Treatment Naïve or Experienced

Glecaprevir-Pibrentasvir in Non-Cirrhotic Genotype 2 ENDURANCE-2

Source: Asselah T, et al. Clin Gastroenterol Hepatol. 2018;16:417-26.

Glecaprevir-Pibrentasvir in Non-Cirrhotic GT 2 *ENDURANCE-2: Study Features

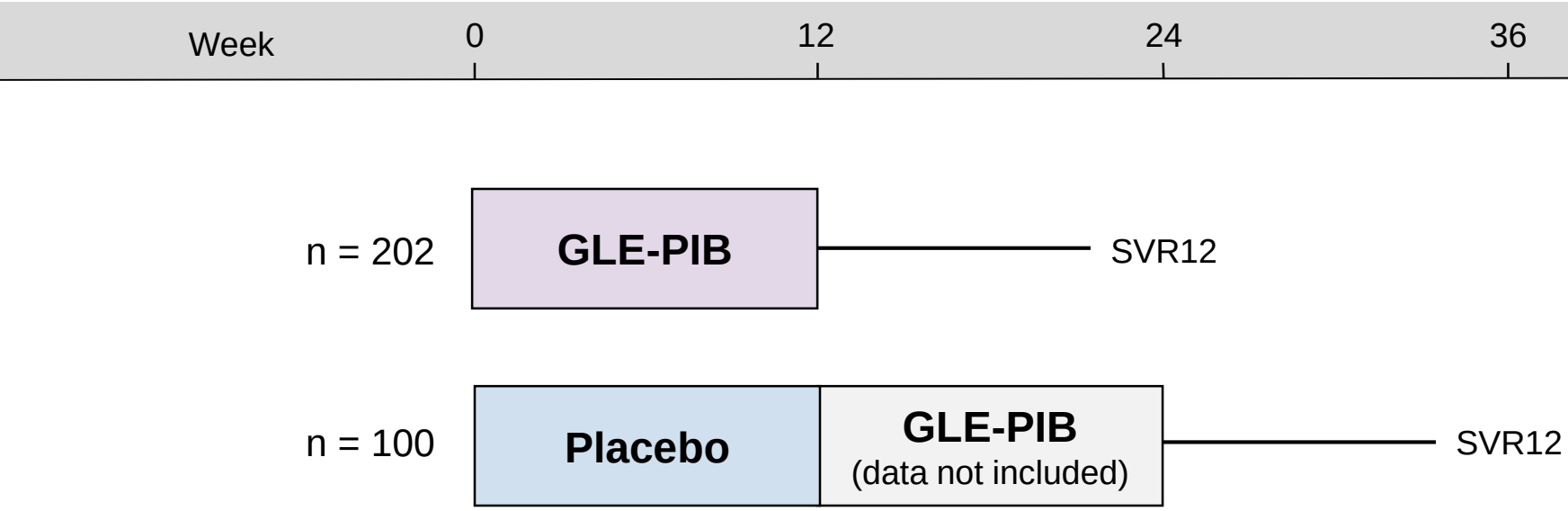
ENDURANCE-2 Trial

- **Design**: Randomized, double-blind, placebo-controlled phase 3 trial to evaluate the safety and efficacy of the fixed-dose combination of glecaprevir-pibrentasvir for 12 weeks in treatment-naïve or treatment-experienced adults with GT 2 chronic HCV infection without cirrhosis.
- **Setting**: Multiple centers in US, Europe and Asia
- **Key Eligibility Criteria**
  - Chronic HCV genotype 2
  - Age ≥18 years
  - HCV RNA ≥1,000 IU/mL at screening
  - Naïve or treated with (1) PEG (or IFN) +/- RBV or (2) SOF + RBV +/- PEG
  - Absence of cirrhosis
  - HIV or HBV coinfection excluded
- **Primary End-Point**: SVR12

***Note**: ENDURANCE-2 was published in conjunction with ENDURANCE-4 and SURVEYOR-II (Part 4)

Source: Asselah T, et al. Clin Gastroenterol Hepatol. 2018;16:417-26.

