

HEPATITIS WEB STUDY  HEPATITIS C ONLINE

Elbasvir-Grazoprevir (*Zepatier*)

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Last Updated: January 29, 2016

ELBASVIR-GRAZOPREVIR (*ZEPATIER*)
Background and Dosing

Elbasvir-Grazoprevir (*Zepatier*)

- **Approval Status**
 - Approval by United States FDA on January 28, 2016
- **Indications and Usage**
 - Indicated for the treatment of chronic HCV genotypes 1 or 4 in adults
 - Indicated for treatment of patients with HIV coinfection
- **Class & Mechanism**
 - Elbasvir: HCV NS5A inhibitor
 - Grazoprevir: HCV NS3/4A inhibitor
- **Dosing:** Elbasvir-Grazoprevir (fixed dose 50 mg/100 mg)
One tablet orally once daily, with or without food
- **Adverse Effects (AE):**
 - Fatigue, headache, and nausea
 - Increase in ALT > 5x normal in 1% of subjects

Elbasvir-Grazoprevir (*Zepatier*) Indications and Usage

Elbasvir-Grazoprevir (EBR-GZR) HCV Treatment in Patients with or without Cirrhosis

| Patient Population | Treatment | Duration |
|---|----------------------------|----------|
| GT 1a: Treatment-naïve or PegIFN/RBV-experienced (<u>without</u> baseline NS5A polymorphisms*) | Elbasvir-Grazoprevir | 12 weeks |
| GT 1a: Treatment-naïve or PegIFN/RBV-experienced (<u>with</u> baseline NS5A polymorphisms*) | Elbasvir-Grazoprevir + RBV | 16 weeks |
| GT 1b: Treatment-naïve or PegIFN/RBV-experienced | Elbasvir-Grazoprevir | 12 weeks |
| GT 1a or 1b: PegIFN/RBV/PI-experienced | Elbasvir-Grazoprevir + RBV | 12 weeks |
| GT 4: Treatment-naïve | Elbasvir-Grazoprevir | 12 weeks |
| GT 4: PegIFN/RBV-Experienced | Elbasvir-Grazoprevir + RBV | 16 weeks |

Abbreviations: PegIFN = peginterferon; RBV = ribavirin; PI = protease inhibitor; EBR-GZR = elbasvir-grazoprevir

*Polymorphisms at amino acid positions 28, 30, 31, or 93

Elbasvir-Grazoprevir (*Zepatier*) Drug-Drug Interactions

HCV GT1a and Impact of Baseline NS5A Polymorphisms on SVR12

| NS5A Polymorphism Status | EBR-GZR x 12 weeks SVR12% (n/N) | EBR-GZR + RBV x 16 weeks SVR12% (n/N) |
|--|------------------------------------|--|
| Without baseline NS5A polymorphism (M28, Q30, L31, or Y93) | 98% (441/450) | 100% (49/49) |
| With baseline NS5A polymorphism (M28*, Q30*, L31*, or Y93*) | 70% (39/56) | 100% (6/6) |

Abbreviations: GT = genotype; EBR = elbasvir; GZR = grazoprevir

*Any change from GT1a reference

Elbasvir-Grazoprevir (*Zepatier*) Drug-Drug Interactions

Drugs that are Contraindicated for Use with Elbasvir-Grazoprevir

Organic ion transporter polypeptide 1B (OATP1B) inhibitors

Antimycobacterials

Rifampin

HIV medications

Atazanavir
Darunavir
Lopinavir
Saquinavir
Tipranavir

Immunosuppressants

Cyclosporine

Strong CYP3A Inducers

Anticonvulsants

Phenytoin
Carbamazepine

Herbal products

St. John's Wort (*Hypericum perforatum*)

HIV medications

Efavirenz

*This is not a complete list of all drugs than inhibit OAT1B

CLINICAL TRIALS

Elbasvir-Grazoprevir

Elbasvir-Grazoprevir (EBR-GZR): Summary of Key Studies

- **Phase 2 Trials**

- **C-SWIFT**: EBR-GZR + Sofosbuvir x 8 or 12 weeks in GT 1 or 3
- **C-WORTHY**: EBR-GZR +/- RBV in TN Cirrhotic or null responders
- **C-WORTHY Coinfection**: EBR-GZR +/- RBV in HIV coinfection
- **C-SALVAGE**: EBR-GZR + RBV in PI-experienced patients
- **C-SCAPE**: EBR +/- GZR +/- RBV in GT 2, 4, 5, or 6 without cirrhosis

Elbasvir-Grazoprevir (EBR-GZR): Summary of Key Studies

- **Phase 3 Trials**

- **C-EDGE TN:** EBR-GZR x 12 weeks in treatment-naïve GT 1, 4 or 6
- **C-EDGE TE:** EBR-GZR +/- RBV x 12 or 16 weeks in TE GT 1, 4 or 6
- **C-EDGE Coinfection:** EBR-GZR x 12 weeks in HIV-HCV coinfecting
- **C-EDGE CO-STAR:** EBR-GZR x 12 weeks in persons who inject drugs
- **C-SURFER:** EBR-GZR x 12 weeks in GT1 and Chronic kidney disease

Elbasvir-Grazoprevir Treatment-Naïve Patients

Treatment Naïve

Elbasvir-Grazoprevir in Treatment-Naïve HCV Genotype 1, 4 or 6 C-EDGE Treatment Naïve (TN)

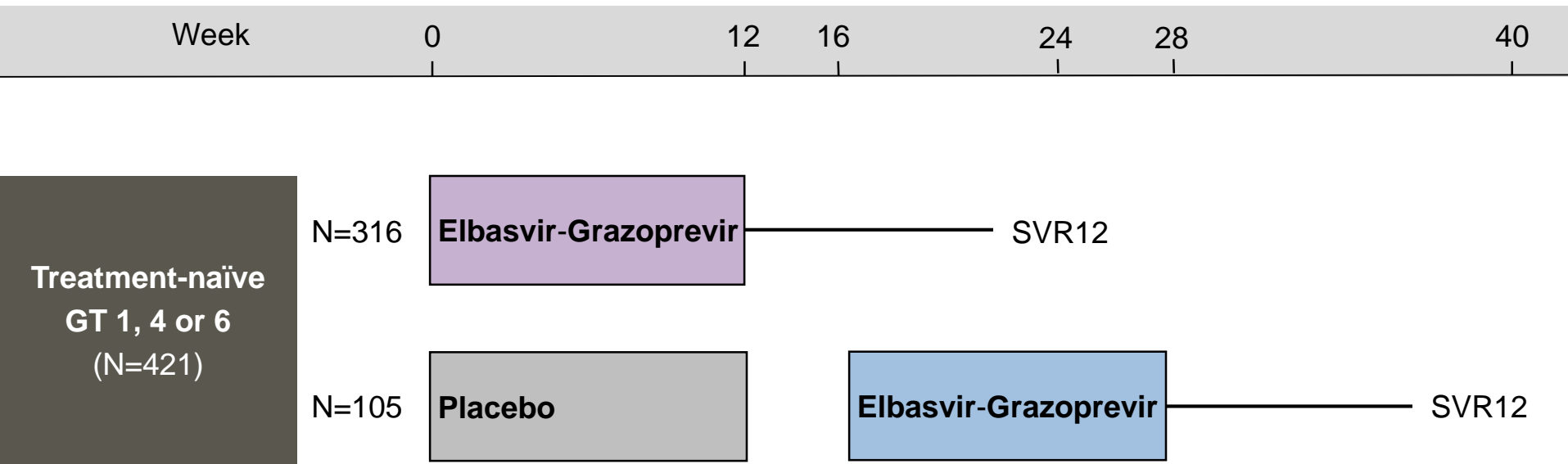
Zeuzem S, et al. Ann Intern Med. 2015;163:1-13.

Elbasvir-Grazoprevir in Treatment-Naïve HCV Genotype 1, 4 or 6 C-EDGE TN Study: Features

C-EDGE TN Trial

- **Design:** Randomized, placebo-controlled, parallel-group, phase 3 trial using a fixed-dose combination of elbasvir-grazoprevir for 12 weeks in treatment-naïve patients with GT 1, 4 or 6 chronic HCV
- **Setting:** 60 sites in United States, Europe, Australia, Scandinavia, & Asia
- **Entry Criteria**
 - Chronic HCV: GT1=91%, GT4=6%, or GT6=3%
 - 18 years or older
 - HCV RNA $\geq 10,000$ IU/mL
 - No prior HCV treatment
 - Patients with compensated cirrhosis accepted
- **Primary End-Point:** SVR12

Elbasvir-Grazoprevir in Treatment-Naïve HCV Genotype 1, 4 or 6 C-EDGE TN: Study Design



Randomized 3:1 ratio to immediate or deferred arm; stratified by cirrhosis, HCV genotype, subtype
After 4 weeks of follow-up, placebo recipients were unblinded and given elbasvir-grazoprevir open label

Drug Dosing

Elbasvir-Grazoprevir (50/100 mg): fixed dose combination; one pill once daily

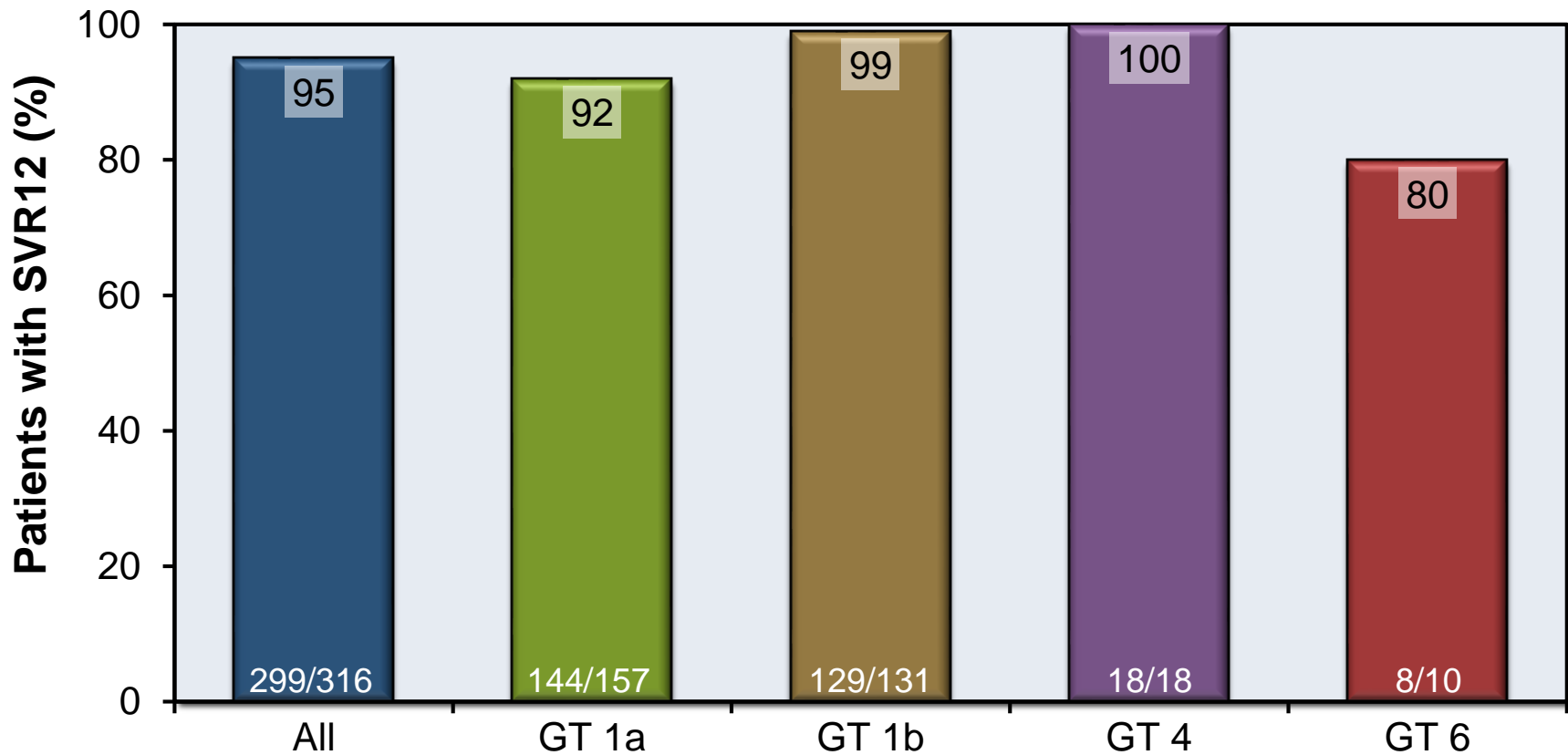
Elbasvir-Grazoprevir in Treatment-Naïve HCV GT 1, 4 or 6 C-EDGE TN: Baseline Characteristics

| Baseline Characteristic | Immediate Arm (N=316) | Delayed Arm (N=105) | All Patients (N=421) |
|---------------------------|--------------------------|------------------------|-------------------------|
| Age, mean | 52 | 54 | 53 |
| Male, % | 54 | 53 | 54 |
| Race, % | | | |
| Asian | 17 | 12 | 16 |
| Black | 19 | 17 | 18 |
| White | 60 | 70 | 63 |
| HCV genotype, n (%) | | | |
| 1a | 157 (50) | 54 (51) | 211 (50) |
| 1b | 131 (42) | 40 (38) | 171 (41) |
| 4 | 18 (6) | 8 (8) | 26 (6) |
| 6 | 10 (3) | 3 (3) | 13 (3) |
| HCV RNA >800,000 IU/ml, % | 222 (70) | 66 (63) | 288 (68) |
| IL28B non-CC, % | 66 | 64 | 65 |
| Fibrosis stage, % | | | |
| F0-2 | 67 | 66 | 66 |
| F3 | 11 | 13 | 12 |
| F4 | 22 | 21 | 22 |

Source: Zeuzem S, et al. Ann Intern Med. 2015;163:1-13.

Elbasvir-Grazoprevir in Treatment-Naïve HCV GT 1, 4 or 6 C-EDGE TN: Results

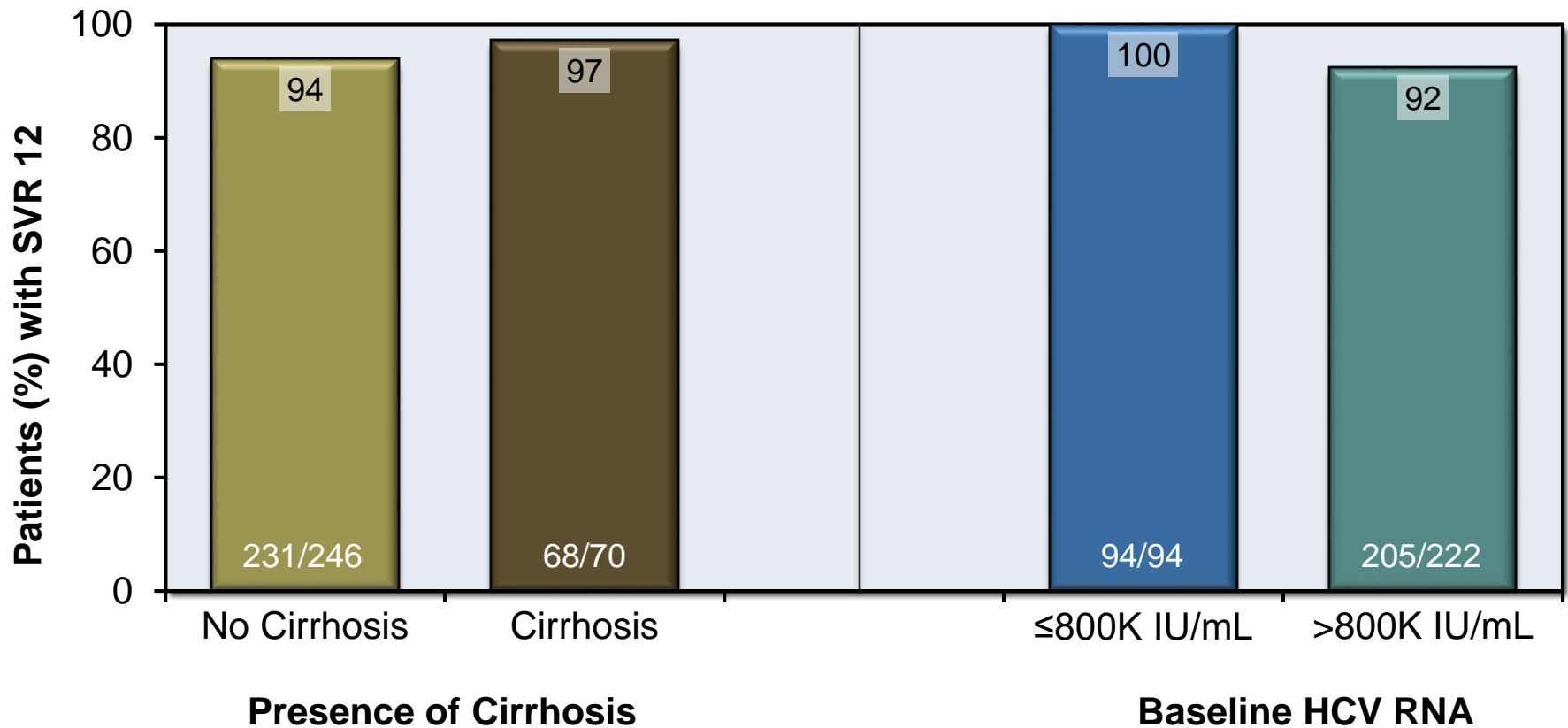
C-EDGE TN: SVR12 Results by Genotype



Primary efficacy analysis included all patients who received ≥ 1 dose of drug.

