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ORIGINAL RESEARCH

Real-World Efficacy and Safety of Universal 8-Week Glecaprevir/Pibrentasvir for Treatment-Naïve Patients from a Nationwide HCV Registry in Taiwan

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ABSTRACT

Introduction: Eight-week glecaprevir/pibrentasvir (GLE/PIB) is indicated for treatment-naïve (TN) patients with chronic hepatitis C (CHC), with or without compensated cirrhosis. Given that the Taiwanese government is committed to eliminating hepatitis C virus (HCV) by 2025, this study aimed to measure real-world evidence for TN patients using 8-week GLE/PIB in the Taiwan HCV Registry (TACR).

Methods: The data of patients with CHC treated with 8-week GLE/PIB were retrieved from TACR, a nationwide registry program organized by the Taiwan Association for the Study of the Liver (TASL). Treatment efficacy, defined as a sustained virologic response at posttreatment

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week 12 (SVR12), was assessed in the modified intention-to-treat (mITT) population, which excluded patients who were lost to follow-up or lacked SVR12 data. The safety profile of the ITT population was assessed.

***Results*:** A total of 7246 (6897 without cirrhosis; 349 with cirrhosis) patients received at least one dose of GLE/PIB (ITT), 7204 of whom had SVR12 data available (mITT). The overall SVR12 rate was 98.9% (7122/7204) among all patients, 98.9% (6780/6856) and 98.3% (342/348) among patients without and with cirrhosis, respectively. For the selected subgroups, which included patients with genotype 3 infection, diabetes, chronic kidney disease, people who injected drugs, and those with human immunodeficiency virus coinfection, the SVR12 rates were 95.1% (272/286), 98.9% (1084/1096), 99.0% (1171/1183), 97.4% (566/581), and

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96.1% (248/258), respectively. Overall, 14.1% (1021/7246) of the patients experienced adverse events (AEs). Twenty-two patients (0.3%) experienced serious AEs, and 15 events (0.2%) resulted in permanent drug discontinuation. Only one event was considered treatment drug related.
***Conclusion*:** Eight-week GLE/PIB therapy was effective and well tolerated in all TN patients, regardless of cirrhosis status.

Keywords: Hepatitis C; Direct-acting antivirals; Glecaprevir; Pibrentasvir; Real world; Taiwan

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Key Summary Points

Why carry out the study?

Chronic hepatitis C virus (HCV) infection has been a human health threat globally.

The World Health Organization (WHO) advocates treatment simplification to patients with HCV infection to facilitating HCV elimination globally.

This study aimed to evaluate the treatment efficacy and safety of a pan-genotypic simplified regimen, 8-weeks glecaprevir/pibretasivir (GLE/PIB), for patients with treatment-naïve HCV with and without liver cirrhosis by using a large real-world cohort from the nationwide Taiwan HCV Registry Program (TACR).

What was learned from the study?

The strategy demonstrated excellent tolerability and achieved a treatment efficacy with a sustained viral response throughout 12 weeks of posttreatment follow-up period (SVR12) rate exceeding 98% in the largest cohort of patients with chronic hepatitis C treated with an 8-week GLE/PIB regimen.

The easily administered, shortened-duration regimen can be applied universally across all subpopulations, regardless of cirrhotic status. This approach would help facilitating HCV elimination through task shifting and treatment simplification.

INTRODUCTION

Hepatitis C virus (HCV) infection is one of the major burdensome liver-related outcomes worldwide. It is estimated that 50 million people are infected with HCV. The World Health Organization (WHO) has committed to the goal of viral control by 2030, and many countries have made progress toward HCV management since 2016. Nevertheless, the majority of countries are still not on track for HCV elimination [1]. To facilitate HCV treatment uptake, the WHO further advocates decentralized testing, task shifting, and treatment simplification with direct-acting antivirals (DAAs) at the primary care level [2].

Glecaprevir/pibrentasvir (GLE/PIB) is now recommended as the standard of care for chronic hepatitis C (CHC). We previously reported that GLE/PIB demonstrates high efficacy in the treatment of Taiwanese patients with CHC, with variable treatment durations [3]. An identical finding was observed in a German registry of people who received either 8- or 12-week GLE/PIB [4]. With solid evidence from clinical trials and the real-world data, an 8-week treatment duration is now approved and applied for both treatment-naïve (TN) patients without and with cirrhosis [5–7]. Therefore, regional guidelines have recommended a universal 8-week treatment duration for TN patients, eliminating concerns about testing for difficult-to-cure genotypes (GT), such as HCV GT3, or resistance-associated substitutions [8, 9]. Uniform and short-duration therapy for HCV may help strengthen patient adherence [10] and attenuate health care burdens, aligning with the WHO's strategy of treatment simplification.

According to the label at the time of registration of Taiwan HCV Registry (TACR), we initially adopted GLE/PIB for 8 to 16 weeks on the basis of the cirrhotic status, treatment experience, and HCV genotypes of the patients with CHC, which was published in 2020 [3]. With the updated indication of the US Food and Drug Administration (FDA), we subsequently demonstrated the real-world evidence of 8-week GLE/PIB regimen in a subset of TN patients with cirrhosis, which was published in 2021 [6]. In response to and alignment with the WHO's new policy of treatment simplification, the current study has further expanded the patient sample, encompassing various patient and viral characteristics.

To this end, the current study aimed to explore the real-world treatment efficacy and tolerability of the 8-week regimen of GLE/PIB in both patients with and without cirrhosis. This study represents the largest CHC cohort to date, utilizing the largest HCV registry worldwide.

