Real-World Outcomes in Patients With Chronic Hepatitis C Virus Infection and Substance Abuse Disorders Treated With Glecaprevir/Pibrentasvir for 8 Weeks: A Pooled Analysis of Multinational Postmarketing Observational Studies

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G/P is Approved for Patients With HCV GT1–6 Infection

Glecaprevir
pangenotypic NS3/4A protease inhibitor

Coformulated: G/P

Pibrentasvir
pangenotypic NS5A inhibitor

- 8-week duration in treatment-naïve patients (without cirrhosis or with compensated cirrhosis)[1]
- Pangenotypic SVR12 rate of 98% in more than 3000 patients in clinical trials
- Favorable safety profile in indicated populations (eg, Child-Pugh A, CKD, patients aged ≥3 years)[1]
- Real-world SVR results have been consistent with the high rates observed in clinical trials[2,3]
- No recommendation for baseline resistance testing (EASL & AASLD guidelines)

AASDL, American Association for the Study of Liver Diseases; CKD, chronic kidney disease; European Association for the Study of the Liver; G/P, Glecaprevir/Pibrentasvir; SVR, sustained virologic response; SVR12, sustained virologic response after 12 weeks post-treatment; G/P dosed as 3 pills taken at the same time once daily with food (total daily dose of 300 mg GLE/120 mg PIB);

1. MAVIRET (SmPC); AbbVie 2021 / MAVYRET (US package insert); AbbVie 2021; 2. Berg T, et al. Aliment Pharmacol Ther. 2019;49:1052–1059; 3. D'Ambrosio R, et al. J Hepatol. 2019;70:379–387.

Background and Objective

The shorter therapy durations possible with G/P could improve outcomes in marginalized patients including PWUD, a critical population to treat in order to meet World Health Organization 2030 HCV elimination targets

Objective

- To examine the real-world effectiveness and safety of 8-week G/P in PWUD and other historically underserved patient groups

G/P, glecaprevir/pibrentasvir; HCV, hepatitis C virus; PWUD, people who use drugs.

Methods – Study Design

Study design

- Data pooled from PMOS across 9 countries on TN patients with HCV treated with 8-week G/P (Nov 13, 2017– Jun 3, 2020)*
- Percentage of patients who achieved SVR12 was assessed overall and by subgroup
  - Illicit drug use was patient-reported

Study population

- Inclusion criteria
  - Aged ≥18 years with HCV GT1–6 infection, without cirrhosis or with CC, who received G/P at the treating physician's discretion

Safety population: All patients who received ≥1 dose of G/P

CPSFU population: All patients who received ≥1 dose of G/P according to current label at the time of the study and had sufficient follow-up

*At the time of the study 8-week G/P treatment was off-label for patients with CC

CC, compensated cirrhosis; CPSFU, core population with sufficient follow up; G/P, glecaprevir/pibrentasvir; GT, genotype; HCV, hepatitis C virus; PMOS, postmarketing observational studies; SVR12, sustained virologic response at posttreatment Week 12; TN, treatment-naïve.

Methods – Outcomes

Effectiveness

- Percentage of patients achieving SVR12 in overall population and by subgroup

Health-related quality of life

- Percentage of patients achieving a minimally important difference (≥2.5) in SF-36 with both the mental and physical component summaries

Safety

- Adverse events and abnormal laboratory measurements in the safety population (patients who received ≥1 dose of G/P)

G/P, glecaprevir/pibrentasvir; SF-36, 36-Item Short-Form Health Survey; SVR12, sustained virologic response at posttreatment Week 12.

Patient Demographics and Disease Characteristics

Characteristics	Safety Population N=1522
Male	834 (54.8)
Age, median years (range)	51 (18–88)
HCV genotype	
1	789 (52.5)
2	144 (9.6)
3	425 (28.3)
4–6	144 (9.6)
Missing	20
Fibrosis stage	
F0–F1	899 (86.9)
F2	60 (5.8)
F3	65 (6.3)
F4	11 (1.1)
Missing	487
No cirrhosis	1508 (99.1)
APRI score	
≤1	836 (82.8)
>1	174 (17.2)
Missing	512
HCV RNA, median (range), Log_{10} IU/mL[a]	6.0 (0.6–8.4)

Characteristics	Safety Population N=1522
Mode of HCV infection	
Contaminated needle or IV drug use	451 (53.9)
Blood product transfusion	187 (22.3)
Vertical transmission (mother to child)	25 (3.0)
Contact with infected individual (other than vertical transmission)	61 (7.3)
Surgery/operation	102 (12.2)
Occupational exposure	11 (1.3)
Unknown/missing	685
Any recreational drug use prior to screening[b]	500 (33.3)
Recreational drug types whose use was ≥3% (PWUD population n=500)	
Heroin	318 (63.6)
Cocaine	110 (22.0)
Marijuana	55 (11.0)
Hashish	38 (7.6)
Opioids	19 (3.8)
History of psychiatric disorder	148 (9.7)
History of alcohol use[c,d]	208 (16.1)
Unemployed or low to no education[e]	592 (42.7)

Data are n (%) unless otherwise stated. [a]n=1441; [b]Drug use was unknown for 19 patients; [c]More than 2 drinks per day; [d]Missing n=229; [e]Missing n=137.
APRI, aspartate aminotransferase to platelet ratio index; HCV, hepatitis C virus; IV, intravenous; RNA, ribonucleic acid.

