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Real-World Effectiveness of Elbasvir/Grazoprevir in HCV-Infected Patients in the US Veterans Affairs Healthcare System

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Summary

Elbasvir/grazoprevir (EBR/GZR) is an all-oral direct-acting antiviral agent (DAA) with high sustained virologic response (SVR) in clinical trials. This study's primary objective was to evaluate effectiveness of EBR/GZR among HCV-infected patients in a real-world clinical setting. We conducted a nationwide retrospective observational cohort study of HCV-infected patients in the US Department of Veterans Affairs (VA) using the VA Corporate Data Warehouse. The study population included patients with positive HCV RNA who initiated EBR/GZR from February 1 to August 1, 2016. We calculated the 95% confidence interval for binomial proportions for SVR overall and by demographic subgroups. Clinical and demographic characteristics were also evaluated. We included 2,436 patients in the study cohort. Most were male (96.5%), African-American (57.5%), with mean age of 63.5 (SD=5.9), and 95.4% infected with genotype (GT) 1 [GT1a (34.7%), GT1b (58.6%)]. Other comorbidities included diabetes (53.2%), depression (57.2%), and HIV (3.0%). More than 50% had history of drug or alcohol abuse (53.9% and 60.5%, respectively). 31.4% of the cohort had cirrhosis. A total of 95.6% (2,328/2,436; 95% CI: 94.7% −96.4%) achieved SVR. The SVR rates by subgroups were: male, 95.5% (2245/2350); female, 96.5% (83/86); GT1a, 93.4%, GT1b, 96.6%, GT4, 96.9%, African-American, 95.9% (1,342/1,400); treatment-experienced, 96.3% (310/322); cirrhosis, 95.6% (732/766); stage 4–5

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Ethical Approval: This study was approved by the VA Central Institutional Review Board and the Michael E. DeBakey VA Medical Center Research & Development subcommittee.

CKD, 96.3% (392/407); and HIV, 98.6% (73/74). SVR rates were high overall and across patient subgroups regardless of gender, race/ethnicity, cirrhosis, renal impairment, or HIV. This study provided important data regarding the effectiveness of EBR/GZR in a large clinical setting.

Keywords

Direct-acting antiviral agents; hepatitis C virus; Veterans Affairs; treatment effectiveness

INTRODUCTION

Chronic hepatitis C virus (HCV) infection affects 1.3% of the U.S. population [1, 2] and is the leading cause of cirrhosis, hepatocellular cancer, and death from liver disease in the U.S. [3]. The new all-oral direct-acting antivirals (DAAs) result in SVR in an unprecedented >90% of patients in clinical trials [4–13]. In early 2016, the US Food and Drug Administration (FDA) approved the fixed dose combination of elbasvir/grazoprevir (EBR/GZR) for the treatment of chronic HCV genotypes (GT) 1 and 4 infections. EBR/GZR demonstrated high sustained virologic response (SVR) overall as well as in special populations of patients including those with advanced chronic kidney disease (CKD), persons who inject drugs, and those with inherited blood disorders with low adverse-event rates [13–15].

Randomized controlled trials of EBR/GZR reported high efficacy for the treatment-naïve and treatment-experienced patients including special populations. In integrated analyses of EBR/GZR trials among GT 1 patients with and without cirrhosis, SVR rates were greater than 95% in all patient subgroups [16, 17]. Among patients infected with HCV GT 1 and stage 4–5 CKD, the phase 3 clinical trial of EBR/GZR showed that the SVR rates were 99% with low adverse-event rates [18]. However, the chasm between efficacy (in clinical trials) and effectiveness (in clinical practice) persists in the DAA era. The few data that are available from real-world experience suggest that SVR rates with all-oral DAAs may be lower than those reported in clinical trials (~75–80% vs. >90%, respectively) [19–22]. In contrast, other data suggest that the effectiveness of DAAs may be comparable to efficacy observed in clinical trials [23, 24]. Previous real-world studies and clinical trials have also reported factors associated with lower response rates including non-adherence, African American race [4, 25, 26], having cirrhosis [22, 24, 26], and male gender [22].

To our knowledge there have been no published reports examining the effectiveness of EBR/GZR regimens in real-world clinical practice. Therefore, the objective of the study was to evaluate effectiveness among HCV-infected patients treated with EBR/GZR in a real-world clinical setting in the US using data from the US Department of Veterans Affairs (VA) healthcare system.

