Treatment Naïve and Treatment Experienced

Elbasvir-Grazoprevir + Sofosbuvir +/- RBV in GT 3

C-ISLE

Source: Foster GR, et al. Hepatology. 2018;67:2113-26.

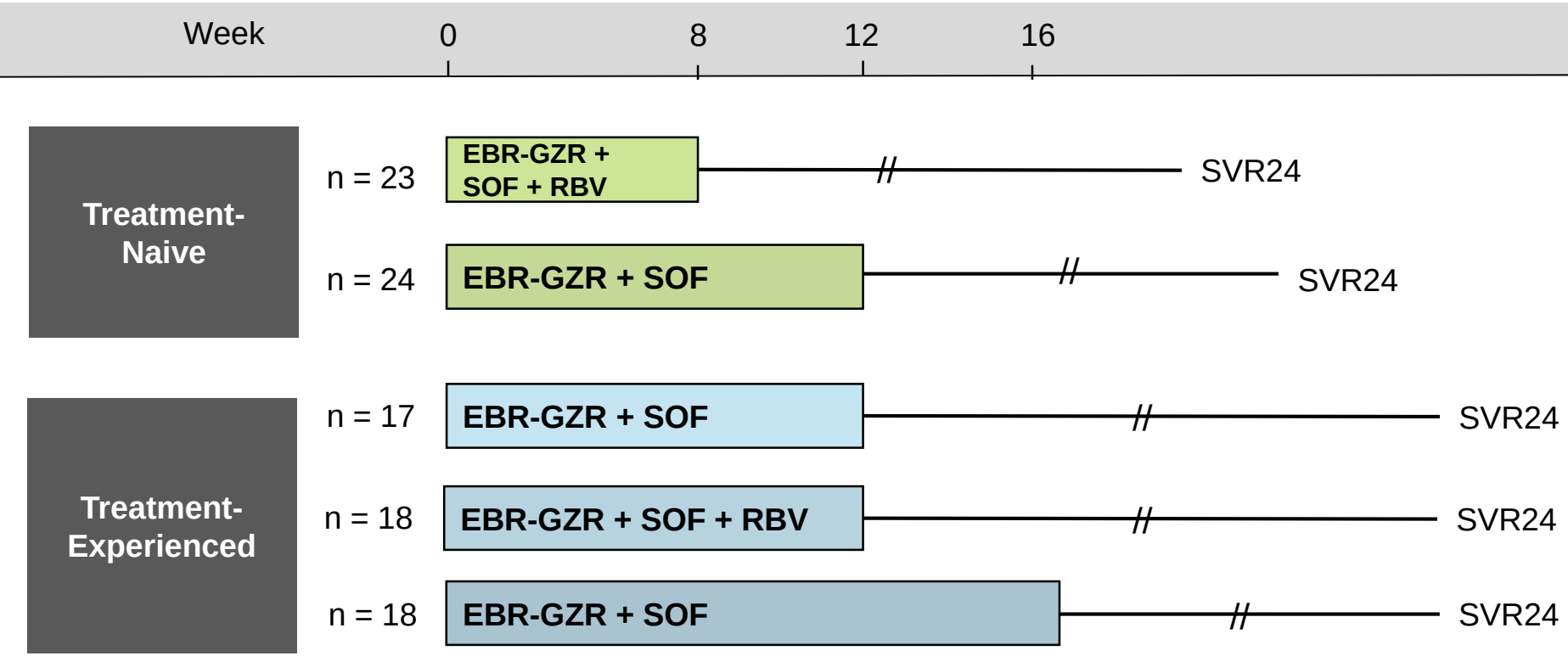
Elbasvir + Grazoprevir +/- Ribavirin in HCV GT3
C-ISLE Study: Features

C-ISLE Trial

- **Design**: Randomized, open label, phase 2 trial examining the safety and efficacy of elbasvir-grazoprevir plus sofosbuvir, with or without ribavirin, for 8 or 12 weeks in treatment-naïve adults with HCV GT3 and compensated cirrhosis, or for 12 or 16 weeks in adults with HCV GT3 and prior with treatment failure with peginterferon plus ribavirin (PR)
- **Entry Criteria**
  - Chronic HCV genotype 3
  - 18 years or older
  - Compensated cirrhosis (Child-Pugh class A) and HIV allowed
  - Exclusions: prior DAA therapy, HBV, Child-Pugh class B or C cirrhosis
- **Primary End-Point**: SVR12

Source: Foster GR, et al. Hepatology. 2018;67:2113-26.

