ORIGINAL PAPER

DOI: http://dx.doi.org/10.15403/jgld-5745

Effectiveness of 8-week Treatment with Glecaprevir/Pibrentasvir in Treatment-naïve or -experienced HCV Patients: Results from an Observational Retrospective Study in Real-life Settings (ODYSSEY)

Anca Trifan[1], Carol Stanciu[1], Adrian Streinu-Cercel[2,3], Augustina Culinescu[4], Liliana Baroiu[5], Eugen Dumitru[6], Cristina Pojoga[7], Ciprian Brisc[8], Mihaela Cristina Brisc[8], Dan Ionut Gheonea[9], Dan Nicolae Florescu[9], Corina Silvia Pop[3,10], Laura Sorina Diaconu[3,10], Laura Munteanu[11], Laura Iliescu[3,12], Mircea Diculescu[3,13], Carmen Ester[3,13], Liliana Gheorghe[3,13]

See **Authors affiliation**s at the end of the paper

Address for correspondence:
Adrian Streinu-Cercel
Prof. Dr. Matei Bals National Institute of Infectious Diseases, Bucharest, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania
astreinucercel@yahoo.com

Received: 06.06.2024
Accepted: 12.07.2024

ABSTRACT

Background & Aims: Pan-genotypic ribavirin-free oral direct-acting antivirals, including the glecaprevir/pibrentasvir combination, are recommended for the treatment of most patients with chronic hepatitis C virus (HCV) infection. In Romania, the HCV-infected patient population receiving glecaprevir/pibrentasvir is not well characterized and data on treatment effectiveness is lacking. The ODYSSEY study aimed to provide insights into the characteristics and treatment outcomes of HCV-infected Romanian patients receiving 8-week therapy with glecaprevir/pibrentasvir.

Methods: This observational, retrospective medical chart review study was based on a Patient Support Program for HCV-infected patients (HCV-PSP) attending clinical practices in Romania and initiating glecaprevir/pibrentasvir between 01 February 2022 and 11 July 2023. Patients ≥18 years of age with compensated liver disease F0-F4 fibrosis grade treatment-naïve or F0-F3 fibrosis grade treatment-experienced on previous interferon-based regimens from the HCV-PSP were included in the ODYSSEY study. Patients received glecaprevir/pibrentasvir for at least 8 weeks. Sustained virological response (SVR) was assessed at 12 weeks after the 8-week treatment (SVR12). Analyses were conducted on the core population (CP) and the CP with sufficient follow-up data (CPSFU).

Results: The CP and CPSFU included 2,240 and 2,165 patients, respectively. In both populations, most patients were female (≥67.57%), aged >50 years (≥73.62%), and treatment-naïve (≥96.47%). F4 fibrosis was reported in 19% of patients. Hypertension was the most common relevant comorbidity, reported for 21% of patients; comorbidity rates increased with age. Overall SVR12 rates were 96.1% [95% confidence interval (CI): 95.2-96.8%) and 99.3% (95%CI: 98.9–99.6) in the CP and CPSFU, respectively. When stratified by gender, age category, comorbidities or fibrosis grade, SVR12 rates were >92% in the CP [except for the subgroups of patients with chronic kidney disease (87.5%) and depressive-/anxiety disorders (86.2%)] and ≥97.0% in the CPSFU. SVR12 rates were higher in female patients. In an exploratory analysis, in the CPSFU, the presence of diabetes mellitus [odds ratio (OR)=3.840; 95%CI: 1.093–13.495] and cardiovascular diseases (OR=7.904; 95%CI: 1.719-36.346) were associated with an increased probability to detect HCV RNA at 12 weeks post-treatment.

Conclusions: The 8-week treatment with glecaprevir/pibrentasvir resulted in high SVR12 rates for multiple HCV-infected patient profiles encountered in real-life settings in Romania.

Key words: hepatitis C virus – chronic hepatis – glecaprevir/pibrentasvir – real-world – sustained virologic response – 8-week treatment.

Abbreviations: CI: confidence interval; CP: core population; CPSFU: CP with sufficient follow-up data; HCV: hepatitis C virus; HCV-PSP: Patient Support Program for HCV-infected patients; OR: odds ratio; SVR: sustained virological response.

INTRODUCTION

Hepatitis C virus (HCV) infection remains a major global public health problem. In 2020, a global prevalence of 0.7% was estimated, corresponding to 56.8 million viremic HCV infections [1]. While this represents a reduction in the number of cases from 2015, it also indicates that at the current pace, the global elimination targets set by the World Health Organization [2] will not be achieved by 2030 [1]. As there is no effective hepatitis C vaccine, prevention of new HCV infections and the use of direct-acting antivirals (DAAs) for the treatment of hepatitis C remain paramount to reduce HCV prevalence and associated morbidity and mortality [2]. In addition, screening

for HCV infections and subsequently ensuring that infected individuals are accessing the most suitable treatment are also certain to play an important role. However, screening strategies differ from one country to another, targeting different at-risk populations and lacking focus on the community [3], leading to the late identification and diagnosis of HCV cases.

