Treatment-Naïve

Glecaprevir-Pibrentasvir in Treatment-Naïve, Non-Cirrhotic GT 3 ENDURANCE-3

Source: Zeuzem S, et al. N Engl J Med. 2018;378:354-69.

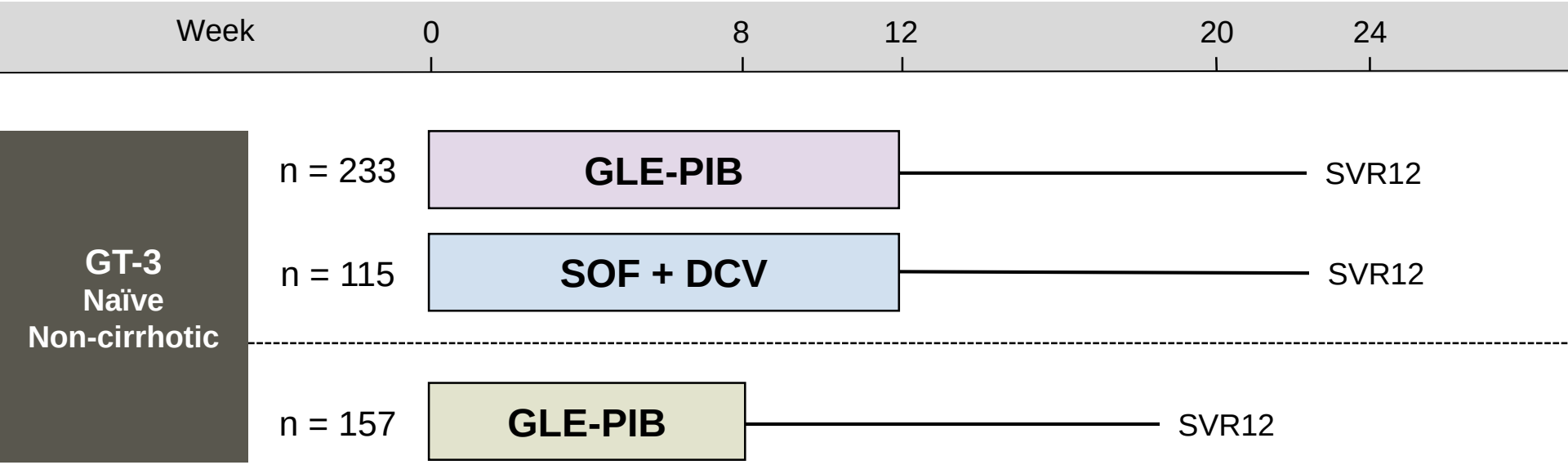
Glecaprevir-Pibrentasvir in Treatment-Naïve, Non-Cirrhotic GT 3
ENDURANCE-3: Study Features

ENDURANCE-3 Trial

- **Design**: Randomized, phase 3 trial to evaluate the safety and efficacy of the fixed-dose combination of glecaprevir-pibrentasvir for 8 or 12 weeks compared with 12 weeks of sofosbuvir and daclatasvir in treatment-naïve adults with GT 3 chronic HCV infection without cirrhosis
- **Key Eligibility Criteria**
  - Chronic HCV GT 3
  - Age ≥18 years
  - HCV RNA ≥1,000 IU/mL at screening
  - Treatment-naïve
  - No cirrhosis (METAVIR score ≤3 or equivalent)
  - HIV or chronic HBV coinfection excluded
- **Primary End-Point**: SVR12

Source: Zeuzem S, et al. N Engl J Med. 2018;378:354-69.

Glecaprevir-Pibrentasvir in Treatment-Naïve Non-Cirrhotic GT 3
ENDURANCE-3: Study Design



348 patients were randomized in 2:1 ratio to 12 weeks of GLE-PIB vs SOF + DCV.
157 were not randomized but assigned to 8 weeks of GLE-PIB.

Abbreviations: GLE-PIB = glecaprevir-pibrentasvir; SOF = sofosbuvir; DCV = daclatasvir

Drug Dosing
Glecaprevir-pibrentasvir: 300/120 mg once daily
Sofosbuvir 400 mg once daily plus Daclatasvir 60 mg once daily

Source: Zeuzem S, et al. N Engl J Med. 2018;378:354-69.