METHODS

Patients

Patients were recruited from the TACR, which is a prospective, observational, nationwide DAA-treated CHC cohort organized by the Taiwan Association for the Study of the Liver (TASL) [3, 6, 11–14]. As of October 31, 2023, a total of 43,685 patients with CHC have been registered in the TACR across 53 hospitals, constituting nearly one-third of DAA-treated patients in Taiwan. DAAs TN patients aged > 18 years who have received at least one dose of GLE/PIB were included in the current analysis. Patients were excluded if they received either the 12- or 16-week GLE/PIB regimen, had a history of liver decompensation, or lacked available liver biochemistry data at baseline or at the end of follow-up. The study protocol was approved by the institutional review boards (IRB) of the participating hospitals and conformed to the guidelines of the International Conference on Harmonization for Good Clinical Practice. Ethics approval was granted by Kaohsiung Medical University Chung-Ho Memorial Hospital (IRB number KMUHIRB-F(I)-20170053). This study was conducted in accordance with the principles outlined in the Helsinki Declaration of 1964 and its later amendments. All patients provided written informed consent before being enrolled in the registry. Full details regarding consent to participate and consent for publication are available upon request.

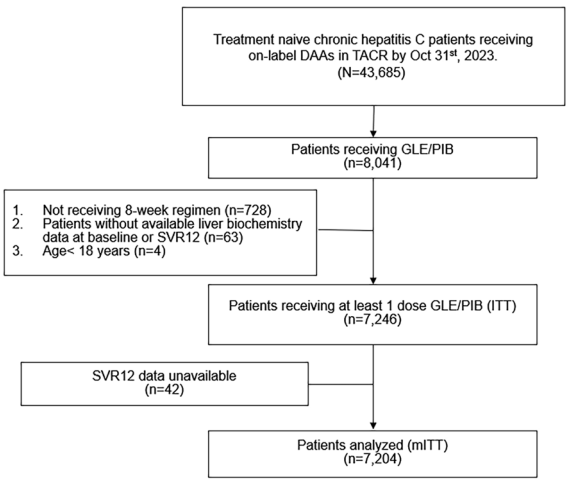

Fig. 1 Patient flowchart. *DAA* direct-acting antiviral. *GLE/PIB* glecaprevir/pibrentasvir, *ITT* intention-to-treat, *mITT* modified intention-to-treat, *SVR* sustained virologic response, *SVR12* undetectable HCV RNA concentration throughout 12 weeks of posttreatment follow-up

The primary objective was to achieve a sustained virologic response (SVR) at 12 weeks, defined as maintaining an undetectable level of HCV ribonucleic acid (RNA) (< 12 IU/mL or < 25 IU/mL depending on individual laboratory testing) throughout the 12 weeks of posttreatment follow-up (SVR12). Chronic kidney disease (CKD) was defined as an estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m^2 or > 60 mL/min/1.73 m^2 with proteinuria for more than 3 months. Liver cirrhosis was defined as previously described, which included any of the following: liver histology, transient elastography (FibroScan®; Echosens, Paris, France, > 12 kPa), acoustic radiation force impulse (> 1.98 m/s), Fibrosis-4 index (> 6.5), or the presence of clinical, radiological, endoscopic, or laboratory evidence of cirrhosis and/or portal hypertension [3, 6]. Health care resource utilization (HCRU) was determined by counting the number of clinic visits from the initiation of GLE/PIB to the SVR12 survey visit. Drug adherence, defined as the percentage of actual dosages of GLE/PIB taken divided by the anticipated 8-week regimen throughout the treatment course (168 pills of GLE/PIB) for each patient, was evaluated. Changes in laboratory parameters were evaluated in patients who achieved an SVR before treatment and at the time of SVR12.

Statistical Analysis

Frequencies were compared between groups using χ^2 tests with Yates' correction or Fisher's exact test. The group means, presented as the means and standard deviations, were compared using analysis of variance, Student's *t* test or the Mann–Whitney *U* test. A paired *t* test was used to compare the changes in laboratory data before and after DAAs therapy. Serum HCV RNA

Table 1 Baseline characteristics and clinical features of the patients

	Overall ($n = 7246$)	Without cirrhosis ($n = 6897$)	With cirrhosis ($n = 349$)	*P* value
Age, years	57.87 ± 13.19	57.62 ± 13.16	62.73 ± 12.79	< 0.01
Age > 70 years, *n* (%)	1398 (19.3)	1290 (18.7)	108 (31.0)	< 0.01
Male, *n* (%)	3831 (52.9)	3642 (52.8)	189 (54.2)	0.66
HCV genotype				
1a/1b, *n* (%)	2325 (32.1)	2217 (32.1)	108 (31.0)	< 0.01
2, *n* (%)	3537 (48.8)	3355 (48.6)	182 (52.2)	
3, *n* (%)	288 (4.0)	280 (4.1)	8 (2.3)	
4/5/6, *n* (%)	859 (11.9)	829 (12.0)	30 (8.6)	
Mixed/unclassified, *n* (%)	237 (3.3)	216 (3.1)	21 (6.0)	
HCV RNA, $\log_{10}$ IU/mL	5.90 ± 1.09	5.90 ± 1.09	5.79 ± 1.19	0.09
HCV RNA > 6,000,000 IU/mL, *n* (%)	1427 (19.7)	1362 (19.8)	65 (18.6)	0.63
AST, U/L	47.44 ± 44.85	46.05 ± 43.26	74.92 ± 63.30	< 0.01
ALT, U/L	60.92 ± 68.76	60.06 ± 68.67	77.90 ± 68.59	< 0.01
Platelet count, × 10^3 U/L	210.06 ± 67.73	212.89 ± 66.09	154.17 ± 75.19	< 0.01
Albumin, g/dL	4.28 ± 0.37	4.29 ± 0.37	4.07 ± 0.42	< 0.01
Total bilirubin, mg/dL	0.72 ± 0.38	0.71 ± 0.38	0.85 ± 0.40	< 0.01
Creatinine, mg/dL[a]	1.00 ± 0.91	1.00 ± 0.92	1.02 ± 0.64	0.64
eGFR,[a] mL/min/1.73 m^2	89.17 ± 28.60	89.36 ± 28.40	85.06 ± 32.34	0.02
FIB-4	2.06 ± 2.26	1.93 ± 2.02	4.75 ± 4.23	< 0.01
Comorbidities, *n* (%)				
Hypertension	2011 (27.8)	1864 (27.0)	147 (42.1)	< 0.01
Diabetes	1278 (17.6)	1181 (17.1)	97 (27.8)	< 0.01
Dyslipidemia	740 (10.2)	696 (10.1)	44 (12.6)	0.15
Cerebrovascular disease	146 (2.0)	138 (2.0)	8 (2.3)	0.69
Cardiovascular disease	525 (7.3)	495 (7.2)	30 (8.6)	0.34
Chronic kidney disease	1506 (20.8)	1396 (20.2)	110 (31.5)	< 0.01
HIV, *n* (%)	261 (3.6)	254 (3.7)	7 (2.0)	0.11
PWID, *n* (%)	585 (8.1)	565 (8.2)	20 (5.7)	0.11
HBsAg (+), *n* (%)	532 (7.3)	505 (7.3)	27 (7.7)	0.75

