Elbasvir-Grazoprevir in Treatment-Naïve HCV Genotype 1, 4, or 6

C-EDGE: Treatment Naïve

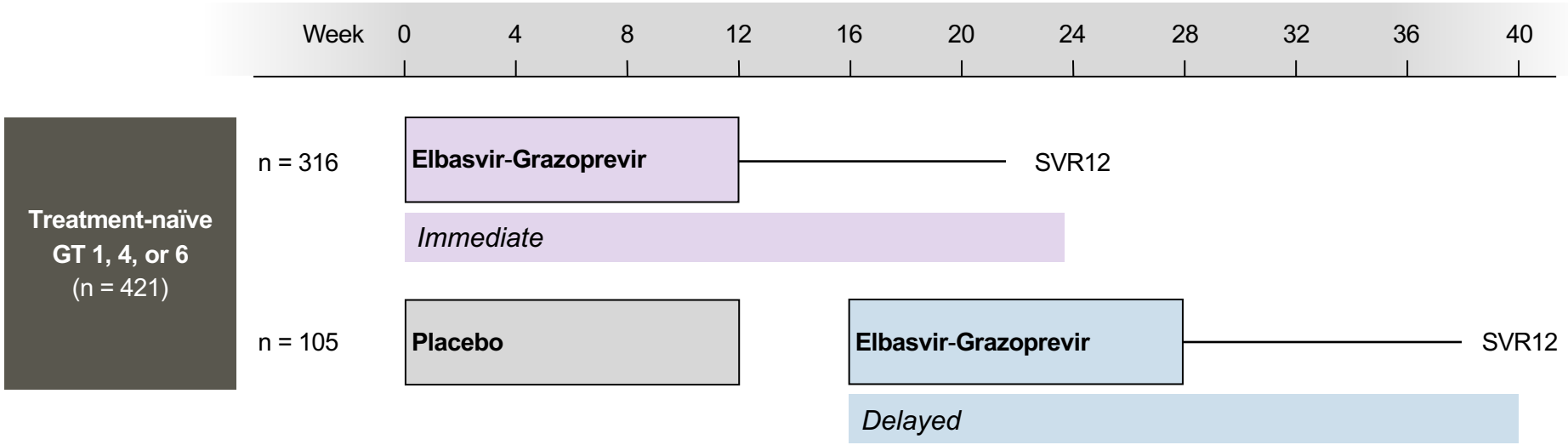
Source: Zeuzem S, et al. Ann Intern Med. 2015;163:1-13.

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

- **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%
  - Age 18 years or older
  - HCV RNA ≥10,000 IU/mL
  - No prior HCV treatment
  - Patients with compensated cirrhosis accepted
- **Primary End-Point**: SVR12