In Europe, in 2021, 14,560 cases of hepatitis C were reported by European Union/European Economic Area member states, corresponding to a rate of 4.1 cases/100,000 population; however, not all countries report the data consistently [4]. In Romania, very low rates were reported from 2016 through 2019 (0.4 cases/100,000 population) and no hepatitis C cases were reported in 2020 and 2021. Nevertheless, Romania is considered to have the highest prevalence of HCV in Europe, with estimates of 2.62% reported in 2019 [5]. This prevalence is likely to differ by region and population. Recent studies showed a prevalence of HCV infection of 2.64% in a village in Northeastern Romania [6] and 2.5% in a southwestern city [7]. In a larger study conducted on patients from medical institutions in four big Romanian cities during 2019–2020, the overall prevalence was 1.39%, with several factors being associated with an increased prevalence: female gender, rural area of residence, older age, and a lower education level [8]. Implementation of screening and linking new cases to care is currently underway in Romania, but unrestricted access to treatment, including DAAs, remains a challenge, especially in rural areas.

Pan-genotypic ribavirin-free oral DAAs are the recommended treatment for most patients with chronic HCV infection. In Europe, the DAAs available and recommended by the European Association for the Study of the Liver are sofosbuvir/velpatasvir, sofosbuvir/velpatasvir/voxilaprevir, glecaprevir/pibrentasvir, and grazoprevir/elbasvir. The therapeutic goal is the cure of HCV infections and the endpoint is a sustained virological response (SVR) in serum or plasma 12 weeks (SVR12) or 24 weeks (SVR24) after the end of therapy, as assessed by a sensitive molecular method [9]. The fixed-dose combination of glecaprevir/pibrentasvir has been approved for the treatment of chronic HCV genotypes 1-6 without cirrhosis or with compensated cirrhosis based on its high efficacy and good safety profile, irrespective of treatment experience [10-14]. Real-world evidence also indicates a high effectiveness of glecaprevir/pibrentasvir for a broad range of patients with HCV infection, with SVR12 rates ≥95% being achieved irrespective of HCV genotype, cirrhosis status, comorbidities, and treatment history [15-23].

In Romania, the glecaprevir/pibrentasvir combination has been made available free of charge for patients with chronic HCV infection since February 2022. However, nationwide disease or treatment registries of HCV-infected patients are lacking; therefore, the patient population with HCV receiving glecaprevir/pibrentasvir is not well characterized. Moreover, it is still unknown to what extent the efficacy of glecaprevir/pibrentasvir observed in clinical trials translates into effectiveness in HCV-infected Romanian patients. To cover these knowledge gaps, in the ODYSSEY study, we collected a minimal set of recent data from medical charts from clinical centers involved in the management of HCV-infected patients. The study aimed to provide relevant insights into the characteristics and treatment outcomes of HCV-infected patients receiving 8-week therapy with glecaprevir/pibrentasvir across the country.

METHODS

Study Design and Participants

We conducted an observational, retrospective medical chart review study based on a Patient Support Program for HCV-infected patients (HCV-PSP) (sponsored by AbbVie SRL, Bucharest, Romania) attending clinical practices in Romania and initiating glecaprevir/pibrentasvir between 01 February 2022 and 11 July 2023. The HCV-PSP enrolled both treatment-naïve and treatment-experienced (previously treated with interferon + ribavirin +/- sofosbuvir, or sofosbuvir + ribavirin) patients.

A total of 278 specialist physicians from 86 private or public clinical outpatient/inpatient centers participated in the HCV-PSP on which the ODYSSEY study was based. The main specialty of the treating physicians was gastroenterology, infectious diseases, or internal medicine.

The ODYSSEY study included patients ≥18 years of age with compensated liver disease F0-F4 fibrosis grade treatment-naïve or F0-F3 fibrosis grade treatment-experienced on previous interferon-based regimens that had recommendations to receive glecaprevir/pibrentasvir treatment for 8 weeks within the HCV-PSP.

This study was notified to the National Bioethics Committee for Medicines and Medical Devices and the National Agency of Medicines and Medical Devices, as required by local laws and regulations (registration number 1520/03 February 2022). All patients included in the ODYSSEY study provided written informed consent within the HCV-PSP, allowing the use of their data for research purposes, in an anonymized manner.

Treatment and Procedures

In the HCV-PSP, treatment-naïve patients received three tablets of 100 mg glecaprevir/40 mg pibrentasvir once daily (*Maviret*, Abbvie Deutschland GmbH & Co. KG), glecaprevir/pibrentasvir for 8 weeks, while treatment-experienced patients could have received the combination regimen for 8 to 12 weeks, depending on the cirrhosis status, according to the approved label [10].

The grade of liver fibrosis was clinically assessed as per routine clinical practice, before initiating the treatment, using a Fibroscan or Fibromax, or aspartate-aminotransferase to platelet ratio index calculation alone for those with scores below 0.5.

Treatment effectiveness was assessed based on SVR12. Serum HCV RNA was measured ≥70 days after the end of treatment for all patients, using a sensitive polymerase chain reaction (PCR) test. SVR12 was defined as HCV RNA level below the lower limit of quantitation.

Data Collection and Management

Collected data included a minimal set of patient demographics (age at inclusion in the HCV-PSP and gender), clinical characteristics (fibrosis grade and method used for determination, comorbidities), and treatment information (treatment-naïve/

experienced category, treatment duration), as well as information on the HCV RNA level (detectable/non-detectable/unknown) at 12 weeks after the end of treatment and viremia.