MATERIALS AND METHODS

This was a retrospective analysis of administrative and clinical data using the VA Corporate Data Warehouse (CDW) which is a national data repository of VA electronic medical records including those of almost 9 million veterans. The CDW includes data from pharmacy, laboratory, inpatient and outpatient encounters by ICD-9/10 diagnosis codes, as

well as vital status from October 1, 1999 through present day. The VA is the largest single provider of HCV care in the US due to the fact that veterans are 3 times more likely to be infected with HCV [27, 28].

Study populations and definitions

The study cohort included subjects who initiated EBR/GZR treatment after the FDA approval beginning on February 1, 2016 to August 1, 2016 from 128 VA Medical Centers nationwide. To allow for adequate follow-up time to determine SVR rates, SVR outcomes were captured through February 15, 2017.

We included subjects who initiated EBR/GZR regimens and were at least 18 years of age. Patients were required to have at least one positive HCV RNA test to confirm chronic HCV and had at least one inpatient or outpatient visit within a one-year period prior to treatment initiation. We excluded patients with undetermined regimen such as having ribavirin (RBV) added ≥30 days after treatment initiation or those treated with EBR/GZR for greater than seventeen weeks because these regimens were not consistent with those approved by the FDA. The index date was defined as the first EBR/GZR initiation date during the study period.

The primary study was conducted among the evaluable population (EP), which included all patients who had HCV RNA test data available at least 4 weeks after the end of treatment. The EP cohort included patients who did not complete treatment regimen. As a sensitivity analysis, we examined the per protocol (PP) population, which included all the patients in the EP who completed treatment regimen of EBR/GZR. Treatment completion was defined as those who were prescribed EBR/GZR for at least 11 weeks (77 days) of treatment. The EBR/GZR regimens consisted of EBR/GZR without RBV, EBR/GZR with RBV, and EBR/GZR + sofosbuvir (SOF) +/− RBV.

Outcomes measures and demographic and clinical variables

SVR was defined as HCV RNA below the limit of quantification performed at least 12 weeks after the end of treatment. If HCV RNA data at ≥12 weeks were not available, SVR was defined based on HCV RNA testing available from week 4 to 12 weeks after the end of treatment to account for variability of clinic visits and availability of laboratory data in clinical practice. This definition of SVR has been used in other similar database studies [25, 29] and SVR4 has been shown to be highly concordant with SVR12 [30]. The end of treatment was calculated from the last day covered by the medication dispensed by totaling the number of days supply. Treatment duration was calculated until there was a gap of at least 45 days without EBR/GZR. HCV patients were considered to have completed 12 weeks and 16 weeks of EBR/GZR regimens if they had received between 77–91 days and 105–119 days of medication, respectively.

Demographic variables included age, gender, race/ethnicity (White, African American, Hispanic, Asian, others). HCV treatment experience was defined as previous exposure to any interferon-based regimen (Peg-IFN) with RBV, first generation (i.e. boceprevir: BOC, telaprevir: TEL), and all-oral DAAs regimens (i.e. simeprevir: SIM, sofosbuvir: SOF, ledipasvir/sofosbuvir: LDV/SOF, ombitasvir/paritaprevir/ritonavir/dasabuvir: PrOD) prior to

EBR/GZR treatment any time after October 1, 1999. If patients received more than one type of previous treatment, they were classified based on the most recent type received prior to EBR/GZR. HCV GT was also determined by using laboratory results for GT tests any time prior to treatment index date. High baseline viral load was defined as those with HCV RNA greater than 6M IU/ml.

Comorbidities such as cirrhosis, diabetes, hypertension, depression, anxiety, history of alcohol and/or drug abuse, and HIV were identified by the presence of at least one ICD-9 or 10 diagnosis codes any time prior to the index date, many of which have been used in previously published studies [31, 32]. Decompensated cirrhosis (end-stage liver disease) was defined as the presence of inpatient or outpatient claims for ascites, variceal bleeding, hepatic encephalopathy, and hepatorenal syndrome based on inpatient or outpatient ICD-9/10 codes. Hepatocellular carcinoma was defined from its diagnosis codes at any time prior to index date. Kidney and liver transplant were defined by presence of CPT or ICD procedure codes any time prior to index date. The Deyo modification of the Charlson comorbidity index was also calculated to determine comorbidity status in the 1 year prior to index date [33].