Source: 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: Design



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

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

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

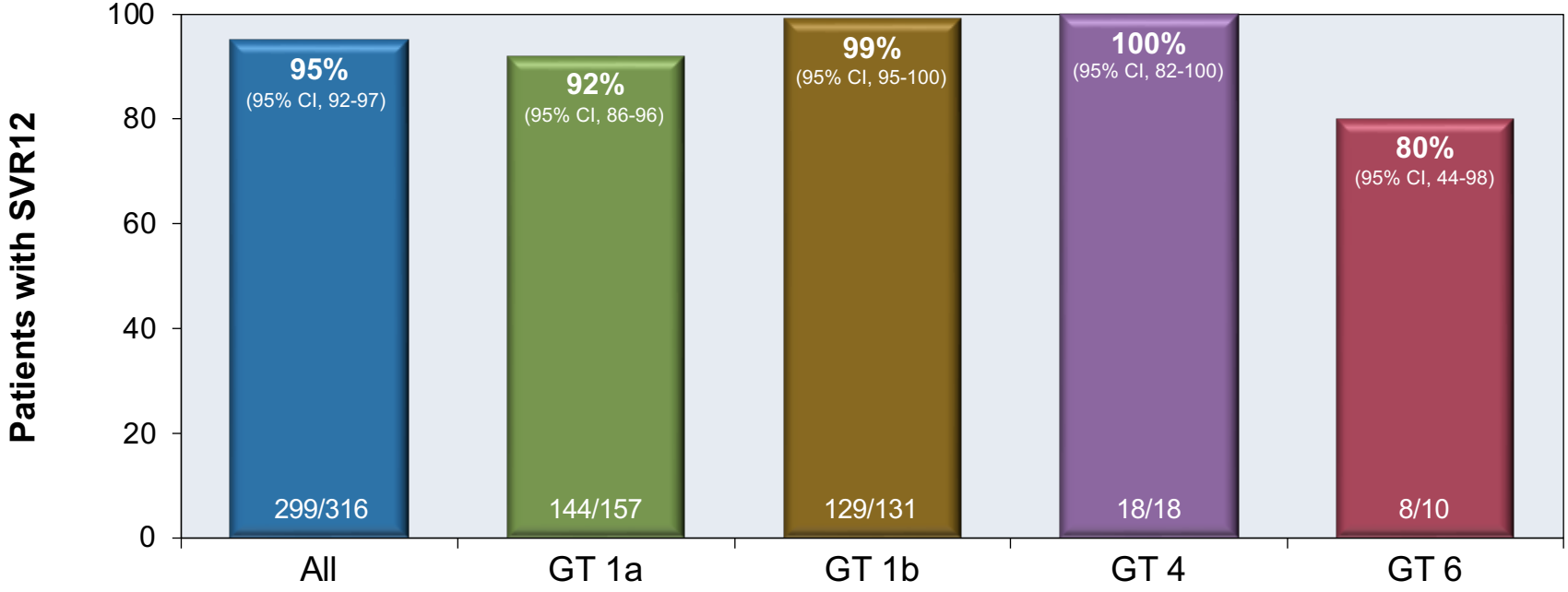
Elbasvir-Grazoprevir in Treatment-Naïve HCV GT 1, 4, or 6
C-EDGE TN: Baseline Characteristics