All data were collected from the patients' medical files, by a third-party service provider and introduced in a Customer Relationship Management-like database.

Statistical Analysis

No formal sample size was calculated for this real-world study. A total number of 2,400 patients were included in the HCV-PSP on which the study was based.

The analyses were conducted on two populations. The core population (CP) included all patients enrolled in the study who had started the recommended treatment with glecaprevir/pibrentasvir as part of the HCV-PSP. The core population with sufficient follow-up data (CPSFU) included all CP patients except those without an HCV RNA evaluation due to reasons not related to safety and efficacy (i.e., patients missing or lost to follow-up in the HCV-PSP).

All analyses were descriptive. Study variables were summarized using univariate statistics, including mean and standard deviation for normally distributed continuous variables, median, interquartile range (IQR), minimum and maximum for non-normally distributed continuous variables, and frequency and proportions for categorical variables. The distribution of continuous variables was examined using histograms or normality tests as appropriate. Missing data were not replaced.

The percentage of patients achieving SVR12 and the two-sided 95% confidence interval (CI) were calculated. Results were stratified mainly by age, gender, fibrosis grade, and comorbidities of interest, and explored through statistical tests for differences, although the study was not powered for any formal comparison. Variables were analyzed using the chi-squared test. In addition, a *post-hoc*, exploratory logistic regression model was used to assess the probability of detecting HCV RNA level 12 weeks after the end of treatment by comorbidities, expressed as odds ratio (OR) with 95% CIs.

Analyses were carried out using SPSS Statistics 26.0.

RESULTS

Patient Characteristics

In total, 2,240 patients participating in the HCV-PSP were enrolled in the ODYSSEY study and included in the CP set; death was reported for 17 (0.76%) patients and 27 (1.20%) dropped out of the study. The CPSFU set included 2,165 patients. All patients received treatment with glecaprevir/pibrentasvir for 8 weeks.

Patient characteristics were similar for the CP and CPSFU sets. Most patients were female (66.88% in CP and 67.57% in the CPSFU set) and over 50 years of age. The most common relevant comorbidity was hypertension, reported for 21.43% of patients in the CP set and 21.48% of those in the CPSFU set. In both populations, ≥96.47% of patients were treatment-naïve (Table I). Fibrosis grade ranged from F0 in 17.99% and 17.88% to F4 in 18.62% and 18.71% of patients in the CP and CPSFU sets, respectively (Fig. 1). For both populations, the most commonly used method to assess fibrosis grade was Fibromax, for 68.35% of CP patients and 68.13% of CPSFU patients (Table I).

Table I. Baseline characteristics in the CP and CPSFU sets, overall and by gender

Characteristic	CP (N=2240)	CPSFU (N=2165)
Gender, n (%)		
Male	742 (33.12)	702 (32.43)
Female	1498 (66.88)	1463 (67.57)
Mean (SD) age, years	58.73 (13.31)	58.8 (13.19)
Median (min, max) age, years	60 (19, 89)	60 (19, 89)
Age category, n (%)		
18–40 years	246 (10.98)	228 (10.53)
41–50 years	345 (15.40)	337 (15.57)
51–60 years	539 (24.06)	527 (24.34)
61–70 years	649 (28.97)	629 (29.05)
>70 years	461 (20.58)	444 (20.51)
At least one comorbidity, n (%)	836 (37.32)	808 (37.32)
Mean number of comorbidities of interest	0.62	0.61
Disease category, n (%)		
Diabetes mellitus	162 (7.23)	155 (7.16)
Hypertension	480 (21.43)	465 (21.48)
Thyroid disease	71 (3.17)	69 (3.19)
Cardiovascular disease	164 (7.32)	155 (7.16)
Chronic kidney disease	33 (1.47)	29 (1.34)
Gastrointestinal disorders	85 (3.79)	83 (3.83)
Depressive/anxious disorders	37 (1.65)	33 (1.52)
Cancer	37 (1.65)	35 (1.62)
HBV co-infection	26 (1.16)	25 (1.15)
Other disorders	283 (12.63)	273 (12.61)
Fibrosis grade assessed, n (%)	2197 (98.08)	2122 (98.01)
Methods used to assess fibrosis grade, n (%)		
Fibromax	1531 (68.35)	1475 (68.13)
Fibroscan	655 (29.24)	636 (29.38)
Liver biopsy	2 (0.09)	2 (0.09)
APRI score	18 (0.80)	18 (0.83)
Not available	34 (1.52)	34 (1.57)
Exposure to previous HCV treatment, n (%)	79 (3.53)	76 (3.51)

APRI: aspartate-aminotransferase to platelet ratio index; CP: core population; CPSFU: core population with sufficient follow-up; HBV: hepatitis B virus; HCV: hepatitis C virus; SD: standard deviation.