Glecaprevir-Pibrentasvir in Non-Cirrhotic GT 2 ENDURANCE-2: Study Design



Note: Four patients enrolled in GT2 arm later determined to be infected with GT1 by phylogenetic analysis

Abbreviations: GLE-PIB= Glecaprevir-pibrentasvir

Drug Dosing
Glecaprevir-pibrentasvir (100/40 mg) fixed-dose combination: three pills (300/120 mg) once daily

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Glecaprevir-Pibrentasvir in Non-Cirrhotic GT 2 ENDURANCE-2: Baseline Characteristics

Baseline Characteristic	GLE-PIB (n = 202)	Placebo (n = 100)
Age, mean ± SD, years	57 ± 12.8	58 ± 12.0
Male, n (%)	98 (49)	45 (45)
Race, n (%) White Black Asian	 121 (60) 7 (3) 69 (34)	 60 (60) 7 (7) 32 (32)
BMI, mean, ± SD kg/m^2	25.8 ± 4.7	26.4 ± 4.1
HCV RNA, median (range), log$_{10}$ IU/mL	6.25 (2.5-7.3)	6.39 (3.4-7.2)
IL28B non-CC, n (%)	111 (55)	50 (50)
Former IDU, n (%)	32 (16)	18 (18)

*One patient in active arm with subtype 2i.

Source: Asselah T, et al. Clin Gastroenterol Hepatol. 2018;16:417-26.

Glecaprevir-Pibrentasvir in Non-Cirrhotic GT 2 ENDURANCE-2: Baseline Characteristics

Baseline Characteristic	GLE-PIB (n = 202)	Placebo (n = 100)
Fibrosis Stage, n (%)		
F0-1	154 (76)	85 (85)
F2	18 (9)	9 (9)
F3	30 (15)	6 (6)
Treatment-naïve, n (%)	141 (70)	71 (71)
Treatment-experienced, n (%)	61 (30)	29 (29)
IFN or PEG ± RBV, n (%)	55 (27)	27 (27)
SOF + RBV ± PEG, n (%)	6 (3)	2 (2)
Concomitant PPI use, n (%)	22 (11)	11 (11)

Source: Asselah T, et al. Clin Gastroenterol Hepatol. 2018;16:417-26.

Glecaprevir-Pibrentasvir in Non-Cirrhotic GT 2 ENDURANCE-2: Baseline Polymorphisms

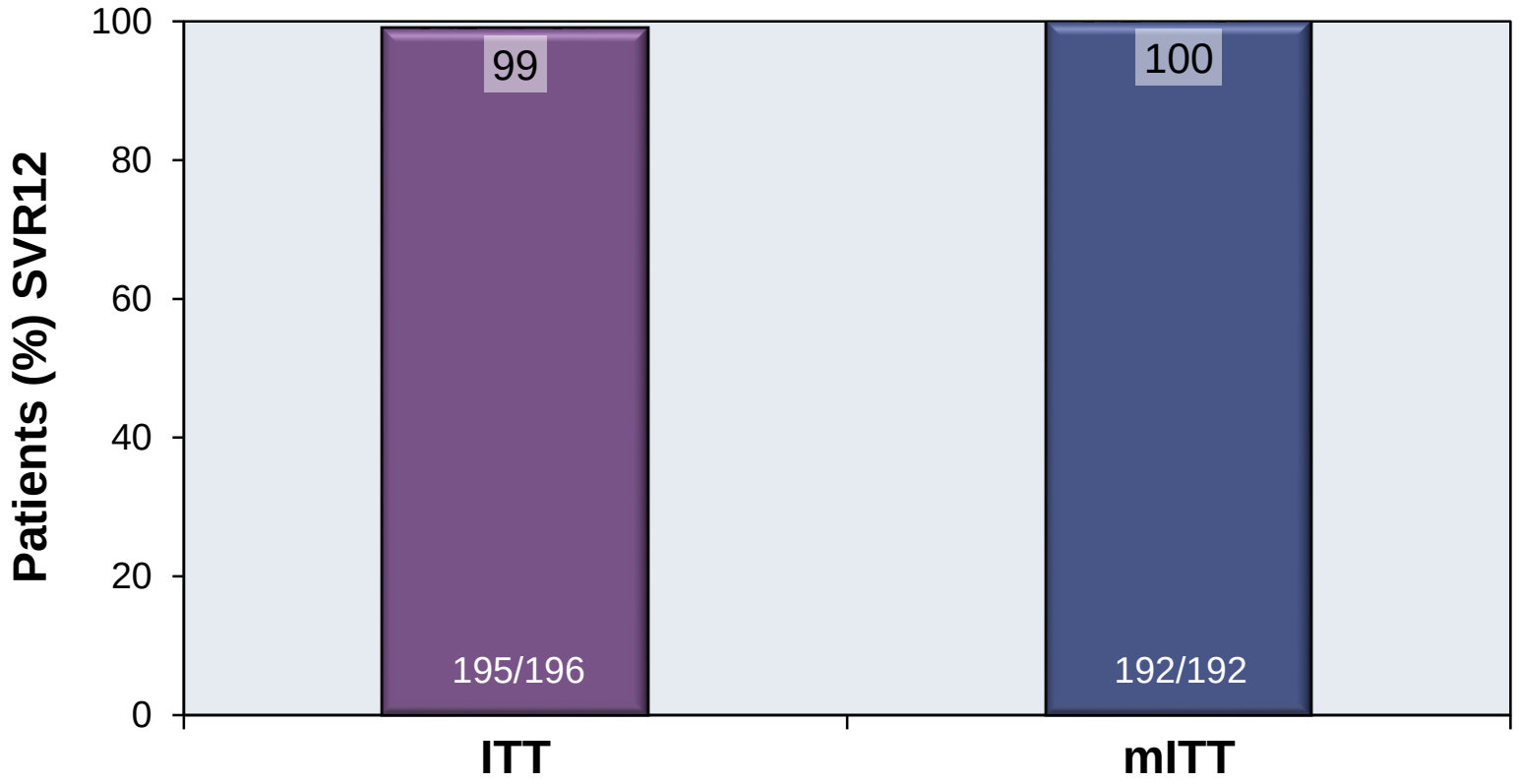
Prevalence of Baseline Polymorphism*, n (%)*	Genotype 2 (n = 160)
None	28 (18)
NS3 only	0
NS5A only	132 (83)
Both NS3 + NS5A	0