Values expressed as mean ± standard deviation or sample size and proportion (%)

AST aspartate aminotransferase, *ALT* alanine aminotransferase, *FIB-4* Fibrosis-4 index, *eGFR* estimated glomerular filtration rate, *HIV* human immunodeficiency virus, *PWID* patients who inject drugs, *HBsAg* hepatitis B surface antigen

[a]Excludes hemodialysis patients ($n = 492$)

Table 2 Treatment response of 8 week glecaprevir/pibrentasvir regimen

	Overall ($n = 7246$)	Without cirrhosis ($n = 6897$)	With cirrhosis ($n = 349$)
SVR12			
ITT, *n/N* (%)	7122/7246 (98.3)	6780/6897 (98.3)	342/349 (98.0)
mITT, *n/N* (%)	7122/7204 (98.9)	6780/6856 (98.9)	342/348 (98.3)[#,&]
Reason for non-SVR12 ($n = 124$)			
Virological failure, *n*	82 (1.1)	76 (1.1)	6 (1.7)
Breakthrough, *n*	1 (0.01)	1 (0.01)	0 (0.0)
Relapse, *n*	81 (1.1)	75 (1.1)	6 (1.7)
Non-virological failure, *n*	42 (0.6)	41 (0.6)	1 (0.3)
Lost follow-up, *n*	8 (0.1)	8 (0.1)	0 (0.0)
Death*, *n*	6 (0.1)	6 (0.1)	0 (0.0)
Data not available, *n*	28 (0.4)	27 (0.4)	1 (0.3)

SVR sustained virological response, *SVR12* undetectable HCV RNA throughout 12 weeks of posttreatment follow-up period, *ITT* intention-to-treat analysis, *mITT* modified intention-to-treat analysis

*Hemorrhagic stroke ($n = 1$); septic shock ($n = 2$); aspiration pneumonia ($n = 1$); Fournier gangrene ($n = 1$); unknown ($n = 1$)

#SVR12 rate: PLT < $50{,}000 \times 10^3$ U/L ($n = 14$) vs. PLT ≥ $50{,}000 \times 10^3$ U/L ($n = 334$), 100% vs. 98.2%, $P = 0.61$

&SVR12 rate: PLT < $75{,}000 \times 10^3$ U/L ($n = 30$) vs. PLT ≥ $75{,}000 \times 10^3$ U/L ($n = 318$), 100% vs. 98.1%, $P = 0.45$

levels were expressed after the logarithmic transformation of the original values. The efficacy of GLE/PIB was evaluated in an intention-to-treat (ITT) population, defined as all enrolled patients who received ≥ 1 dose of GLE/PIB, and a modified intention-to-treat (mITT) population, defined as subjects who received ≥ 1 dose of DAAs and with HCV RNA data available at posttreatment week 12. Safety assessments were reported as adverse events (AEs), serious adverse events (SAEs), and laboratory abnormalities in the ITT population. The eGFR was calculated using the Modification of Diet in Renal Disease (MDRD) equation [11, 15]. The Fibrosis-4 score (FIB-4) was calculated as age (years) × aspartate transaminase (AST) [U/L]/{platelets [10^9/L] × (alanine transaminase [ALT] [U/L])}$^{1/2}$. Stepwise logistic regression analysis was performed to determine factors associated with treatment failure by analyzing the covariates with a p value < 0.1 in the univariate analysis. All the statistical analyses were conducted with SPSS 14.0 statistical software (SPSS, Chicago, IL, USA).

RESULTS

Among the 8041 patients treated with GLE/PIB, 728 patients who were allocated to 12- or 16-week regimens were excluded. Sixty-three patients were excluded because of unavailable liver biochemistry data, and four were excluded because they were younger than 18 years. Of the remaining 7246 patients [non-cirrhosis ($n = 6897$); cirrhosis ($n = 349$)], 7204 patients with available treatment outcomes were included in the mITT analysis (Fig. 1). The mean age was 57.9 years, and men accounted for 52.9% of the population. The dominant viral genotype was HCV GT2 (48.8%), followed by GT1 (32.1%). A total of 288 patients (4.0%) had GT3 infection; 1427 patients (19.7%) had a baseline HCV RNA concentration > 6,000,000 IU/ml. A total of 532 (7.3%) and 261 (3.6%) patients were coinfected with hepatitis B virus (HBV) and human immunodeficiency virus (HIV), respectively; 1506 (20.8%)

