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# Real-world Clinical Outcomes of Bebtelovimab and Sotrovimab Treatment of High-risk Persons With Coronavirus Disease 2019 During the Omicron Epoch

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***Background.*** Antispike monoclonal antibodies are recommended for early treatment of high-risk persons with mild to moderate coronavirus disease 2019 (COVID-19). However, clinical outcomes of their use during the severe acute respiratory syndrome coronavirus 2 Omicron wave are limited.

***Methods.*** This is a descriptive retrospective study of high-risk adult patients who received treatment with sotrovimab (January 1–March 20, 2022) or bebtelovimab (March 21–April 30, 2022). The primary outcome was the proportion of patients who progressed to severe outcome within 30 days after receiving antispike-neutralizing monoclonal antibody infusion.

***Results.*** A total of 3872 high-risk patients (median age, 62.7 years; 41.1% male) with mild to moderate COVID-19 received sotrovimab (n = 2182) or bebtelovimab (n = 1690). Among sotrovimab-treated patients, the most common comorbidities were an immunosuppressed condition (46.7%), hypertension (38.2%), and diabetes (21.2%). The rates of severe outcome, intensive care unit (ICU) admission, and mortality were 2.2%, 1.0%, and 0.4%, respectively, after sotrovimab infusion. Among bebtelovimab-treated patients, the most common comorbidities were hypertension (42.7%), diabetes (17.1%), and an immunosuppressed condition (17.0%). The rates of severe disease, ICU admission, and mortality were 1.3%, 0.5%, and 0.2%, respectively, after bebtelovimab infusion. Older age, immunosuppressed status, and several comorbidities were associated with severe disease progression, while COVID-19 vaccination was associated with lower risk. No anaphylaxis was reported during monoclonal antibody infusion.

***Conclusions.*** This real-world analysis of a large cohort of high-risk patients demonstrates low rates of severe disease after treatment with sotrovimab during the era dominated by Omicron B.1.1.529 and after treatment with bebtelovimab during the era dominated by BA.2 and Omicron subvariants.

**Keywords.** bebtelovimab; sotrovimab; COVID-19; monoclonal antibodies; hospitalization.

Antispike-neutralizing monoclonal antibodies are effective for early treatment of high-risk persons with mild to moderate coronavirus disease 2019 (COVID-19) [1]. Randomized controlled trials have shown that early treatment with bamlanivimab-etesevimab, casirivimab-imdevimab, or sotrovimab results in reduction in hospitalization rates and death [2–4]. These clinical benefits have been shown in real-world

settings among large cohorts of patients treated under US Food and Drug Administration (FDA) Emergency Use Authorization (EUA) [5–8].

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) continues to evolve into variants of concern (VOC) characterized by spike protein mutations that allow the virus to escape monoclonal antibody–mediated neutralization [9]. The spike mutations of SARS-CoV-2 Omicron variants made bamlanivimab-etesevimab and casirivimab-imdevimab ineffective for treatment [9]. However, pseudovirus experiments have demonstrated that sotrovimab maintained activity against SARS-CoV-2 Omicron (B.1.1.529), making it the only antispike-neutralizing monoclonal antibody recommended for treatment in January 2022. Further evolution of SARS-CoV-2 Omicron led to the emergence of several subvariants, including BA.2, that escape neutralization by sotrovimab [9, 10]. On April 5, 2022, the FDA rescinded the EUA for sotrovimab when the US Centers for Disease Control

and Prevention (CDC) estimated that the proportion of COVID-19 cases caused by the SARS-CoV-2 Omicron BA.2 variant exceeded 50% in all US regions [11]. Based on limited data, the FDA granted EUA for bebtelovimab as an alternative antispike monoclonal antibody for treatment of high-risk persons with mild to moderate COVID-19 on February 11, 2022 [12]. Pseudovirus experimental data suggest that bebtelovimab maintains activity against SARS-CoV-2 Omicron subvariants [9], but the clinical data to support its use are very limited. In this report, we describe the clinical characteristics and outcomes of high-risk patients who received treatment with sotrovimab during the period dominated by SARS-CoV-2 Omicron B.1.1.529 or bebtelovimab during the period dominated by BA.2 and its subvariants.