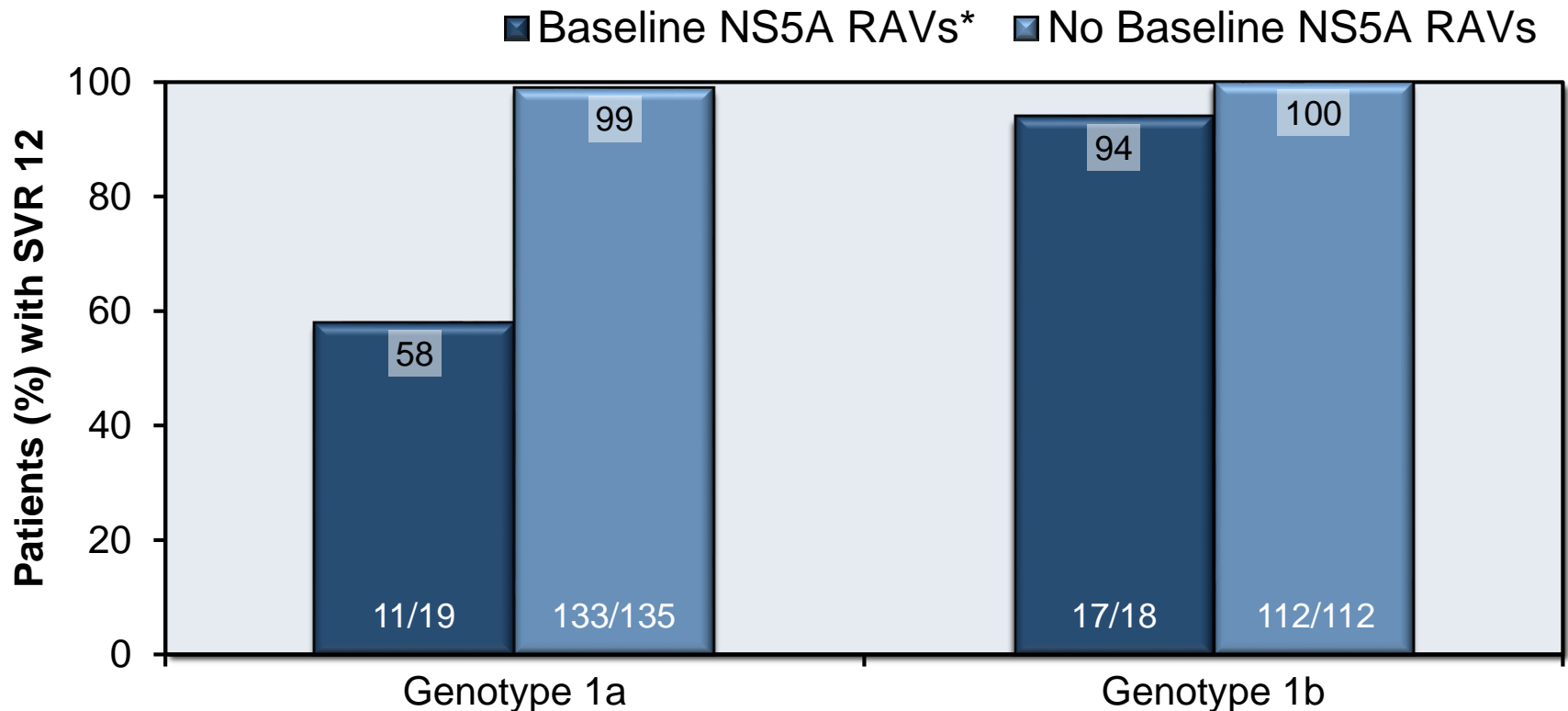
Elbasvir-Grazoprevir in Treatment-Naïve HCV GT 1, 4 or 6 C-EDGE TN: Results

C-EDGE TN: SVR12 by Presence of Cirrhosis or High HCV RNA Level



Elbasvir-Grazoprevir in Treatment-Naïve HCV GT 1, 4 or 6 C-EDGE TN: Results

Baseline NS5A Resistance-Associated Variants and SVR12 in GT1

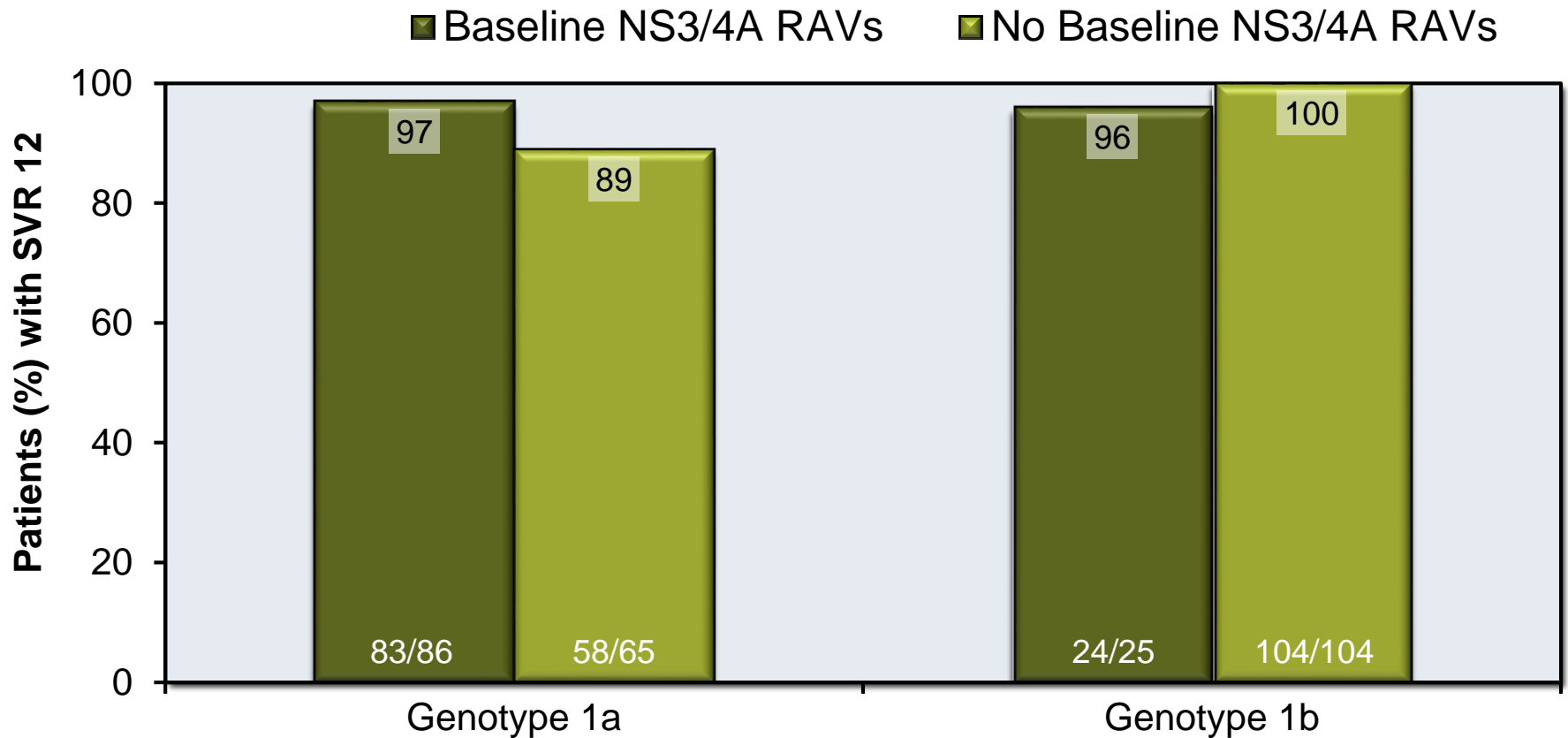


*Patients with baseline GT1a RAVs with a ≤ 5 -fold shift to elbasvir: SVR12=90% (9 of 10)

*Patients with baseline GT1a RAVs with a > 5 -fold shift to elbasvir: SVR12=22% (2 of 9)

Elbasvir-Grazoprevir in Treatment-Naïve HCV GT 1, 4 or 6 C-EDGE TN: Results

Baseline NS3/4A Resistance-Associated Variants and SVR12 in GT1



Elbasvir-Grazoprevir in Treatment-Naïve HCV GT 1, 4 or 6 C-EDGE TN: Adverse Events

| Adverse Event (AE) | Elbasvir-Grazoprevir | |
|---|-----------------------|-------------------------------|
| | Immediate (n=316) | Deferred (Placebo) (n=105) |
| Discontinuation due to AE | 3 (0.9%) | 1 (1%) |
| Serious AEs | 9 (3%) | 3 (3%) |
| Deaths | 2 (0.6%) [§] | 0 |
| Any AE in ≥10% of patients | | |
| Headache | 52 (17%) | 19 (18%) |
| Fatigue | 49 (16%) | 18 (17%) |
| Laboratory AEs | | |
| ALT >5 x baseline | 3 (0.9%) | 0 |
| AST >5 x baseline | 1 (0.3%) | 0 |
| Total bilirubin elevation >5 x baseline | 1 (0.3%) | 0 |
| Grade 3 or 4 hemoglobin | 0 | 0 |
| Grade 3 or 4 neutrophils | 1 (0.3%) | 1 (1%) |
| Grade 3 or 4 creatinine | 0 | 0 |

[§] Neither death was considered to be study-related.

Source: Zeuzem S, et al. *Ann Intern Med.* 2015;163:1-13.

Elbasvir-Grazoprevir in Treatment-Naïve HCV GT 1, 4 or 6 C-EDGE TN: Conclusions

Conclusions: “Grazoprevir-elbasvir achieved high SVR12 rates in treatment-naive cirrhotic and noncirrhotic patients with genotype 1, 4, or 6 infection. This once-daily, all-oral, fixed-combination regimen represents a potent new therapeutic option for chronic HCV infection.”

Treatment Naïve

Elbasvir-Grazoprevir + Sofosbuvir in Treatment-Naïve HCV Genotype 1 or 3
C-SWIFT

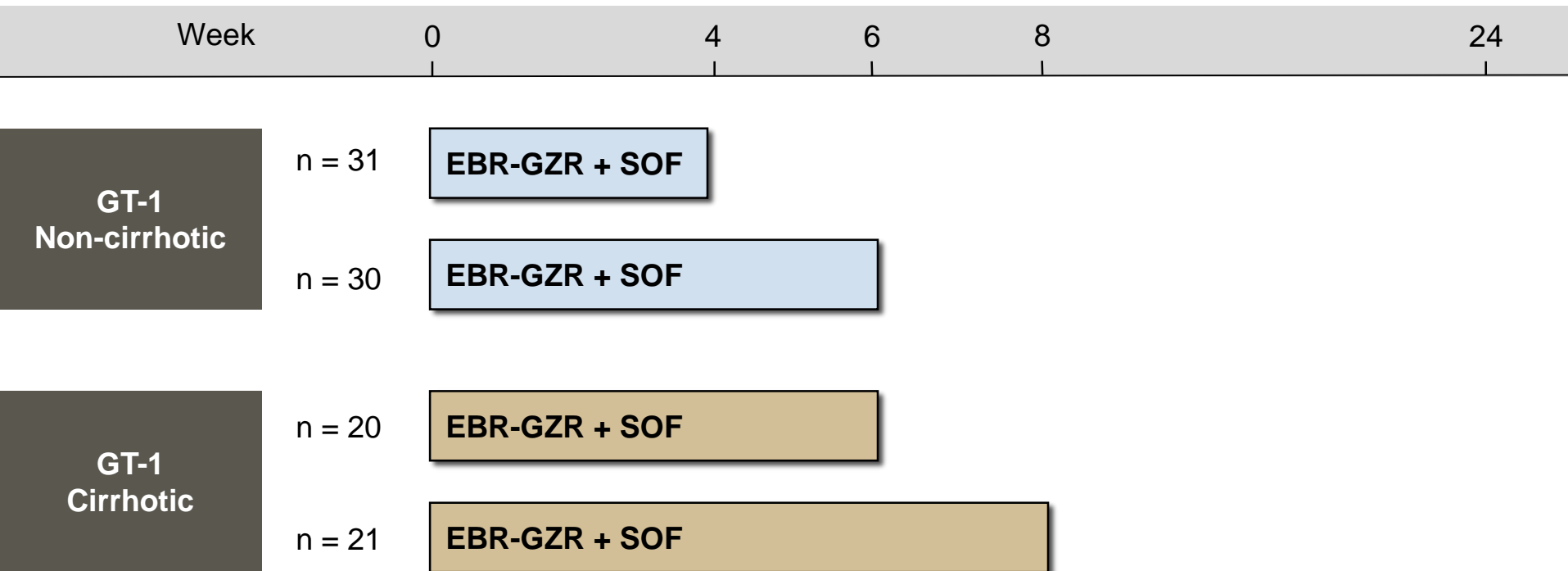
Poordad F, et al. EASL 2015; Abstract O006.

Elbasvir-Grazoprevir + Sofosbuvir in Treatment-Naïve GT 1 or 3 C-SWIFT Study: Features

C-SWIFT Trial

- **Design:** Open-label phase 2 trial to evaluate the efficacy and safety of short duration therapy with elbasvir-grazoprevir + sofosbuvir in treatment-naïve GT 1 or 3 infection, with or without cirrhosis
- **Entry Criteria**
 - Chronic HCV Genotype 1 (n=102) or Genotype 3 (n=41)
 - 18 years or older
 - No prior HCV treatment
 - HCV RNA $\geq 10,000$ IU/ml
 - ALT and AST < 350 IU/L
 - Cirrhosis allowed
- **Primary End-Point:** SVR12

Elbasvir-Grazoprevir + Sofosbuvir in Treatment-Naïve GT 1 or 3 C-SWIFT Study: Study Design for GT 1



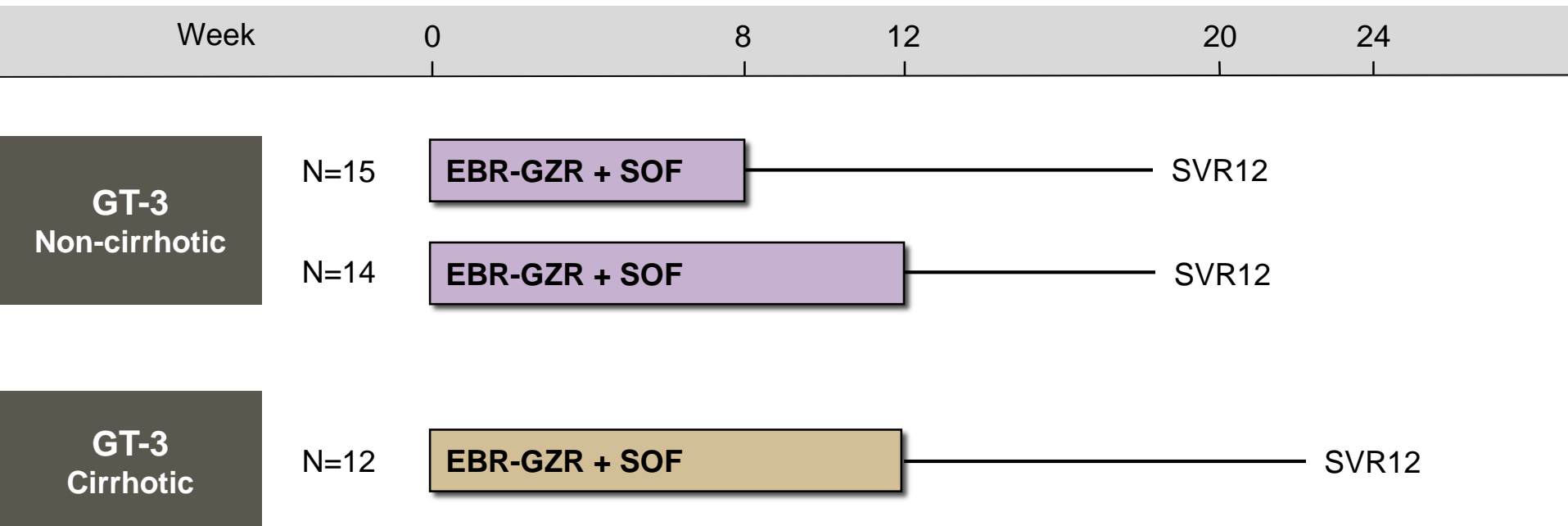
Abbreviations: EBR-GZR = elbasvir-grazoprevir; SOF = sofosbuvir

Drug Dosing

Elbasvir-grazoprevir (50/100 mg): fixed-dose combination; one pill once daily

Sofosbuvir: 400 mg once daily

Elbasvir-Grazoprevir + Sofosbuvir in Treatment-Naïve GT 1 or 3 C-SWIFT Study: Study Design for GT 3