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 for Immediate Group

C-EDGE TN: SVR12 Results by Genotype

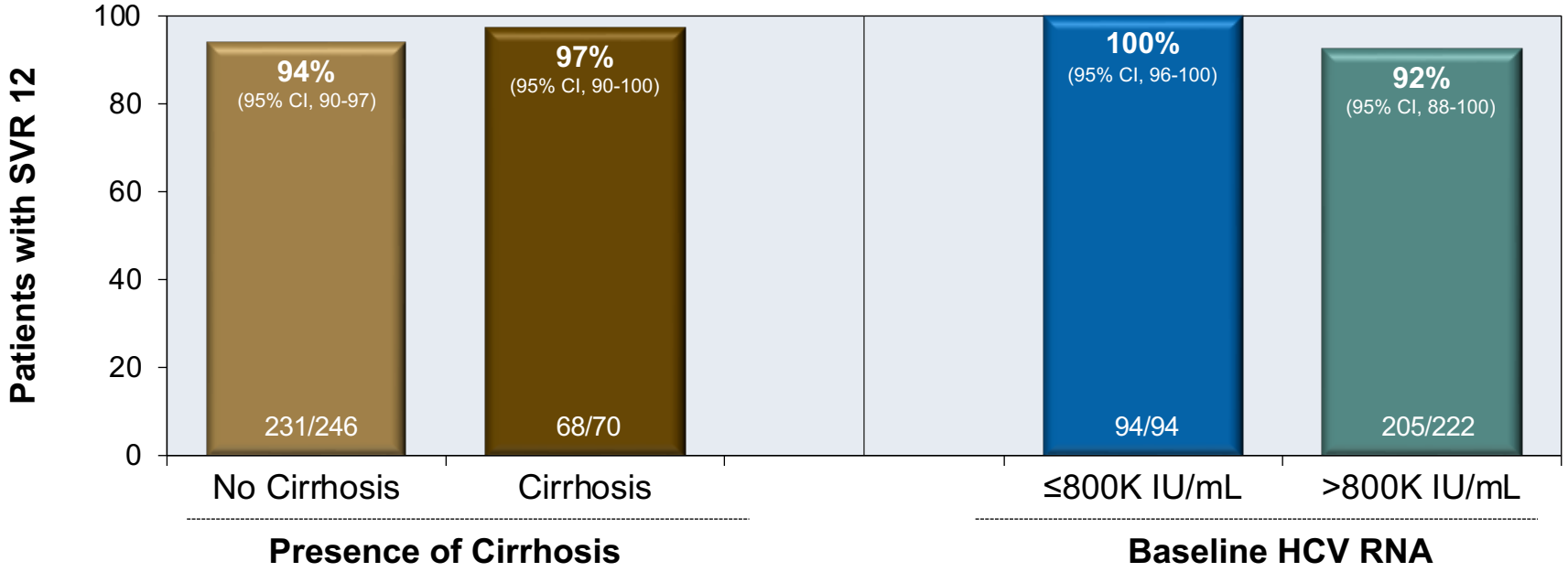


Primary efficacy analysis included all patients who received ≥1 dose of drug.

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 for Immediate Group

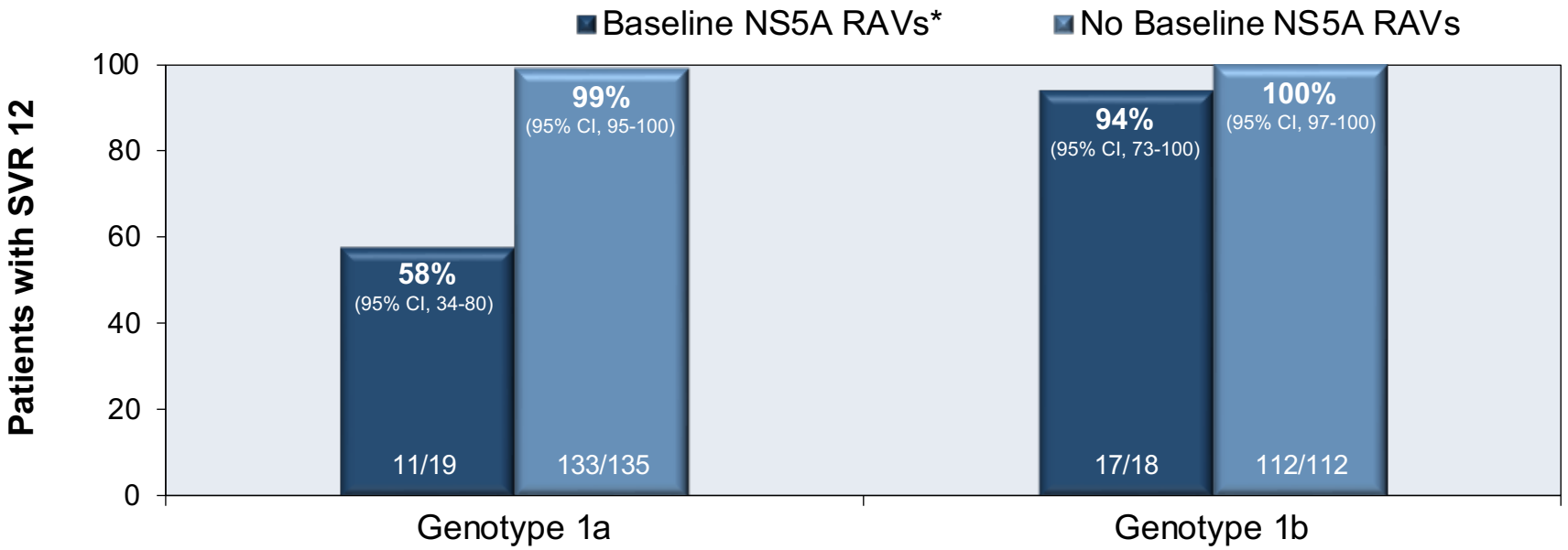
C-EDGE TN: SVR12 by Presence of Cirrhosis or High HCV RNA Level