## METHODS

### Study Period and Setting

The Mayo Clinic is an integrated health care delivery network serving >1 million patients each year across Southern Minnesota, Northeastern Iowa, Western Wisconsin, and the metropolitan areas of Jacksonville, Florida, and Phoenix, Arizona. On November 7, 2020, the Mayo Clinic established its Monoclonal Antibody Treatment (MATRx) program to administer antispike monoclonal antibodies to high-risk patients with mild to moderate COVID-19. The MATRx program, protocols, and procedures have been described [13]. Real-world clinical outcomes of antispike monoclonal antibody treatment of patients treated by MATRx before the SARS-CoV-2 Omicron wave have been reported [5–8]. For this study, only patients who received treatment during a 4-month period between January 1 and April 30, 2022, were included. Based on guidance from the FDA, the MATRx program switched to sotrovimab as its sole monoclonal antibody treatment option when Omicron B.1.1.529 became the dominant variant on January 1, 2022. With the impending surge of the BA.2 Omicron subvariant, the MATRx program switched to bebtelovimab as the only antispike monoclonal antibody treatment option starting the week of March 21, 2022, which was 2 weeks before the FDA rescinded the EUA for sotrovimab on April 5, 2022.

### Study Population and Design

This was a descriptive retrospective study of adult patients, 18 years or older, who were identified from the Mayo Clinic electronic health records (EHRs) as having received treatment with sotrovimab or bebtelovimab between January 1 and April 30, 2022. All patients were followed for at least 30 days, with May 30, 2022, as the end period for this analysis. Although high-risk adolescents aged 12–<18 years received antispike monoclonal antibody therapies, they were not included in this study due to differences in eligibility criteria. For this descriptive study, the population was divided into 2 separate and independent cohorts (bebtelovimab or sotrovimab cohort) based on the specific neutralizing monoclonal antibody received.

### Antispike Monoclonal Antibodies

Sotrovimab and bebtelovimab were distributed to our facilities by the federal government. The specific neutralizing monoclonal antibody administered to an eligible patient was based solely on the FDA-recommended product during the date of treatment. Sotrovimab (500-mg dose as a 1-time infusion) was used solely from January 1 until the week of March 21, 2022, when the program switched to bebtelovimab (175 mg intravenously over 1 minute). All patients received education about the specific neutralizing monoclonal antibody product, the potential benefits and adverse effects, and the EUA and investigational status. All patients provided consent for treatment with the antispike-neutralizing monoclonal antibody products.

### Clinical Eligibility Criteria and Risk Factor Scores

Adult patients were eligible to receive antispike-neutralizing monoclonal antibodies if they had mild to moderate COVID-19 confirmed by a positive SARS-CoV-2 polymerase chain reaction or antigen test and were within 7 days of symptom onset. Asymptomatic patients were not eligible for treatment. In compliance with the FDA EUA criteria, patients had to have ≥1 of the following criteria: age ≥65 years, body mass index (BMI) >25 kg/m$^2$, immunocompromised status, pregnancy, hypertension, diabetes mellitus, chronic kidney disease, chronic lung disease, cardiovascular disease, sickle cell disease, neurodevelopmental disorders, or medico-technological dependence [14]. In November 2020, our MATRx program developed a Monoclonal Antibody Screening Score (MASS) [15–17]. MASS assigned points to each of the initial eligibility criteria set forth by the FDA in November 2020, with subsequent modifications as follows: age ≥65 (2 points), BMI ≥35 (1 point), diabetes mellitus (2 points), chronic kidney disease (3 points), cardiovascular disease in a patient age ≥55 years (2 points), chronic respiratory disease in a patient age ≥55 years (2 points), hypertension in a patient age ≥55 years (1 point), and immunocompromised status (4 points). For this study, we used MASS and Charlson Comorbidity Index scores as composite measures of high-risk characteristics or medical comorbidity.

### Outcome

The primary outcome of this descriptive study, which was assessed separately for the 2 treatment cohorts, was the proportion of patients who progressed to severe outcomes within 30 days after receiving antispike-neutralizing monoclonal antibody infusion. "Severe outcome" was defined according to the World Health Organization (WHO) Ordinal Scale of ≥4 (hospitalized and requiring oxygen supplementation by mask or nasal prongs, invasive mechanical ventilation, extracorporeal membrane

oxygenation, and death). Variables associated with severe outcomes were assessed for the 2 antibody treatment cohorts. In addition, we described the proportion of patients who required an intensive care unit (ICU) level of care and all-cause mortality at day 30 as secondary outcomes.