Within the CP set, female patients had a lower mean age than males (53.3 versus 61.3 years) and a larger proportion was >70 years of age (24.5% versus 12.67%). The proportion of patients with at least one comorbidity was higher in females and in patients >70 years of age. (Supplementary file). The distribution of comorbidities by gender differed significantly for hypertension ($p<0.001$), thyroid disease

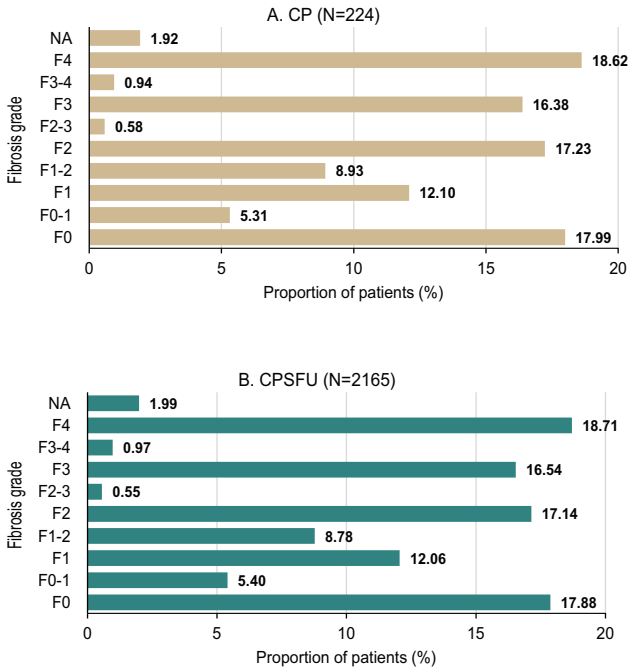

Fig. 1. Fibrosis severity in the core population (A) and core population with sufficient follow-up (B) sets. NA; not available (data missing).

(p<0.001), and depressive/anxiety disorders (p=0.004), with the higher values observed in female patients. Distribution by age category differed significantly for diabetes mellitus (p<0.001), hypertension (p<0.001), thyroid disease (p<0.001), cardiovascular disease (p<0.001), chronic kidney disease (p=0.039) and other comorbidities (p=0.003). The severity of fibrosis increased with age; the distribution of fibrosis age differed significantly by both gender and age categories (p<0.001 for both).

Within the CPSFU set, females had a higher mean age compared to males (61.3 versus 53.5 years), as a considerably higher proportion of females were >50 years of age (82.09% versus 56.83% for males). The rates of comorbidities increased with age and more females than males had hypertension, which was the most commonly reported comorbidity across the cohort. The proportion of patients with F4 fibrosis tended to be higher in males and older individuals (Supplementary file). The distribution of comorbidities by gender differed significantly for hypertension (p<0.001), thyroid disease (p<0.001), and depressive/anxiety disorders (p=0.001); the higher values were always observed in female patients. Distribution by age category was significantly different for diabetes mellitus (p<0.001), hypertension (p<0.001), thyroid disease (p<0.001), and depressive/anxiety disorders (p=0.001). The distribution of fibrosis grade also differed significantly by gender and age category (p<0.001 for both).

Treatment Effectiveness

In the CP set, the overall SVR12 rate was 96.1% (95% CI: 95.2%-96.8%). When stratified by gender, age category, comorbidities or fibrosis grade, SVR12 rates were >92% except for the subgroups of patients with chronic kidney disease and depressive-/anxiety disorders, where lower rates (87.5% and 86.2%, respectively) were observed (Fig. 2A). The distribution of SVR12 rates differed significantly for age categories (p=0.002), gender (p<0.001), diabetes mellitus (p=0.015), and cardiovascular diseases (p=0.010).

