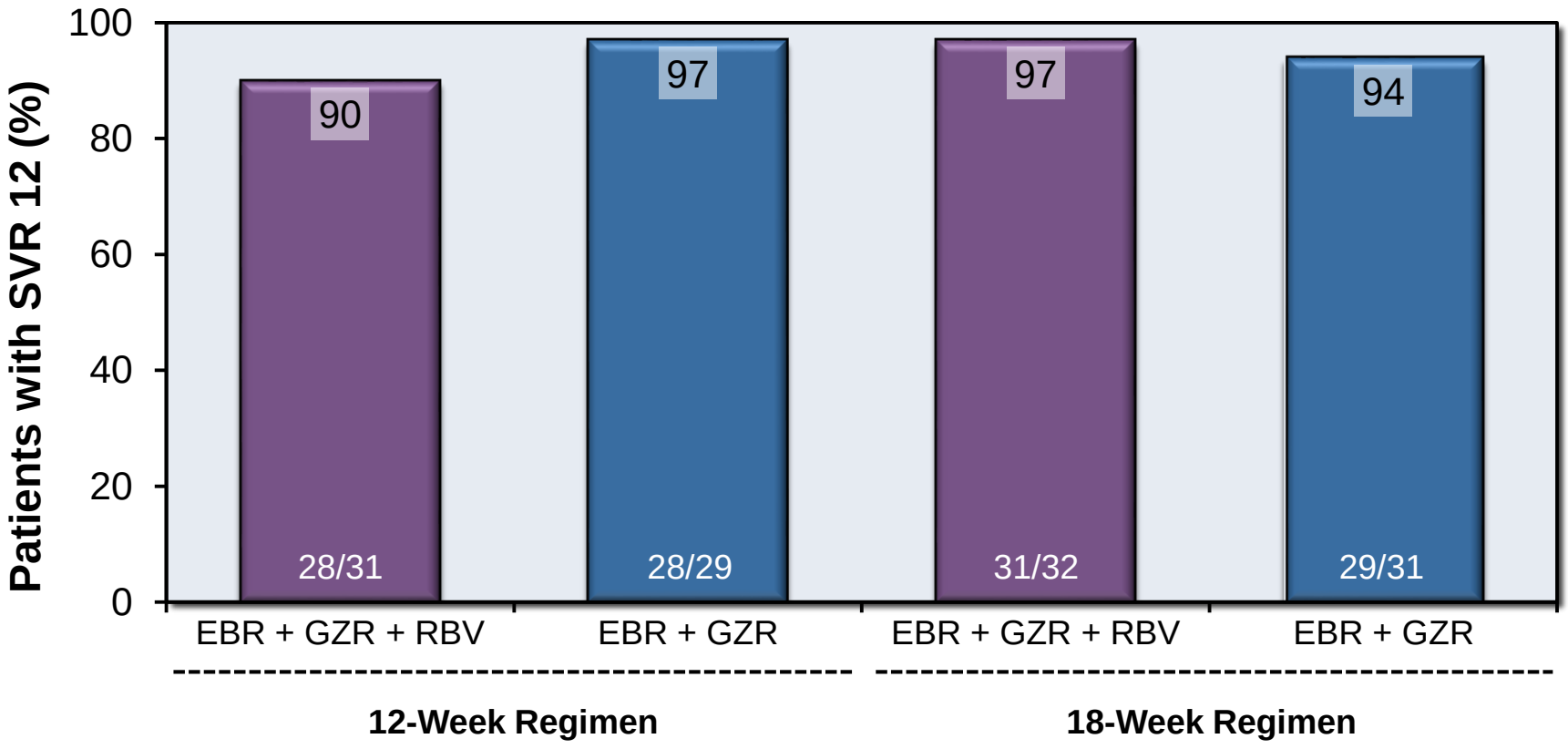
Baseline Characteristic	Treatment-naïve + cirrhosis		Null responders	
	EBR + GZR + RBV N=63	EBR + GZR N=60	EBR + GZR + RBV N=65	EBR + GZR N=65
Mean age, y (range)	58 (41-79)	59 (42-82)	54 (24-76)	54 (18-77)
Male, %	54	67	55	58
Race White Non-white	 90 10	 92 8	 92 8	 94 6
Hispanic/Latino, %	11	7	0	2
HCV Genotype, % 1a 1b Unclassified	 70 29 2	 72 25 3	 57 43 0	 60 40 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.