Abbreviations: EBR-GZR= grazoprevir-elbasvir; SOF = sofosbuvir

Drug Dosing

Grazoprevir/elbasvir (100/50 mg): fixed dose combination; one pill once daily

Sofosbuvir 400 mg once daily

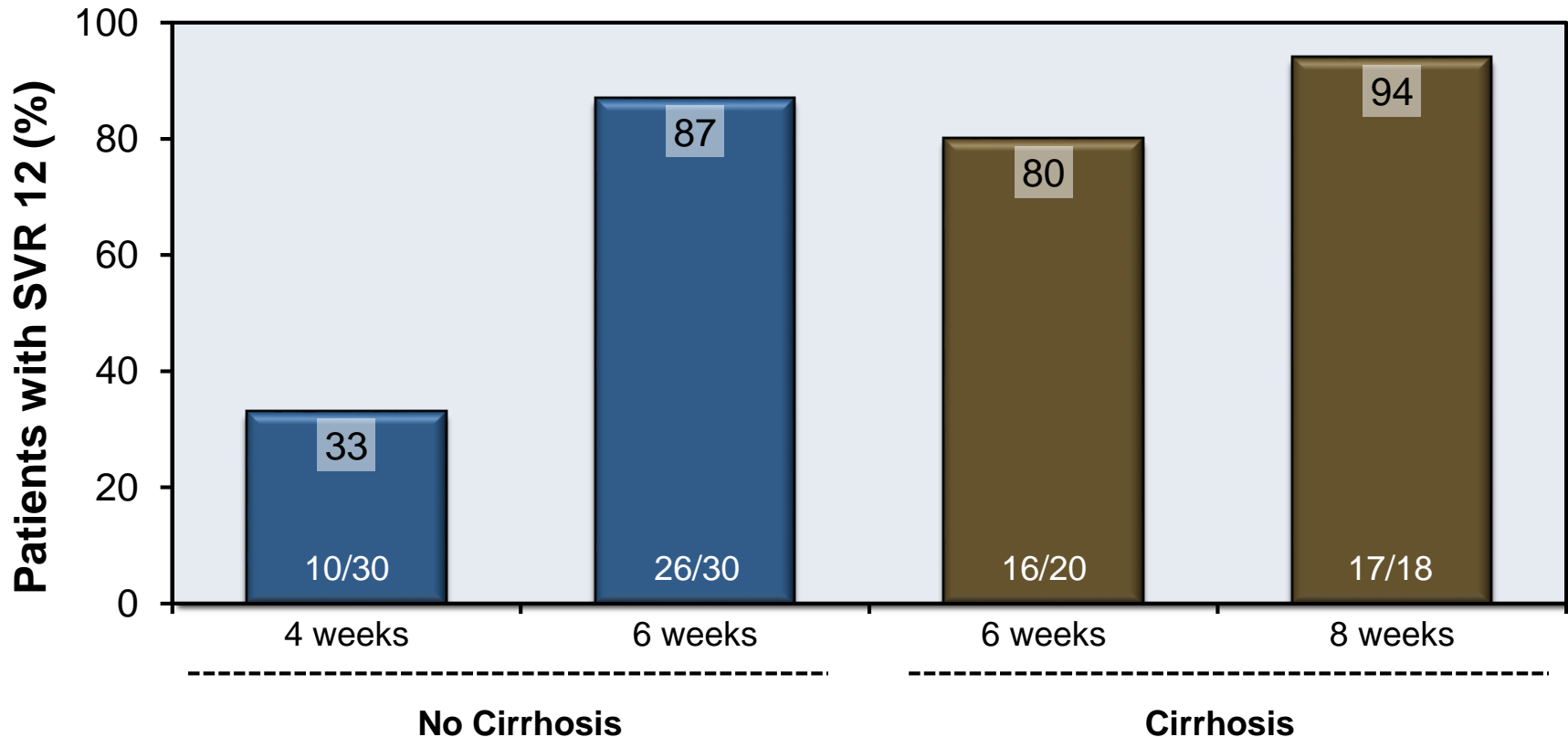
Elbasvir-Grazoprevir + Sofosbuvir in Treatment-Naïve GT 1 or 3 C-SWIFT Study: Baseline Characteristics

| Baseline Characteristic | Genotype 1 | | | | Genotype 3 | | |
|---------------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|------------------|------------------|
| | No cirrhosis | | Cirrhosis | | No Cirrhosis | | Cirrhosis |
| | 4 weeks N=31 | 6 weeks N=30 | 6 weeks N=20 | 8 weeks N=21 | 8 weeks N=15 | 12 weeks N=14 | 12 weeks N=12 |
| Mean age, years | 52 | 51 | 56 | 57 | 51 | 42 | 55 |
| Male sex, % | 65 | 63 | 65 | 62 | 73 | 57 | 83 |
| Race, % | | | | | | | |
| White | 97 | 93 | 100 | 95 | 100 | 100 | 100 |
| Hispanic/Latino | 29 | 47 | 65 | 48 | 40 | 57 | 50 |
| HCV Genotype, % | | | | | | | |
| 1a | 84 | 87 | 80 | 76 | -- | -- | -- |
| 1b | 16 | 13 | 20 | 24 | -- | -- | -- |
| 3 | -- | -- | -- | -- | 100 | 100 | 100 |
| IL28B CC, % | 36 | 27 | 30 | 24 | 40 | 21 | 50 |
| Cirrhosis, % | 0 | 0 | 100 | 100 | 0 | 0 | 100 |
| HCV RNA, 10 ⁶ IU/ml (mean) | 3.7 | 3.1 | 1.7 | 2.4 | 3.3 | 2.6 | 2.3 |

Source: Poordad F, et al. EASL 2015; Abstract O006.

Elbasvir-Grazoprevir + Sofosbuvir in Treatment-Naïve GT 1 or 3 C-SWIFT Study: Results for GT 1

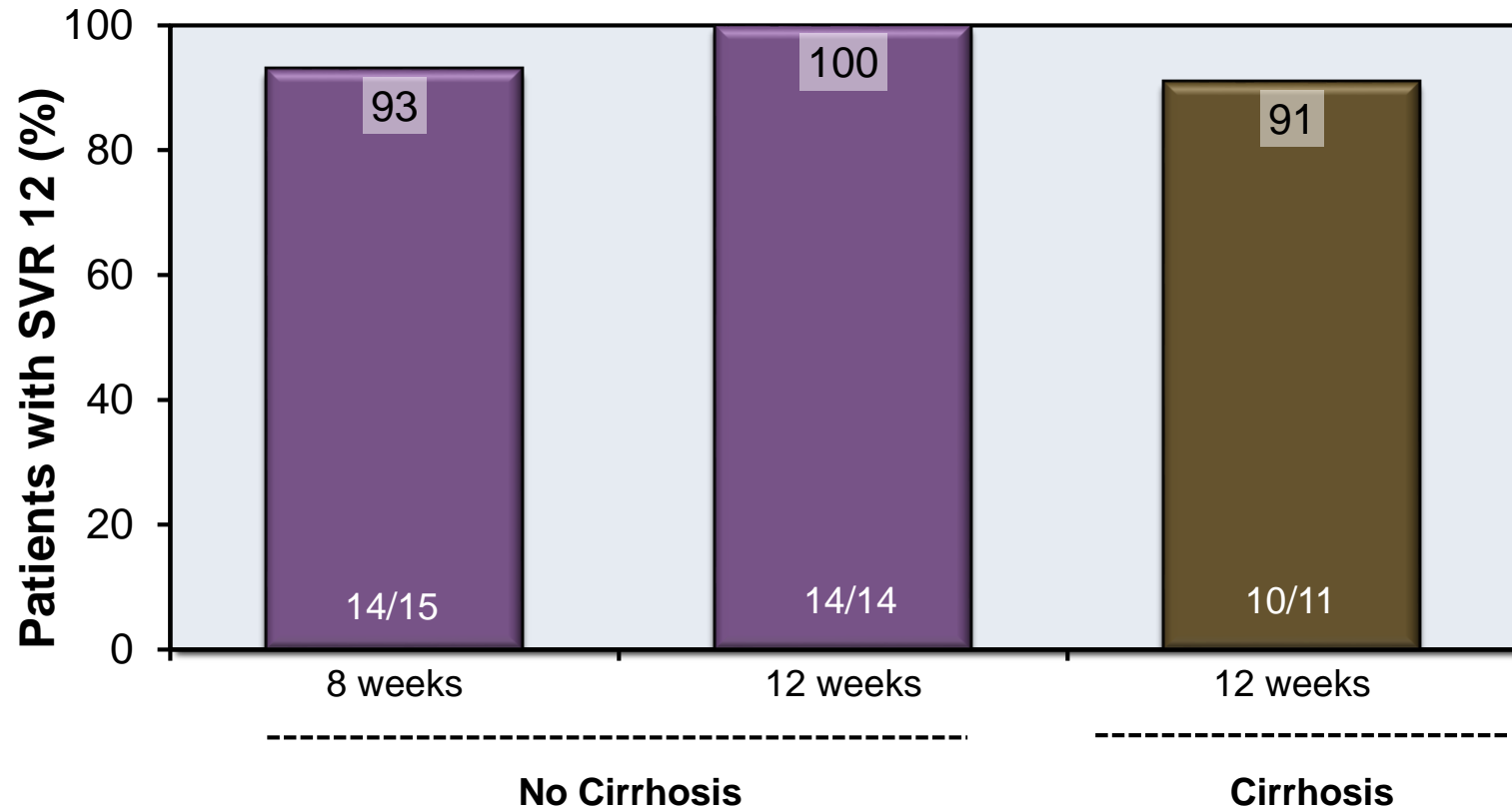
C-SWIFT: SVR 12* for GT 1 by Treatment Duration and Cirrhosis



*Analysis by modified intention-to-treat analysis (excluded patients who discontinued due to reasons other than virologic failure)

Elbasvir-Grazoprevir + Sofosbuvir in Treatment-Naïve GT 1 or 3 C-SWIFT Study: Results for GT 3

C-SWIFT: SVR 12* for GT 3 by Treatment Duration and Cirrhosis



Analysis by modified intention-to-treat analysis (excluded patients who discontinued due to reasons other than virologic failure)

Elbasvir-Grazoprevir + Sofosbuvir in Treatment-Naïve GT 1 or 3 C-SWIFT Study: Conclusions

Conclusions: “A novel regimen of grazoprevir/elbasvir with sofosbuvir was able to shorten treatment duration to 8 weeks or less among cirrhotic and non-cirrhotic HCV genotype 1-infected patients.”
“Genotype 3 patients achieved high SVR12 rates with 8-12 weeks of therapy, including patients with cirrhosis.”

Treatment Naïve

Elbasvir + Grazoprevir +/- Ribavirin in Treatment-Naïve HCV GT 2, 4, 5, or 6

C-SCAPE

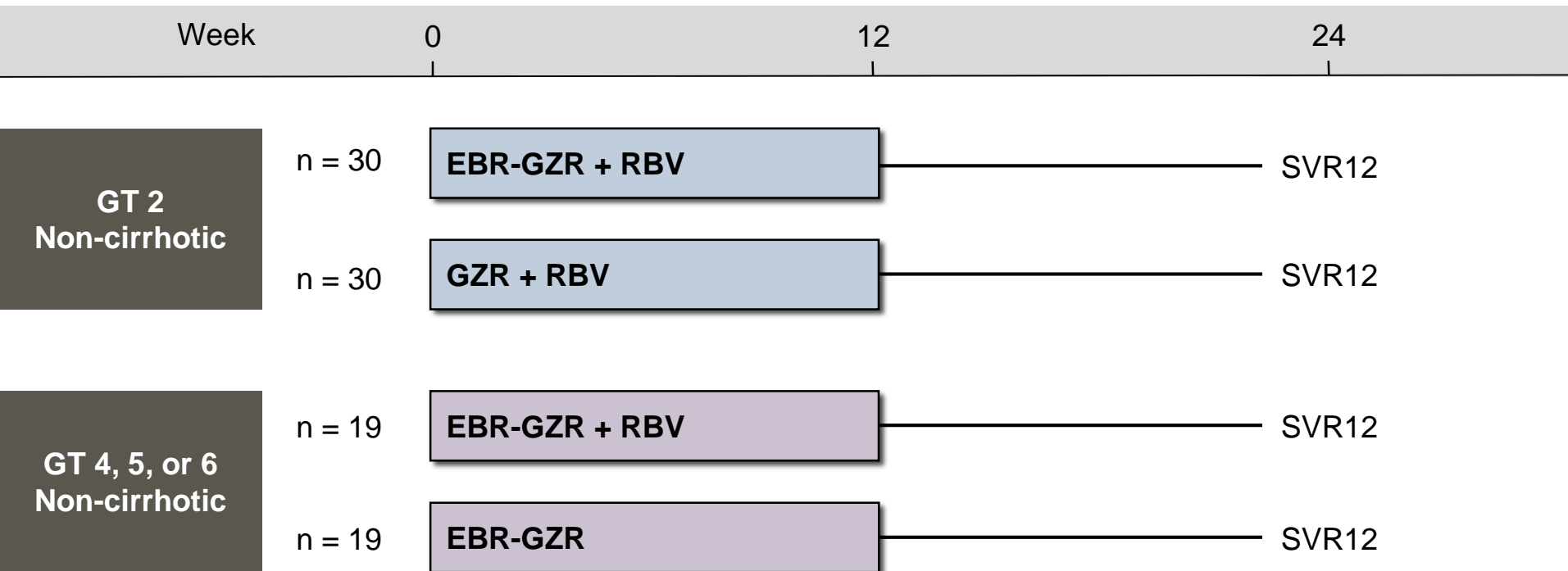
Brown A, et al. EASL 2015; Abstract P0771.

Elbasvir + Grazoprevir +/- RBV in Treatment-Naïve GT 2, 4, 5 or 6 C-SCAPE Study: Features

C-SWIFT Trial

- **Design:** Open-label, phase 2 trial to evaluate the efficacy and safety of elbasvir + grazoprevir + ribavirin versus elbasvir + grazoprevir versus grazoprevir + ribavirin in non-cirrhotic, treatment-naïve patients with GT 2, 4, 5, or 6 chronic hepatitis C infection
- **Entry Criteria**
 - Chronic HCV GT2 (n=60), GT4 (n=20), GT5 (n=8), or GT6 (n=10)
 - 18 years or older
 - No prior HCV treatment
 - HCV RNA $\geq 10,000$ IU/ml
 - No evidence of cirrhosis
- **Primary End-Point:** SVR12

Elbasvir + Grazoprevir +/- RBV in Treatment-Naïve GT 2, 4, 5 or 6 C-SCAPE Study: Study Design for GT 1



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

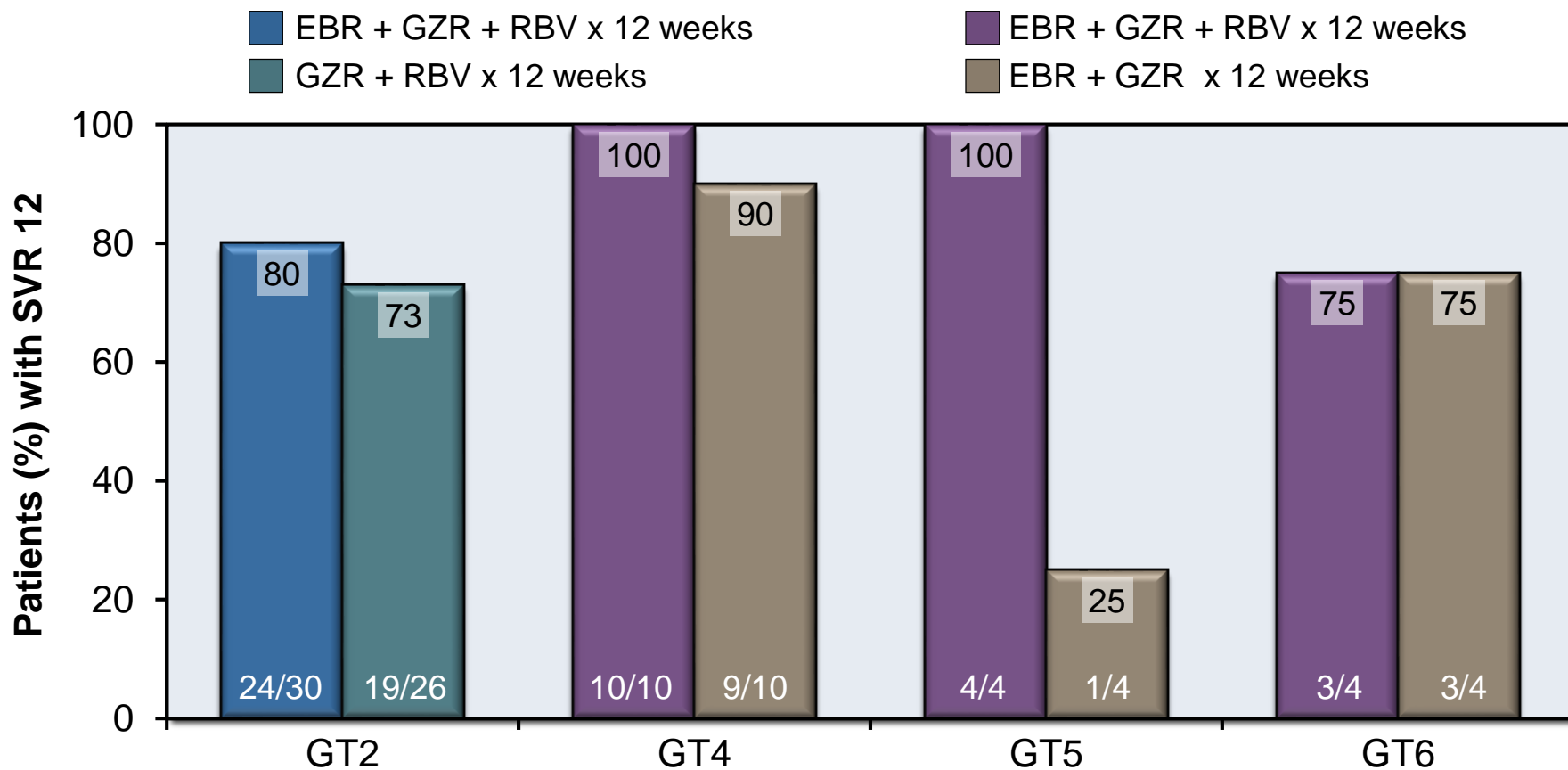
Elbasvir + Grazoprevir +/- RBV in Treatment-Naïve GT 2, 4, 5 or 6 C-SCAPE Study: Baseline Characteristics

| Baseline Characteristic | Genotype 2 | | Genotype 4, 5, 6 | |
|-------------------------|------------------------|-------------------|-------------------------|-----------------|
| | EBR + GZR+ RBV n=30 | GZR + RBV n=30 | EBR + GZR + RBV n=19 | EBR-GZR n=19 |
| Mean age, y (range) | 47.3 | 48.3 | 52.2 | 52.8 |
| Male sex, % | 63.3 | 56.7 | 42.1 | 63.2 |
| Race, % | | | | |
| White | 100 | 86.7 | 73.7 | 68.4 |
| Other | 0 | 13.3 | 26.3 | 31.6 |
| HCV Genotype, n | | | | |
| 2 | 30 | 26 | 0 | 0 |
| 4 | 0 | 0 | 10 | 10 |
| 5 | 0 | 0 | 4 | 4 |
| 6 | 0 | 0 | 4 | 4 |
| 1 | -- | 4 | -- | -- |
| HCV RNA | | | | |
| ≤ 2 million | 36.7 | 36.7 | 57.9 | 36.8 |
| >2 million | 63.3 | 63.3 | 42.1 | 63.2 |

*Excluded from modified intent-to-treat analysis due to discordant genotype

Elbasvir + Grazoprevir +/- RBV in Treatment-Naïve GT 2, 4, 5 or 6 C-SCAPE Study: Results

C-SCAPE: SVR12 by Genotype and Regimen



Elbasvir + Grazoprevir +/- RBV in Treatment-Naïve GT 2, 4, 5 or 6 C-SCAPE Study: Conclusions

Conclusions: “These data support the inclusion of patients with HCV GT4 and GT6 infection in the phase 3 program.”