*Baseline polymorphisms detected by next generation sequencing at a 15% threshold in samples that had sequences available for both targets (N) at the following amino acid positions:
- NS3: 155, 156, 168
- NS5A: 24, 28, 30, 31, 58, 92, 93

Source: Asselah T, et al. Clin Gastroenterol Hepatol. 2018;16:417-26.

Glecaprevir-Pibrentasvir in Non-Cirrhotic GT 2
ENDURANCE-2: Results

ENDURANCE-2: Overall SVR, by Analysis



ITT, intent-to-treat: excludes 6 sofosbuvir-experienced patients, all of whom achieved SVR12
mITT, modified intent-to-treat: xcludes patients with non-virologic failure and those with ineligible genotype

Source: Asselah T, et al. Clin Gastroenterol Hepatol. 2018;16:417-26.

Glecaprevir-Pibrentasvir in Non-Cirrhotic GT 2 ENDURANCE-2: Adverse Events

Adverse Event (AE), n (%)	**GLE-PIB** 12 weeks (n = 202)	**Placebo** (n = 100)
Discontinuation due to AE	0	0
Serious AEs[§]	3 (1)	1 (1)
Deaths	0	0
Any AE in >10% of patients		
Headache	24 (12)	12 (12)
Fatigue	23 (11)	10 (10)
Laboratory AEs		
AST elevation, grade 3-4 (>5x ULN)	2 (1)	1 (1)
ALT elevation, grade 3-4 (>5x ULN)*	1 (0.5)	2 (2)
Total bilirubin, grade 3 (3-10x ULN)[#]	1 (0.5)	0

AST, aspartate aminotransferase; ALT, alanine aminotransferase; ULN, upper limit normal
[§] No serious AEs were deemed to be DAA-related; no SAEs led to drug discontinuation.
Event occurred with grade 3 AST and grade 3 alkaline phosphatase elevation in context of cholelithiasis.
[#]Indirect hyperbilirubinemia; no associated ALT elevation. Declined with treatment.

Source: Asselah T, et al. Clin Gastroenterol Hepatol. 2018;16:417-26.

Glecaprevir-Pibrentasvir in Non-Cirrhotic GT 2 *ENDURANCE-2: Conclusions

Conclusion: “The SVR12 rate in all genotype 2-infected patients treated for 12 weeks (including those with sofosbuvir experience) was 99.5%, with no virologic failures.”

***Note**: ENDURANCE-2 was published in conjunction with ENDURANCE-4 and SURVEYOR-II (Part 4)

Source: Asselah T, et al. Clin Gastroenterol Hepatol. 2018;16:417-26.

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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.

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