### Patient Consent

The Mayo Clinic Institutional Review Board reviewed this study and designated it as exempt. Patient consent was waived and not required for this study. However, per Minnesota law, only patients who had previously provided research authorization were included in this study.

### Statistical Analysis

The baseline demographics, clinical characteristics, and outcomes of patients who received infusions with sotrovimab or bebtelovimab were separately described using standard descriptive statistics including mean, median, interquartile range (IQR), percentage, and 95% confidence interval. As appropriate, groups were compared using a Kruskal-Wallis rank-sum test, Fisher exact test, or Pearson chi-square test, as appropriate, and adjusted for multiple comparisons. Analyses were performed using the Rstudio integrated development environment [18]. Charlson Comorbidity Index features were computed using the comorbidity package (version 1.0.2) [19]. Tables were generated using the Arsenal package (version 3.6.3) [20]. Univariate hazard ratios were generated using the modelsum function of Arsenal and visualized with the forestploter package in R. Statistical significance was set at $P < .05$.

## RESULTS

### Patient Population

During the 4-month study period, a total of 3872 high-risk patients with mild to moderate COVID-19 received antispike-neutralizing monoclonal antibody treatment. The median age (IQR) was 62.7 (44.7–72.1) years (45.8% were ≥65 years), and 41.1% were male. The population was predominantly non-Hispanic (94.9%) and White (93.6%). The most common underlying conditions for the whole cohort were hypertension (40.2%), immunosuppressed status (33.7%), and diabetes mellitus (19.4%). The majority of patients (89.2%) had received a primary COVID-19 vaccination series; 69.5% had received a booster dose.

During the 30 days after antispike-neutralizing monoclonal antibody infusion, a total of 71 patients (1.8%) developed the primary outcome of severe COVID-19. An additional 74 high-risk patients with mild to moderate COVID-19 were hospitalized for indications not related to COVID-19, including those who were diagnosed incidentally during hospital admission screening procedures; none of these patients required oxygen supplementation or qualified as having severe COVID-19.

### Sotrovimab Cohort

During the 11-week period from January 1 to March 20, 2022, a total of 2182 high-risk patients were treated with sotrovimab for mild to moderate COVID-19. The median age (IQR) was 60.4 (40.8–70.8) years (41.2% were age ≥65 years); 41.1% were male. The most common medical comorbidities were immunosuppressed status (46.7%), hypertension (38.2%), and diabetes mellitus (21.2%). Malignancy (18.1%), organ transplant (12.3%), and rheumatologic diseases (8.4%) were the most common immunocompromising conditions. The majority (86.3%) had received a primary COVID-19 vaccine series; 63.5% had received a booster dose.

During the 30 days after sotrovimab infusion, 49 patients developed severe outcomes (2.2%; 95% CI, 1.9%–2.6%). The rates of severe outcomes were 2.0% in January, 2.4% in February, and 2.4% in March 2022. Patients who developed severe outcomes after sotrovimab infusion were significantly older than those who did not develop severe disease, and they had significantly more comorbidities, as reflected by higher MASS and Charlton Comorbidity Index scores (Table 1). In particular, there were significantly higher proportions of chronic cardiac disease, chronic lung disease, chronic kidney disease, diabetes mellitus, hypertension, and immunocompromising conditions among patients who progressed to severe outcomes vs those who did not. Conversely, COVID-19 vaccination rates were lower among those who developed severe COVID-19. Primary vaccination (odds ratio [OR], 0.24; 95% CI, 0.13–0.44) and booster (OR, 0.5; 95% CI, 0.28–0.88) were associated with lower risk of severe disease (Supplementary Table 1, Supplementary Figure 1).

Twenty-one patients (1.0%) required an ICU level of care within 30 days after sotrovimab infusion. Nine patients (0.4%) died from underlying malignancy (n = 4), COVID-19 pneumonia (n = 1), renal failure (n = 1), subarachnoid hemorrhage (n = 1), and unknown causes (n = 2). No patient developed anaphylactic reaction during sotrovimab infusion.