Elbasvir-Grazoprevir + Sofosbuvir +/- RBV in HCV GT3 Cirrhosis
C-ISLE Study: Study Design



Abbreviations: EBR = elbasvir; GRZ = grazoprevir; SOF = sofosbuvir; RBV = ribavirin

Drug Dosing

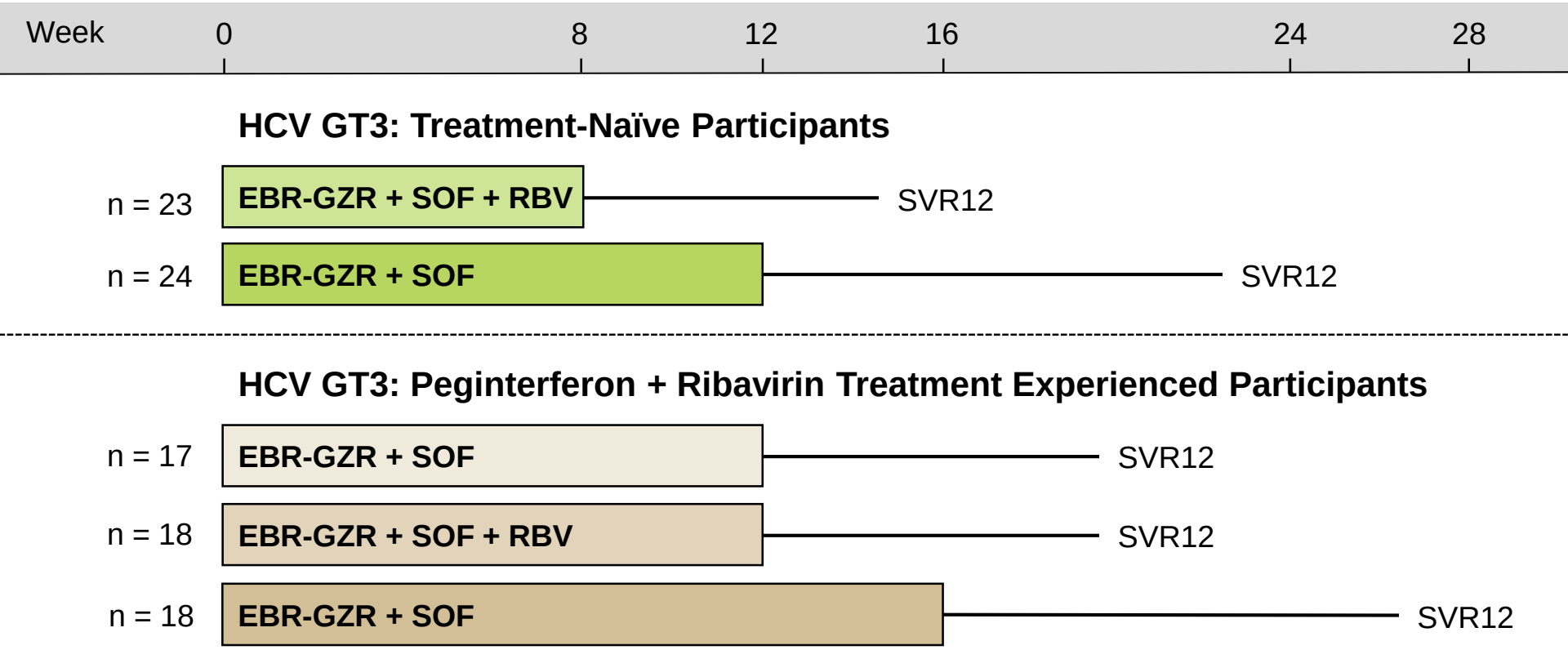
Elbasvir: 50 mg once daily, Grazoprevir: 100 mg once daily, Sofosbuvir: 400 mg once daily
Ribavirin (weight-based and divided bid): 800 to 1400 mg/day

Source: Foster G, et al. Hepatology 2018;67:2113-6.