Elbasvir-Grazoprevir in Treatment-Experienced Patients

Treatment Experienced

Elbasvir-Grazoprevir +/- Ribavirin in HCV Genotype 1, 4 or 6 C-EDGE Treatment Experienced (TE)

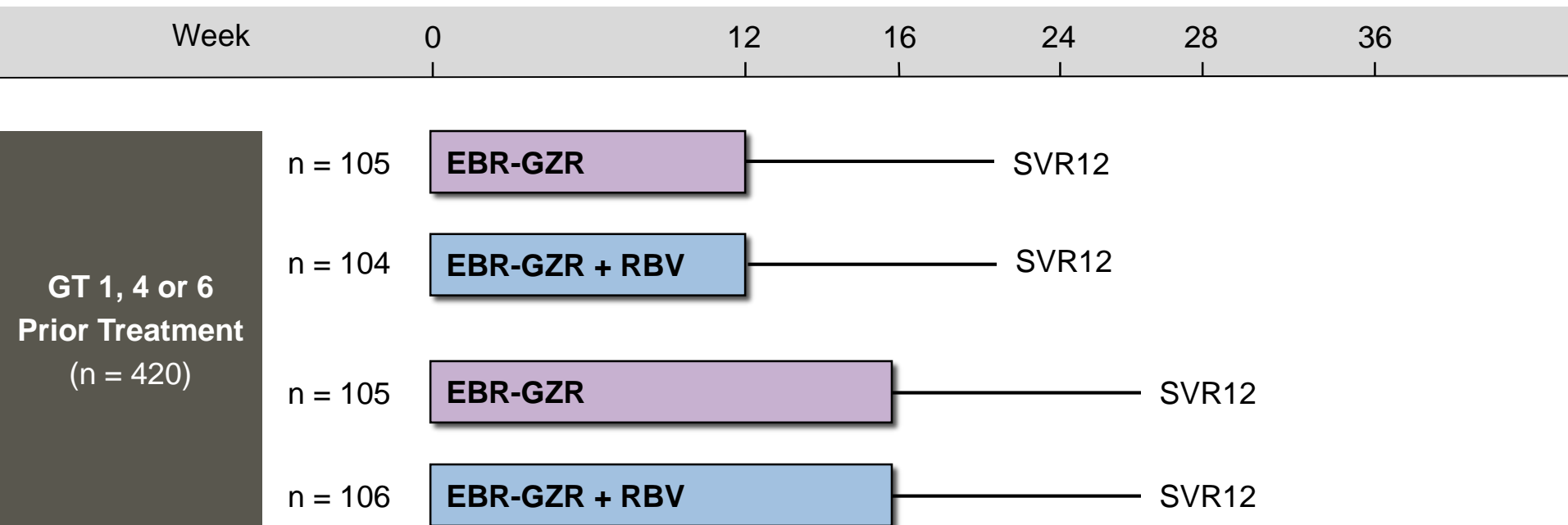
Kwo P, et al. EASL 2015. Abstract P0886.

Elbasvir-Grazoprevir +/- Ribavirin in HCV Genotype 1, 4 or 6 C-EDGE TE Study: Features

C-EDGE TE Trial

- **Design:** Randomized, open label, parallel-group phase 3 trial examining the safety and efficacy of a fixed-dose combination of elbasvir-grazoprevir with or without ribavirin for 12 or 16 weeks in treatment-experienced patients with GT 1, 4, or 6 HCV and previous failure of peginterferon plus ribavirin
- **Entry Criteria**
 - Chronic HCV Genotype 1, 4 or 6
 - 18 years or older
 - HCV RNA $\geq 10,000$ IU/mL
 - History of peginterferon plus ribavirin treatment failure
 - Patients with compensated cirrhosis accepted
- **Primary End-Point:** SVR12

Elbasvir-Grazoprevir +/- Ribavirin in HCV Genotype 1, 4 or 6 C-EDGE TE: Study Design



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

Drug Dosing

Elbasvir-grazoprevir (50/100 mg): fixed dose combination; one pill once daily

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

Elbasvir-Grazoprevir +/- Ribavirin in HCV Genotype 1, 4 or 6

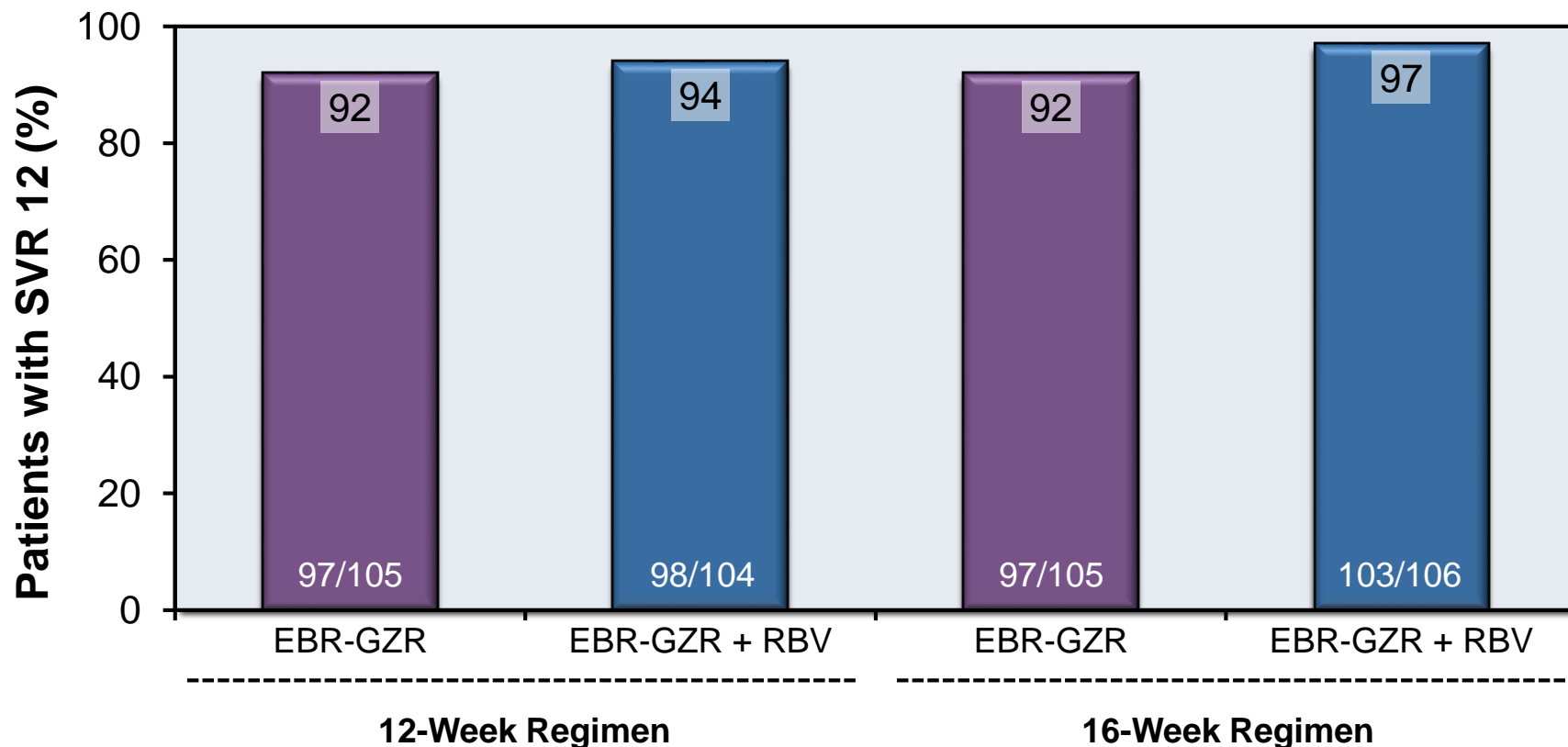
C-EDGE TE: Baseline Characteristics

| Baseline Characteristic | 12-Week Treatment | | 16-Week Treatment | |
|--------------------------|-------------------|------------------------|-------------------|------------------------|
| | EBR-GZR n=105 | EBR-GZR + RBV n=104 | EBR-GZR n=105 | EBR-GZR + RBV n=106 |
| Mean age, y (range) | 56 (25–76) | 56 (23–75) | 55 (31–73) | 55 (19–77) |
| Male sex, % | 63 | 69 | 66 | 60 |
| Race, % | | | | |
| White | 63 | 67 | 69 | 74 |
| Black | 22 | 23 | 9 | 14 |
| Asian | 14 | 9 | 21 | 9 |
| HCV Genotype, % | | | | |
| 1a | 58 | 58 | 46 | 55 |
| 1b | 33 | 28 | 46 | 36 |
| 4 | 9 | 14 | 5 | 8 |
| 6 | -- | -- | 4 | 2 |
| Cirrhosis, % | 35 | 34 | 36 | 35 |
| HIV coinfection, % | 6 | 5 | 6 | 4 |
| Prior treatment response | | | | |
| Relapse, % | 33 | 37 | 36 | 38 |
| Partial response, % | 20 | 21 | 20 | 22 |
| Relapse, % | 47 | 42 | 44 | 41 |

Source: Kwo P et al. EASL 2015. Abstract P0886.

Elbasvir-Grazoprevir +/- Ribavirin in HCV Genotype 1, 4 or 6 C-EDGE TE: Results

C-EDGE TE: SVR 12* by Treatment Duration and Regimen

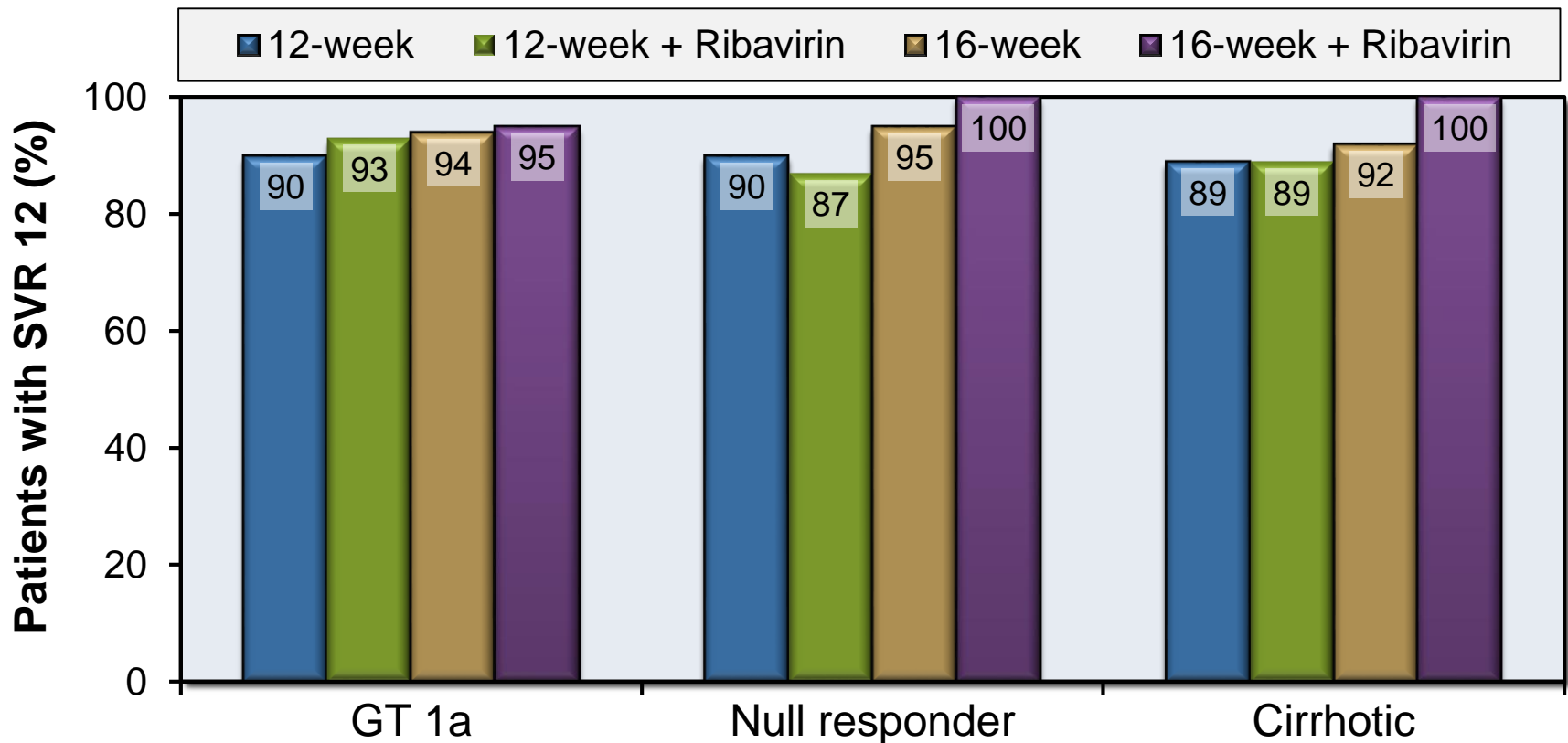


* Analysis per protocol: excluding patients who dropped out due to reasons other than virologic failure

Elbasvir-Grazoprevir +/- Ribavirin in HCV Genotype 1, 4 or 6

C-EDGE TE: Results

C-EDGE TE: SVR 12* by Key Subgroups



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

Elbasvir-Grazoprevir +/- Ribavirin in HCV Genotype 1, 4 or 6 C-EDGE TE: Results

Conclusions: “This is an ongoing, Phase III study among subjects with HCV GT1 or 4 infection who failed prior PR therapy, including large numbers of Black/African-American and cirrhotic patients. Preliminary results showed a 12 week regimen of GZR/EBR FDC was highly efficacious with respect to SVR4 among these hard-to-cure patients, and had a favorable safety profile.”

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 ≥ 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

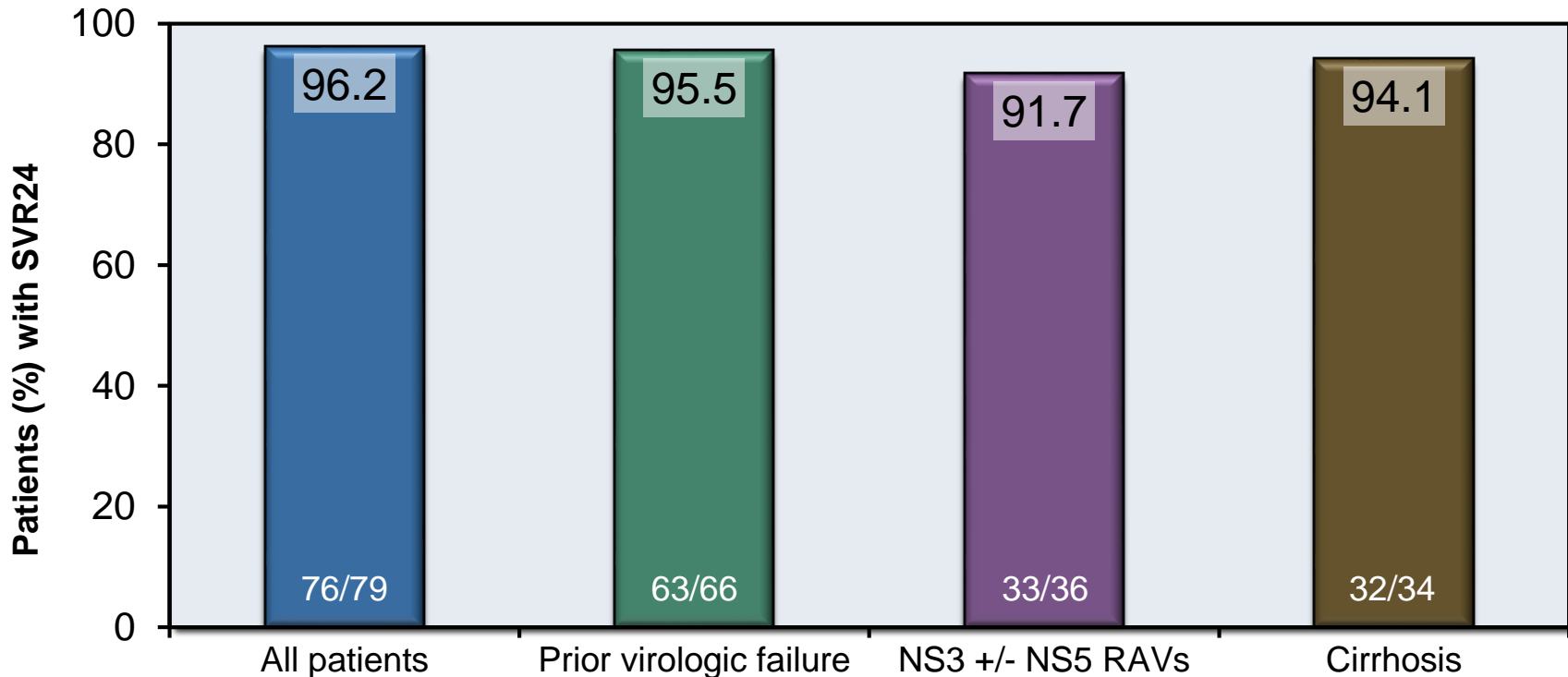
| Baseline Characteristic | All Patients (N=79) | Baseline NS3 RAVs* (N=34) | No Baseline NS3 RAVs* (N=44) |
|--|---------------------|---------------------------|------------------------------|
| Mean age, years | 54.4 | 53.9 | 54.6 |
| Male/Female, % | 58.2/41.8 | 61.8/38.2 | 54.5/45.5 |
| HCV genotype, % | | | |
| 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 ⁺ , % | 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)

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 ≥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.”