Table 3 SVR12 (mITT) in subgroups stratified by cirrhotic status

	Overall ($n = 7204$)		Without cirrhosis ($n = 6856$)		With cirrhosis ($n = 348$)	
	n/N	% (95% CI)	*n/N*	% (95% CI)	*n/N*	% (95% CI)
HCV genotype						
1	2292/2303	99.5 (99.1–99.7)	2186/2195	99.6 (99.2–99.8)	106/108	98.1 (93.5–99.5)
2	3483/3526	98.8 (98.4–99.1)	3306/3345	98.8 (98.4–99.1)	177/181	97.8 (94.5–99.1)
3	272/286	95.1 (92.0–97.1)	264/278	95.0 (91.7–97.0)	8/8	100.0 (67.6–100.0)
4/5/6*	841/853	98.6 (97.6–99.2)	811/823	98.5 (97.5–99.2)	30/30	100.0 (88.6–100.0)
Mixed/unclassified	234/236	99.2 (97.0–99.8)	213/215	99.1 (96.7–99.7)	21/21	100.0 (84.5–100.0)
Diabetes						
No	5871/5936	98.9 (98.6–99.1)	5623/5684	98.9 (98.6–99.2)	248/252	98.4 (96.0–99.4)
Yes	1251/1268	98.7 (97.9–99.2)	1157/1172	98.7 (97.9–99.2)	94/96	97.9 (92.7–99.4)
Chronic kidney disease						
No	5630/5699	98.8 (98.5–99.0)	5392/5460	98.8 (98.4–99.0)	238/239	99.6 (97.7–99.9)
Yes	1475/1487	99.2 (98.6–99.5)	1371/1378	99.5 (99.0–99.8)	104/109	95.4 (89.7–98.0)
HCV RNA						
> 6,000,000 IU/mL	1388/1418	97.9 (97.0–98.5)	1327/1353	98.1 (97.2–98.7)	61/65	93.9 (85.2–97.6)
≤ 6,000,000 IU/mL	5729/5779	99.1 (98.9–99.3)	5448/5496	99.1 (98.8–99.3)	281/283	99.3 (97.5–99.8)
Cerebrovascular disease						
No	6979/7060	98.9 (98.6–99.1)	6645/6720	98.9 (98.6–99.1)	334/340	98.2 (96.2–99.2)
Yes	143/144	99.3 (96.2–99.9)	135/136	99.3 (96.0–99.9)	8/8	100.0 (67.6–100.0)
PWID						
No	6556/6623	99.0 (98.7–99.2)	6234/6295	99.0 (98.8–99.2)	322/328	98.2 (96.1–99.2)
Yes	566/581	97.4 (95.8–98.4)	546/561	97.3 (95.6–98.4)	20/20	100.0 (83.9–100.0)
HIV						
No	6874/6946	99.0 (98.7–99.2)	6539/6605	99.0 (98.7–99.2)	335/341	98.2 (96.2–99.2)
Yes	248/258	96.1 (93.0–97.9)	241/251	96.0 (92.8–97.8)	7/7	100.0 (64.6–100.0)
Drug adherence						
≥ 80%	7107/7186	98.9 (98.6–99.1)	6768/6842	98.9 (98.6–99.1)	339/344	98.5 (96.6–99.4)
< 80%	15/18	83.3 (60.8–94.2)	12/14	85.7 (60.1–96.0)	3/4	75.0 (30.1–95.4)

SVR sustained virological response, *SVR12* undetectable HCV RNA throughout 12 weeks of posttreatment follow-up period, *mITT* modified intention-to-treat analysis, *PWID* persons who inject drugs, *HIV* human immunodeficiency virus

*HCV-4 ($n = 3$, SVR12 rate 100%), HCV-5 ($n = 1$, SVR12 rate 100%), HCV-6 ($n = 850$; SVR12 rate: all patients 98.6% [838/850], LC 100% (30/30), non-LC 98.5% [808/820])

and 1278 (17.6%) patients had CKD and diabetes, respectively. Regarding high-risk behaviors, 585 patients (8.1%) were documented to have a history of intravenous drug abuse (Table 1). Compared to patients without cirrhosis, those with compensated liver cirrhosis were older and had a greater proportion of hypertension, diabetes, CKD, and GT2 infection. These patients also had higher AST, ALT, and bilirubin

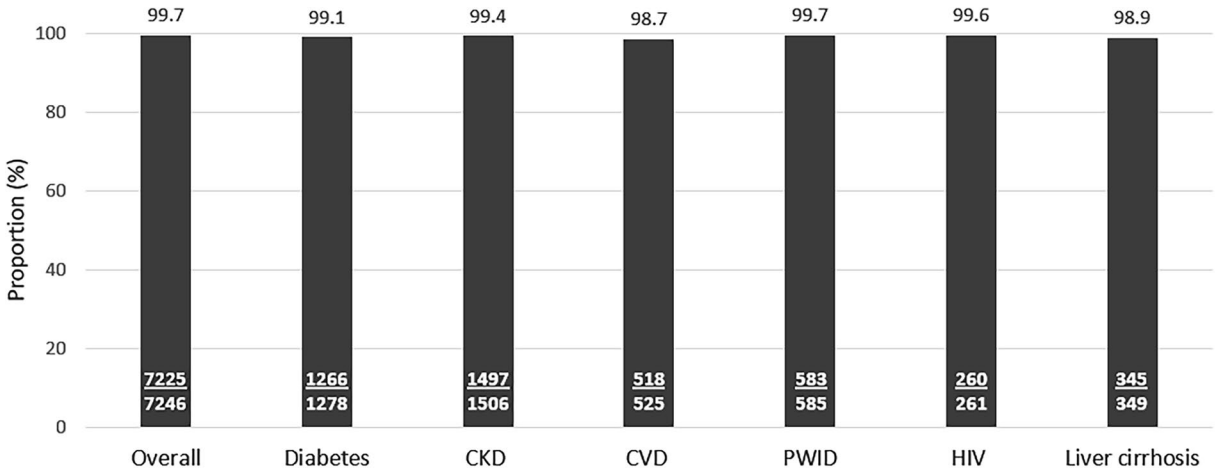

Fig. 2 Proportion of patients with drug compliance > 80% in the overall patients and subpopulations. *CKD* chronic kidney disease, *CVD* cardiovascular disease, *PWID* persons who inject drugs, *HIV* human immunodeficiency virus

levels and FIB-4 scores and lower eGFRs, albumin levels, and platelet counts (Table 1).

