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Letter to the Editor

High Real-World Sustained Virologic Response Rate with Glecaprevir/Pibrentasvir at a Racially Diverse Urban Academic Medical Center

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To the Editor:

We read with interest your recent publication by Park *et al.*[1] which described real-world glecaprevir/pibrentasvir use in Korean patients at a single institution. We would like to present additional real-world data on glecaprevir/pibrentasvir use.

Hepatitis C virus (HCV) affects about 1% of the American population and is the most common blood-borne infection in the United States.[2] It disproportionately affects non-White racial groups in the United States. Recent HCV prevalence data estimate that non-Hispanic African American/Black patients account for a higher share of the HCV infections in the United States compared to other ethnic/racial groups (1.8% vs 0.8%; relative risk=2.2).[3]

Non-Hispanic African American/Black individuals represent 13.4% of the United States population per the 2019 census, yet 23% of HCV infections occurred within this racial group between 2013 and 2016.[3,4] About 18.5% of Americans are of Hispanic/LatinX ethnic origin per the 2019 census; 6% of known-race, newly reported chronic HCV infections occurred within this group in 2019.[4,5] The Centers for Disease Control and Prevention remarked that non-Hispanic African American/Black and Hispanic individuals had the most notable relative increase in HCV rates from 2010 to 2019.[5]

Despite differences in infection rates among racial and ethnic groups, clinical trial data for direct-acting antivirals often include mostly White patients. Potential reasons for lack of racially diverse clinical trial participation include lack of understanding the value of participation, fear of new treatment and/or stigma of participating, financial burden, transportation, and time commitment.

Treatment with glecaprevir/pibrentasvir demonstrated high success in phase 2 and 3 clinical trials with sustained virologic response (SVR) rates greater than 97%. Pooled clinical trial data from 1,248 patients who received 8-week treatment courses from eight phase 2 and 3 trials predominantly included White (79.6%) and non-Hispanic (89.2%) participants.[6] One phase 3b clinical trial included a high percent of Black patients (44%) compared to other trials. However, this trial had a narrow focus, specifically on the use of glecaprevir/pibrentasvir in 177 patients after treatment failure with sofosbuvir-based treatment regimens.[7]

Published multi-site cohort data on glecaprevir/pibrentasvir use in Japanese, German, Polish, and Italian centers are available, but they do not represent the racially and ethnically diverse patient populations that comprise the United States.[4,8-11] It is important to demonstrate effectiveness and safety with medication use across races and ethnicities. Our real-world experience offers insight on clinical outcomes with use of

glecaprevir/pibrentasvir in a diverse patient population.

Authors at an urban academic medical center performed a retrospective cohort review of the electronic medical records of adult patients from the UI Health Liver Clinic who were prescribed chronic HCV treatment with glecaprevir 300 mg/pibrentasvir 120 mg daily for 8 or 12 weeks from August 2017 through August 2020. Data were collected and managed using electronic data capture tools hosted at the University of Illinois at Chicago. The data collected included baseline characteristics, comorbidities, HCV treatment-related details, and laboratory values throughout treatment and until SVR was assessed. Statistical analysis was descriptive; counts and percentages were presented for categorical variables and means and standard deviations were used for continuous data.

The study was approved by the Institutional Review Board of University of Illinois at Chicago (IRB number: 2020-0354). A waiver of consent authorization was granted for this retrospective chart review. The primary outcome was SVR, defined as an undetectable HCV RNA test result at least 12 weeks following completion of treatment with glecaprevir/pibrentasvir. Secondary outcomes included adverse drug reactions and safety.

Between September 2017 and August 2020, 155 patients aged 28 to 80 years old began HCV treatment with glecaprevir/pibrentasvir. Most patients were male (n=81, 52%), most were African American/Black (n=89, 57%; 87 of whom were non-Hispanic), and 24 (16%) patients were Hispanic/LatinX.