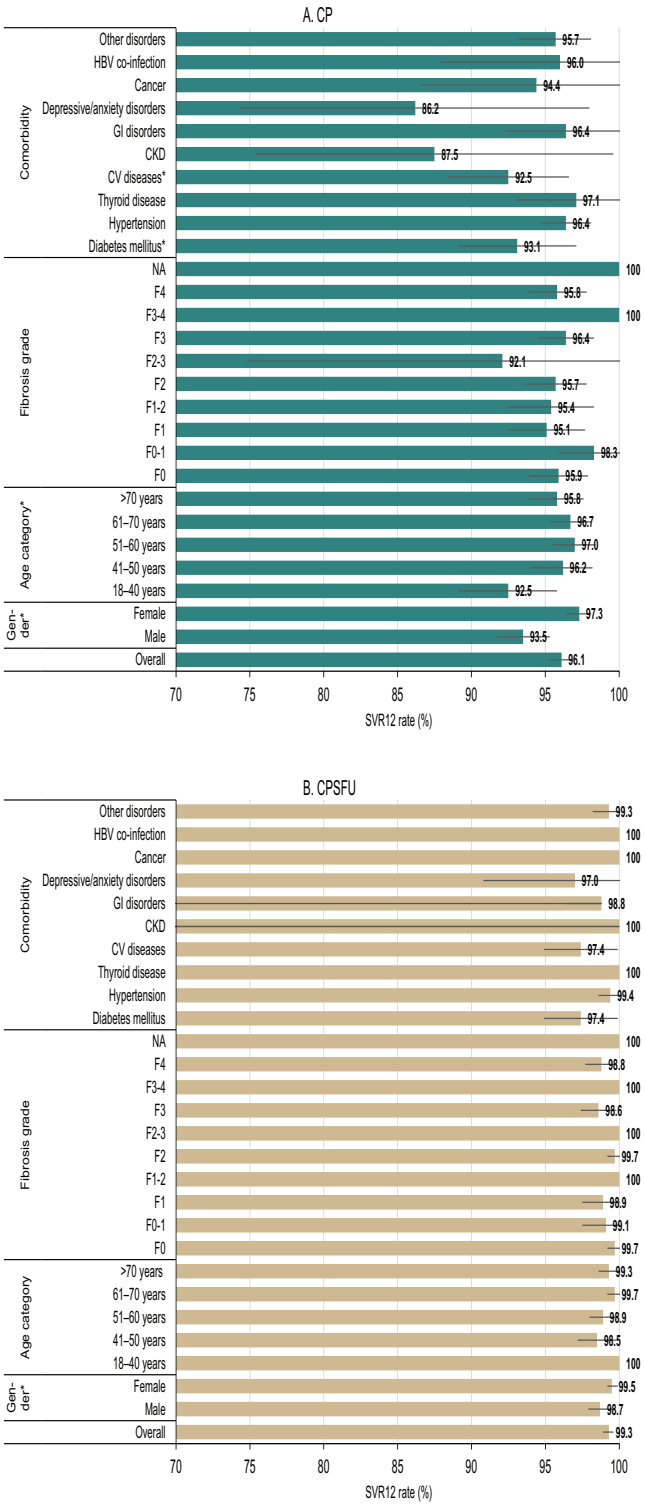

Fig. 2. SVR12 rates in the core population (A) and core population with sufficient follow-up (B) sets, overall and by gender, age category, fibrosis grade, and comorbidities of interest. CKD: chronic kidney disease; CV: cardiovascular; GI: gastrointestinal; HBV: hepatitis B virus; NA: not available (data missing); SVR12: sustained virological response at 12 weeks after the end of treatment; *The distribution of SVR rates differed significantly. Error bars represent 95% confidence intervals. For clarity, only the 70–100 interval is shown for the X-axis.

In an exploratory analysis, the presence of diabetes mellitus (OR=3.869, 95%CI: 1.101–13.567; p=0.035) and cardiovascular diseases (OR=7.876, 95%CI: 1.707–36.344; p=0.008) was shown to increase the probability to detect HCV RNA at 12 weeks post-treatment.

In the CPSFU set, the SFR12 rates were 99.3% (95%CI: 98.9–99.6) overall and ranged between 97.0% and 100% across subgroups (Fig. 2B). The distribution of SVR12 rates differed significantly for gender (p=0.041). In an exploratory analysis, SVR12 rates were compared between patients with or without a specific comorbidity (Fig. 3); the presence of diabetes mellitus (OR=3.840, 95%CI: 1.093–13.495; p=0.036) and cardiovascular diseases (OR=7.904, 95%CI: 1.719-36.346, p=0.008) were associated with an increased probability to detect HCV RNA at 12 weeks post-treatment.

DISCUSSION

This is the first study to provide comprehensive information on the characteristics and response to treatment of Romanian HCV-infected patients receiving 8-week therapy with glecaprevir/pibrentasvir, in real-life settings. Treatment resulted in high rates of SVR12 in both the CP and the CPSFU, including across various subgroups based on age, fibrosis stage, and comorbidities of interest.

The patient population was characterized by a median age of around 60 years and approximately half of the patients were >60 years of age, with two-thirds of patients being women, more than one-third having at least one comorbidity, and the vast majority of patients being treatment-naïve. The median age and the proportion of female patients in our study are higher than that reported from other European populations in which therapy with glecaprevir/pibrentasvir was evaluated [18, 19, 22-25]. This suggests some particularities for the Romanian HCV-infected patients, in particular, a possible rise of HCV infection in females. Comorbidities were reported for around 37% of patients and hypertension was the most prevalent, described in approximately 20% of patients, with diabetes mellitus and cardiovascular disease also being reported in 7% of patients, as in other populations treated with glecaprevir/pibrentasvir [16, 18]. Nearly 20% of patients had cirrhosis and this proportion increased with increasing age category, but all grades of fibrosis were present in our study population. Most patients were treatment-naïve, although glecaprevir/pibrentasvir is also recommended for the treatment of patients who failed prior therapy with interferon + ribavirin +/- sofosbuvir, or sofosbuvir + ribavirin [10].

The SVR12 rates observed in our study following treatment with glecaprevir/pibrentasvir for the overall CP and CPSFU populations were high, in line with previous observations in real-world settings across different geographies and subgroups of interest [11, 26] and regardless of HCV genotype [27]. Our results were also consistent with the data reported from clinical trials [14]. High SVR12 rates (>97.0%) were observed in our study across all subgroups considered in the CPSFU population, which excluded the patients without an HCV RNA evaluation at 12 weeks after the end of treatment. In the Romanian patients with cirrhosis, the SVR12 rate was 98.8%, reinforcing the effectiveness demonstrated by glecaprevir/pibrentasvir in international populations with compensated cirrhosis [16, 18, 28, 29]. The treatment also resulted in an SVR12 rate of 99.7% in patients >70 years of age. This rate was slightly higher than the rate of 97.9% reported from a recent retrospective multicenter real-world study conducted in Italian patients with chronic HCV infection ≥75 years of age, in which a similar proportion of patients had grade F4 fibrosis [29]. In a different study comprising 1177 Italian patients with HCV infection, older age at treatment was associated with higher treatment success rates [24]. Other reports identified other predictors for increasing the risk of treatment failure in real-life settings: being an intravenous drug user [23], having high HCV viral load [16, 17] and creatinine levels [24]. Using a logistic regression model, we found that the presence of diabetes mellitus and cardiovascular diseases increased the odds of treatment failure. However, between-study comparisons are hindered by the heterogeneity of the populations and the methods used.