Treatment Responses

The overall SVR12 rates were 98.3% (7122/7246) and 98.9% (7122/7204) according to the ITT and mITT analyses, respectively. When patients were stratified according to cirrhosis status, the SVR12 rates were 98.3% (6780/6897) and 98.9% (6780/6856) among patients without cirrhosis and 98.0% (342/349) and 98.3% (342/348) among patients with cirrhosis in the ITT and mITT analyses, respectively. Of the 82 patients with virological failure, 81 experienced relapse after the end of treatment, and only one experienced virological breakthrough during treatment (Table 2).

Subgroup analysis using mITT analysis revealed that the high SVR12 rates were generalized to all subgroups regardless of cirrhosis status, including viral GT, comorbidity, and special population subgroups. There was a lower SVR12 rate (83.3%; 15/18) among patients whose DAAs compliance was <80%. Patients with GT3 responded less well than those with other genotypes [95% (274/286) vs. 99% (6850/6918)] (Table 3). Logistic regression analysis of factors associated with SVR12 including HCV non-GT3 [odds ratio (OR)/95% confidence intervals (CI) 4.31/2.33–7.96, $P<0.01$], HCV RNA < 6,000,000 IU/mL (OR/CI 2.27/1.42–3.61, $P<0.01$), non-HIV (OR/CI 2.45/1.21–4.98, $P=0.01$), and drug adherence>80% (OR/CI 25.45/6.70–96.63, $P<0.01$) (Supplementary Table 1).

Up to 99.7% of patients maintained a drug adherence rate > 80% throughout the 8-week regimen. This high drug adherence rate was observed across diverse populations, including persons who inject drugs (PWID) (99.7%), patients with HIV (99.6%) and patients with liver cirrhosis (98.9%) (Fig. 2).

Safety

As shown in Table 4, 1021 patients (14.1%) experienced AEs. The most common AEs (≥1% of total patients) were fatigue (5.6%), pruritus (5.4%), insomnia (1.7%), and headache (1.7%). Twenty-two patients (0.3%) had documented serious AEs, and only one patient with symptoms of jaundice and pruritus was identified as having a potentially DAA-related event. The proportions of patients with abnormal liver function are also displayed. The causal relationships between adverse events and laboratory abnormalities were not fully addressed as these data are not generally recorded in the TACR database. The mean number

Table 4 Safety profile of 8-week glecaprevir/pibrentasvir regimen

Event, *n* (%)	Overall (*n* = 7246)	Without cirrhosis (*n* = 6897)	With cirrhosis (*n* = 349)
Any adverse event	1021 (14.1)	950 (13.8)	71 (20.3)
Serious adverse event	22 (0.3)	21 (0.3)	1 (0.3)
DAA-related serious adverse event*	1 (0.01)	1 (0.01)	0 (0.0)
Discontinuation due to adverse event			
Temporary†	12 (0.2)	10 (0.2)	2 (0.6)
Permanent‡	15 (0.2)	12 (0.2)	3 (0.9)
Adverse event occurring in ≥ 1% of patients			
Fatigue	409 (5.6)	379 (5.5)	30 (8.6)
Headache	89 (1.2)	86 (1.3)	3 (0.9)
Pruritus	392 (5.4)	363 (5.3)	29 (8.3)
Insomnia	123 (1.7)	116 (1.7)	7 (2.0)
Total blood bilirubin increased[a]			
Grade 1	1454 (20.1)	1360 (19.7)	94 (26.9)
Grade 2	234 (3.2)	220 (3.2)	14 (4.0)
Grade 3–4	13 (0.2)	10 (0.1)	3 (0.9)
Grade 3–4 AST or ALT elevation	0 (0.0)	0 (0.0)	0 (0.0)
AST increased[b]			
Grade 1	215 (3.0)	198 (2.9)	17 (4.9)
Grade 2	16 (0.2)	14 (0.2)	2 (0.6)
Grade 3–4	17 (0.2)	17 (0.3)	0 (0.0)
ALT increased[b]			
Grade 1	189 (2.6)	179 (2.6)	10 (2.9)
Grade 2	16 (0.2)	16 (0.2)	0 (0.0)
Grade 3–4	16 (0.2)	15 (0.2)	1 (0.3)

DAA directly acting antivirals, *AST* aspartate aminotransferase, *ALT* alanine aminotransferase

*Jaundice with pruritus

†Elevated bilirubin (*n* = 5), pruritus (*n* = 3), sepsis (*n* = 2), admission due to psychiatric disease (*n* = 1), COVID-19 infection (*n* = 1)

‡Elevated bilirubin (*n* = 2), pruritus (*n* = 3), skin rash (*n* = 1), incarceration (*n* = 1), traumatic accident (*n* = 1), psoas muscle abscess (*n* = 1), cachexia due to hepatocellular carcinoma (*n* = 1), sepsis (*n* = 2), not depicted (*n* = 3)