We used estimated glomerular filtration rate (eGFR) to categorize patients by severity of CKD if they had at least two eGFR values ≥3 months apart within 2 years prior to the index date as follows: eGFR >60, Stage 3 CKD (eGFR of 30–59), and Stages 4–5 CKD (eGFR <30). We ascertained eGFR from automated reporting of VA laboratory tests that used the Modification of Diet in Renal Disease (MDRD) equation [34]. If the two tests classified a patient in discrepant stages, the patient was classified using the most recent stage. Stage of CKD was assigned based on the criteria published by the National Kidney Foundation [35].

Data analysis—Descriptive statistics were used to describe demographic and clinical characteristics such as HCV GT, baseline HCV viral load, HIV co-infection, alcohol or substance use, depression, and comorbid physical health conditions by treatment regimen type. Mean or median values were compared using chi-squared test, Fisher Exact test, or the Wilcoxon signed-rank test for continuous variables, as appropriate. We conducted primary data analysis in the EP cohort. The SVR rates were calculated overall and by demographic and clinical variables defined above. We calculated the 95% confidence interval for binomial proportions for SVR overall and by demographic and clinical subgroups. SVR rates by treatment regimen and treatment experience were also analyzed. We further stratified by GT 1 and GT 4 and calculated SVR by prior treatment status, treatment regimen, and duration while excluding patients with history of decompensated cirrhosis or who had prior use of all-oral DAAs. We calculated 95% confidence intervals (CIs) for SVR rates using the binomial distribution. Overall SVR was calculated in the PP cohort as a sensitivity analysis. We used SAS® (version 9.4, SAS Institute Inc., Cary, NC, USA) for analyses. The study was approved by the VA Central Institutional Review Board.

RESULTS

During the study period, we identified 2,985 chronic HCV-infected patients who initiated EBR/GZR regimens. After applying study inclusion and exclusion criteria, 2,436 patients

were included in the EP cohort as a primary study population. When excluding those who did not complete treatment regimen (7.3%, n=179), the PP cohort included 2,257 patients (Figure 1).

Cohort characteristics overall and by treatment regimen

Baseline demographic and clinical characteristics of EP by EBR/GZR treatment regimen are shown in Table 1. Of 2,436 patients in the evaluable population, 2,246 (92.2%) were prescribed EBR/GZR without RBV, followed by EBR/GZR+RBV (6.4%, n = 156) and EBR/GZR +SOFs+/−RBV (1.4%, n = 34). The mean age was 63.5 years old (SD = 5.9); and the majority were African American (57.5%) and male (96.5%). There were 2,324 patients (95.4%) infected with GT 1 [GT1a (34.7%, n = 844), GT 1b (58.6%, n = 1428)]. The prevalence of co-morbidities was as follows: diabetes (53.2%), depression (57.2%), CKD stage 3–5 (32.8%), and HIV co-infection (3%). A third (31.4%) of the cohort had a diagnosis of cirrhosis; 13.6% overall had decompensated cirrhosis. Additionally, more than half of the patients had a history of drug (53.9%) or alcohol (60.5%) abuse. The population included 448 treatment-experienced patients (18.4%). We observed that EBR/GZR were given to some patient populations that are not indicated by the US FDA labelling such as the 117 patients (4.8%) who had prior NS5A-exposure of LDV/SOF or PrOD and the 332 patients (13.6%) who had decompensated cirrhosis. We also observed 4 GT 3 patients and 2 GT 2 patients.

Comparing baseline characteristics across regimens, patients receiving EBR/GZR+RBV were slightly younger than patients receiving other regimen types. Patients receiving EBR/GZR alone were more likely to be Black (58.8% vs. 41.7% and 41.2% for EBR/GZR +RBV and EBR/GZR+SOF+/−RBV, respectively) and infected with GT1b (62.3% vs. 16% and 11.8% for EBR/GZR+RBV and EBR/GZR+SOF+/−RBV, respectively) than other regimens. There were 91.2% (31/35) of patients treated with EBR/GZR+SOF+/−RBV who had prior LDV/SOF or PrOD treatment compared with only 11.5% for EBR/GZR+RBV and 3% for EBR/GZR. Comorbidities were similar across regimen types except for cirrhosis, which was higher among patients who received EBR/GZR+SOF+/−RBV (58.8% any cirrhosis vs. 31.1% and 30.1% in EBR/GZR and EBR/GZR+RBV, respectively). EBR/GZR +SOF+/−RBV patients were also less likely to have CKD stage 3–5 than the other regimens (11.8% vs. 33.8% and 23.7% in EBR/GZR and EBR/GZR+RBV, respectively).