Concomitant Medications

Characteristics	Safety Population N=1522	PWUD N=500
Number of concomitant medications		
1	257 (16.9)	104 (20.8)
2–4	300 (19.7)	116 (23.2)
5–8	86 (5.7)	33 (6.6)
>8	21 (1.4)	5 (1.0)
none	858 (56.4)	242 (48.4)
Drugs used in addiction disorders	102 (6.7)	101 (20.2)
Anxiolytics	97 (6.4)	63 (12.6)
ACE inhibitors	94 (6.2)	19 (3.8)
Antidepressants	86 (5.7)	41 (8.2)
Beta blocking agents	85 (5.6)	7 (1.4)
Antithrombotic agents	84 (5.5)	21 (4.2)
Drugs for peptic ulcer and gastroesophageal reflux	64 (4.2)	8 (1.6)
Antipsychotics	46 (3.0)	32 (6.4)

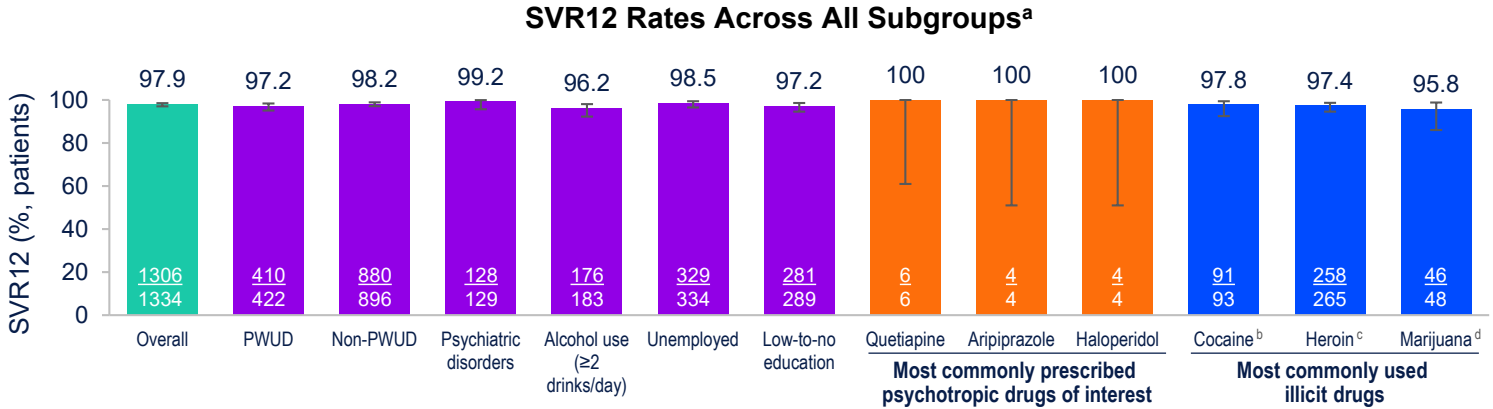
In the safety population, the most commonly used prescribed psychotropic drugs with a potential interaction with G/P were quetiapine (0.5%), aripiprazole (0.3%), and haloperidol (0.3%)

The most common drugs used with addiction disorder in the safety population were methadone (3.8%), buprenorphine (2.1%), and temgesic-nx (0.6%)

Data are n (%).
ACE, angiotensin-converting enzyme; G/P, glecaprevir/pibrentasvir; PWUD, people who use drugs.

Results – SVR12 Rate

SVR12 rate was 97.9% (1306/1334) overall, 97.2% (410/422) in PWUD, and ≥95.8% across subgroups



Reasons for virologic failure													
On-treatment virologic failure	6	1	5	1	2	2	2	0	0	0	1	0	0
Relapse	11	4	7	0	1	1	1	0	0	0	0	2	0
Discontinuation of treatment	4	2	2	0	1	1	2	0	0	0	1	1	1
Missing SVR12 data	2	2	0	0	1	1	2	0	0	0	0	2	1
Other	5	3	2	0	2	0	1	0	0	0	0	2	0

[a]Error bars represent 95% confidence intervals. Data are from the core population with sufficient follow-up; [b]An additional 22 TN/TE patients using cocaine received G/P for 12 weeks; all (100%) achieved SVR12; [c]An additional 44 TN/TE patients using heroin received G/P for 12 weeks; all (100%) achieved SVR12; [d]An additional 10 TN/TE patients using marijuana received G/P for 12 weeks; all (100%) achieved SVR12.
G/P, glecaprevir/pibrentasvir; PWUD, people who use drugs; SVR12, sustained virologic response at posttreatment Week 12; TE, treatment-experienced; TN, treatment-naïve.