[a]Total blood bilirubin increased: Grade 1, 1.0–1.5 × ULN if baseline was normal; > 1.0 to 1.5 × baseline if baseline was abnormal. Grade 2, > 1.5 to 3.0 × ULN if baseline was normal; > 1.5 to 3.0 × baseline if baseline was abnormal. Grade 3, > 3.0 to 10.0 × ULN if baseline was normal; > 3.0 to 10.0 × baseline if baseline was abnormal. Grade 4, > 10.0 × ULN if baseline was normal; > 10.0 × baseline if baseline was abnormal

[b]Alanine aminotransferase/aspartate aminotransferase increased: Grade 1, > 1.0 to 3.0 × ULN if baseline was normal; > 1.5 to 3.0 × baseline if baseline was abnormal. Grade 2. > 3.0 to 5.0 × ULN if baseline was normal; > 3.0 to 5.0 × baseline if baseline was abnormal. Grade 3, > 5.0 to 20.0 × ULN if baseline was normal; > 5.0 to 20.0 × baseline if baseline was abnormal. Grade 4, > 20.0 × ULN if baseline was normal; > 20.0 × baseline if baseline was abnormal

Table 5 Laboratory examinations changes before and after HCV eradication

n = 1278	Baseline	SVR12	*P* value[a]
HbA1c (%)	5.98 ± 1.21	5.83 ± 0.94	< 0.01*
FPG, mg/dL	109.52 ± 43.24	109.33 ± 35.93	0.15
AST, U/L	47.54 ± 49.18	24.94 ± 38.74	< 0.01*
ALT, U/L	57.68 ± 62.06	21.62 ± 25.61	< 0.01*
Total bilirubin, mg/dL	0.66 ± 0.33 + 0.60	0.67 ± 0.36	0.78
INR, sec	1.02 ± 0.27	1.00 ± 0.09	0.10
Albumin, g/dL	4.16 ± 0.43	4.24 ± 0.40	< 0.01*
Platelet, × 10^3 U/L	200.03 ± 66.63	205.05 ± 64.68	0.01*
FIB-4	2.35 ± 1.60	2.00 ± 1.51	< 0.01*

Values expressed as mean ± standard deviation or sample size and proportion (%)

SVR sustained virological response, *SVR12* undetectable HCV RNA throughout 12 weeks of posttreatment follow-up period, *HbA1C* hemoglobin A1C, *FPG* fasting plasma glucose, *AST* aspartate aminotransferase, *ALT* alanine aminotransferase, *INR* international normalized ratio, *FIB-4* Fibrosis-4 index

[a]Excludes hemodialysis patients (*n* = 492)

(mean ± SD) of outpatient visits during GLE/PIB treatment was 4.9 ± 0.9.

Changes in Laboratory Data Before and After Patients Achieved SVR12

A total of 1278 patients had available laboratory data at baseline and at SVR12. Liver-related biochemical parameters, including AST, ALT, and albumin levels, along with platelet counts and the FIB-4 score, showed significant improvement. In addition, hemoglobin A1C levels decreased significantly (5.98% to 5.83%, $P<0.01$) (Table 5). Among patients with CKD, there was a significant increase in eGFR from 48.30 to 50.58 mL/min/1.73 m^2 ($P<0.001$), with a more pronounced improvement observed in those with a baseline eGFR < 60 mL/min/1.73 m^2 (from 39.25 to 42.23 mL/min/1.73 m^2, $P<0.001$). (Supplementary Table 2).

DISCUSSION

To the best of our knowledge, this is the largest CHC cohort to receive a universal 8-week regimen of GLE/PIB for both patients without and with cirrhosis. Our findings demonstrated that the regimen was highly effective and well tolerated among patients with CHC in Taiwan. The high SVR12 rate was generalized across all HCV genotypes and special populations, with a satisfactory safety profile observed in the real-world setting.

While addressing the characteristics of DAA-treated patients in recent years, there has been a notable rise in the proportion of TN and noncirrhotic individuals reported in both Eastern [3, 13, 14] and Western populations [16]. In Taiwan, more than 90% of patients with CHC were TN according to recent nationwide studies [3, 13]. As a consequence, an 8-week regimen of GLE/PIB or 12-week regimen of sofosbuvir/velpatasvir is currently the preferred treatment choice in the real-world setting [8, 9]. As demonstrated in the present study, the SVR12 rates were as high as 98.3% and 98.9% according to the ITT and mITT analyses, respectively. A short course of 8 weeks regimen of GLE/PIB in TN patients with cirrhosis was first approved by the US FDA in 2019 and by the Taiwan FDA (TFDA) in 2020, on the basis of the 99.7% SVR12 rate in the EXPEDITION-8 study [5]. Along these lines, certain small-scale and collaborative

studies have proven the applicability of the regimen in clinical practice [3, 6, 17–22]. The present study recruited a large number of patients from the nationwide registry, enabling a more extensive and detailed subgroup analysis. The results align with previous studies and demonstrate that 8 weeks of GLE/PIB treatment is highly effective in TN patients with cirrhosis, regardless of patient characteristics such as HCV-GT3 infection, PWID status, and HIV coinfection (SVR12 rates were all 100% in the present study).

A relatively low SVR12 rate of 83.3% was noted among patients whose drug adherence was < 80%. Poor drug compliance is a predictive factor of treatment failure in the DAAs era [14, 23]. A prolonged treatment duration of GLE/PIB of 16 weeks has been reported to lead to an increased proportion of nonadherent patients [23]. Similarly, a pooled analysis of 10 clinical trials of GLE/PIB demonstrated that drug adherence decreased substantially with increasing treatment duration from week 4 to week 12 [24]. In the real world, a study assessing 7203 PWID revealed that, in comparison to patients who received the 12-week regimen of GLE/PIB, those who received an 8-week regimen had greater pill refill persistence [25]. Owing to the truncated 8-week treatment course in the registry, only 18 (0.2%) patients exhibited a drug adherence rate less than 80%. A short-course treatment regimen was selected on the basis of patient preference [26]. Imperatively, this approach helps to ensure drug adherence and facilitate the decentralization or outreach HCV care [27].

