Glecaprevir-Pibrentasvir in Patients with and without Cirrhosis

Pooled Analysis

Source: Gane E, et al. Clin Infect Dis. 2019;69:1657-64.

Glecaprevir-Pibrentasvir in Patients with and without Cirrhosis Pooled Analysis: Study Features

- **Design**: Integrated analysis of pooled data from nine phase 2 & 3 trials to evaluate the safety and efficacy of the fixed-dose combination of glecaprevir-pibrentasvir for 8, 12 or 16 weeks in treatment-naïve and treatment-experienced adults with GT 1-6 chronic HCV infection with and without cirrhosis
- **Setting:** US, Canada, Europe, Australia, New Zealand and South Africa
- **Key Eligibility Criteria**
  - Chronic HCV GT 1-6
  - HCV RNA ≥1,000 IU/mL at screening
  - Treatment naïve
  - Prior treatment with (1) PEG (or INF) +/- RIB or (2) Sofosbuvir + RIB +/- PEG
  - Patients with compensated cirrhosis permitted in some trials
  - Patients with chronic HBV excluded
- **End Points**: Safety and efficacy, stratified by cirrhosis status

Source: Gane E, et al. Clin Infect Dis. 2019;69:1657-64.

Glecaprevir-Pibrentasvir in Patients +/- Cirrhosis (Pooled Analysis) Baseline Characteristics

Characteristics	Cirrhosis* (n = 308)	No Cirrhosis (n = 2,061)	Overall (n = 2,369)
Age ≥65 years	64 (21)	264 (13)	328 (14)
Male sex, n (%)	199 (65)	1119 (54)	1318 (56)
Race, n (%)			
White	261 (85)	1637 (80)	1898 (80)
Black	25 (8)	124 (6)	149 (6)
Asian	17 (6)	255 (12)	272 (11)
Other	5 (2)	42 (2)	47 (2)
BMI ≥30 kg/m^2, n (%)	115 (37)	387 (19)	502 (21)
HCV genotype, n (%)			
GT 1	123 (40)	864 (42)	987 (42)
GT 2	38 (12)	439 (21)	477 (20)
GT 3	116 (38)	527 (26)	643 (27)
GT 4	22 (7)	160 (8)	182 (8)
GT 5 / 6	2 (<1) / 7 (2)	30 (1)/ 41 (2)	32 (1) / 48 (2)

*All with cirrhosis had compensated cirrhosis
Abbreviations: BMI = body mass index; GT = genotype

Source: Gane E, et al. Clin Infect Dis. 2019;69:1657-64.

Glecaprevir-Pibrentasvir in Patients +/- Cirrhosis (Pooled Analysis) Baseline Characteristics

Characteristics	Cirrhosis* (n = 308)	No Cirrhosis (n = 2,061)	Overall (n = 2,369)
Treatment experienced, n (%)	126 (41)	603 (29)	729 (31)
PRS experienced**	99 (79)	517 (86)	616 (84)
PI and/or NS5A experienced**	27 (21)	86 (14)	113 (16)
HCV RNA ≥1 million IU/ml, n (%)	183 (59)	1224 (59)	1407 (59)
Fibrosis stage, n (%)			
F0-1	0	1651 (80)	1651 (70)
F2	0	163 (8)	165 (7)
F3	0	243 (12)	245 (10)
F4	307 (99)***	0	307 (13)
Child-Pugh score, n (%)			
5	264 (86)	4 (<1)	268 (11)
6	41 (13)	0	41 (2)
>6	2 (<1)	0	2 (<1)
Platelet count <100 x 10^9 cells/L	70 (23)	7 (<1)	77 (3)

*Compensated
**Percentage out of total number of treatment-experienced
***Missing in n=1
Abbreviations: PRS = pegIFN, ribavirin or sofosbuvir plus ribavirin; PI = protease inhibitor

Source: Gane E, et al. Clin Infect Dis. 2019;69:1657-64.

Glecaprevir-Pibrentasvir in Patients +/- Cirrhosis (Pooled Analysis) Baseline Characteristics

Characteristics	Cirrhosis* (n = 308)	No Cirrhosis (n = 2,061)	Overall (n = 2,369)
G/P treatment duration, n (%)			
8 weeks	0	828 (40)	828 (35)
12 weeks	245 (80)	1176 (57)	1421 (60)
16 weeks	63 (20)	57 (3)	120 (5)
Albumin <3.5 g/dl, n (%)	23 (7)	5 (<1)	28 (1)
CKD stage 4 or 5 (eGFR <30 ml/min/1.73 m^2)	20 (7)	83 (4)	103 (5)
History of diabetes**	63 (20)	141 (7)	204 (9)
History of cardiovascular disease**	154 (50)	622 (30)	776 (33)

*Compensated
**Statistically significant difference between those with versus without cirrhosis at p-value <0.05 level

Abbreviation: CKD = chronic kidney disease

Source: Gane E, et al. Clin Infect Dis. 2019;69:1657-64.