SVR rates overall and by subgroups

In the EP cohort (n=2,436), 95.6% (95%CI: 94.7%−96.4%) of veterans prescribed EBR/GZR regimens achieved SVR (Table 2). When including only patients who completed at least 11 weeks of treatment, the SVR rate in the PP cohort was 97.0% (2,190/2,257; 95%CI: 96.3%−97.7%).

Table 2 showed that SVR rates by baseline characteristics ranged from 93% to 97%. SVR by these subgroups were reported as follows: male, 95.5% (2,245/2,350); female, 96.5% (83/86); African American, 95.9% (1,342/1,400); Hispanic, 95.1% (77/81); White, 95.0% (783/824); previously untreated, 96.1% (1,910/1,988); cirrhosis, 95.5% (772/808); without cirrhosis, 95.6% (1556/1628); stage 3 CKD, 96.7% (380/393); stage 4–5 CKD, 96.3%

(392/407); HIV positive, 98.6% (73/74); HIV negative, 95.5% (2,255/2,362); history of alcohol abuse, 95.9% (1,412/1,473); no history of alcohol abuse, 95.1% (916/963); history of drug abuse, 95.3% (1,251/1,313); and no history of drug abuse, 95.9% (1,077/1,123). The SVR rate for treatment-experienced patients was 93.3% (418/448); of those, 117 patients (26.1%) had prior NS5A exposure of LDV/SOF or PrOD with SVR rates of 82.9% and 88.6%, respectively.

SVR in the 34 patients treated with EBR/GZR +SOFs+/−RBV was 97.1% (33/34) (data not shown). The one treatment failure was a >65 year old black male, with GT1a, treated with EBR/GZR+SOF without RBV who did not complete the treatment course (i.e. had less than 11 weeks of treatment). He was previously treated by LDV/SOF with baseline HCV RNA ≥ 6 million copies, and had HIV infection, stage 4/5 CKD, and prior exposure of drug abuse.

SVR rates among GT1- and GT4 HCV-infected patients by treatment regimen

In the subgroup analysis that excluded patients with prior treatment experience with all-oral DAAs or those who had decompensated cirrhosis which were not indicated in the US FDA labeling for EBR/GZR, the majority of patients were treated with EBR/GZR without RBV (94% in GT1 and 96.6% in GT4) (Table 3). Overall SVR (EP) rates among GT1 patients were 96.2% (1842/1915); . SVR was 96.4% (1737/1801) for those treated with EBR/GZR without RBV; 92% (104/113) for EBR/GZR+RBV; and 100% (1/1) for EBR/GZR+SOF+/−RBV. Of those who had GT1a (N = 647), 546 patients (84.4%) received 12 weeks of treatment, 49 patients (7.6%) received 16 weeks of treatment, and 52 (8%) patients did not receive at least 11 weeks of treatment. SVR rates of EBR/GZR-based regimens for 12 weeks was 97% (531/546) and 90% (44/49) among those treated for 16 weeks. Specifically, SVR for EBR/GZR without RBV for 12 weeks was 98% (471/481) and SVR for EBR/GZR+RBV for 16 weeks was 83.3% (20/24).

Of 1,668 GT1 treatment-naïve patients, majority (93%) were treated with EBR/GZR without RBV. SVR rates were 96.2% overall [EBR/GZR: 96.5% (1501/1555), EBR/GZR+RBV: 92% (104/113)]. In 247 GT1 treatment-experienced (i.e. Peg-IFN or BOC or TEL) patients, SVR was 95.9%. Finally, among 59 patients with GT4, 98.3% achieved SVR overall ranging from 98.2%−100% by regimen and treatment duration.

DISCUSSION

This study evaluated the real-world effectiveness of EBR/GZR in the first 6 months after approval in the large VA national health care system. Our study showed that EBR/GZR was highly effective, with an SVR of 95.6% overall and 97% in patients who completed a full course of treatment. SVR rates were high across patient subgroups regardless of gender, race/ethnicity, presence of cirrhosis, renal impairment, or HIV co-infection. To our knowledge, this is the largest real-world effectiveness study of EBR/GZR of 2,436 patients. Randomized controlled trials demonstrated high SVR rates for EBR/GZR ranging from 90% to100% [13–15]. Compared to the integrated analysis of 6 clinical trials among patients with HCV GT 1, 4, and 6 infection [36], HCV patients in this study were older, had a higher prevalence of comorbidities, and had a higher percent of treatment experience including those with prior use of all-oral DAAs. Our findings show that the real-world effectiveness of

EBR/GZR among HCV-infected GT1 or GT4 patients in the VA population is comparable to efficacy rates reported in clinical trials.