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.

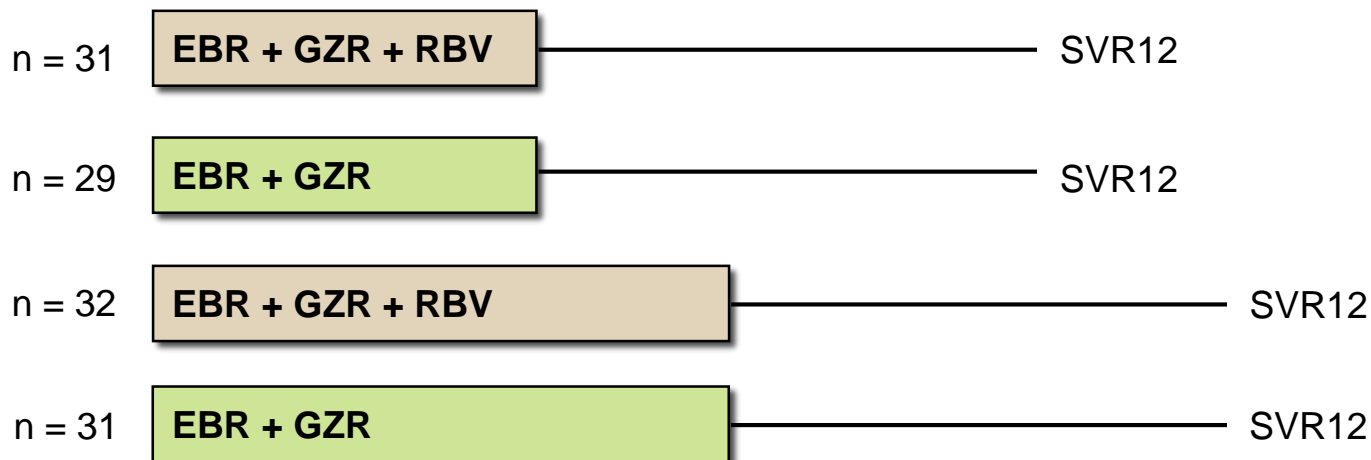
Elbasvir + Grazoprevir +/- Ribavirin in HCV GT1 C-WORTHY Study: Features

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 $\geq 10,000$ 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



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

Drug Dosing

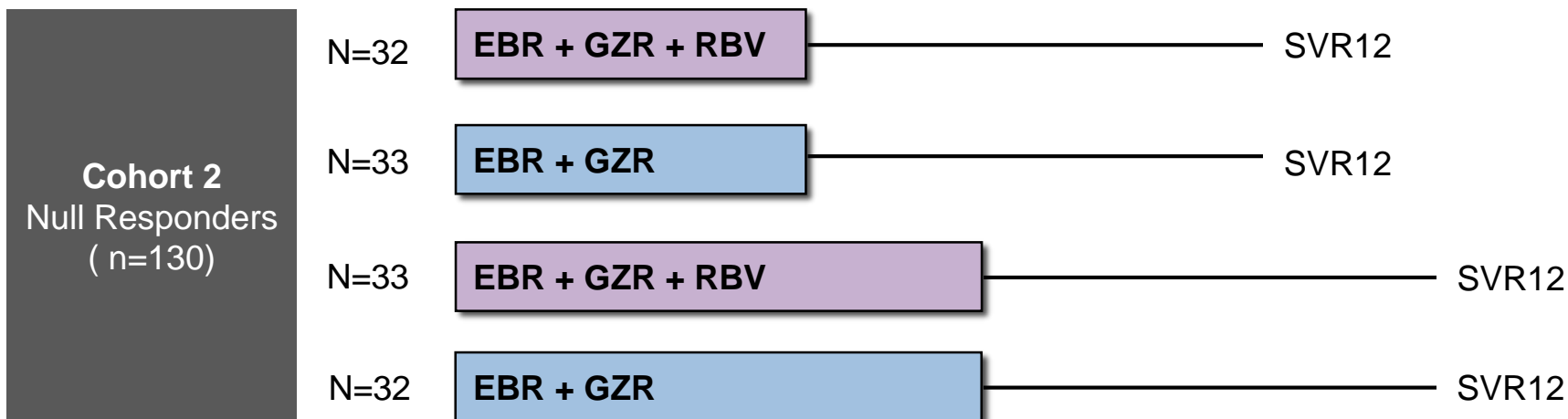
Elbasvir: 50 mg once daily

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

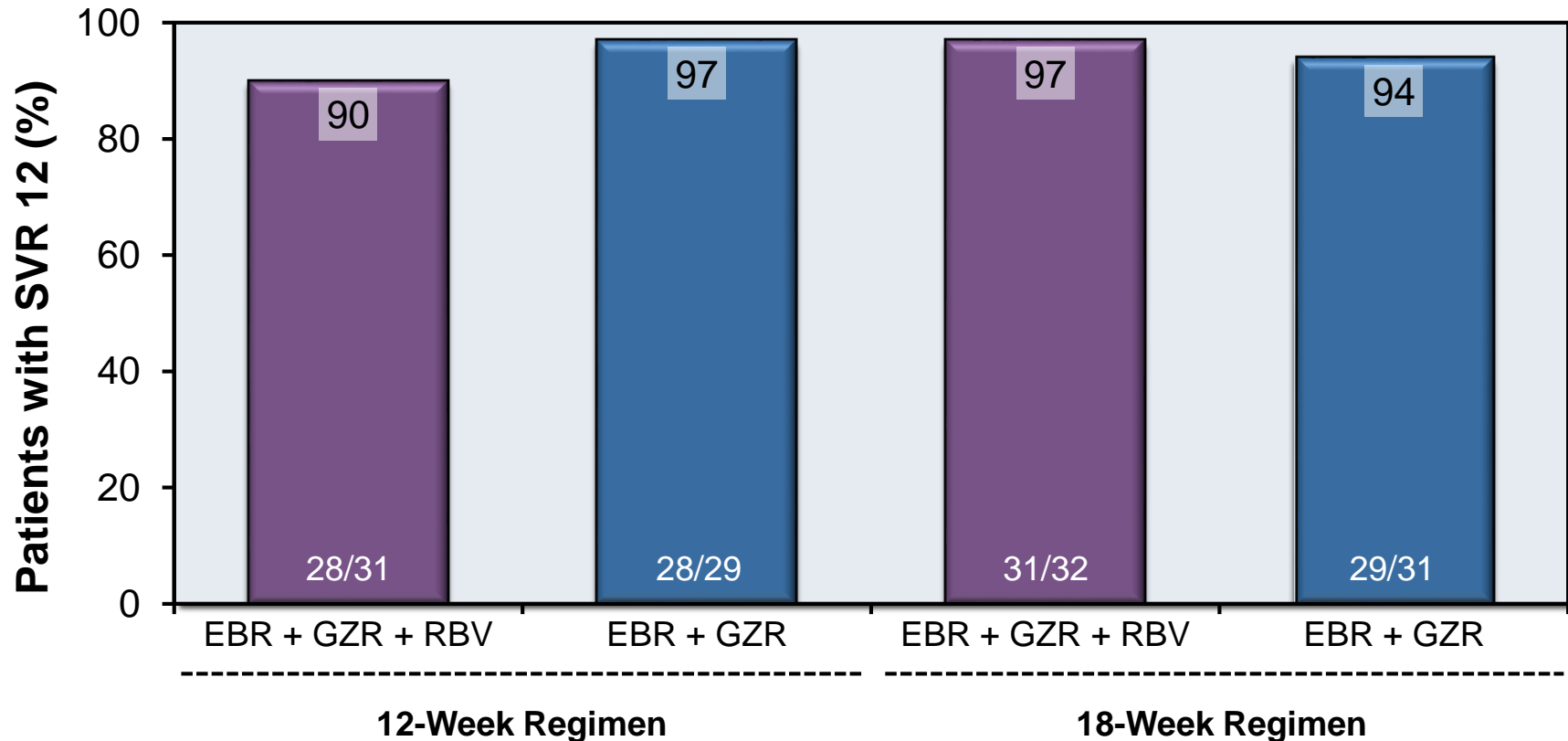
Ribavirin (weight-based and divided bid): 800 to 1400 mg/day

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 |

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

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



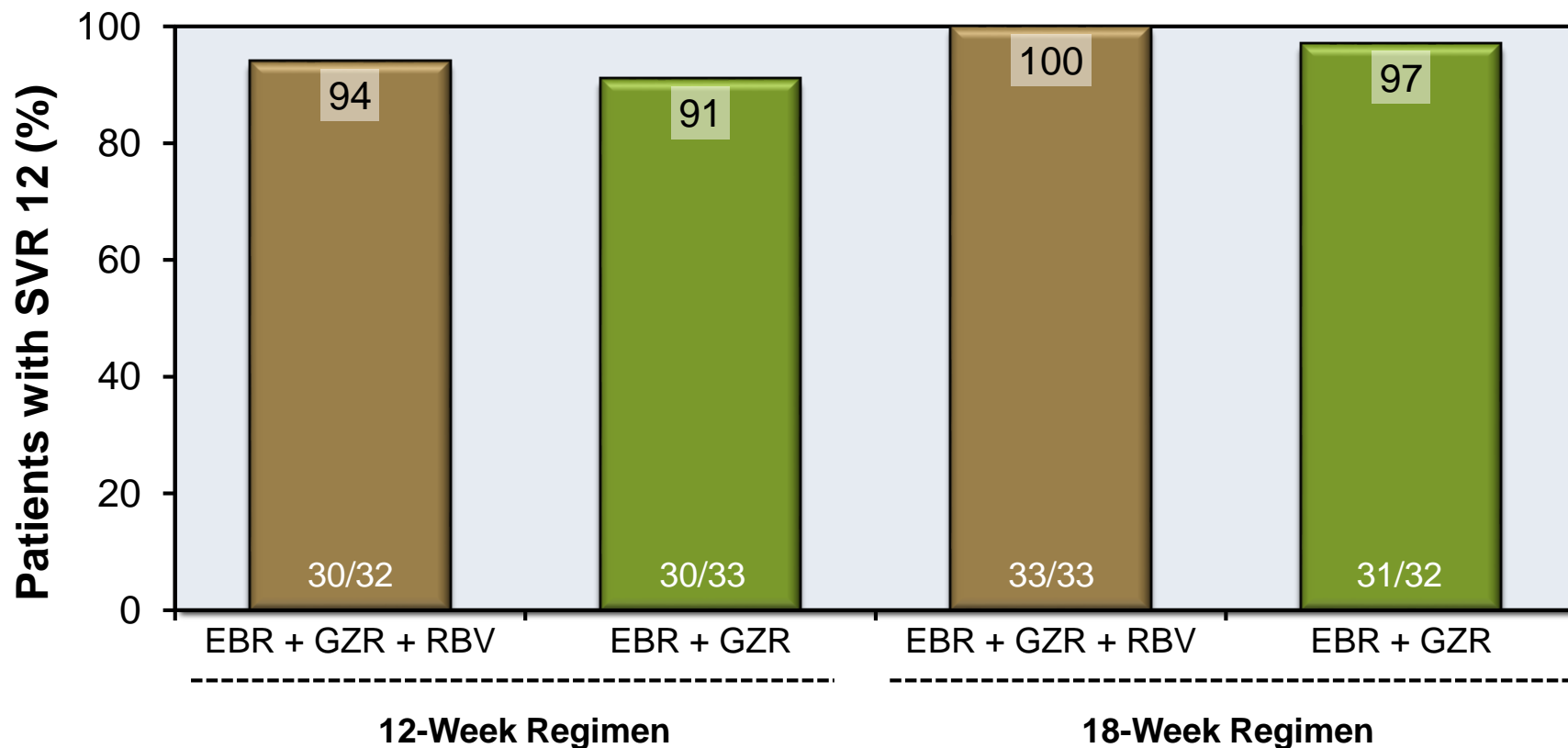
Abbreviations: EBR = elbasvir; GZR = grazoprevir; RBV = ribavirin

*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



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

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

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.”

Elbasvir-Grazoprevir in HIV Coinfection

Treatment Naïve

HIV Coinfection

Elbasvir-Grazoprevir in HCV and HIV Coinfection, GT 1, 4 or 6 C-EDGE CO-INFECTION

Rockstroh JK, et al. Lancet HIV. 2015;2:e319-27.

Elbasvir-Grazoprevir in HCV-HIV Coinfection GT 1, 4 or 6

C-EDGE CO-INFECTION: Study Features

C-EDGE Trial

- **Design:** Prospective, open-label, single-arm study examining the safety and efficacy of a fixed-dose combination of elbasvir-grazoprevir for 12 weeks in treatment-naïve patients with chronic HCV genotype 1, 4, or 6 and HIV coinfection.
- **Entry Criteria**
 - Chronic HCV Genotype 1, 4, or 6
 - 18 years or older
 - HCV RNA $\geq 10,000$ IU/mL
 - No prior treatment
 - Compensated cirrhosis permitted
 - HIV infection
- **Primary End-Point:** SVR12

Elbasvir-Grazoprevir in HCV-HIV Coinfection GT 1, 4 or 6 C-EDGE CO-INFECTION: Study Design

Week

0

12

24

HIV-HCV Coinfected
Treatment-naïve
GT 1, 4 or 6

N=218

Elbasvir-Grazoprevir

SVR12

Drug Dosing

Elbasvir-grazoprevir (50/100 mg): fixed dose combination; one pill once daily

Elbasvir-Grazoprevir in HCV-HIV Coinfection GT 1, 4 or 6 C-EDGE CO-INFECTION: Participants

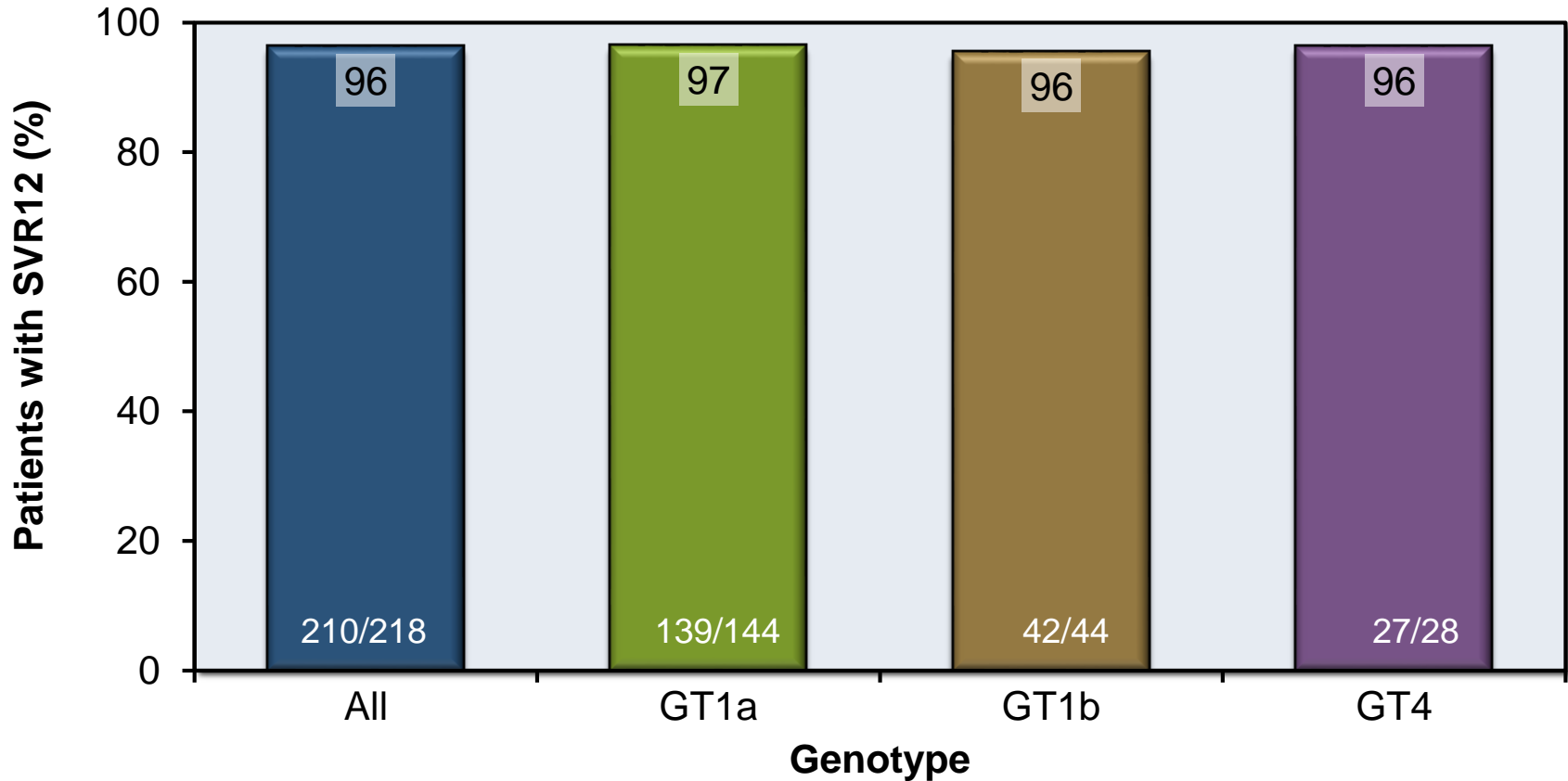
| Baseline Characteristic | Elbasvir-Grazoprevir (N=218) |
|--|------------------------------|
| Age, mean | 49 |
| Male, n (%) | 183 (84%) |
| Race, n (%) | |
| White | 167 (77%) |
| Black or African-American | 38 (17%) |
| Other | 13 (6%) |
| HCV genotype, n (%) | |
| 1a | 144 (66%) |
| 1b | 44 (20%) |
| 4 | 28 (13%) |
| 6 | 2 (1%) |
| Fibrosis stage, n (%) | |
| F0-2 | 160 (73%) |
| F3 | 23 (11%) |
| F4 | 35 (16%) |
| Mean baseline HCV RNA, log ₁₀ IU/ml | 6.03 |