HEPATITIS C ONLINE

Elbasvir-Grazoprevir + Sofosbuvir +/- Ribavirin in HCV GT3

C-ISLE: Study Design



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Hepatitis C Online

Elbasvir-Grazoprevir + Sofosbuvir +/- Ribavirin in HCV GT3
C-ISLE Study: Baseline Characteristics

Baseline Characteristic	Treatment-Naïve		Treatment-Experienced		
	EBR-GZR + SOF + RBV 8 weeks (n = 23	EBR-GZR + SOF 12 weeks (n = 24)	EBR-GZR + SOF 12 weeks (n = 17)	EBR-GZR + SOF + RBV 12 weeks (n = 18)	EBR-GZR + SOF 16 weeks (n = 18)
Median age, y (range)	51 (37-68)	48 (32-64)	58 (48-68)	56 (38-70)	53 (43-66)
Male, %	56.5	70.8	64.7	66.7	83.3
Female, %	43.5	29.2	35.3	33.3	16.7
Race					
White, %	69.6	79.2	76.5	50.0	66.7
Asian, %	26.1	16.7	23.5	50.0	33.3
BMI, %					
<30 kg/m^2	73.9	75.0	76.5	72.2	61.1
≥30 kg/m^2	26.1	25.0	23.5	27.8	38.9
Baseline HCV RNA					
≤2 million IU/mL, %	52.2	41.7	58.8	44.4	61.1
>2 million IU/mL, %	47.8	58.3	41.2	55.6	38.9

Source: Foster GR, et al. Hepatology. 2018;67:2113-26.

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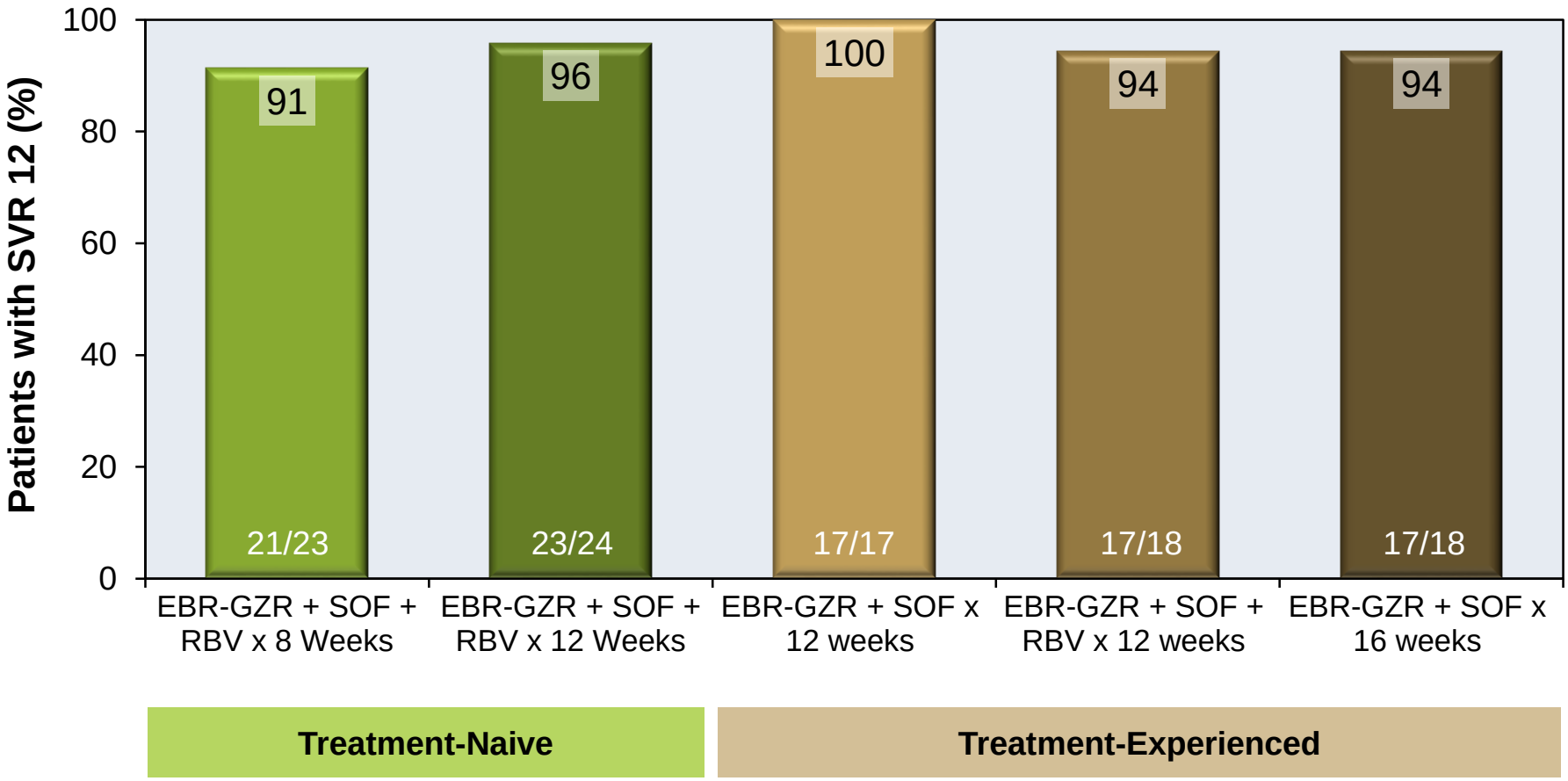
Elbasvir-Grazoprevir + Sofosbuvir +/- Ribavirin in HCV GT3 C-ISLE Study: Results