The effectiveness of EBR/GZR reported in this study is slightly higher than other previous VA studies of all-oral DAAs (not including EBR/GZR). Backus et al. reported an overall SVR of 88%−91% in 21,242 VA patients with GT 1 who received LDV/SOF or PrOD [26], and Fox et al. reported SVR rates of 83–92% for 11,464 VA patients on all-oral DAAs through July 1, 2015 [22]. Ioannou et al. evaluated 17,487 VA patients treated with SOF, LDV/SOF and PrOD regimens from January 2014 to June 2015. The SVR12 was 92.8% for those with HCV GT 1 and 89.6% for those with GT 4 [29]. The study population in this study was comparable to other studies in using the intent-to-treat definition that included those who discontinued treatment early. Compared to other VA studies, some differences in baseline characteristics were observed that could be important for the interpretation of SVR rates. First, the percentage of African Americans in this cohort was higher than in other VA studies (i.e. 59% in this study vs. 39%, Backus et al.; 34%, Fox et al.; and 29%, Ioannou et al.) [22, 26, 29]. Second, this study cohort had higher percentages of patients with depression and diabetes, but lower percentages of patients with HIV-co infection compared with the above studies. Third, about 30–35% of patients with cirrhosis were observed among all these findings. While the other three studies reported negative impact on response rates in patients with cirrhosis, patients with cirrhosis in our study did not have an attributably lower SVR than patients without cirrhosis as the SVR rates were 95.6% in both groups.

Table 2 showed that SVR rates of EBR/GZR were 95% or higher across many patient subgroups including GTs, those with HIV-coinfection, cirrhosis, history of drug/alcohol abuse, and moderate to severe CKD. Although several studies of other DAAs demonstrated negative impact of high viral load, African American race, cirrhosis, decompensated liver disease, and those with concomitant proton pump inhibitors (PPI) upon treatment response among those treated with LDV/SOF in the VA [25, 26]. In contrast, we observed slightly higher SVR rates among African Americans compared to the overall cohort. Our findings reported a slightly lower SVR rate of 92.5% in patients with high viral load compared with SVR overall. In addition, high SVR was achieved in HCV-infected patients with CKD across all CKD stages. One-third of patients treated had CKD stage 3–5, which was higher than those treated with other all-oral DAAs observed in literature (i.e. 6.9%−27.3%) [37, 38]. Our results suggest that HCV can be effectively treated among these highly vulnerable patients with CKD or in the high-risk population. Finally, although the US FDA labelling of EBR/GZR is not indicated for those with prior exposure to NS5A DAAs or those with decompensated cirrhosis, about 5% had prior use of NS5A and 14% had decompensated cirrhosis. Our finding reported slightly lower SVR rates than overall in patients with prior exposure to LDV/SOF or PrOD (i.e. 82.9%−88.6%) during the first six months after the approval.

Our study has several strengths. First, we used data from the nationwide VA database, which is the largest integrated healthcare data source for patients with HCV, including those who are racially and clinically diverse. Second, missing data is relatively low because the VA healthcare system has an established electronic medical record system as well as a robust pharmacy benefits management system including prescriptions data across all VA facilities. However, this study is subject to certain limitations. The VA population may not be

generalizable to the entire U.S. population due to the potential for differing demographic risk factors. Misclassification bias may exist, as diagnoses and co-morbidities were identified through ICD-9/10 codes. Sample sizes were low for some subgroups (i.e. EBR/GZR+RBV for 16 weeks) and larger studies are needed to determine more robust results. Additionally, some laboratory data, including data on the presence of baseline NS5A resistance-associated substitutions (RAS), was not available at the time of this analysis. Adverse events data was also not available in this study. Future studies are needed to examine the impact of RAS and RBV on real-world effectiveness of EBR/GZR.

In conclusion, EBR/GZR regimens were highly effective, with an overall SVR of 96% and 97% in the EP and PP cohorts, respectively. SVR rates were high across patient subgroups regardless of gender, race/ethnicity, presence of cirrhosis, history of drug or alcohol abuse, renal impairment, or HIV co-infection. This studied provides important data regarding the effectiveness of EBR/GZR in a large clinical setting.