Elbasvir-Grazoprevir in HCV-HIV Coinfection GT 1, 4 or 6 C-EDGE CO-INFECTION: Participants

| HIV Characteristics | Elbasvir-Grazoprevir (N=218) |
|---|------------------------------|
| Median CD4 cell count, (IQR) | 568 (424-766) |
| ART Status | |
| On ART with undetectable HIV RNA | 211 (97%) |
| ART naïve | 7 (3%) |
| ART nucleos(t)ide pair | |
| Abacavir-containing | 47 (22%) |
| Tenofovir-containing | 164 (75%) |
| None | 7 (3%) |
| ART Third Agent | |
| Raltegravir | 113 (52%) |
| Dolutegravir | 59 (27%) |
| Rilpivirine | 38 (17%) |
| None | 8 (4%) |
| IQR = interquartile range; ART = antiretroviral therapy | |

Elbasvir-Grazoprevir in HCV-HIV Coinfection GT 1, 4 or 6 C-EDGE CO-INFECTION: Results

C-EDGE CO-INFECTION: SVR12 Results by Genotype



Overall SVR12 results includes the 2 patients with GT 6, who both achieved SVR12.

Elbasvir-Grazoprevir in HCV-HIV Coinfection GT 1, 4 or 6 C-EDGE CO-INFECTION: Adverse Events

| Adverse Event (AE), n (%) | Elbasvir-Grazoprevir (N=218) | |
|-------------------------------------|------------------------------|----------------|
| Discontinuation due to AE | 0 | |
| Serious AEs | 2 (1%) | |
| Deaths | 0 | |
| Any AE in >5% of patients | | |
| Fatigue | 29 (13%) | |
| Headache | 27 (12%) | |
| Nausea | 20 (9%) | |
| Upper respiratory tract infection | 18 (8%) | |
| Diarrhea | 16 (7%) | |
| Insomnia | 15 (7%) | |
| Grade 3 or 4 laboratory abnormality | <u>Grade 3</u> | <u>Grade 4</u> |
| Total bilirubin | 1 (<1%) | 0 |
| ALT elevation | 3 (1%) | 2 (1%) |
| AST elevation | 0 | 1 (<1%) |
| Hemoglobin | 0 | 0 |

Elbasvir-Grazoprevir in HCV-HIV Coinfection GT 1, 4 or 6 C-EDGE CO-INFECTION: Conclusions

Conclusions: “This HCV treatment regimen seems to be effective and well tolerated for patients co-infected with HIV with or without cirrhosis. These data are consistent with previous trials of this regimen in the monoinfected population. This regimen continues to be studied in phase 3 trials.”

Treatment Naïve

HIV Coinfection

Elbasvir + Grazoprevir +/- RBV: HCV GT1 +/- HIV Coinfection C-WORTHY Coinfection

Sulkowski M, et al. Lancet. 2015;385:1087-97.

Elbasvir + Grazoprevir +/- RBV in HCV GT1 +/- HIV Coinfection

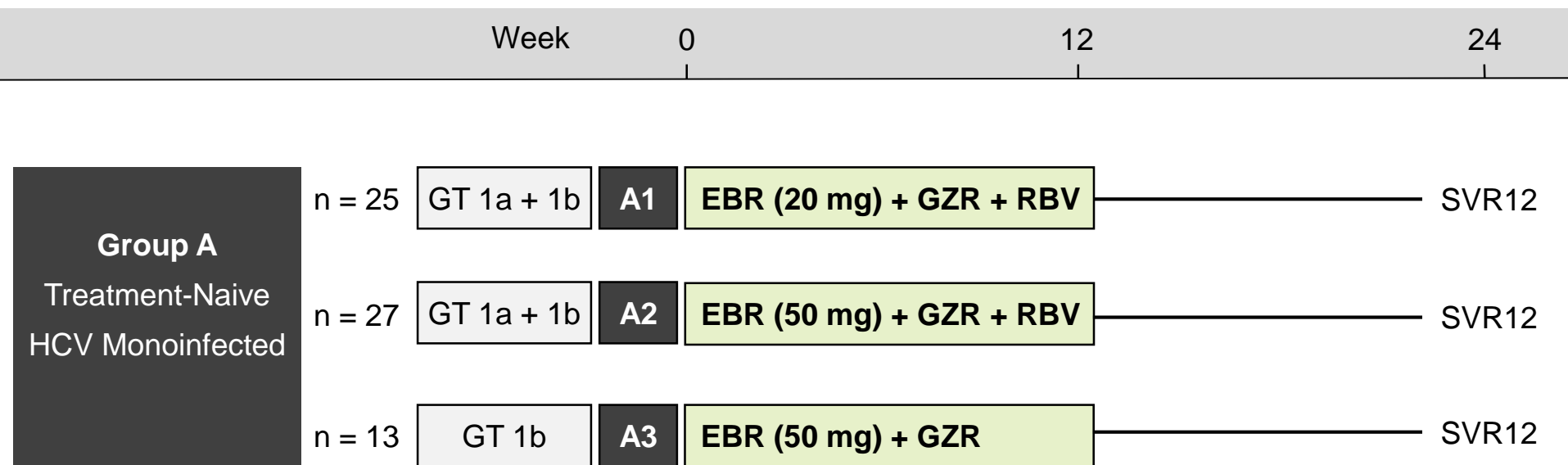
C-WORTHY Coinfection: Study Features

C-WORTHY (Protocol 035) Trial

- **Design:** Randomized, open-label phase 2 trial examining the safety and efficacy of a fixed-dose combination of elbasvir plus grazoprevir, with or without ribavirin, in treatment-naïve HCV-monoinfected (part A) or HCV-HIV coinfecting (part B) patients without cirrhosis
- **Entry Criteria**
 - Chronic HCV Genotype 1
 - 18 years or older
 - HCV RNA $\geq 10,000$ IU/mL
 - No prior treatment
 - No cirrhosis
 - Part B: well-controlled HIV infection (on antiretroviral therapy ≥ 8 weeks, HIV RNA undetectable $\times \geq 24$ weeks and CD4 count ≥ 300 cells/mm³)
- **Primary End-Point:** SVR12

Elbasvir + Grazoprevir +/- RBV in HCV GT1 +/- HIV Coinfection

C-WORTHY Coinfection: Study: Study Design Part A



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

Drug Dosing

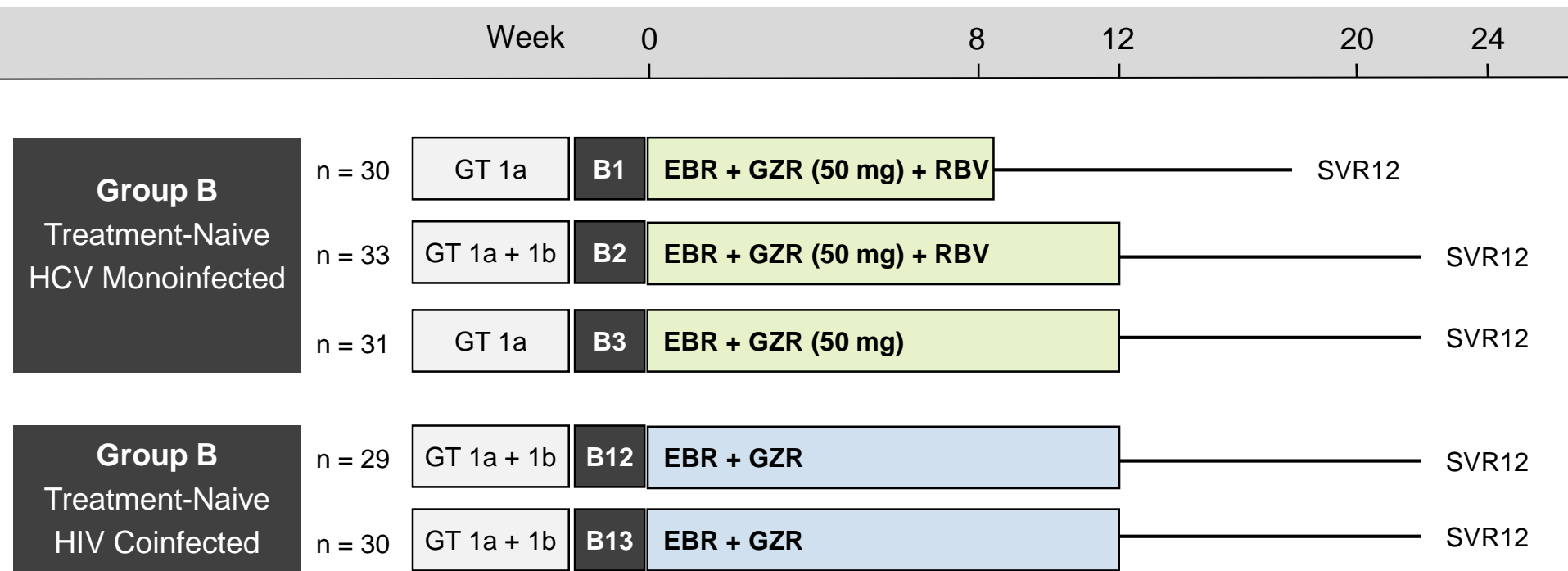
Elbasvir (20 mg or 50 mg) once daily

Grazoprevir (100 mg) once daily

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

Elbasvir+ Grazoprevir +/- RBV in HCV GT1 +/- HIV Coinfection

C-WORTHY Coinfection: Study: Study Design Part B



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

Drug Dosing

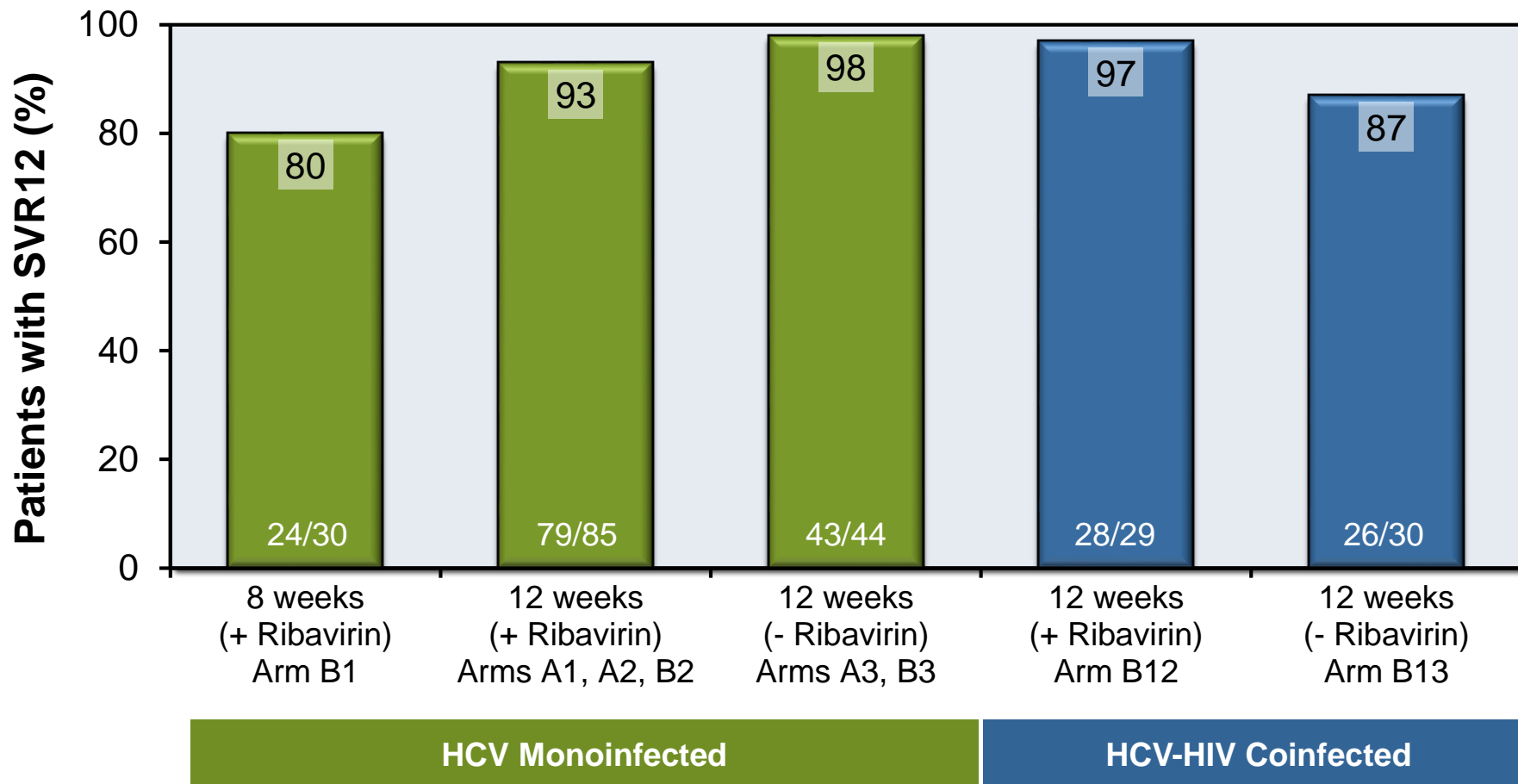
Elbasvir (50 mg) once daily

Grazoprevir (100 mg) once daily

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

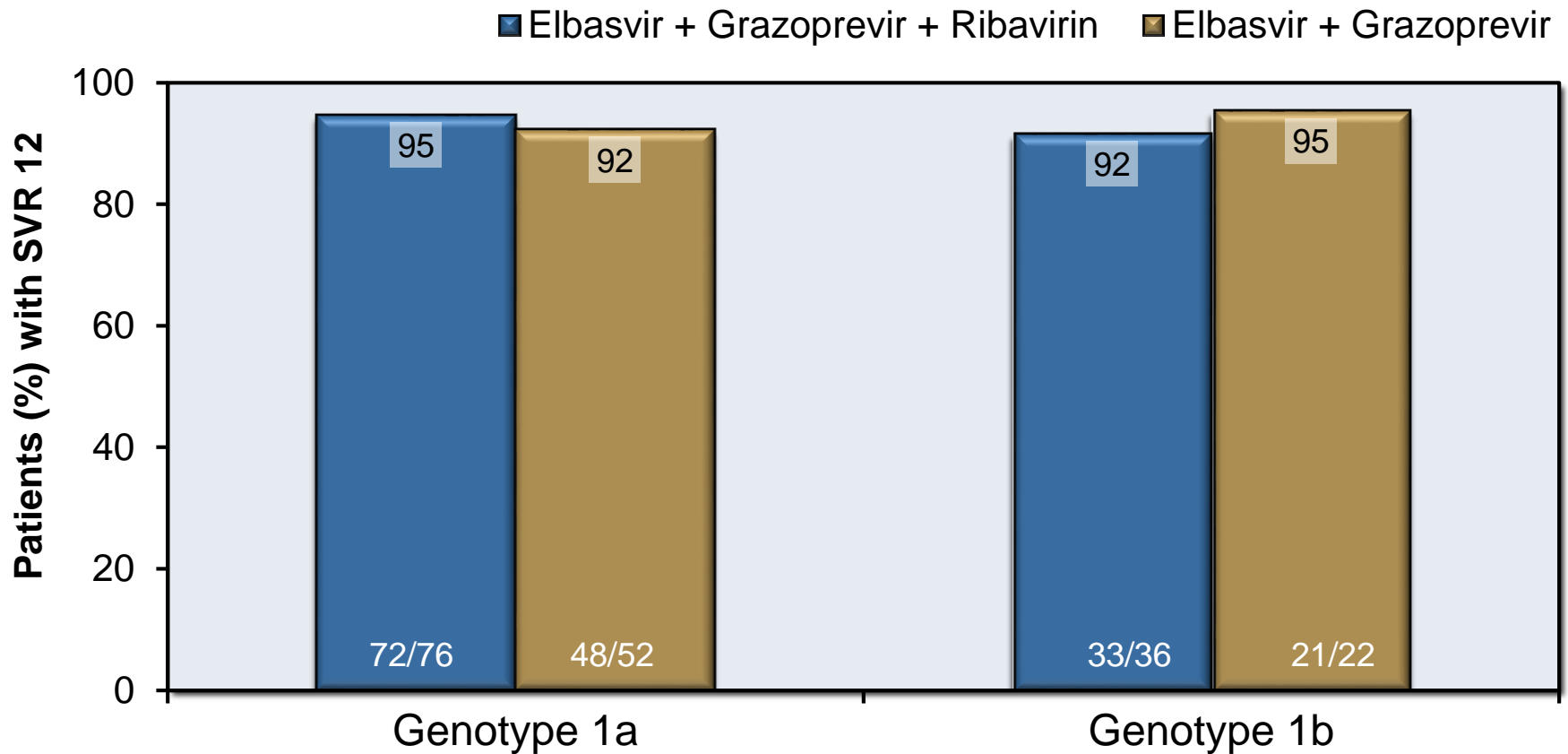
Elbasvir + Grazoprevir +/- RBV in HCV GT1 +/- HIV Coinfection C-WORTHY Coinfection: Results

C-WORTHY: SVR12 Results by Treatment and HIV Coinfection Status



Elbasvir + Grazoprevir +/- RBV in HCV GT1 +/- HIV Coinfection C-WORTHY Coinfection: Study: Results

C-WORTHY: SVR12 Rates by HCV GT1 Subtype and Use of Ribavirin



Elbasvir + Grazoprevir +/- RBV in HCV GT1 +/- HIV Coinfection C-WORTHY Coinfection: Study Features

Interpretation: “Once-daily grazoprevir plus elbasvir with or without ribavirin for 12 weeks in previously untreated HCV-mono-infected and HIV/HCV-co-infected patients without cirrhosis achieved SVR12 rates of 87-98%. These results support the ongoing phase 3 development of grazoprevir plus elbasvir.”