The most common AEs were fatigue and pruritus in the present study, which were predictable and manageable. A recent cohort study demonstrated that protease inhibitor (PI)-containing DAAs were as well tolerated as non-PI DAAs in terms of patient safety, even among patient with advanced cirrhosis [28]. Another study indicated the absence of specific safety signals in patients with compensated cirrhosis receiving GLE/PIB, even in cases where patients presented with overt thrombocytopenia or a Child–Pugh score of A6 [29]. A pooled analysis of nine clinical trials revealed only three liver decompensation events among patients with portal hypertension, which were judged as non-investigational drug-related events [30]. According to the current registry of the present study, only one SAE, jaundice and pruritus, was considered DAA related. We did not address drug–drug interactions in the large registry, which could be a potential concern issue, especially for PI-containing DAAs. However, this should not pose a critical concern provided that pretreatment assessments are conducted by experienced or trained care providers. Studies have demonstrated that GLE/PIB could be safely used for patients with multiple comorbidities and complex comedications, such as those with severe mental illness [27] and hemodialysis [31]. According to the current database, only one patient with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, who took Paxlovid (nirmatrelvir/ritonavir), had transiently discontinued GLE/PIB for 5 days, but the outcomes still resulted in treatment success. This result may reinforce the strategy of simplifying treatment by shifting tasks toward other marginalized populations, such as underserved drug users [32] and incarcerated individuals [33, 34].

The present study has several limitations. Despite the sizable cohort in the present study, the very low prevalence rates of GT 3, 4, and 5 infections in Taiwan restricted the exploration of the real-world efficacy of GLE/PIB in our study to other populations in Western countries. Since these were registry-based data rather than clinical trial data, it is possible that the incidence of adverse events may have been underreported. We tried our best to overcome reporting bias by adopting, utilizing, and cross-verifying the results on a uniform database platform. Finally, we also failed to explore the long-term outcome in the post-SVR era in the cohort.

CONCLUSION

This Taiwanese cohort study stands as the largest real-world report, demonstrating that an 8-week regimen of GLE/PIB was highly effective and well tolerated in TN patients with HCV, irrespective of cirrhosis status.

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Data Availability. The data that support the findings of this study are available upon reasonable request from the corresponding author.

Declarations

Conflict of Interest. All named authors declare that they have no competing interests.

Ethical Approval. It is required to access the data of TACR with the permission of the owner, TASL. The study protocol was approved by the institutional review boards (IRB) of the participating hospitals and conformed to the guidelines of the International Conference on Harmonization for Good Clinical Practice. Ethics approval was granted by Kaohsiung Medical University Chung-Ho Memorial Hospital (IRB number KMUHIRB-F(I)-20170053). This study was conducted in accordance with the principles outlined in the Helsinki Declaration of 1964 and its later amendments. All patients provided written informed consent before being enrolled in the registry. Full details regarding consent to participate and consent for publication are available upon request.

REFERENCES

1. Polaris Observatory HCV Collaborators. Global change in hepatitis C virus prevalence and cascade of care between 2015 and 2020: a modelling study. Lancet Gastroenterol Hepatol. 2022;7(5):396–415.

2. World Health Organization. Hepatitis C. Geneva: WHO, 2022. https://www.who.int/news-room/fact-sheets/detail/hepatitis-c. Accessed 20 Dec 2023.

3. Huang CF, Kuo HT, Chang TS, et al. Nationwide registry of glecaprevir plus pibrentasvir in the treatment of HCV in Taiwan. Sci Rep. 2021;11(1):23473.

4. Cornberg M, Stoehr A, Naumann U, et al. Real-world safety, effectiveness, and patient-reported outcomes in patients with chronic hepatitis C virus infection treated with glecaprevir/pibrentasvir: updated data from the German Hepatitis C-Registry (DHC-R). Viruses. 2022;14(7):122.

5. Brown RS Jr, Buti M, Rodrigues L, et al. Glecaprevir/pibrentasvir for 8 weeks in treatment-naïve patients with chronic HCV genotypes 1–6 and compensated cirrhosis: the EXPEDITION-8 trial. J Hepatol. 2020;72(3):441–9.

6. Chang TS, Huang CF, Kuo HT, et al. Effectiveness and safety of 8-week glecaprevir/pibrentasvir in HCV treatment-naïve patients with compensated cirrhosis: real-world experience from Taiwan nationwide HCV registry. Hep Int. 2023;17(3):550–61.

7. Zuckerman E, Gutierrez JA, Dylla DE, et al. Eight weeks of treatment with glecaprevir/pibrentasvir is safe and efficacious in an integrated analysis of treatment-naïve patients with hepatitis C virus infection. Clin Gastroenterol Hepatol. 2020;18(11):2544–2553.e2546.

8. Bhattacharya D, Aronsohn A, Price J, Lo Re V. Hepatitis C guidance 2023 update: AASLD-IDSA recommendations for testing, managing, and treating hepatitis C virus infection. Clin Infect Dis. 2023:ciad319.

9. European Association for the Study of the Liver. EASL recommendations on treatment of hepatitis C: final update of the series. J Hepatol. 2020;73(5):1170–1218.

10. Emmanuel B, Wilson EM, O'Brien TR, Kottilil S, Lau G. Shortening the duration of therapy for chronic hepatitis C infection. Lancet Gastroenterol Hepatol. 2017;2(11):832–6.