Results – PROs

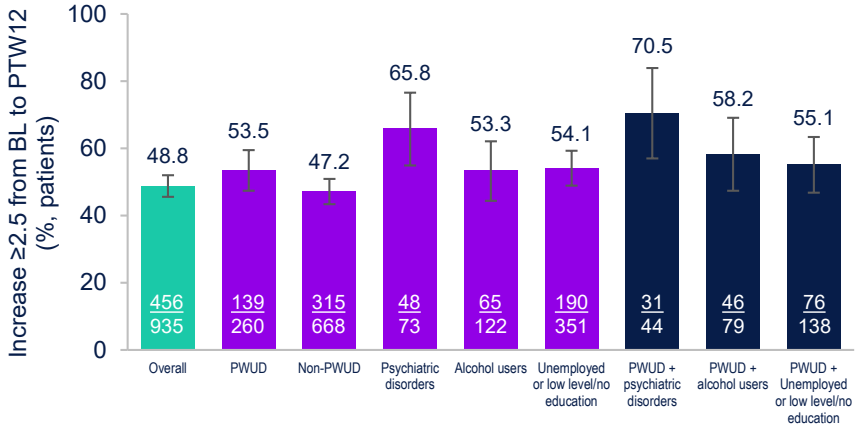
At SVR12 visit, percentages of patients who achieved improvements ≥2.5 in SF-36 MCS from baseline were:

- 53.5% (139/260) in PWUD
- 65.8% (48/73) in patients with psychiatric disorder
- 70.5% (31/44) in PWUD with psychiatric disorder

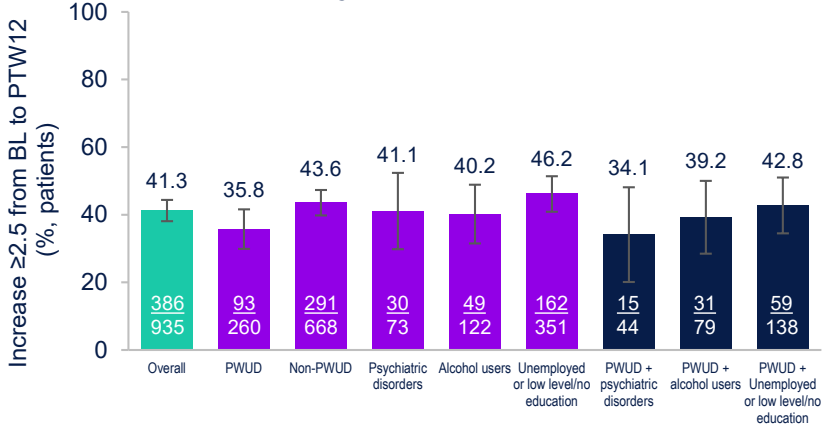
At SVR12 visit, percentages of patients who achieved improvements ≥2.5 in SF-36 PCS from baseline were:

- 35.8% (93/260) in PWUD
- 41.1% (30/73) in patients with psychiatric disorder
- 34.1% (15/44) in PWUD with psychiatric disorder

Improvements ≥2.5 in SF-36 Mental Component Summary from Baseline at SVR12 Visit



Improvements ≥2.5 in SF-36 Physical Component Summary from Baseline at SVR12 Visit



BL, baseline; PCS, physical component summary; PWUD, people who use drugs; MCS, mental component summary; PRO, patient reported-outcome; PTW12, posttreatment Week 12; PWUD, people who use drugs; SF-36, 36-Item Short-Form Health Survey; SVR12, sustained virologic response at posttreatment Week 12.

Safety

AE	N=1522
Any AE	170 (11.2)
DAA-related AEs	92 (6.0)
Any SAE	13 (0.9)
DAA-related SAEs[a]	1 (<0.1)
AE leading to discontinuation of study drug	5 (0.3)
DAA-related AEs leading to discontinuation of study drug	3 (0.2)
SAEs leading to discontinuation of study drug	0 (0)
Fatal AEs	3 (0.2)
Deaths[b,c]	5 (0.3)
Common AEs (occurring in ≥1.0% of patients)	
Fatigue	29 (1.9)
Headache	29 (1.9)
Asthenia	28 (1.8)
Nausea	15 (1.0)
Laboratory abnormalities	
Post-nadir ALT >5 × ULN	2/774 (0.3)
Total bilirubin ≥2 × ULN	10/774 (1.3)

G/P demonstrated a favorable safety profile

Most common reported AEs were fatigue, headache, asthenia, and nausea

There was one G/P-related SAE which did not result in study drug discontinuation[a]

Data are n (%) unless otherwise stated.
[a]Acute pericarditis, considered DAA-related by investigator; [b]There were no DAA-related deaths; [c]Includes non–treatment-emergent deaths.
AE, adverse event; ALT, alanine aminotransferase; DAA, direct-acting antiviral; G/P, glecaprevir/pibrentasvir; SAE, serious adverse event; ULN, upper limit of normal.

Conclusion

- Data show that G/P is a highly effective and well-tolerated pangenotypic treatment option for a broad range of patients
- These results further support the use of 8-week G/P in underserved populations including those with substance abuse and psychiatric comorbidities
- This study helps to address barriers to HCV elimination, including stigma and lack of confidence in treating marginalized patients

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