### Bebtelovimab Cohort

During the 6-week period from March 21 to April 30, 2022, a total of 1690 high-risk patients received bebtelovimab infusion for mild to moderate COVID-19. The median age of the cohort (IQR) was 65.4 (49.9–74.0) years (51.8% were age ≥65 years); 41.1% were male. The most common medical comorbidities were hypertension (42.7%), diabetes mellitus (17.1%), and immunosuppressed status (17.0%). Malignancy is the most common immunocompromising condition (12.5%). The majority of patients (92.9%) had received a primary COVID-19 vaccine series; 77.2% had received a booster dose.

During the 30 days after bebtelovimab infusion, 22 patients (1.3%; 95% CI, 1.0%–1.6%) developed severe disease. Patients who progressed to severe COVID-19 were significantly older and had a higher number of medical comorbidities, as reflected

by MASS. In particular, patients who developed severe outcomes had significantly higher proportions of having chronic kidney disease, congestive heart failure, diabetes mellitus, hypertension, and immunosuppressed status when compared with those who did not progress to severe disease (Table 2). In contrast, the proportions of having completed a primary COVID-19 vaccination series and a booster vaccine dose were significantly lower among those who developed severe outcomes. Having received primary vaccination (OR, 0.16; 95% CI, 0.06–0.42) and booster (OR, 0.42; 95% CI,

0.18–1.03) was associated with a lower risk of severe disease (Supplementary Table 2, Supplementary Figure 2).

Eight bebtelovimab-treated patients (0.5%) subsequently required an ICU level of care. Three patients (0.2%) died within 30 days of bebtelovimab treatment due to progressive respiratory failure from COVID-19 (n = 1), progression of metastatic malignancy (n = 1), and cardiac arrest associated with ventricular fibrillation (n = 1). One patient developed chills and palpitations during bebtelovimab infusion that required evaluation in the emergency department but without the need for

**Table 1.** Demographic and Clinical Characteristics of 2182 High-risk Patients Treated With Sotrovimab for Mild to Moderate COVID-19 During the SARS-CoV-2 Omicron Surge, January 1–March 20, 2022

| Characteristics | No Severe Disease (n = 2133) | Severe Disease (n = 49) | P Value[b] | All Patients (n = 2182) |
|---|---|---|---|---|
| Age, median (IQR), y | 60.2 (40.4–70.6) | 69.6 (59.1–77.9) | <.01 | 60.4 (40.8–70.8) |
| Sex, male, No. (%) | 871 (40.8) | 26 (53.1) | .22 | 897 (41.1) |
| Race, White, No. (%) | 1968 (92.3) | 43 (87.8) | .26 | 2011 (92.2) |
| Ethnicity, non-Hispanic, No. (%) | 2015 (94.5) | 42 (85.7) | .03 | 2057 (94.3) |
| Charlson Comorbidity Index, median (IQR) | 1.0 (0.0–2.0) | 2.0 (1.0–4.0) | <.01 | 1.0 (0.0–2.0) |
| Monoclonal Antibody Screening Score, median (IQR) | 4.0 (2.0–7.0) | 8.0 (6.0–11.0) | <.01 | 5.0 (2.0–7.0) |
| Body mass index, median (IQR), kg/m$^2$ | 27.6 (24.7–30.9) | 25.8 (22.3–27.4) | <.01 | 27.6 (24.6–30.8) |
| Chronic lung disease, No. (%) | 278 (13.0) | 16 (32.7) | <.01 | 294 (13.5) |
| Chronic renal disease, No. (%) | 101 (4.7) | 12 (24.5) | <.01 | 113 (5.2) |
| Congestive heart failure, No. (%) | 157 (7.4) | 10 (20.4) | <.01 | 167 (7.7) |
| Diabetes mellitus, No. (%) | 440 (20.6) | 22 (44.9) | <.01 | 462 (21.2) |
| Hypertension, No. (%) | 805 (37.7) | 29 (59.2) | <.01 | 834 (38.2) |
| Immunocompromised status, No. (%) | 984 (46.1) | 34 (69.4) | <.01 | 1018 (46.7) |
| Primary COVID-19 vaccination, No. (%)[a] | 1854 (86.9) | 30 (61.2) | <.01 | 1884 (86.3) |
| COVID-19 booster dose, No. (%) | 1363 (63.9) | 23 (46.9) | .01 | 1386 (63.5) |

Abbreviations: COVID-19, coronavirus disease 2019; IQR, interquartile range; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

[a]Primary COVID-19 vaccination: completion of a primary series consisting of receipt of 2 doses of an mRNA vaccine or a single dose of an adenovirus vector vaccine.