Elbasvir-Grazoprevir in Patients with Renal Disease

Treatment Naïve and Treatment Experienced

Elbasvir + Grazoprevir in GT 1 and Chronic Renal Disease C-SURFER

Roth D, et al. Lancet 2015;386:1537-45.

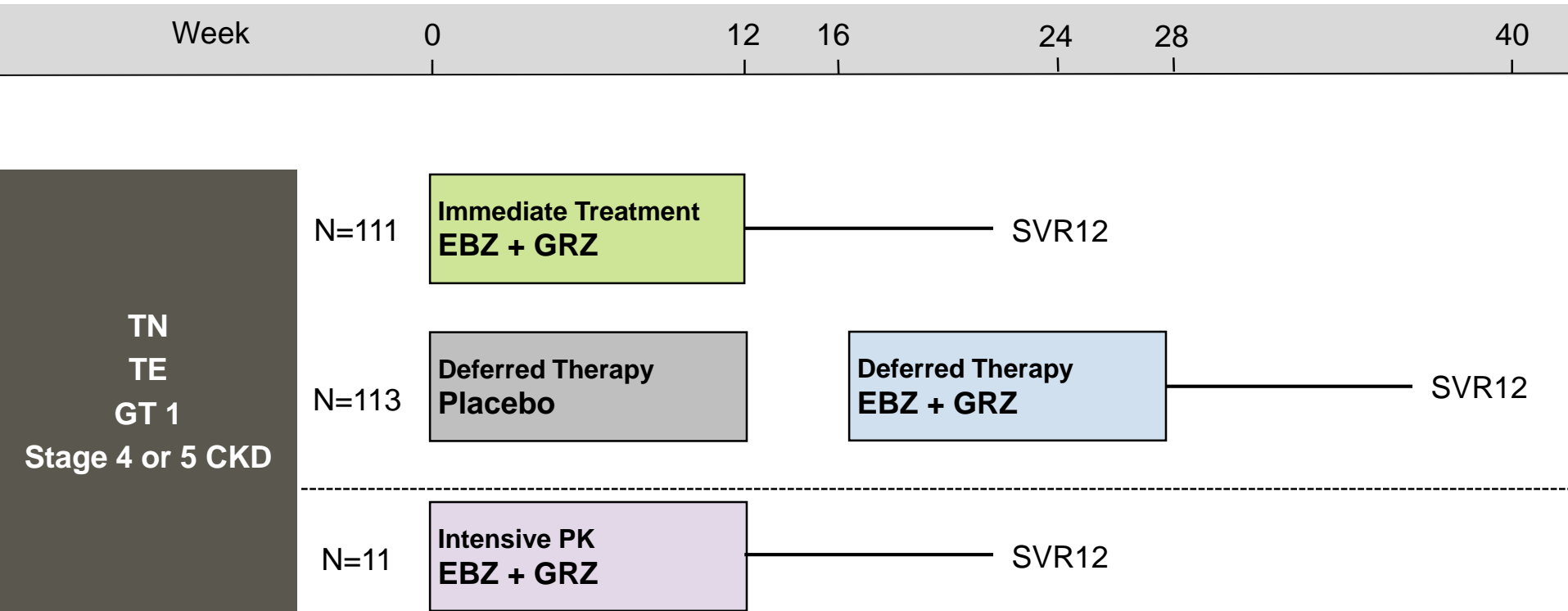
Elbasvir + Grazoprevir in HCV GT1 and Renal Disease

C-SURFER Study: Features

C-SURFER

- **Design:** Randomized, phase 3, double-blind trial examining the safety and efficacy of elbasvir plus grazoprevir for 12 weeks in treatment-naïve or treatment-experienced patients genotype 1 chronic HCV and stage 4 or 5 chronic renal disease, including patients on hemodialysis.
- **Setting:** 68 international sites
- **Entry Criteria**
 - Chronic HCV Genotype 1
 - Chronic kidney disease (Stage 4 or 5) +/- hemodialysis
 - 18 years or older
 - Treatment naïve or treatment-experienced
 - Cirrhosis allowed
- **Primary End-Point:** SVR12

Elbasvir + Grazoprevir in HCV GT1 and Renal Disease C-SURFER Study: Study Design



Drug Dosing

Grazoprevir 100 mg once daily and Elbasvir 50 mg once daily; given as separate medications in Immediate treatment and Intensive PK arms; given as fixed dose combination in Deferred arm

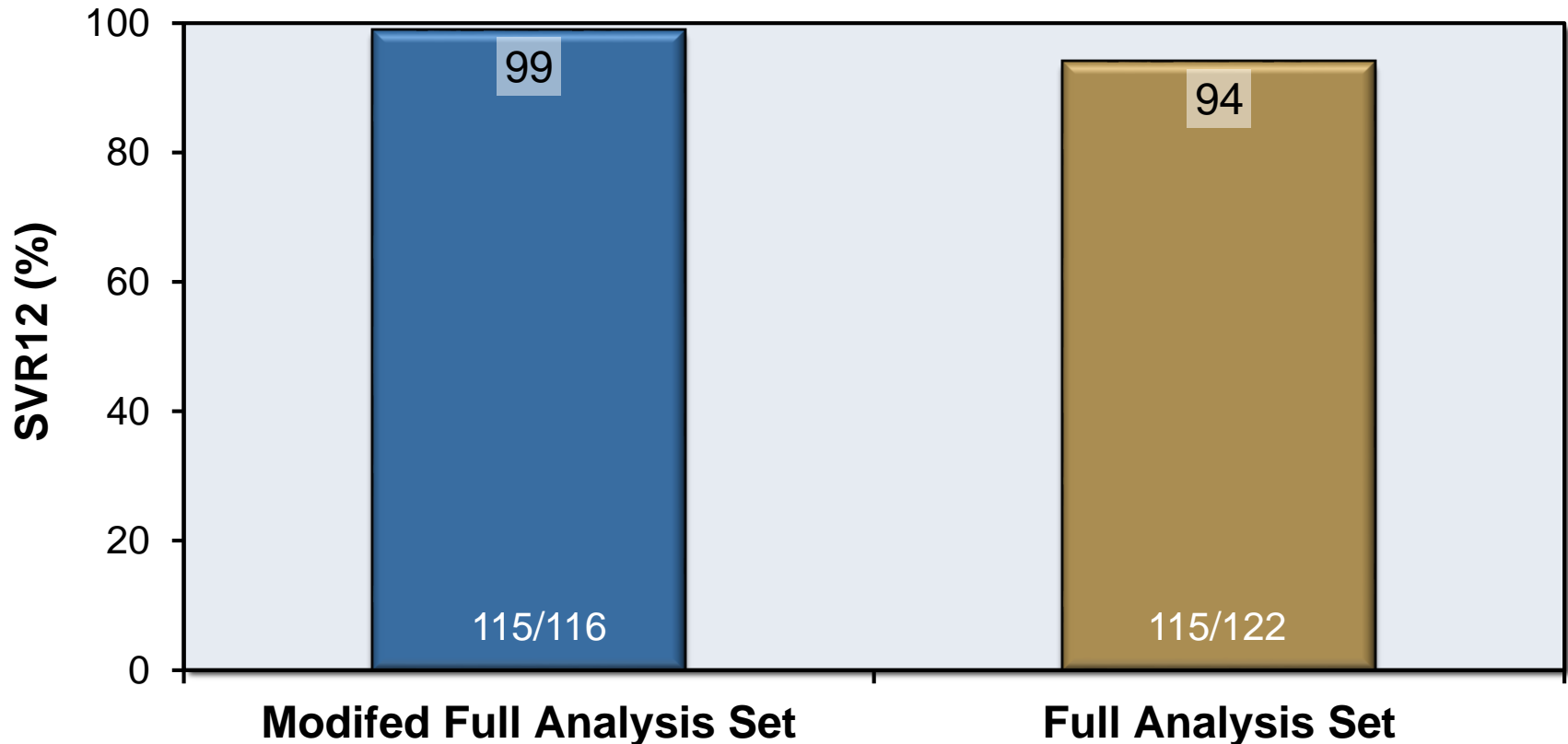
Elbasvir + Grazoprevir in HCV GT1 and Renal Disease C-SURFER Study: Participants

| Baseline Characteristic | EBR + GZR Immediate n=111 | EBR + GZR Deferred n=113 | EBR + GZR PK n=11 | Total N=235 |
|-------------------------|---------------------------------|--------------------------------|-------------------------|----------------|
| Mean age, years (SD) | 56.5 (9.1) | 55.2 (10.1) | 58.2 (6.8) | 56 (9.5) |
| Male sex, % | 73 | 71 | 100 | 73 |
| Race, % | | | | |
| White | 50 | 43 | 54 | 47 |
| Black | 45 | 47 | 45 | 46 |
| Asian | 5 | 8 | 0 | 6 |
| HCV Genotype, % | | | | |
| 1a | 48 | 52 | 91 | 52 |
| 1b | 52 | 47 | 9 | 48 |
| 1 other | 0 | 1 | 0 | 0 |
| Cirrhosis, % | 6 | 6 | 0 | 6 |
| Treatment-naïve, % | 82 | 78 | 91 | 80 |
| Diabetes, % | 34 | 32 | 55 | 34 |
| Kidney disease severity | | | | |
| Stage 4, % | 16 | 20 | 36 | 19 |
| Stage 5, % | 84 | 80 | 64 | 81 |
| On dialysis, % | 78 | 77 | 55 | 76 |

Source: Roth D, et al. Lancet 2015;386:1537-45.

Elbasvir + Grazoprevir in HCV GT1 and Renal Disease C-SURFER Study: Results

C-SURFER: SVR12 Results



Modified analysis excluded patients who did not receive ≥ 1 dose of drug or who died or discontinued early for reasons unrelated to HCV treatment.

Elbasvir + Grazoprevir in HCV GT1 and Renal Disease C-SURFER Study: Safety

| Adverse Event (AE), n (%) | Elbasvir + Grazoprevir | |
|---|------------------------|-------------------------------|
| | Immediate (n=111) | Deferred (Placebo) (n=113) |
| Discontinuation due to AE | 0 | 5 (4.4) |
| Serious AEs | 16 (14.4) | 19 (16.8) |
| Deaths | 1 (0.8) | 3 (2.7) |
| Any AE in ≥10% of patients | 84 (75.7) | 95 (84.1) |
| Headache | 19 (17.1) | 19 (16.8) |
| Nausea | 17 (15.3) | 18 (15.9) |
| Fatigue | 11 (9.9) | 17 (15.9) |
| Insomnia | 7 (6.3) | 12 (10.6) |
| Dizziness | 6 (5.4) | 18 (15.9) |
| Diarrhea | 6 (5.4) | 15 (13.3) |
| Laboratory AEs | | |
| Hemoglobin <8.5 g/dl | 5 (4.5) | 5 (4.4) |
| ALT 1.1-2.5 x baseline | 2 (1.8) | 36 (31.9) |
| Creatinine [§] >2.5 x baseline | 1 (1.2) | 0 |

§ Among patients not on dialysis at baseline.

Source: Roth D, et al. Lancet 2015;386:1537-45.

Elbasvir + Grazoprevir in HCV GT1 and Renal Disease C-SURFER Study: Conclusions

Interpretation: “Once-daily grazoprevir and elbasvir for 12 weeks had a low rate of adverse events and was effective in patients infected with HCV genotype 1 and stage 4-5 chronic kidney disease.”

Elbasvir-Grazoprevir in Persons who Inject Drugs

Elbasvir-Grazoprevir in HCV GT 1,4, or 6 in PWID* on Opiate Agonist Therapy
C-EDGE CO-STAR

*PWID = Persons Who Inject Drugs

Dore G, et al. AALSD. 2015; Abstract 40.

Elbasvir-Grazoprevir in HCV GT 1, 4, or 6 in PWID on Opiate Agonist Therapy

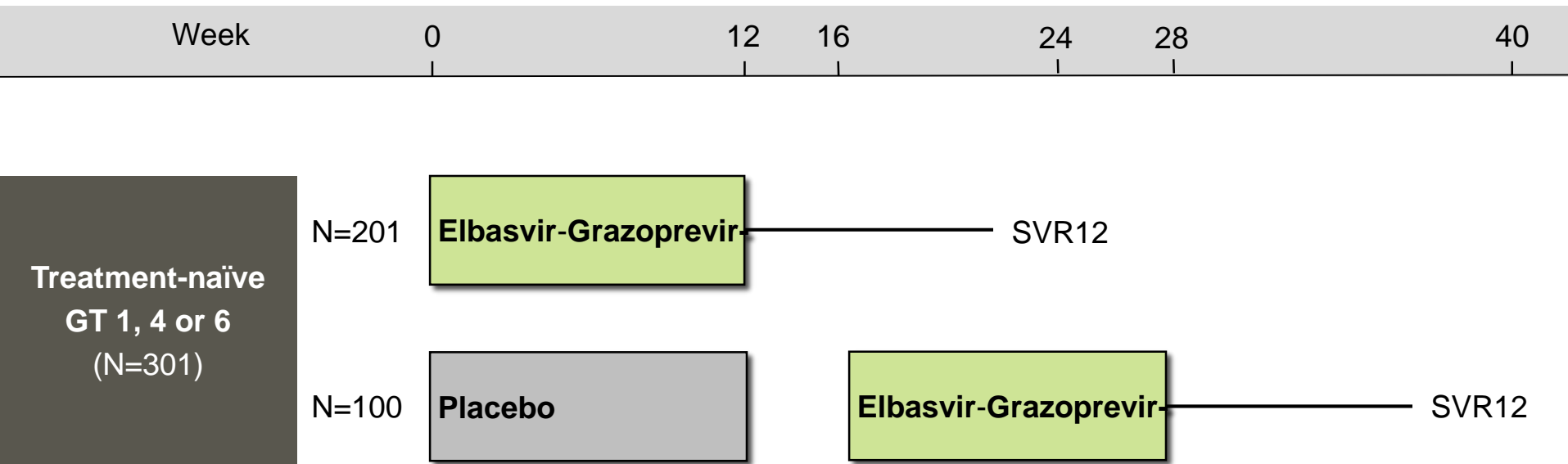
C-EDGE CO-STAR: Study Features

C-EDGE CO-STAR

- **Design:** Randomized, phase 3, parallel group, placebo-controlled trial using a fixed-dose combination of elbasvir-grazoprevir in treatment-naïve chronic HCV genotype 1, 4, or 6 in persons who inject drugs who are receiving opiate agonist therapy
- **Entry Criteria**
 - Chronic HCV Genotype 1, 4, or 6
 - No prior treatment
 - 18 years or older
 - Opiate Agonist Therapy for ≥ 3 months and kept $\geq 80\%$ of appointments
 - HCV RNA $\geq 10,000$ IU/mL
 - Cirrhosis allowed with goal 20% of subjects with cirrhosis
 - HIV infection allowed
- **Primary End-Point:** SVR12