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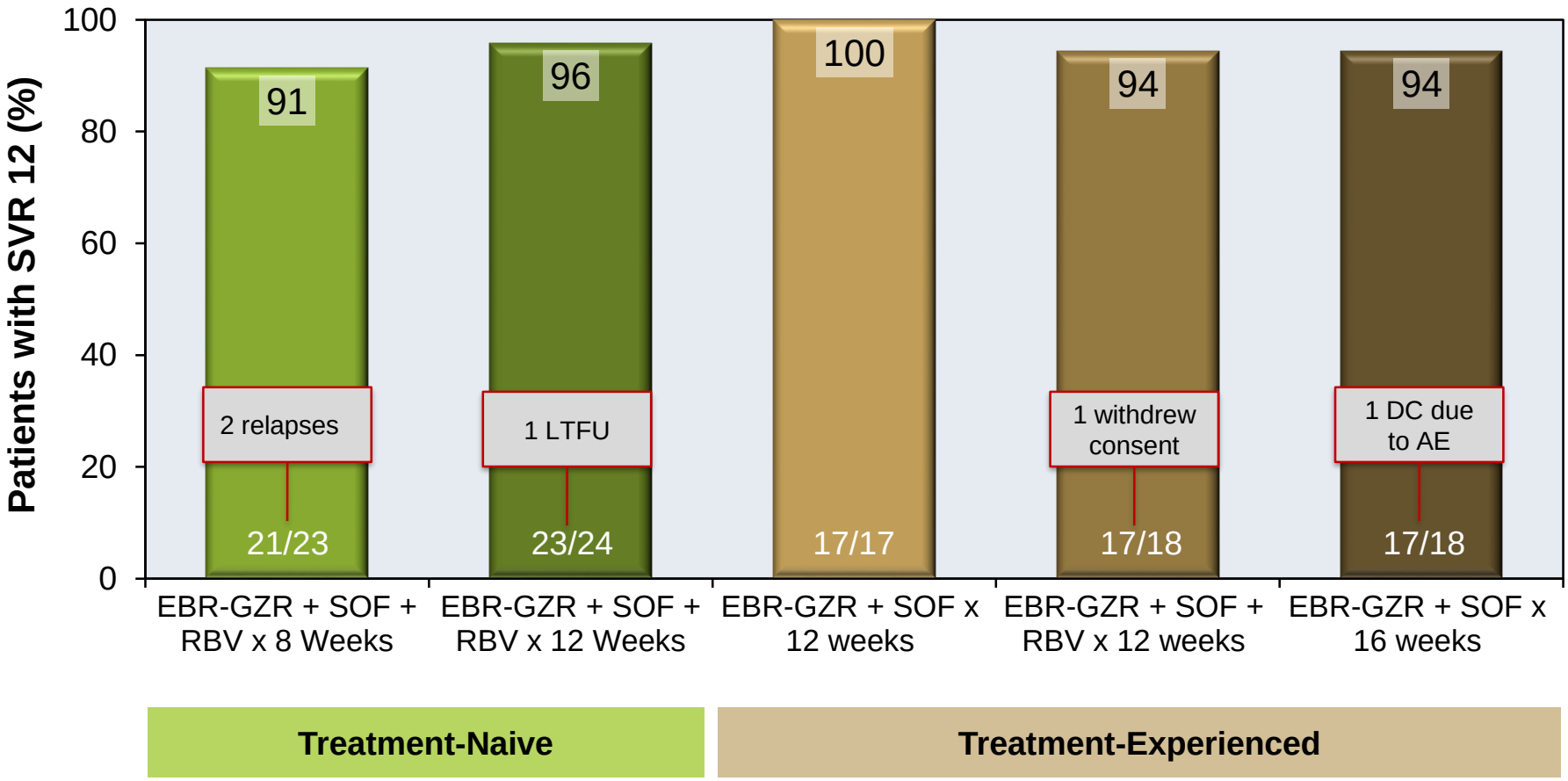
HEPATITIS C ONLINE

Elbasvir-Grazoprevir + Sofosbuvir +/- Ribavirin in HCV GT3 C-ISLE Study: Results



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Source: Foster GR, et al. Hepatology. 2018;67:2113-26.

