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Real-world Experience of Sotrovimab in High-risk, Immunocompromised COVID-19 Patients

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We completed a real-world analysis of 498 consecutive high-risk nonimmunocompromised and immunocompromised patients who received sotrovimab during the B.1.1.529 surge. Emergency department visits/hospitalizations and 30-day all-cause mortality between the 2 groups were similar. When administered early, sotrovimab is effective at preventing coronavirus disease 2019 progression in immunocompromised and nonimmunocompromised patients.

Keywords. COVID-19; monoclonal antibody; sotrovimab; immunocompromised hosts; outcomes.

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has resulted in >5.8 million deaths worldwide and >900 000 deaths in the United States [1]. Monoclonal antibodies (MABs) have been evaluated to treat COVID-19 in the outpatient setting to prevent disease progression and subsequent hospitalization in high-risk patients. MABs block the interaction between viral proteins and human cells, preventing the viral agents from entering the target cells [2]. They are most effective when utilized early in COVID-19 [2].

The Omicron (B.1.1.529) variant was first detected in November 2021 and quickly became the dominant SARS-CoV-2 variant [3]. This variant has significant mutations, including 37 substitutions in the spike protein, the majority clustered in the receptor-binding domain (RBD) [3]. The main target of MAB is the RBD, and these mutations in B.1.1.529 made many MAB therapies ineffective, including the combination therapies casirivimab/imdevimab and bamlanivab/etesevimab [3]. Sotrovimab, an engineered human MAB, retained activity against B.1.1.529 through recognition of antigenic sites outside the RBD [3]. The registration clinical trial demonstrated the effectiveness of sotrovimab in preventing hospitalizations in high-risk COVID-19 patients [4]. However, there are no reports that have examined the effectiveness specifically in high-risk immunocompromised patients.

By December 31, 2021, B.1.1.529 became the dominant variant in the United States [1]. At Henry Ford Health System (HFHS) in Michigan, sotrovimab has been the only MAB administered under Food and Drug Administration (FDA) Emergency Use Authorization (EUA) since December 27, 2021, due to the rapid increase in cases of B.1.1.529. We report our real-world experience with sotrovimab in immunocompromised and nonimmunocompromised patients with COVID-19 at high risk for disease progression.

METHODS

We performed a retrospective analysis of high-risk patients with COVID-19 who were referred for sotrovimab treatment from December 27, 2021, to January 3, 2022. All patients were >18 years of age and had a positive SARS-CoV-2 test by polymerase chain reaction or antigen. All patients received a 500-mg infusion of sotrovimab within 10 days of symptom onset.

High risk was defined as patients with any of the following conditions identified in the FDA EUA: age >65 years, body mass index (BMI) >30, pregnancy, chronic lung disease, diabetes, cardiovascular disease, end-stage renal disease on dialysis, and immunosuppressive disease or immunosuppressive treatment [5]. Immunocompromised patients were defined as those with primary immunodeficiency, people with HIV, organ transplant recipients, or those receiving chemotherapy, biologic immunomodulators, immunosuppressive drugs, or high-dose corticosteroids [6]. Demographic data, underlying comorbidities, and COVID-19 vaccination status were collected. A descriptive analysis was performed of all consecutive patients who met study inclusion criteria. The primary outcome was emergency department (ED) visits and/or hospitalizations, and the secondary outcome was all-cause mortality. All outcomes were measured at 30 days after administration of sotrovimab. Additionally, we completed a nested case–control analysis to compare outcomes of immunocompromised patients with those of nonimmunocompromised patients.

RESULTS

Of the 498 patients who met inclusion criteria, 88 patients were classified as immunocompromised and 410 as nonimmunocompromised. Patient characteristics are shown in Table 1.

Table 1. Characteristics and Outcomes in Immunocompromised vs Nonimmunocompromised Patients Receiving Sotrovimab