Glecaprevir-Pibrentasvir in Treatment-Naïve Non-Cirrhotic GT 3
ENDURANCE-3: Baseline Characteristics

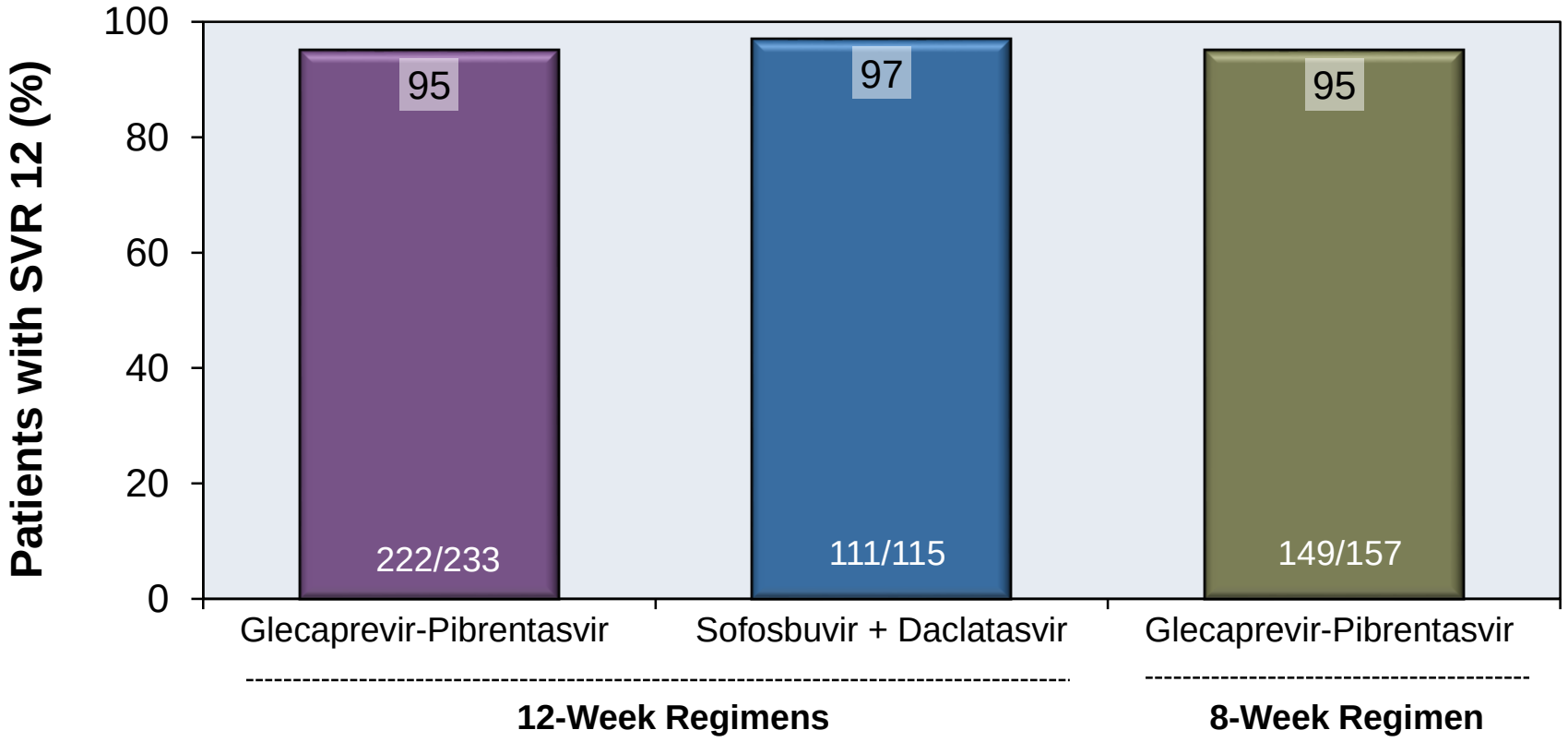
Characteristics	2:1 randomization		Non-randomized
	GLE-PIB 12 wk n = 233	SOF + DCV 12 wk n = 115	GLE-PIB 8 wk n = 157
Median age, (range) years	48 (22-71)	49 (20-70)	47 (20-76)
Male sex, n (%)	121 (52)	52 (45)	92 (59)
Black race, n (%)	4 (2)	4 (3)	3 (2)
History of injection drug use, n (%)	149 (64)	73 (63)	104 (66)
BMI, median kg/m^2 (range)	25 (17-49)	25 (18-42)	26 (18-44)
Median HCV RNA (range), $\log_{10}$ IU/ml	6.1 (3.5-7.5)	6.0 (3.8-7.4)	6.1 (1.2-7.6)
Fibrosis stage, n (%) F0 or F1 F2 F3	 201/233 (86) 12/233 (5) 20/233 (9)	 97/115 (84) 8/115 (7) 10/115 (9)	 122/157 (78) 8/157 (5) 27/157 (17)
HCV subtype 3a, n (%)	217 (93)	110 (96)	151 (96)

GLE-PIB = glecaprevir-pibrentasvir; SOF = sofosbuvir; DCV = daclatasvir; BMI = body mass index

Source: Zeuzem S, et al. N Engl J Med. 2018;378:354-69.