Glecaprevir-Pibrentasvir in Patients +/- Cirrhosis (Pooled Analysis) Adverse Events (without chronic kidney disease stage 4-5)

Adverse Event (AE), n (%)	Cirrhosis[1] (n = 288)	No Cirrhosis (n = 1,977)	Overall (n = 2,265)
Any AE	213 (74)	1316 (67)	1529 (68)
Any grade ≥3 AE	20 (7)	45 (2)	65 (3)
Serious AE	17 (6)	31 (2)	48 (2)
DAA-related serious AE	0	1 (<1)	1 (<1)
AE leading to drug discontinuation	0	8 (<1)[2]	8 (<1)
AEs in 10% patients			
Headache	47 (16)	363 (18)	410 (18)
Fatigue	58 (20)	272 (14)	330 (15)
Nausea	27 (9)	181 (9)	208 (9)
Pruritus	18 (6)	85 (4)	103 (5)
Deaths	1 (<1)[3]	5 (<1)[4]	6 (<1)

[1]Compensated. [2] Of these 8 patients, 3 experienced a total of 9 DAA-related AEs that led to study drug discontinuation, including abdominal pain, diarrhea, nausea, fatigue, malaise, dizziness, headache, and transient ischemic attacks.
[3]Due to cerebral hemorrhage. [4]Due to pneumonia, accidental overdose, adenocarcinoma, hepatic cancer metastatic, and acute ethanol and combined methadone toxicity
Abbreviation: CKD, chronic kidney disease

Source: Gane E, et al. Clin Infect Dis. 2019;69:1657-64.

Glecaprevir-Pibrentasvir in Patients +/- Cirrhosis (Pooled Analysis) Adverse Events (with CKD stage 4-5)

Adverse Event (AE), n (%)	Cirrhosis[1] (n = 20)	No Cirrhosis (n = 84)	Overall (n = 104)
Any AE	20 (100)	54 (64)	74 (71)
Any grade ≥3 AE	11 (55)	14 (17)	25 (24)
Serious AE	11 (55)	14 (17)	25 (24)
DAA-related serious AE	0	0	0
AE leading to drug discontinuation	2 (10)	2 (2)	4 (4)[2]
AEs in 10% patients			
Headache	1 (5)	8 (10)	9 (9)
Fatigue	1 (5)	14 (17)	15 (14)
Nausea	4 (20)	8 (10)	12 (12)
Pruritus	6 (30)	15 (18)	21 (20)
Deaths	1 (5)[3]	0	1 (<1)

[1]Compensated cirrhosis
[2]Of these 4 patients, 2 with compensated cirrhosis experienced a DAA-related AE: 1 had Grade 2 diarrhea, and 1 had Grade 3 pruritus.
[3]Cause of death was cerebral hemorrhage.
Abbreviation: CKD, chronic kidney disease

Source: Gane E, et al. Clin Infect Dis. 2019;69:1657-64.

Glecaprevir-Pibrentasvir in Patients +/- Cirrhosis (Pooled Analysis) Laboratory Abnormalities

Grade ≥3, n (%)	Cirrhosis* (n = 308)	No Cirrhosis (n = 2,061)	Overall (n = 2,369)
ALT >5 x ULN	0	2 (<1)	2 (<1)
AST >5 x ULN	0	6 (<1)	6 (<1)
Total bilirubin >3 x ULN	3 (1)	6 (<1)	9 (<1)
Platelets <50 x 10^9/L	4 (1)	0	4 (<1)