	Total (n = 498)	Immunocompromised (n = 88)	Nonimmunocompromised (n = 410)	P Value
Male, No. (%)	181 (36.3)	34 (38.6)	147 (35.9)	.622
Age, median (IQR), y	64 (40–74)	60.5 (44.5–71)	65 (40–74.75)	.434
Age >65 y, No. (%)	246 (49.4)	210 (51.2)	36 (40.9)	.079
Self-reported race/ethnicity				
Black, No. (%)	138 (27.7)	22 (25)	116 (28.3)	.531
White, No. (%)	300 (60.2)	60 (68.2)	240 (58.5)	.093
Other, No. (%)	41 (8.2)	5 (5.7)	36 (8.8)	.337
Unknown, No. (%)	19 (3.8)	1 (1.1)	18 (4.4)	.221
BMI,[a] median (IQR), kg/m^2	31.1 (26.5–39)	29.4 (26.1–34.7)	31.6 (26.6–39.5)	.020
Cardiac risk factors,[b] No. (%)	315 (63.3)	59 (67.0)	256 (62.4)	.416
Pulmonary risk factors,[c] No. (%)	160 (32.1)	23 (26.1)	137 (33.4)	.185
Diabetes, No. (%)	115 (23.1)	28 (31.8)	87 (21.2)	.032
CKD/ESRD, No. (%)	62 (12.4)	23 (26.1)	39 (9.5)	<.001
Pregnancy, No. (%)	52 (10.4)	2 (2.3)	50 (12.2)	.003
Symptoms to dose, median (IQR), d	5 (4–7)	5 (4–6.25)	5 (4–7)	.272
Vaccinated (≥1 dose), No. (%)	334 (67.1)	74 (84.1)	260 (63.4)	<.001
COVID-related ED visit or admission, No. (%)	11 (2.2)	4 (4.5)	7 (1.7)	.111
COVID-related admission, No. (%)	8 (1.6)	4 (4.5)	4 (1.0)	.036
COVID-related ED visit, No. (%)	3 (0.6)	0 (0)	3 (0.7)	.421
Death, No. (%)	3 (0.6)	2 (2.3)	1 (0.2)	.082

Abbreviations: BMI, body mass index; CKD, chronic kidney disease; ED, emergency department; ESRD, end-stage renal disease; IQR, interquartile range.

[a]Calculated as weight in kilograms divided by height in meters squared.

[b]Included myocardial infarction, coronary disease, hyperlipidemia, hypertension, or congestive heart failure.

[c]Included asthma, chronic obstructive pulmonary disease, or obstructive sleep apnea.

The immunocompromised group included patients with rheumatological diseases, multiple sclerosis, HIV infection, hematological malignancy, solid organ malignancy, inflammatory bowel disease, interstitial lung disease, and organ transplant recipients. The immunocompromised group had lower median BMI, higher rates of diabetes, chronic kidney disease or end-stage renal disease, lower rates of pregnancy, and were more likely to be vaccinated. The rest of the demographics and underlying comorbidities were comparable in both groups.

Overall, the primary outcome was met in 11 patients (2.2%), ED visits in 3 patients (0.6%), and hospital admissions in 8 patients (1.6%). Death occurred in 3 patients (0.6%). In the immunocompromised group, the primary outcome was met in 4 patients (4.5%), compared with 7 patients (1.7%) in the nonimmunocompromised group (P .111). All the immunocompromised patients were hospitalized, compared with 4 patients (1.0%) in the nonimmunocompromised group (P = .036). Thirty-day all-cause mortality occurred in 2 patients (2.3%) in the immunocompromised group, compared with 1 patient (0.2%) in the nonimmunocompromised group (P = .082). No immediate adverse events were observed after sotrovimab administration.

DISCUSSION

Our real-world study of 498 patients demonstrates the effectiveness of sotrovimab in preventing hospitalizations and mortality in immunocompromised and high-risk nonimmunocompromised COVID-19 patients.

Previous studies have not evaluated the effectiveness of sotrovimab, specifically in immunocompromised patients at high risk for COVID-19 disease progression. In the COMET-ICE registration trial [4], of 291 patients administered sotrovimab, 1% of patients were hospitalized and 0 patients died (Supplementary Table 1). Compared with our study, overall, 1.6% of patients were hospitalized and 0.6% died. The slightly higher rate of hospitalization and death in our real-world study can be accounted for by the higher rate of median comorbidities, older age, and later administration of sotrovimab. While COMET-ICE patients had a median of 1 high-risk comorbidity, our patients had a median of 3. The median age in COMET-ICE was 53 years, and our patients' median age was 64 years. The median time to dose in COMET-ICE was documented as <3 days, and our median time to dose was 5 days. COMET-ICE did not report on outcomes in immunocompromised patients. We found no significant difference in ED visits and hospitalizations between the immunocompromised and nonimmunocompromised groups. All patients who presented to the hospital in the immunocompromised group were hospitalized; however, there was no significant difference in 30-day all-cause mortality between the 2 groups.

Other studies investigating sotrovimab include the TICO trial [7]. This study found no significant difference in patients administered sotrovimab compared with placebo; however, the population studied was hospitalized patients, and sotrovimab

was administered 8 days from symptom onset, later than an average of 5 days in our population [7].

Our study is limited due to its retrospective nature and limited sample size. Due to logistical issues, we were not able to compare COVID-19-positive patients who did not receive sotrovimab with those who did. In our study, 67.07% of patients were vaccinated, and it is unknown what effect this has on studied outcomes. Additionally, we could not analyze the role of COVID-19 seropositivity in all patients.

We conclude that in a real-world setting, early administration of sotrovimab has low rates of COVID-19 disease progression among high-risk patients, including those who are immunocompromised.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Acknowledgments

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