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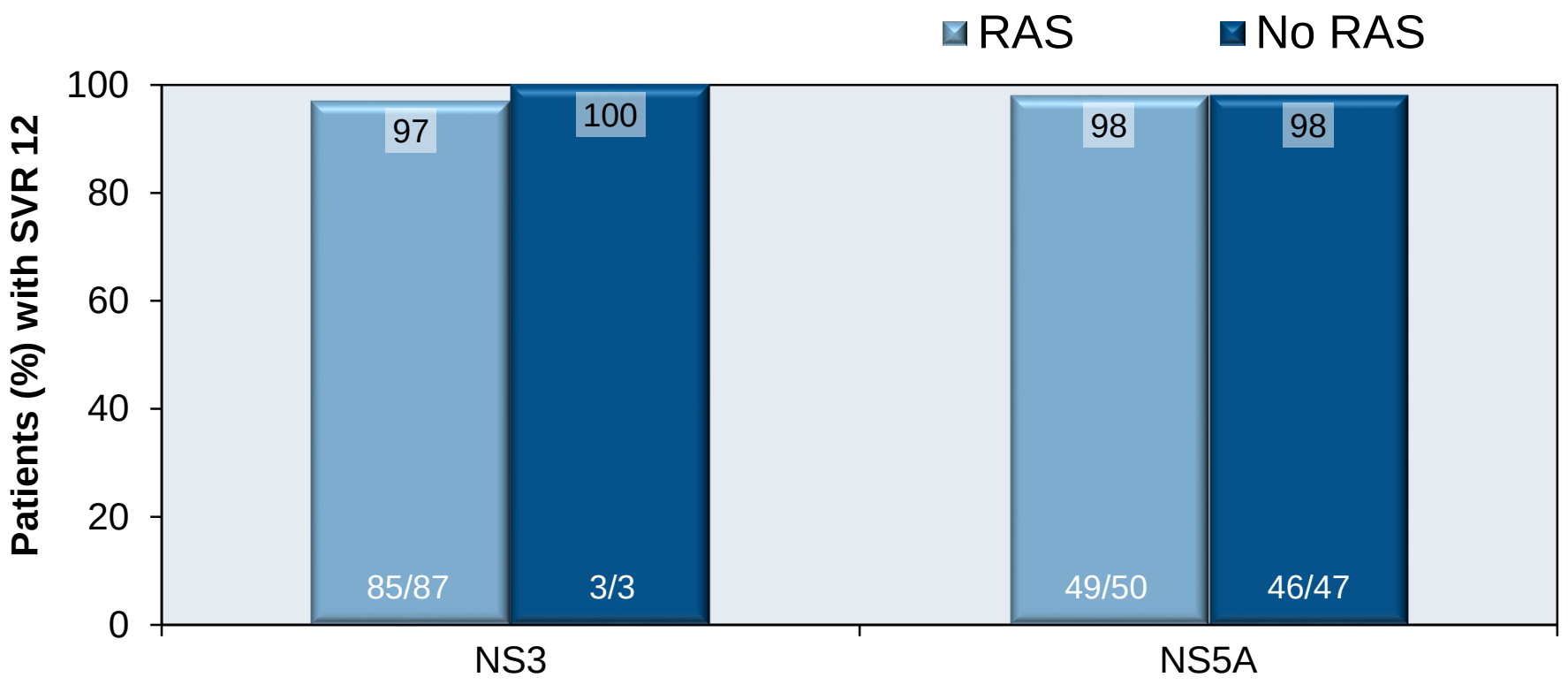
Elbasvir-Grazoprevir + Sofosbuvir +/- RBV in HCV GT3 Cirrhosis
C-ISLE Study: Results by Presence of RAS

C-ISLE: SVR12 Rates by Presence of RAS



RAS = resistance-associated substitution. 97 patients contributed to RAS analysis.
Of these, 90 had sequences available for NS3 analysis and all 97 for NS5A analysis.