Most patients (69%) were prescribed 8 weeks of treatment; (31%) were prescribed 12 weeks. The indications for 12-week treatment included compensated cirrhosis with treatment prior to the approval for 8-week therapy in this population in 2019 (63%), history of solid organ transplant (33%), and prior treatment with a protease inhibitor (4%). Eight-week treatment was prescribed for treatment-naïve or interferon-experienced, non-cirrhotic patients, and after the guideline change, this group was expanded to include compensated cirrhotic patients in 2019. All 36 cirrhotic patients (23%) had compensated cirrhosis (Child-Turcotte-Pugh class A); 24 (66.7%) of whom were Black. See Table 1 for additional patient details and treatment outcomes.

Of the patients who started treatment, 94.1% achieved SVR. Excluding eight patients who were lost-to-follow-up and three patients who self-discontinued treatment early, 100% achieved SVR. Two of the three patients who self-discontinued treatment early still achieved SVR. One patient took 26 doses, was lost to follow up for months due to substance use and never refilled his medication, but later returned to clinic and achieved SVR. One patient received 8 of 12 prescribed weeks of therapy and was non-adherent; missed at least 9 doses in the first 8 weeks, but obtained SVR. The only patient (genotype 1a, Metavir F3) who did not achieve SVR took 4 weeks of medication intermittently and never refilled the medication to complete the prescribed 8-week course.

Of the 36 cirrhotic patients who started treatment, 16.7% received 8-week treatment and 83.3% received 12-week treatment. Thirty-four (94.4%) cirrhotic patients achieved SVR, and two (5.6%) Black cirrhotic patients who were prescribed 12 weeks of treatment were lost-to-follow-up. Table 1 shows patient SVR rates by intended length of therapy and treatment completion.

Overall rates of patient-reported fatigue and headache during treatment were 16.8% and 16.1%, respectively. No patients experienced serious adverse events, discontinued due to adverse events, or died during treatment.

The objective of our study was to report a diverse patient population's real-world SVR rate after treatment with glecaprevir/pibrentasvir. Treatment with this direct-acting antiviral regimen offered high SVR rates across all racial and ethnic groups.

Treatment length was 8 weeks for most patients. Twelve-week treatment was used mostly for post-transplant patients, and compensated cirrhotic patients who were treated prior to the manufacturer's label change on September 26, 2019 and the American Association for the Study of Liver Diseases and the Infectious Diseases Society of America (AASLD/IDSA) guideline change for the recommended treatment length to be 8 instead of the initially-recommended 12 weeks for treatment-naïve compensated cirrhotic patients.

Other published real-world studies primarily offer insight into racially homogeneous patient populations.[8-11] Our real-world SVR results increase the available literature on glecaprevir/pibrentasvir outcomes, including a patient population with a high total proportion of non-Hispanic Black and Hispanic White patients. Data were limited to chart documentation for patients at one urban academic medical center. Our proportion of Hispanic patients was similar to the proportion in the United States, and our proportion of Black patients was over 4-fold the proportion in the United States.[4]

HCV SVR rates were high after 8- and 12-week treatment courses with glecaprevir/pibrentasvir at our institution. Our data adds to available literature on real-world treatment outcomes of a racially diverse patient population.

Table 1. Baseline Characteristics and Treatment Outcomes (n=155)