[b]P value comparing severe and nonsevere cohorts was calculated using a Kruskal-Wallis rank-sum test, Fisher exact test, or Pearson chi-square test, as appropriate.

**Table 2.** Demographic and Clinical Characteristics of 1690 High-risk Patients Treated With Bebtelovimab for Mild to Moderate COVID-19 During the SARS-CoV-2 Omicron Surge, March 21–April 30, 2022

| Characteristics | No Severe Disease (n = 1668) | Severe Disease (n = 22) | P Value[b] | All Patients (n = 1690) |
|---|---|---|---|---|
| Age, median (IQR), y | 65.3 (49.3–73.6) | 75.1 (68.2–82.8) | <.01 | 65.4 (49.9–74.0) |
| Sex, male, No. (%) | 679 (40.7) | 15 (68.2) | <.01 | 694 (41.1) |
| Race, White, No. (%) | 1593 (95.5) | 21 (95.5) | .58 | 1614 (95.5) |
| Ethnicity, non-Hispanic, No. (%) | 1596 (95.7) | 20 (90.9) | .25 | 1616 (95.6) |
| Charlson Comorbidity Index, median (IQR) | 0.0 (0.0–2.0) | 1.0 (0.0–4.0) | .22 | 0.0 (0.0–2.0) |
| Monoclonal Antibody Screening Score, median (IQR) | 3.0 (2.0–5.0) | 8.0 (5.0–9.0) | <.01 | 3.0 (2.0–5.0) |
| Body mass index, median (IQR), kg/m$^2$ | 27.7 (24.9–30.6) | 25.9 (23.7–29.2) | .26 | 27.7 (24.9–30.6) |
| Chronic lung disease, No. (%) | 231 (13.8) | 3 (13.6) | .98 | 234 (13.8) |
| Chronic renal disease, No. (%) | 37 (2.2) | 2 (9.1) | .03 | 39 (2.3) |
| Congestive heart failure, No. (%) | 110 (6.6) | 8 (36.4) | <.01 | 118 (7.0) |
| Diabetes mellitus, No. (%) | 280 (16.8) | 9 (40.9) | <.01 | 289 (17.1) |
| Hypertension, No. (%) | 703 (42.1) | 18 (81.8) | <.01 | 721 (42.7) |
| Immunocompromised status, No. (%) | 279 (16.7) | 9 (40.9) | <.01 | 288 (17.0) |
| Primary COVID-19 vaccination, No. (%)[a] | 1555 (93.2) | 15 (68.2) | <.01 | 1570 (92.9) |
| COVID-19 booster dose, No. (%) | 1291 (77.4) | 13 (59.1) | .04 | 1304 (77.2) |

Abbreviations: COVID-19, coronavirus disease 2019; IQR, interquartile range; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

[a]Primary COVID-19 vaccination: completion of a primary series consisting of receipt of 2 doses of an mRNA vaccine or a single dose of an adenovirus vector vaccine.

[b]P value comparing severe and nonsevere cohorts was calculated using a Kruskal-Wallis rank-sum test, Fisher exact test, or Pearson chi-square test, as appropriate.

hospitalization. No case of anaphylaxis was reported during bebtelovimab infusion.

## DISCUSSION

Bebtelovimab is recommended as an alternative treatment for COVID-19 in patients who are unable to receive a 3-day course of outpatient intravenous remdesivir or a 5-day course of oral nirmatrelvir-ritonavir [21]. The alternative status of bebtelovimab is due to a lack of robust clinical data to support its efficacy. In the FDA EUA document, the rates of COVID-19-related hospitalization and death through day 29 were reported to be generally lower among patients who received bebtelovimab alone or in combination with other monoclonal antibodies (bamlanivimab and etesevimab) when compared with placebo cohorts in prior trials [12]. Our findings in this retrospective study of 1690 high-risk patients who received bebtelovimab infusion concur with this observation. The rate of progression to severe disease among high-risk patients treated with bebtelovimab in our study during the Omicron BA.2 period was 1.3% by day 30, which was comparable to the rates observed with other antispike monoclonal antibodies during the pre-Delta and Delta epochs [2–5, 7, 15, 16, 22]. While there was no direct statistical comparison between the bebtelovimab cohort and the sotrovimab cohort in this study, it is reassuring to observe that the rate of severe disease progression after bebtelovimab during the BA.2-dominant period is lower than what was observed among patients who received sotrovimab during the Omicron period, which was dominated by B.1.1.529.