Elbasvir-Grazoprevir in HCV GT 1, 4, or 6 in PWID on Opiate Agonist Therapy

C-EDGE CO-STAR: Study Features

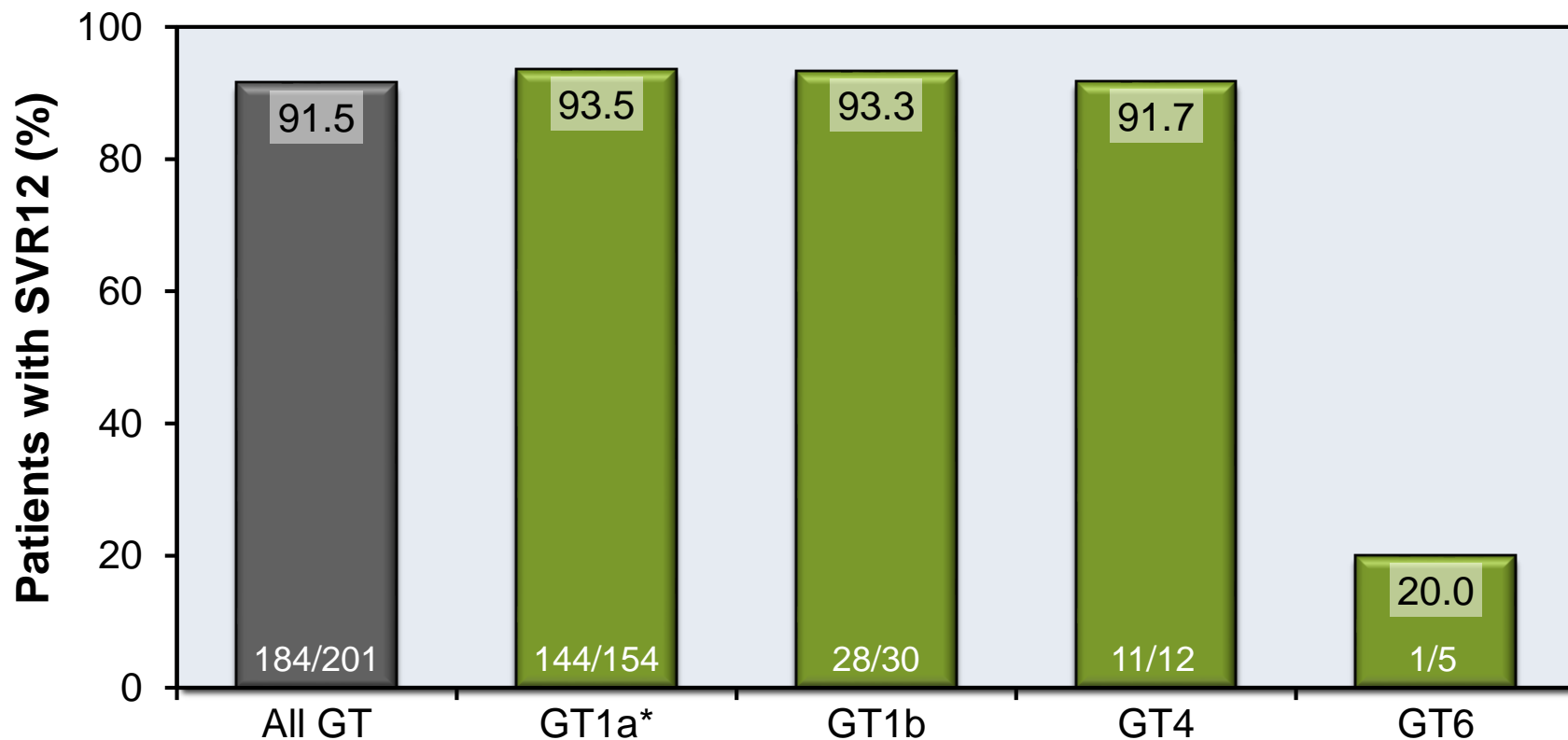


Drug Dosing

Grazoprevir-elbasvir (100/50 mg): fixed dose combination; one pill once daily

Elbasvir-Grazoprevir in HCV GT 1, 4, or 6 in PWID on Opiate Agonist Therapy C-EDGE CO-STAR: Results in Immediate Treatment Group

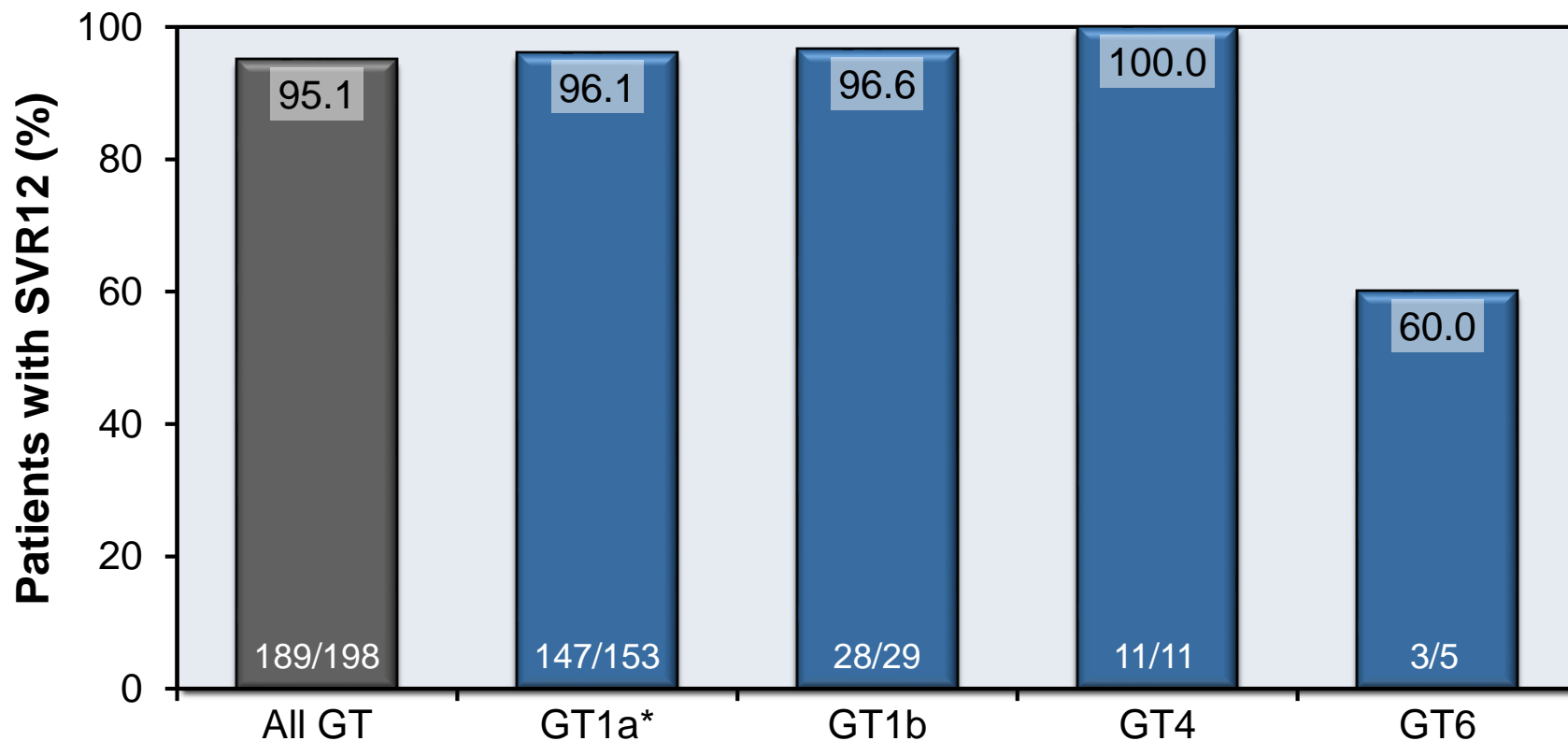
C-EDGE CO-STAR: SVR12 Results with Full Analysis Set



*Includes one subject with mixed infection (GT 1a and 1b) who achieved SVR12

Elbasvir-Grazoprevir in HCV GT 1, 4, or 6 in PWID on Opiate Agonist Therapy C-EDGE CO-STAR: Results in Immediate Treatment Group

C-EDGE CO-STAR: SVR12 Results with Modified Full Analysis Set[^]



[^]Excludes patients who discontinued trial for non-treatment related reasons

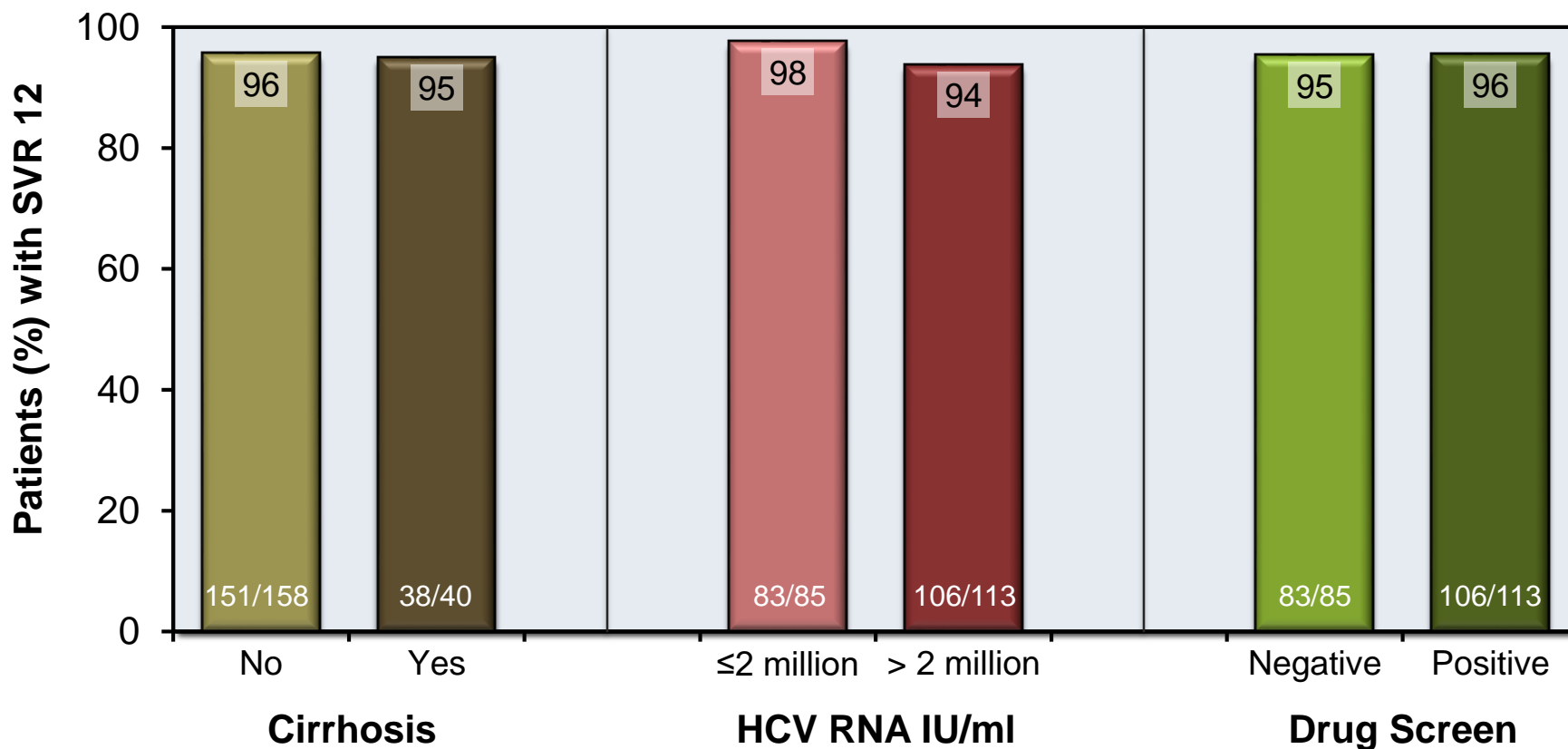
*Includes one subject with mixed infection (GT 1a and 1b) who achieved SVR12

Source: Dore G, et al. AALSD. 2015; Abstract 40.

Elbasvir-Grazoprevir in HCV GT 1, 4, or 6 in PWID on Opiate Agonist Therapy

C-EDGE CO-STAR: Results

C-EDGE CO-STAR: SVR12 Results with Modified Full Analysis Set[^]



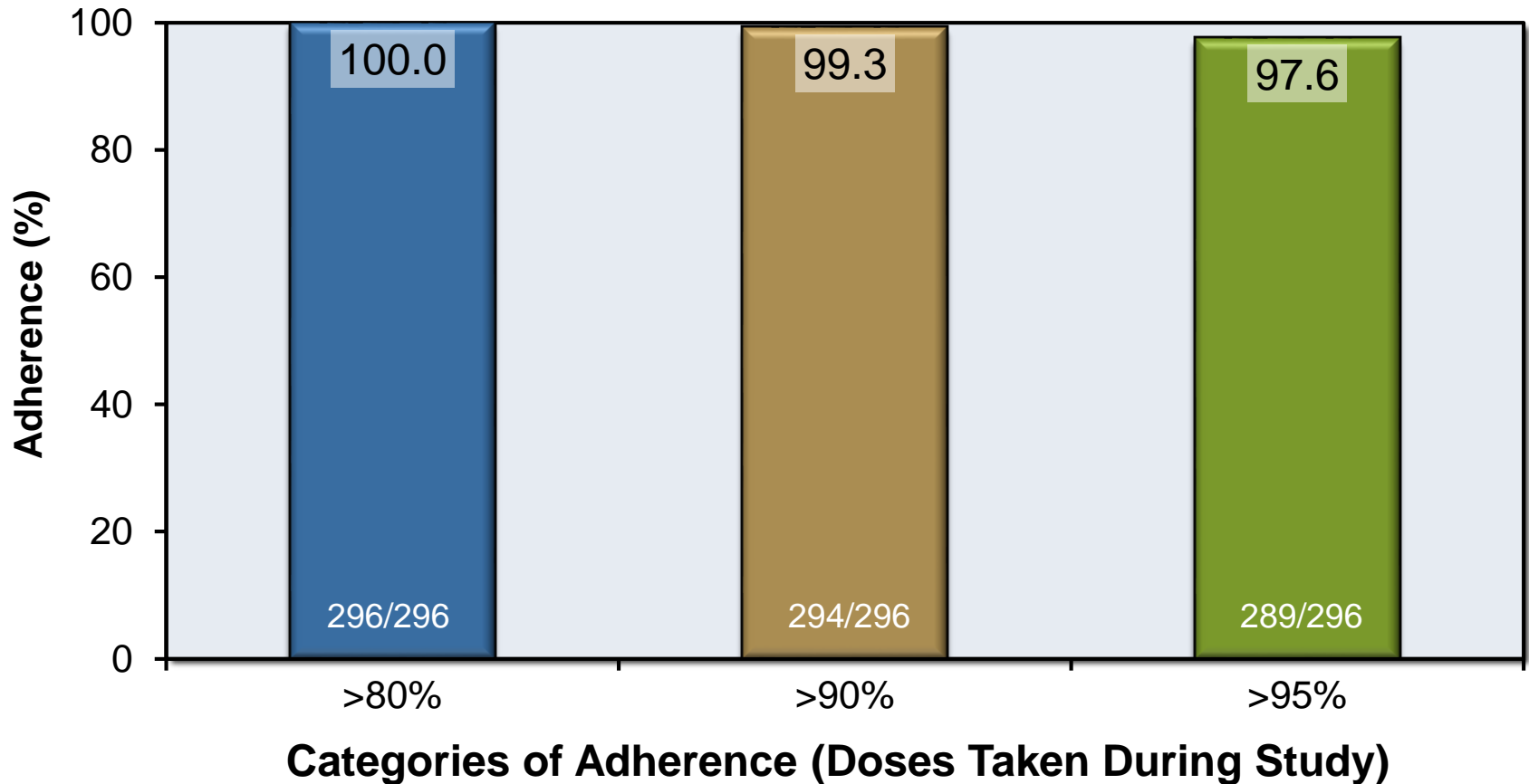
[^]Excludes patients who discontinued trial for non-treatment related reasons

Source: Dore G, et al. AALSD. 2015; Abstract 40.

Elbasvir-Grazoprevir in HCV GT 1, 4, or 6 in PWID on Opiate Agonist Therapy

C-EDGE CO-STAR: Results

C-EDGE CO-STAR: Adherence Overall



Elbasvir-Grazoprevir in HCV GT 1, 4, or 6 in PWID on Opiate Agonist Therapy

C-EDGE CO-STAR: Safety

| Adverse Event (AE), n (%) | Elbasvir-Grazoprevir | |
|----------------------------|----------------------|-------------------------------|
| | Immediate (n=201) | Deferred (Placebo) (n=100) |
| Discontinuation due to AE | 2 (1) | 2 (2) |
| Serious AEs | 7 (3.5) | 4 (4) |
| Deaths | 0 | 1 (1) |
| Any AE in ≥10% of patients | 166 (82.6) | 83 (83) |
| Fatigue | 32 (15.9) | 20 (20) |
| Headache | 26 (12.9) | 14 (14) |
| Nausea | 23 (11.4) | 9 (9) |
| Diarrhea | 20 (10) | 9 (9) |
| Laboratory AEs | | |
| Hemoglobin <8.5 g/dl | 0 | 0 |
| Late ALT/AST >5 x ULN* | 0 | 0 |
| Bilirubin >2.6 x ULN* | 0 | 1 (1) |
| Creatinine >2.5 x baseline | 0 | 0 |

*ULN = upper limit of normal

Elbasvir-Grazoprevir in HCV GT 1, 4, or 6 in PWID on Opiate Agonist Therapy C-EDGE CO-STAR: Conclusions

Conclusions: “Elbasvir-grazoprevir demonstrated high efficacy in GT1 and 4- infected patients receiving Opiate Agonist Therapy. Data demonstrate support for treating HCV among subjects receiving Opiate Agonist Therapy.”