Hepatitis web study

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

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



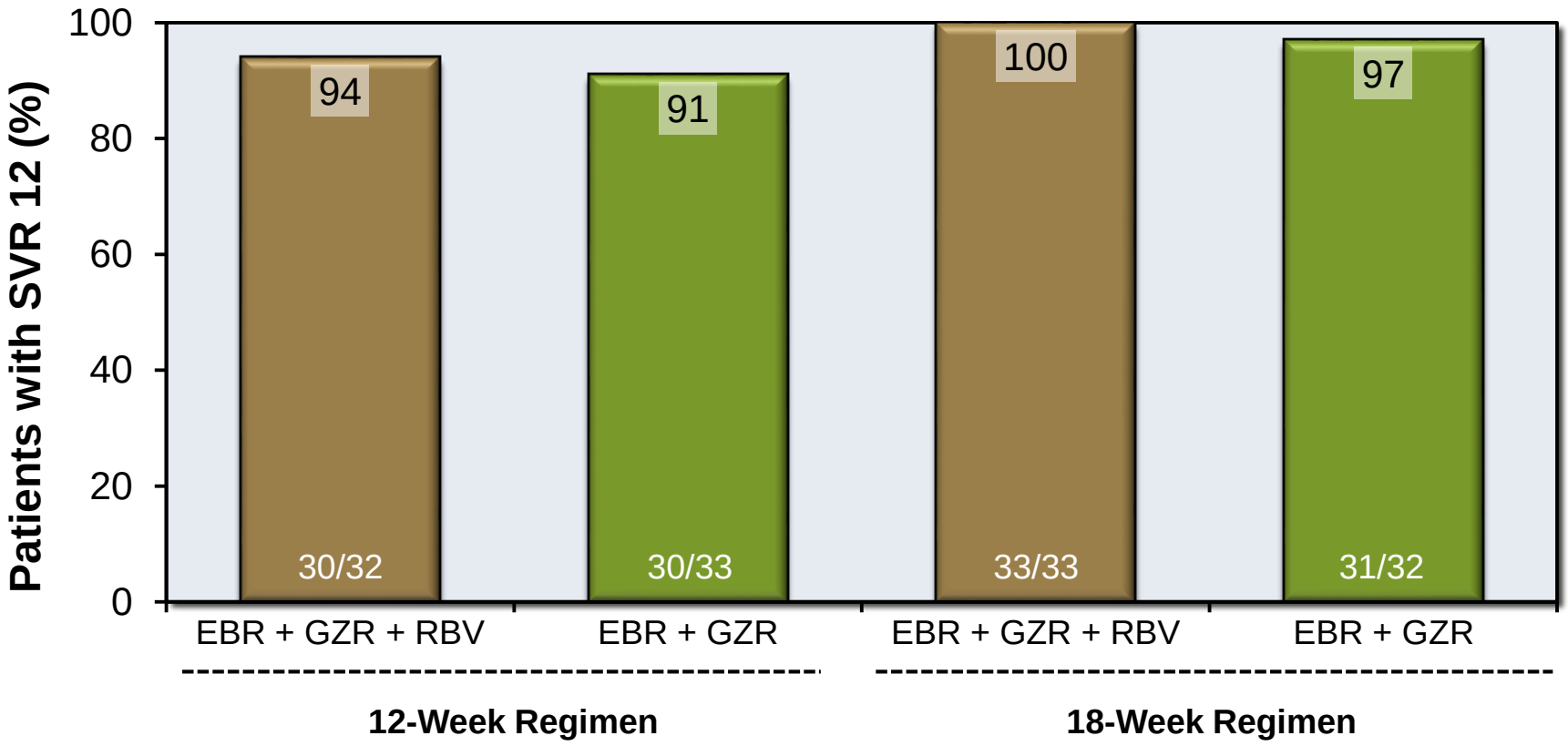
Abbreviations: EBR = elbasvir; GZR = grazoprevir; RBV = ribavirin

*Analysis per protocol: excluding patients who dropped out due to reasons other than virologic failure

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



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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

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

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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.”

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