Characteristic	All patients (n=155)	8-Week course (n=107)	12-Week course (n=48)
Age, mean±SD, yr	57.4±10.3	57.1±11.1	58.2±8.4
Born between 1945–1965	119 (76.8)	80 (74.8)	39 (81.3)
Sex			
Female	74 (47.7)	56 (52.3)	18 (37.5)
Male	81 (52.3)	51 (47.7)	30 (62.5)
Race/ethnicity			
African American/Black, non-Hispanic	87 (56.1)	60 (56.1)	27 (56.3)
Caucasian/White, non-Hispanic	35 (22.6)	24 (22.4)	11 (22.9)
Hispanic	24 (15.5)	16 (15.0)	8 (16.7)
Asian/Pacific Islander	7 (4.5)	5 (4.7)	2 (4.2)
Unknown race, non-Hispanic	2 (1.3)	2 (1.9)	0
Body mass index, mean±SD, kg/m^2	29.4±6.7	29.4±7.0	29.4±6.0
Body mass index			
<18.5 kg/m^2	5 (3.2)	4 (3.7)	1 (2.1)
18.5–24.99 kg/m^2	40 (25.8)	29 (27.1)	11 (22.9)
25–29.99 kg/m^2	45 (29.0)	28 (26.2)	17 (35.4)
30–39.99 kg/m^2	54 (34.8)	37 (34.6)	17 (35.4)
≥40 kg/m^2	11 (7.1)	9 (8.4)	2 (4.2)
HCV genotype			
1a	83 (53.5)	58 (54.2)	25 (52.1)
1b	43 (27.7)	33 (30.8)	10 (20.8)
1a-1b/mixed/indistinguishable	3 (1.9)	2 (1.9)	1 (2.1)
2	8 (5.2)	6 (5.6)	2 (4.2)
3	14 (9.0)	6 (5.6)	8 (16.7)
4	2 (1.3)	1 (0.9)	1 (2.1)
6	2 (1.3)	1 (0.9)	1 (2.1)
HCV treatment history			
Naïve	148 (95.5)	104 (97.2)	44 (91.7)
Experienced	7 (4.5)	3 (2.8)	4 (8.3)
Stage (non-cirrhotic)			
F0	13 (8.4)	9 (8.4)	4 (8.3)
F1	25 (16.2)	22 (20.6)	3 (6.3)
F2	38 (24.5)	33 (30.8)	5 (10.5)
F3	38 (24.5)	36 (33.6)	2 (4.2)
F0-F3 (non-cirrhotic)	5 (3.2)	1 (0.9)	4 (8.3)
Cirrhotic (all Child-Turcotte-Pugh class A)	36 (23.2)	6 (5.6)	30 (62.5)
Comorbid psychiatric illness	47 (30.3)	33 (30.8)	14 (29.2)
History of hepatocellular carcinoma	6 (3.9)	1 (0.9)	5 (10.4)
History of solid organ transplant	16 (10.3)	0	16 (33.3)
Concurrent medication for opioid use disorder	20 (6.0)	16 (15.0)	4 (8.3)
Hemodialysis	5 (3.2)	4 (3.7)	1 (2.1)
Hepatitis B virus coinfection	2 (1.3)	0	2 (4.3)
HIV coinfection	5 (3.2)	3 (2.8)	2 (4.3)
Insurance			
Medicaid	95 (61.3)	63 (58.9)	32 (66.7)
Medicare part D	33 (21.3)	24 (22.4)	9 (18.8)
Private/commercial	26 (16.8)	19 (17.8)	7 (14.6)
No Insurance	1 (0.6)	1 (0.9)	0
Treatment course and outcomes			
Overall SVR rate (intent-to-treat)	146 (94.1)	100 (93.5)	46 (95.8)
Completed full treatment course	144 (92.9)	99 (92.5)	45 (93.8)
SVR (full treatment completion)	144 (100)	99 (100)	45 (100)
Early self-discontinuation of treatment	3 (1.9)	2 (1.9)	1 (2.1)
SVR (early discontinuation)	2 (66.7)	1 (50.0)	1 (100)
Lost-to-follow-up	8 (5.2)	6 (5.6)	2 (4.2)

Data are presented as number (%) unless otherwise indicated.
HCV, hepatitis C virus; HIV, human immunodeficiency virus; SVR, sustained virologic response.

CONFLICTS OF INTEREST

M.T.M. serves on the speakers' bureau for AbbVie, has received grant funding from Gilead and Merck, served on the advisory board for AbbVie and Gilead, and is a minor shareholder of AbbVie, Gilead, and Merck stock. N.W. and A.N. do not have any conflicts of interest to disclose.

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Some patients may have received off-label use of glecaprevir/pibrentasvir.

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