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Abbreviations

BOC	boceprevir
CI	confidence interval
CKD	chronic kidney disease
DAA	direct-acting antiviral agent
EBR/GZR	elbasvir/grazoprevir
eGFR	estimated glomerular filtration rate
EP	evaluable population
FDA	Food and Drug Administration
GT	genotype
HCV	hepatitis C virus
LDV	ledipasvir
MDRD	Modification of Diet in Renal Disease
Peg-IFN	pegylated interferon

PP	per protocol
PPI	proton pump inhibitor
PrOD	ombitasvir/paritaprevir/ritonavir/dasabuvir
RAS	resistance-associated substitution
RBV	ribavirin
SIM	simeprevir
SOF	sofosbuvir
SVR	sustained virologic response
TEL	telaprevir
VA	Veterans Affairs
VA CDW	Veterans Affairs Corporate Data Warehouse

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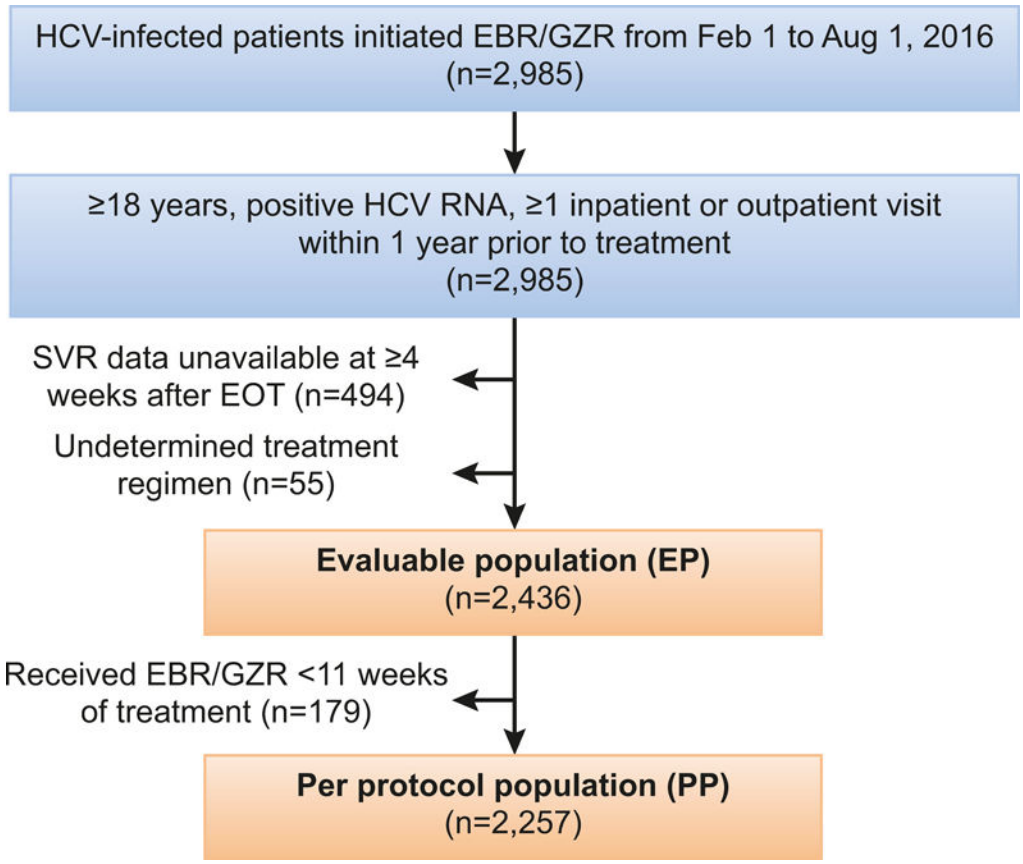

Fig. 1.
Study cohort diagram

Table 1.

Baseline and clinical characteristics among chronic HCV-infected patients treated with EBR/GZR in the evaluable population