11. Huang CF, Tseng KC, Cheng PN, et al. Impact of sofosbuvir-based direct-acting antivirals on renal function in chronic hepatitis C patients with impaired renal function: a large cohort study from the Nationwide HCV Registry Program (TACR). Clin Gastroenterol Hepatol. 2022;20(5):1151–1162.e1156.

12. Lo CC, Huang CF, Cheng PN, et al. Ledipasvir/sofosbuvir for HCV genotype 1, 2, 4–6 infection: real-world evidence from a nationwide registry in Taiwan. J Formosan Med Assoc Taiwan Yi Zhi. 2022;121(8):1567–1578.

13. Cheng PN, Mo LR, Chen CT, et al. Sofosbuvir/velpatasvir for hepatitis C virus infection: real-world effectiveness and safety from a Nationwide Registry in Taiwan. Infect Dis Ther. 2022;11(1):485–500.

14. Chen CY, Huang CF, Cheng PN, et al. Factors associated with treatment failure of direct-acting antivirals for chronic hepatitis C: a real-world nationwide hepatitis C virus registry programme in Taiwan. Liver Int. 2021;41(6):1265–77.

15. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. Ann Intern Med. 1999;130(6):461–70.

16. Hüppe D, Stoehr A, Buggisch P, et al. The changing characteristics of patients infected with chronic hepatitis C virus from 2014 to 2019: real-world data from the German Hepatitis C-Registry (DHC-R). J Viral Hepatitis. 2021;28(10):1474–83.

17. Flamm SL, Kort J, Marx SE, et al. Effectiveness of 8-week glecaprevir/pibrentasvir for treatment-naïve, compensated cirrhotic patients with chronic hepatitis C infection. Adv Ther. 2020;37(5):2267–74.

18. Su PY, Chen YY, Lai JH, et al. Real-world experience of chronic hepatitis C-related compensated

liver cirrhosis treated with glecaprevir/pibrentasvir: a multicenter retrospective study. J Clin Med. 2021;10(22):17.

19. Wedemeyer H, Erren P, Naumann U, et al. Glecaprevir/pibrentasvir is safe and effective in hepatitis C patients with cirrhosis: real-world data from the German Hepatitis C-Registry. Liver Int. 2021;41(5):949–55.

20. Klinker H, Naumann U, Rössle M, et al. Glecaprevir/pibrentasvir for 8 weeks in patients with compensated cirrhosis: safety and effectiveness data from the German Hepatitis C-Registry. Liver Int. 2021;41(7):1518–22.

21. Lu YH, Lu CK, Chen CH, et al. Comparison of 8- versus 12-weeks of glecaprevir/pibrentasvir for Taiwanese patients with hepatitis C and compensated cirrhosis in a real-world setting. PLoS ONE. 2022;17(8):e0272567.

22. Cornberg M, Ahumada A, Aghemo A, et al. Safety and effectiveness using 8 weeks of glecaprevir/pibrentasvir in HCV-infected treatment-naïve patients with compensated cirrhosis: the CREST Study. Adv Ther. 2022;39(7):3146–58.

23. Brown A, Welzel TM, Conway B, et al. Adherence to pan-genotypic glecaprevir/pibrentasvir and efficacy in HCV-infected patients: a pooled analysis of clinical trials. Liver Int. 2020;40(4):778–86.

24. Zamor PJ, Brown A, Dylla DE, et al. High sustained virologic response rates of glecaprevir/pibrentasvir in patients with dosing interruption or suboptimal adherence. Am J Gastroenterol. 2021;116(9):1896–904.

25. Martinez A, Cheng WH, Marx SE, et al. Shorter duration hepatitis C virus treatment is associated with better persistence to prescription refills in people who inject drugs: a real-world study. Adv Ther. 2023;40(8):3465–77.

26. Welzel TM, Yang M, Sajeev G, et al. Assessing patient preferences for treatment decisions for new direct acting antiviral (DAA) therapies for chronic hepatitis C virus infections. Adv Ther. 2019;36(9):2475–86.

27. Huang CF, Jang TY, Yu SC, et al. Patient-centered and integrated outreach care for chronic hepatitis C patients with serious mental illness in Taiwan. Kaohsiung J Med Sci. 2024;40(1):86–93.

28. Wong YJ, Tran S, Huang CF, et al. Real-world treatment outcome with protease inhibitor direct-acting antiviral in advanced hepatitis C cirrhosis: a REAL-C study. Hep Int. 2023;17(5):1150–61.

29. Feld JJ, Forns X, Dylla DE, et al. Safety analysis of glecaprevir/pibrentasvir in patients with markers of advanced liver disease in clinical and real-world cohorts. J Viral Hepatitis. 2022;29(12):1050–61.

30. Brown RS Jr, Collins MA, Strasser SI, et al. Efficacy and safety of 8- or 12 weeks of glecaprevir/pibrentasvir in patients with evidence of portal hypertension. Infect Dis Ther. 2022;11(2):913–24.

31. Hu TH, Su WW, Yang CC, et al. Elimination of hepatitis C virus in a dialysis population: a collaborative care model in Taiwan. Am J Kidney Dis. 2021;78(4):511–519.e511.

32. Aghemo A, Horsmans Y, Bourgeois S, et al. Real-world outcomes in historically underserved patients with chronic hepatitis C infection treated with glecaprevir/pibrentasvir. Infect Dis Ther. 2021;10(4):2203–22.

33. Yang TH, Fang YJ, Hsu SJ, et al. Microelimination of chronic hepatitis C by universal screening plus direct-acting antivirals for incarcerated persons in Taiwan. Open Forum Infect Dis. 2020;7(8):ofaa301.

34. Huang CF, Chen GJ, Hung CC, Yu ML. HCV microelimination for high-risk special populations. J Infect Dis. 2023;228(Suppl 3):S168–S179.