Overall, our results add to the current evidence of the high effectiveness for the 8-week therapy with glecaprevir/pibrentasvir in patients with HCV infection. Of note, no significant difference was observed in SVR12 rates following 8- or 12-week treatment durations in real-world practice [24, 28, 29]. The 8-week regimen could help reducing the burden of pre-treatment assessments, clinic visits, and thus, indirectly and to various extent, the overall HCV-related healthcare resource utilization, as compared with the 12- or 16-week treatments. The shorter duration may also translate into higher adherence to treatment [16] and could therefore be beneficial in reaching underserved areas or in

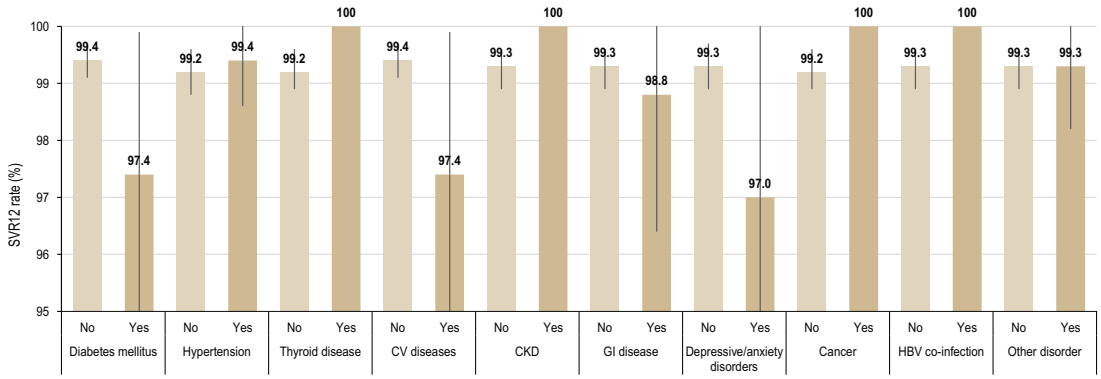

Fig. 3. SVR12 rates by comorbidities group in the CPSFU dataset. For abbreviations see Fig. 2.

specific patient populations in Romania, as the 8-week therapy with glecaprevir/pibrentasvir demonstrated high effectiveness in these situations [19, 23-25, 30, 31].

Our study provides information on HCV-infected patients treated with glecaprevir/pibrentasvir, based on data collected in a centralized and standardized manner from clinical centers involved in the management of hepatitis C. However, the study has several limitations, due mainly to its non-interventional, retrospective design. ODYSSEY used real-world data from a PSP, which has the disadvantage of a limited collection of variables, and missing information in medical charts. Nevertheless, this reflects the real-world situation in clinical practice. Moreover, while the HCV-PSP was conducted in more than 80 medical centers routinely managing HCV-infected patients, not all eligible patients for treatment with glecaprevir/pibrentasvir were included in the program due to the patient's or their treating physician's decision. We performed no stratification by hard-to-reach subpopulations, such as those who have been incarcerated, patients with psychiatric disorders, and people who inject drugs. Still, the results observed in the ODYSSEY study are likely to be generalizable to the entire Romanian population of HCV-infected patients. In addition, the HCV genotype was not determined and we did not assess reasons for treatment discontinuation and non-response to treatment.

CONCLUSIONS

The 8-week treatment with glecaprevir/pibrentasvir resulted in high SVR12 rates in multiple HCV-infected patient profiles encountered in routine clinical practice in Romania. Our findings contribute to the real-world evidence for the effectiveness of this short, pan-genotypic treatment regimen in clinical practice settings across various geographies and can inform the Romanian healthcare community and decision-makers about current and future needs in the management of patients with HCV infection.

Data sharing statement

AbbVie is committed to responsible data sharing regarding the clinical trials we sponsor. This includes access to anonymized, individual, and trial-level data (analysis data sets), as well as other information (e.g., protocols, clinical study reports, or analysis plans), as long as the trials are not part of an ongoing or planned regulatory submission. This includes requests for clinical trial data for unlicensed products and indications.

These clinical trial data can be requested by any qualified researchers who engage in rigorous, independent, scientific research, and will be provided following review and approval of a research proposal, statistical analysis plan, and execution of a Data Sharing Agreement. Data requests can be submitted at any time after approval in the United States and Europe and after acceptance of this manuscript for publication. The data will be accessible for 12 months, with possible extensions considered. For more information on the process or to submit a request, visit the following link: https://vivli.org/ourmember/abbvie/ then select "Home".

Conflicts of interest: L.M. is an employee of AbbVie Romania and may hold stock or options. The other authors have no conflicts of interest to declare.