Characteristics	EBR/GZR N=2246	EBR/GZR+ RBV N=156	EBR/GZR+ SOF+/−RBV n = 34	All patients N=2436	P-value[+]
Age, mean (S.D.)	63.7 (5.9)	61.9 (6.6)	63.6 (5.5)	63.5 (5.9)	0.003
Race/ethnicity, N (%)					
White (non-Hispanic)	726 (32.3)	80 (51.3)	18 (53.0)	824 (33.8)	N/A[*]
African American	1321 (58.8)	65 (41.7)	14 (41.2)	1400 (57.5)	
Hispanic	77 (3.4)	3 (1.9)	1 (2.9)	81 (3.3)	
Others	33 (1.5)	1 (0.6)	1 (2.9)	35 (1.4)	
Missing	89 (4.0)	7 (4.5)	0 (0)	96 (4.0)	
Male, N (%)	2169 (96.6)	148 (94.9)	33 (97.1)	2350 (96.5)	0.529
Genotype, N (%)					
GT1a	699 (31.1)	122 (78.2)	23 (67.6)	844 (34.7)	N/A[*]
GT1b	1399 (62.3)	25 (16.0)	4 (11.8)	1428 (58.6)	
GT1 unknown subtype	42 (1.9)	5 (3.2)	5 (14.7)	52 (2.1)	
GT2	2 (0.1)	0 (0)	0 (0)	2 (0.1)	
GT3	1 (0.04)	1 (0.6)	2 (5.9)	4 (0.2)	
GT4	62 (2.7)	2 (1.3)	0 (0)	64 (2.6)	
Missing GT	41 (1.8)	1 (0.7)	0 (0)	42 (1.7)	
Treatment-naïve, N (%)	1853 (82.5)	133 (85.3)	2 (5.9)	1988 (81.6)	<0.001
Treatment-experienced, N (%)	393 (17.5)	23 (14.7)	33 (94.1)	448 (18.4)	
Prior interferon	314 (14.0)	1 (0.6)	1 (2.9)	316 (13.0)	
Prior BOC/TEL	6 (0.3)	0 (0)	0 (0)	6 (0.2)	
Prior SIM+SOF, SOF	5(0.2)	4 (2.6)	0 (0)	9 (0.4)	
Prior LVD/SOF and PrOD	68 (3.0)	18 (11.5)	31 (91.2)	117 (4.8)	
Deyo Charlson Comorbidity Index - mean (S.D.)	2.3 (2.6)	1.9 (2.2)	1.2 (1.3)	2.3 (2.5)	0.042
Anxiety, N (%)	640 (28.5)	47 (30.1)	11 (32.4)	698 (28.7)	0.810
Cirrhosis, N (%)	699 (31.1)	47 (30.1)	20 (58.8)	766 (31.4)	0.002
Compensated cirrhosis, N (%)	400 (17.8)	23 (14.7)	11 (32.4)	434 (17.8)	0.052
Decompensated cirrhosis, N (%)	299 (13.3)	24 (15.4)	9 (26.5)	332 (13.6)	0.069
Ascites, N (%)	83 (3.7)	10 (6.4)	2 (5.9)	95 (3.9)	0.199
Hepatic encephalopathy, N (%)	129 (5.7)	6 (3.9)	1 (2.9)	136 (5.6)	0.484
Depression, N (%)	1279 (57.0)	92 (59.0)	23 (67.7)	1394 (57.2)	0.412
Hepatocellular carcinoma, N,(%)	45 (2.0)	4 (2.6)	3 (8.8)	52 (2.1)	0.039
Diabetes, N (%)	1208 (53.8)	73 (46.8)	14 (41.2)	1295 (53.2)	0.088
History of drug abuse, N (%)	1202 (53.5)	91 (58.3)	20 (58.8)	1313 (53.9)	0.428
History of alcohol abuse, N (%)	1361 (60.6)	93 (59.6)	19 (55.9)	1473 (60.5)	0.834

Characteristics	EBR/GZR N=2246	EBR/GZR+ RBV N=156	EBR/GZR+ SOF+/−RBV n = 34	All patients N=2436	P-value[+]
HIV, N (%)	68 (3.0)	6 (3.9)	0 (0)	74 (3.0)	0.566
History of kidney transplant, N (%)	33 (1.5)	1 (0.6)	1 (3.0)	35 (1.4)	0.478
History of liver transplant, N (%)	13 (0.6)	1 (0.6)	0 (0)	14 (0.6)	0.680
eGFR, Mean (S.D.)	68.9 (35.8)	75.6 (36.9)	96.9 (25.8)	69.7 (35.9)	<0.001
CKD stage 3–5, N (%)	759 (33.8)	37 (23.7)	4 (11.8)	800 (32.8)	0.014
Baseline HCV RNA ≥6M IU/ml[*], N (%) (missing n = 110)	373 (16.6)	23 (14.7)	4 (11.8)	400 (16.4)	0.522

[+] Fisher's exact test calculated for variables with sample size less than 5.

[*] Insufficient memory space to process Fisher exact test.

Table 2.