Glecaprevir-Pibrentasvir in Treatment-Naïve Non-Cirrhotic GT 3 ENDURANCE-3 Study: Results

ION-3: SVR 12 by Treatment Duration and Regimen (ITT Analysis)



GLE-PIB = glecaprevir-pibrentasvir; SOF = sofosbuvir; DCV = daclatasvir
ITT = Intent-to-treat

Source: Zeuzem S, et al. N Engl J Med. 2018;378:354-69.

Glecaprevir-Pibrentasvir in Treatment-Naïve Non-Cirrhotic GT 3
ENDURANCE-3: Treatment Outcomes

Outcomes, n (%)	2:1 randomization		Non-randomized
	GLE-PIB 12 x 12 weeks n=233	SOF + DCV x 12 weeks n=115	GLE-PIB x 8 weeks n=157
SVR12	222 (95)	111 (97)	149 (95)
Virologic Failure			
Breakthrough	1 (<1)	0	1 (1)
Relapse	3 (1)	1 (1)	5 (3)
Failure due to other reasons			
Discontinuation due to AE	1 (<1)	1 (1)	0
Withdrawal of consent	1 (<1)	0	0
Non-compliance	1 (<1)	0	0
Lost to follow-up / missing SVR12	4 (2)	2 (2)	2 (1)

SVR = Sustained virologic response; GLE-PIB = glecaprevir-pibrentasvir; SOF = sofosbuvir; DCV = daclatasvir

Source: Zeuzem S, et al. N Engl J Med. 2018;378:354-69.

Glecaprevir-Pibrentasvir in Treatment-Naïve Non-Cirrhotic GT 3 ENDURANCE-3: Resistance Analysis

SVR12 by Baseline Polymorphism, n (%)	2:1 randomization		Non-randomized
	GLE-PIB 12 wk	SOF + DCV 12 wk	GLE-PIB 8 wk
NS3 only	26/26 (100)	--	14/15 (93)
NS5A only	35/36 (97)	20/21 (95)	34/36 (94)
NS3 + NS5A	6/7 (86)	--	5/7 (71)
None	151/153 (99)	89/89 (100)	94/95 (99)

*Detected at 15% threshold by next-generation sequencing in samples that had sequences available at a key subset of amino acid positions:
NS3: 36, 55, 56, 80, 155, 156, 166, 168; NS5A at 24, 28, 29, 30, 31, 32, 58, 92, 93

GLE-PIB = glecaprevir-pibrentasvir; SOF = sofosbuvir; DCV = daclatasvir

Source: Zeuzem S, et al. N Engl J Med. 2018;378:354-69.

Glecaprevir-Pibrentasvir in Treatment-Naïve Non-Cirrhotic GT 3 ENDURANCE-3: Adverse Events

Adverse Event (AE), n (%)	Randomized		Non-randomized
	GLE-PIB 12 wk n=233	SOF + DCV 12 wk n=115	GLE-PIB 8 wk n=157
Any adverse event	177 (76)	80 (70)	98 (62)
AE possibly drug-related	112 (48)	50 (43)	63 (40)
Serious adverse event	5 (2)	2 (2)	3 (2)
AE leading to drug discontinuation	3 (1)	1 (1)	0
AE occurring in ≥10% patients			
Headache	60 (26)	23 (20)	31 (20)
Fatigue	44 (19)	16 (14)	20 (13)
Nausea	32 (14)	15 (13)	19 (12)
Laboratory abnormalities			
Grade ≥3 ALT (>5 x ULN)	0	1 (1)	0
Grade ≥3 total bilirubin (>3 x ULN)	0	0	1 (1)
Grade ≥3 neutrophil count (< 1 x 10^9/L)	1 (<1)	0	0

Source: Zeuzem S, et al. N Engl J Med. 2018;378:354-69.

Hepatitis web study

Glecaprevir-Pibrentasvir for 8 or 12 weeks in Non-Cirrhotic GT 1 *ENDURANCE-3: Conclusions

Conclusion: “Once-daily treatment with glecaprevir–pibrentasvir for either 8 weeks or 12 weeks achieved high rates of sustained virologic response among patients with HCV genotype 1 or 3 infection who did not have cirrhosis.”

***Note**: ENDURANCE-3 was published in conjunction with ENDURANCE-1

Source: Zeuzem S, et al. N Engl J Med. 2018;378:354-69.

This slide deck is from the University of Washington's *Hepatitis C Online* and *Hepatitis Web Study* projects.

Hepatitis C Online

www.hepatitisc.uw.edu

Hepatitis Web Study

http://depts.washington.edu/hepstudy/

Funded by a grant from the Centers for Disease Control and Prevention.

Hepatitis
web study