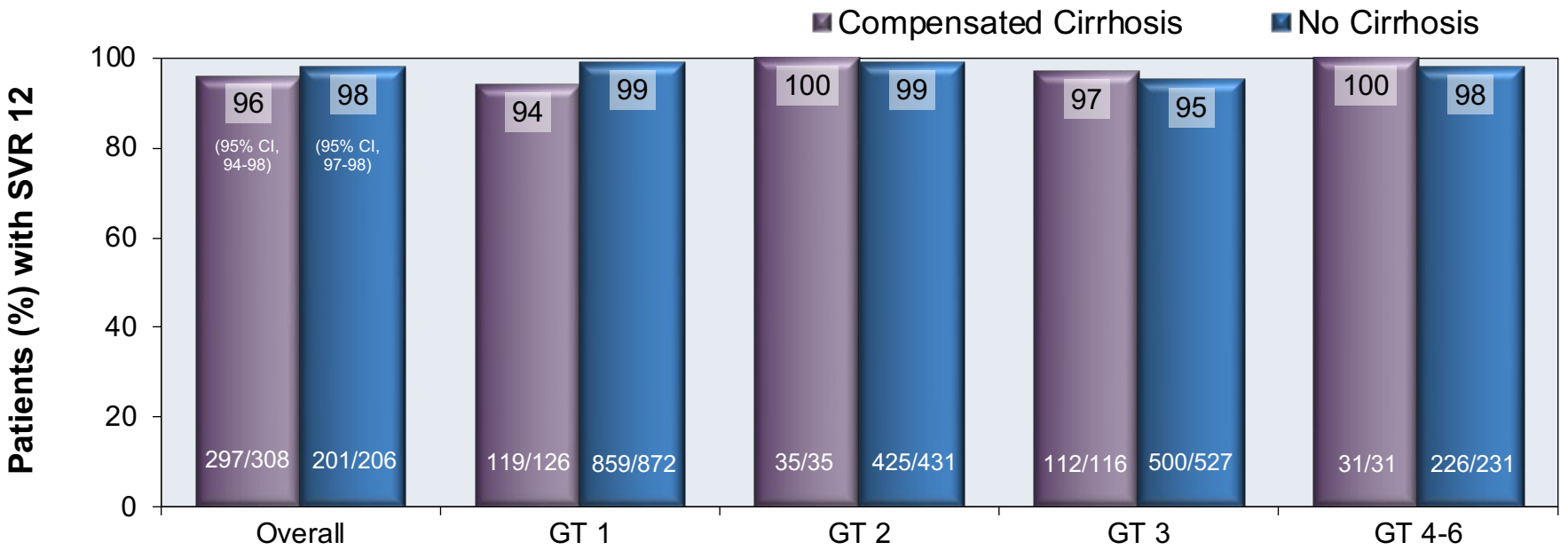
*All with cirrhosis had compensated cirrhosis

Abbreviations: ALT = alanine aminotransferase; AST = aspartate aminotransferase, ULN = upper limit of normal

Source: Gane E, et al. Clin Infect Dis. 2019;69:1657-64.

Glecaprevir-Pibrentasvir in Patients +/- Cirrhosis (Pooled Analysis) Results

Overall SVR by Intention-to-Treat Analysis



Note – duration of treatment 12 (80%) or 16 (20%) weeks for cirrhosis.

Source: Gane E, et al. Clin Infect Dis. 2019;69:1657-64.

Glecaprevir-Pibrentasvir in Patients +/- Cirrhosis (Pooled Analysis) Outcomes

Outcome	Cirrhosis* (n = 308)	No Cirrhosis (n = 2,061)
SVR12, n (%, [95% CI])	297 (96.4 [93.7-98.0])	2010 (97.5 [96.8-98.1])
Non-response, n (%)		
On-treatment virologic failure	5**	6
Viral relapse	3	19
Premature drug discontinuation	1	11
Missing SVR12 data	2	15

*Compensated. Abbreviation: SVR12, sustained virologic response 12 weeks post-treatment; CI, confidence interval.
**2 patients had prior treatment experience with both a NS5A inhibitor and NS3/4A protease inhibitor. Glecaprevir-pibrentasvir not recommended for treatment in this dual DAA-experienced patient population.

Source: Gane E, et al. Clin Infect Dis. 2019;69:1657-64.

Glecaprevir-Pibrentasvir in Patients +/- Cirrhosis (Pooled Analysis) Conclusions

Conclusions: “Glecaprevir-pibrentasvir was safe and efficacious in patients with compensated liver disease, including those with CKD 4/5.”

Source: Gane E, et al. Clin Infect Dis. 2019;69:1657-64.

Acknowledgments

Hepatitis C Online is funded by a cooperative agreement from the Centers for Disease Control and Prevention (CDC-RFA- PS21-2105). This project is led by the University of Washington Infectious Diseases Education and Assessment (IDEA) Program.

HEPATITIS B ONLINE

HEPATITIS C ONLINE

IDEA INFECTIOUS DISEASES EDUCATION & ASSESSMENT