Authors' contributions: All authors had access to relevant data and participated in the analysis and interpretation of data, writing, reviewing, and approval of this publication. A.T., C.S., A.S.-C., A.C., L.B., E.D., C.P., C.B., M.C.B., D.I.G., D.N.F., C.S.P., L.S.D., L.I., M.D., C.E., L.G. had substantial contributions to acquisition of data. All authors agree to be accountable for all aspects of the work. No honoraria or payments were made for authorship.

Acknowledgements: AbbVie funded this study and participated in the study design, research, analysis, data collection, interpretation of data, reviewing, and approval of the publication. Data collection for the Patient Support Program were provided by CEBIS International, Romania and were funded by AbbVie. Medical writing support was provided by Petronela M. Petrar (PhD) and Ana Maria Iordan (MD, MSc) and statistical analyses were provided by Bogdan Voicu (PhD) (all from MedInteractiv Bucharest, Romania) and funded by AbbVie.

Authors' affiliation: 1) Institute of Gastroenterology and Hepatology, Iasi; Grigore T. Popa University of Medicine and Pharmacy, Iasi; 2) Prof. Dr. Matei Bals National Institute of Infectious Diseases, Bucharest; 3) Carol Davila University of Medicine and Pharmacy, Bucharest; 4) Dr. Victor Babes Clinical Hospital of Infectious and Tropical Diseases, Bucharest; 5) Sf. Cuvioasa Parascheva Clinical Hospital of Infectious Diseases, Galati; Faculty of Medicine and Pharmacy, Dunărea de Jos University of Galati; 6) Sf. Apostol Andrei County Clinical Emergency Hospital, Constanţa; Faculty of Medicine, Ovidius University Constanţa; 7) Prof. Dr. Octavian Fodor Regional Institute of Gastroenterology and Hepatology; UBB Med, Babes-Bolyai University, Department for Clinical Psychology and Psychotherapy, Cluj-Napoca; 8) Bihor County Clinical Emergency Hospital; Faculty of Medicine and Pharmacy, University of Oradea; 9) Craiova County Clinical Emergency Hospital; University of Medicine and Pharmacy of Craiova; 10) University Emergency Hospital of Bucharest; 11) AbbVie Romania; 12) Department of Internal Medicine, Fundeni Clinical Institute, Bucharest; 13) Digestive Diseases and Liver Transplantation Center, Fundeni Clinical Institute, Bucharest, Romania.

Supplementary material: To access the supplementary material visit the online version of the *J Gastrointestin Liver Dis* at http://dx.doi.org/10.15403/jgld-5745n

REFERENCES

1. The 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;7:396-415. doi:10.1016/s2468-1253(21)00472-6
2. World Health Organization. Global health sector strategies on, respectively, HIV, viral hepatitis and sexually transmitted infections for the period 2022-2030. Available from: http://www.who.int/publications/i/item/9789240053779