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

Baseline NS5A Resistance-Associated Variants and SVR12 in GT1

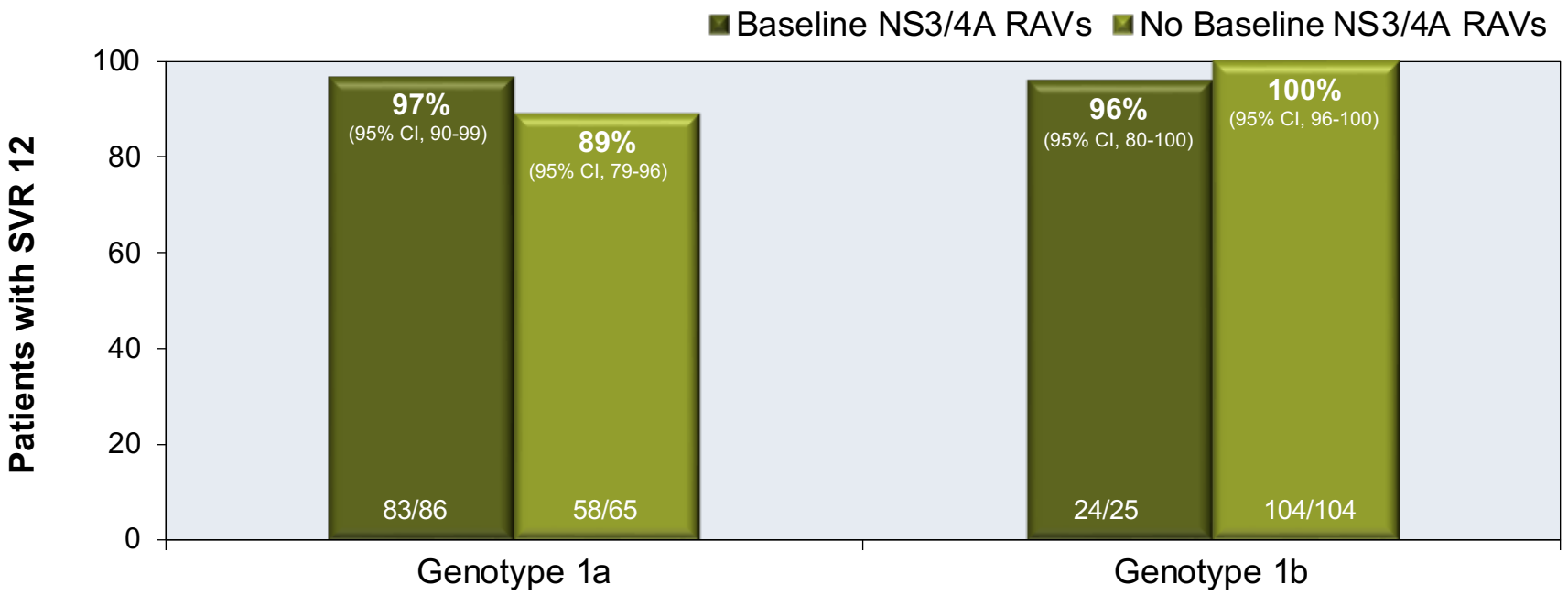


*Patients with baseline GT1a RAVs with a ≤5-fold shift to elbasvir: SVR12=90% (9 of 10)
*Patients with baseline GT1a RAVs with a >5-fold shift to elbasvir: SVR12=22% (2 of 9)

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

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



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: Adverse Events

Adverse Event (AE)	Elbasvir-Grazoprevir	
	Immediate (n = 316)	**Delayed** (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.”

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

Acknowledgments

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