Source: Foster G, et al. Hepatology 2018;67:2113-6.

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Elbasvir-Grazoprevir + Sofosbuvir +/- RBV in HCV GT3 Cirrhosis
C-ISLE Study: Adverse Events

Adverse Event (AE), n (%)	Treatment-naïve		Treatment-Experienced		
	EBR-GZR + SOF + RBV 8 weeks (n = 23)	EBR-GZR + SOF 12 weeks (n = 24)	EBR-GZR + SOF + RBV 12 weeks (n = 17)	EBR-GZR + SOF 12 weeks (n = 18)	EBR-GZR + SOF 16 weeks (n = 18)
Drug-related AE	14 (61)	13 (54)	5 (29)	15 (83)	11 (61)
Any AE	20 (87)	21 (88)	14 (82)	17 (94)	17 (94)
Fatigue	6 (26)	8 (33)	6 (35)	10 (56)	6 (33)
Nausea	4 (17)	3 (13)	3 (18)	6 (33)	3 (17)
Headache	5 (22)	7 (29)	5 (29)	11 (61)	7 (39)
Rash	3 (13)	1 (4)	1 (6)	3 (17)	1 (6)
Serious AE	0	0	1 (6)	3 (17)	1 (6)
Discontinuation due to AE	0	0	0	0	1 (6)
Deaths	0	0	0	0	0
Hemoglobin <10 mg/dL	0	0	1 (6)	2 (11)	0
Bilirubin <5x baseline	0	0	0	0	0
ALT/AST >5x baseline	0	0	0	0	0

Source: Foster G, et al. Hepatology 2018;67:2113-6.

HEPATITIS C ONLINE

Elbasvir-Grazoprevir + Sofosbuvir +/- Ribavirin in HCV GT3
C-ISLE Study: Conclusions

Conclusion: “Data from this study support the use of elbasvir-grazoprevir plus sofosbuvir for 12 weeks without reibavirin for treatment-naive and peginterferon/ribavirin-experienced people with GT3 infection and cirrhosis.”

Source: Foster GR, et al. Hepatology. 2018;67:2113-26.

Treatment Naïve and Treatment Experienced

Elbasvir-Grazoprevir + Sofosbuvir +/- RBV in GT 3 Patients with Compensated Cirrhosis

C-ISLE

Source: Foster G, et al. Hepatology 2018;67:2113-6.

Elbasvir-Grazoprevir + Sofosbuvir +/- RBV in HCV GT3 Cirrhosis
C-ISLE Study: Baseline Characteristics

Baseline Characteristic	Treatment-naïve		Treatment-Experienced		
	EBR-GZR + SOF + RBV 8 wks (n = 23)	EBR-GZR + SOF 12 wks (n = 24)	EBR-GZR + SOF + RBV 12 wks (n = 17)	EBR-GZR + SOF 12 wks (n = 18	EBR-GZR + SOF 16 wks n = 18)
Median age, yrs (range)	51 (37-68)	48 (32-64)	58 (48-68)	56 (38-70)	53 (43-66)
Male, %	56.5	70.8	64.7	66.7	83.3
Race White Asian Other	 69.6 26.1 4.3	 79.2 16.7 4.2	 76.5 23.5 0	 50 50 0	 66.7 33.3 0
BMI ≥30 kg/m^2, %	26.1	25	23,5	27.8	38.9
Prior PR history, % Intolerant Null responder Relapser	n/a	n/a	 0 0 100	 0 5.6 94.4	 5.6 0 94.4
IL28B non-CC, %	39.1	33.3	64.7	61.1	61.1
HCV RNA >2 million IU/mL, %	47.8	58.3	41.2	55.6	38.9

Source: Foster G, et al. Hepatology 2018;67:2113-6.

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Elbasvir-Grazoprevir + Sofosbuvir +/- RBV in HCV GT3 Cirrhosis C-ISLE Study: Conclusions

Conclusion: “In conclusion, high efficacy was demonstrated in treatment-naive and peginterferon/ribavirin treatment–experienced participants with HCV GT3 infection and cirrhosis, with SVR12 rates of 100% achieved in participants receiving elbasvir-grazoprevir plus sofosbuvir with or without ribavirin for 12 weeks.”

Source: Foster G, et al. Hepatology 2018;67:2113-6.