3. Avramovic G, Oprea C, Surey J, et al. HepCare Europe-A service innovation project. HepCheck: Characteristics of the patient population with active infection as defined by HCV RNA. Int J Infect Dis 2020;91:246-251. doi:10.1016/j.ijid.2019.11.027
4. European Centre for Disease Prevention and Control. Hepatitis C - Annual Epidemiological Report for 2021. Available from: https://www.ecdc.europa.eu/en/publications-data/hepatitis-c-annual-epidemiological-report-2021
5. Thomadakis C, Gountas I, Duffell E, et al. Prevalence of chronic HCV infection in EU/EEA countries in 2019 using multiparameter evidence synthesis. Lancet Reg Health Eur 2023;36:100792. doi:10.1016/j.lanepe.2023.100792.
6. Huiban L, Stanciu C, Muzica CM, et al. Hepatitis C Virus Prevalence and Risk Factors in a Village in Northeastern Romania-A Population-Based Screening-The First Step to Viral Micro-Elimination. Healthcare (Basel) 2021;9:651. doi:10.3390/healthcare9060651
7. Butaru AE, Doica IP, Gheonea DI, Rogoveanu I, Diculescu M, Oancea CN. Preliminary Results of the Micro-Elimination Project of Hepatitis C in a Disadvantaged Town in South-West of Romania-Orşova. Curr Health Sci J 2020;46:217-221. doi:10.12865/chsj.46.03.01
8. Gheorghe L, Iacob S, Csiki IE, et al. The Prevalence of HCV Infection and Risk Factors in a Hospital- Based Population Screening, a First Step to the Micro-Elimination of HCV Infection in Medical Institutions from Romania - Results of the HepC ALERT Study. J Gastrointestin Liver Dis 2020;29:587-593. doi:10.15403/jgld-3084
9. European Association for the Study of the Liver. EASL recommendations on treatment of hepatitis C: Final update of the series. J Hepatol 2020;73:1170-1218. doi:10.1016/j.jhep.2020.08.018
10. European Medicines Agency. Maviret: Summary of Product Characteristics. Available from: http://www.ema.europa.eu/en/documents/product-information/maviret-epar-product-information_en.pdf
11. Liu X, Hu P. Efficacy and Safety of Glecaprevir/Pibrentasvir in Patients with Chronic HCV Infection. J Clin Transl Hepatol 2021;9:125-132. doi:10.14218/jcth.2020.00078
12. Shen C, Fan H, Ge Z, et al. Efficacy and Safety of Glecaprevir/Pibrentasvir in HCV Patients With Previous Direct-Acting Antiviral Therapy Failures: A Meta-Analysis. Front Med (Lausanne) 2020;7:592472. doi:10.3389/fmed.2020.592472
13. Wang X, Fan X, Deng H, et al. Efficacy and safety of glecaprevir/pibrentasvir for chronic hepatitis C virus genotypes 1-6 infection: A systematic review and meta-analysis. Int J Antimicrob Agents 2019;54:780-789. doi:10.1016/j.ijantimicag.2019.07.005
14. Xu HQ, Wang CG, Xiao P, Gao YH. Efficacy and Safety of Glecaprevir/Pibrentasvir for Chronic Hepatitis C Patients: A Systematic Review and Meta-analysis. J Clin Transl Hepatol 2020;8:267-276. doi:10.14218/jcth.2020.00047
15. Al-Ahmari TS, Alotaibi AF, Aljasser AI, Aljasser AI, Eldaw AM, Abd-Ellatif EE. The Effectiveness and Safety of Direct-Acting Antivirals in the Treatment of Hepatitis C Virus in Saudi Arabia: A Nationwide Study Based on the Saudi Ministry of Health Surveillance Data From 2017 to 2021. Cureus 2023;15:e42780. doi:10.7759/cureus.42780
16. 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. Hepatol Int 2023;17:550-561. doi:10.1007/s12072-023-10506-z
17. Chen JJ, Chiu YC, Lee PL, et al. Real-world effectiveness and safety of sofosbuvir/velpatasvir and glecaprevir/pibrentasvir for genotype 6 chronic hepatitis C. J Formos Med Assoc 2022;121:2265-2272. doi:10.1016/j.jfma.2022.04.020
18. 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;39:3146-3158. doi:10.1007/s12325-022-02158-6
19. 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;14:1541. doi:10.3390/v14071541
20. Lu M, Rupp LB, Melkonian C, et al. Real-World Safety and Effectiveness of an 8-Week Regimen of Glecaprevir/Pibrentasvir in Patients with Hepatitis C and Cirrhosis. Adv Ther 2024;41:744-758. doi:10.1007/s12325-023-02748-y
21. Ryu JE, Song MJ, Kim SH, et al. Safety and effectiveness of direct-acting antivirals in patients with chronic hepatitis C and chronic kidney disease. Korean J Intern Med 2022;37:958-968. doi:10.3904/kjim.2021.486
22. Vera J, Gomes A, Póvoas D, et al. Real-World Effectiveness and Safety of Glecaprevir/Pibrentasvir for the Treatment of Chronic Hepatitis C: A Prospective Cohort Study in Portugal. Acta Med Port 2024;37:323-333. doi:10.20344/amp.19178
23. Yaras S, Demir M, Barutcu S, et al. The efficacy and tolerability of glecaprevir/pibrentasvir treatment in a real-world chronic hepatitis C patients cohort. Hepatol Forum 2023;4:92-96. doi:10.14744/hf.2023.2023.0001
24. Persico M, Aglitti A, Milella M, et al. Real-life glecaprevir/pibrentasvir in a large cohort of patients with hepatitis C virus infection: The MISTRAL study. Liver Int 2019;39:1852-1859. doi:10.1111/liv.14170
25. Reau N, Cheng WH, Shao Q, Marx SE, Brooks H, Martinez A. Real-World Effectiveness of 8-Week Glecaprevir/Pibrentasvir in Treatment-Naïve, Compensated Cirrhotic HCV Patients. Infect Dis Ther 2023;12:1849-1860. doi:10.1007/s40121-023-00823-z
26. Lampertico P, Carrión JA, Curry M, et al. Real-world effectiveness and safety of glecaprevir/pibrentasvir for the treatment of patients with chronic HCV infection: A meta-analysis. J Hepatol 2020;72:1112-1121. doi:10.1016/j.jhep.2020.01.025
27. Yen HH, Chen YY, Lai JH, et al. Pan-Genotypic Direct-Acting Antiviral Agents for Undetermined or Mixed-Genotype Hepatitis C Infection: A Real-World Multi-Center Effectiveness Analysis. J Clin Med 2022;11:1853. doi:10.3390/jcm11071853
28. 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:e0272567. doi:10.1371/journal.pone.0272567
29. Pugliese N, Calvaruso V, Masarone M, et al. Glecaprevir/Pibrentasvir is safe and effective in Italian patients with chronic hepatitis C aged 75 years or older: A multicentre study. Liver Int 2023;43:1440-1445. doi:10.1111/liv.15599
30. Çölkesen F, Tarakçi A, Kacar F, Eroğlu E, Özdemir Armağan Ş. Real Life Data for Glecaprevir/Pibrentasvir: A Single-Center Study. Arch Curr Med Res 2021;2:14-18. doi:10.47482/acmr.2021.9
31. Tsai YC, Yu ML, Ko CY, Hsin YH, Tsai QZ, Huang CW. Treatment effectiveness and side effects of patients with hepatitis C in the prisons of Southern Taiwan: a real-life retrospective analysis. BMJ Open 2023;13:e070490. doi:10.1136/bmjopen-2022-070490