SVR in patients treated with EBR/GZR+/− RBV (all genotypes) by baseline characteristics in the evaluable population (N=2,436)

Characteristics	N	N	SVR (%)	Confidence Interval
All patients (SVR)	2328	2436	95.6%	94.7%−96.4%
Gender				
Male	2245	2350	95.5%	94.6%−96.3%
Female	83	86	96.5%	90.1%−99.3%
Age				
>65 years	828	866	95.6%	94.0%−96.9%
≤65 years	1500	1570	95.5%	94.4%−96.5%
Cirrhosis				
No	1556	1628	95.6%	94.5%−96.5%
Yes	732	766	95.6%	93.9%−96.9%
Compensated	420	434	96.8%	94.6%−98.2%
Decompensated	312	332	94.0%	90.9%−96.3%
Race				
African American	1342	1400	95.9%	94.7%−96.8%
Hispanic	77	81	95.1%	87.8%−98.6%
White	783	824	95.0%	93.3%−96.4%
Other	33	35	94.3%	80.8%−99.3%
Missing race	93	96	96.9%	91.1%−99.4%
Genotype				
Genotype 1 (all)	2218	2324	95.4%	94.5%−96.3%
Genotype 1a	788	844	93.4%	91.5%−94.9%
Genotype 1b	1379	1428	96.6%	95.5%−97.5%
Genotype 2 or 3	6	6	100.0%	54.1%−100%
Genotype 4	62	64	96.9%	89.2%−99.6%
Unknown genotype	42	42	100.0%	91.6%−100%
Treatment history				
Treatment-naïve	1910	1988	96.1%	95.1%−96.9%
Treatment-experienced (IFN or BOC/TEL)	310	322	96.3%	93.6%−98.1%
Treatment-experienced (including all-oral DAAs)	418	448	93.3%	90.6%−95.4%
LDV/SOF	68	82	82.9%	73.0%−90.3%
PrOD	31	35	88.6%	73.3%−96.8%
SIM+SOF, SOF+RBV	9	9	100.0%	66.3%−100%
BOV/TEL	5	6	83.3%	35.9%−99.6%
IFN+/−RBV	305	316	96.5%	93.9%−98.2%
CKD*				

Characteristics	N	N	SVR (%)	Confidence Interval
eGRF ≥60ml	1533	1611	95.2%	94.0%−96.2%
Stage 3 CKD	380	393	96.7%	94.4%−98.2%
Stage 4–5 CKD	392	407	96.3%	94.0%−97.9%
HIV				
Positive	73	74	98.6%	92.7%−99.9%
Negative	2255	2362	95.5%	94.6%−96.3%
History of drug abuse				
Yes	1251	1313	95.3%	94.0%−96.4%
No	1077	1123	95.9%	94.6%−97.0%
History of alcohol abuse				
Yes	1412	1473	95.9%	94.7%−96.8%
No	916	963	95.1%	93.6%−96.4%
Baseline HCV RNA				
≥6M IU/ml	370	400	92.5%	89.5%−94.9%
<6M IU/ml	1853	1926	96.2%	95.3%−97.0%

* Patients without 2 or more eGFR values are not included in this subgroup.

Table 3.

SVR by treatment regimen and prior HCV treatment among GT1- and GT4 HCV-infected patients in the evaluable population

		Treatment-naïve		Treatment-experienced (Peg-IFN+RBV, BOC, TEL)		Total
	N	%	N	%	N	%
Genotype 1 (n=1915)						
Overall	1605/1668	96.2	237/247	96.0	1842/1915	96.2
By regimen						
EBR/GZR	1501/1555	96.5	236/246	95.9	1737/1801	96.4
EBR/GZR+RBV	104/113	92.0	--	--	104/113	92.0
EBR/GZR+SOF+/−RBV	--	--	1/1	100	1/1	100
By treatment regimen						
EBR/GZR 12 wk	1387/1416	98.0	208/213	97.7	1595/1629	97.9
EBR/GZR 16 wk	28/28	100	16/18	88.9	44/46	95.7
EBR/GZR+RBV 12 wk	74/79	93.7	--	--	74/79	93.7
EBR/GZR+RBV 16 wk	27/31	87.1	--	--	27/31	87.1
EBR/GZR+SOF+/−RBV 12 wk	--	--	1/1	100	1/1	100
Genotype 4 (n=59)						
Overall	53/54	98.2	5/5	100	58/59	98.3
By regimen						
EBR/GZR	51/52	98.1	5/5	100	56/57	98.2
EBR/GZR+RBV	2/2	100	--	--	2/2	100
By treatment regimen						
EBR/GZR 12 wk	49/49	100	1/1	100	50/50	100
EBR/GZR 16 wk	--	--	2/2	100	2/2	100
EBR/GZR+RBV 12 wk	--	--	--	--		
EBR/GZR+RBV 16 wk	2/2	100	--	--	2/2	100

Note: excluding decompensated cirrhosis.