Sotrovimab was the antispike-neutralizing monoclonal antibody for outpatient treatment of mild to moderate COVID-19 during the height of the SARS-CoV-2 Omicron B.1.1.529 surge. Due to scarce sotrovimab supply, our MATRx program prioritized its use for the treatment of the highest-risk populations [14]. This program decision explains the high proportion of patients with high-risk comorbidities in the sotrovimab cohort, including a large population of immunocompromised patients. Almost half of the sotrovimab cohort was labeled immunocompromised—a group that is considered at highest risk of severe outcomes [6, 23]. Reassuringly, despite a high-risk cohort enriched with immunodeficient patients, the rate of progression to severe disease was only 2.2% after sotrovimab infusion. We hypothesize that this overall good outcome could be related to high rates of vaccination in our patients, the timely infusion of neutralizing monoclonal antibody therapies, and the potentially low virulence of the Omicron variant. The rate of severe outcomes after sotrovimab infusion in our study is comparable to the outcomes reported in previous randomized placebo-controlled trials conducted before Delta and Omicron and lower than the 6% rate among patients who received placebo in those trials [4, 22].

Older age, immunosuppressed status, and having a higher number of medical comorbidities, as measured by MASS, were significantly associated with a higher risk of severe disease progression after bebtelovimab or sotrovimab treatment. This observation is consistent with previous reports indicating higher risk of disease progression despite neutralizing monoclonal antibody treatment among persons with multiple medical comorbidities [6, 24]. Likewise, our findings are consistent with previous reports that highlight significant protection from severe disease among persons who received COVID-19 vaccination [25]. Nonetheless, our study also emphasizes that, despite having received COVID-19 vaccination and a booster dose, some patients may remain at risk of progression to severe outcomes, and this risk could be mitigated by early administration of antispike monoclonal antibodies [16]. In a prior study, our group demonstrated that the number of patients needed to treat with monoclonal antibodies in order to prevent 1 hospitalization for breakthrough COVID-19 was as low as 4 among those with MASS ≥4 during the Delta epoch [16]. This implies that neutralizing antispike monoclonal antibodies provides added benefit over the baseline immune protection afforded by active vaccination. The combined effect of active immunization supplemented by passive immunotherapy could account for the low rates of severe disease, ICU level of care, and death, despite a population with high proportions of comorbidities and immunocompromising conditions.

The results of our study should be interpreted in the context of its numerous limitations. Because of its retrospective and observational design, some variables such as vaccination status and clinical outcomes may not have been captured in patients who sought subsequent care in other centers. Viral genetic sequencing was not performed to determine specific variants in the treatment cohorts, so we can only assume, based on data tracking reported by the Centers for Disease Control and Prevention, that our cases were predominantly due to SARS-CoV-2 Omicron (B.1.1.529) during the early part of the study when sotrovimab was used for treatment and due to BA.2 and other subvariants during the latter part of the study when bebtelovimab was used for treatment [26]. It is possible that some sotrovimab-treated patients progressed to severe disease because they were infected with nonsusceptible SARS-CoV-2 Omicron BA.2 and its subvariants. Likewise, it is possible that the progression to severe disease was due to underlying high-risk medical comorbidities [6, 16]. The study population consisted of disproportionately high numbers of immunocompromised hosts. The imbalance in the clinical characteristics between the 2 treatment cohorts were limitations that prevented us from performing a direct comparative analysis of outcomes between the 2 cohorts. Moreover, the sequential use of the 2 neutralizing monoclonal antibodies limited the conduct of a true head-to-head comparison of outcomes. Because the 2 cohorts were not concurrently treated, it is

impossible to account for any potential biologic differences in disease severity among different SARS-CoV-2 Omicron subvariants. Our study population was largely non-Hispanic White persons who sought care at a large academic medical center, and our results may not be generalizable to communities of underrepresented populations. The MATRx program proactively screened eligible patients, which resulted in a rapid time to neutralizing monoclonal antibody treatment (median of 2 days from diagnosis), and our outcomes may not reflect those of programs with a different infrastructure [13]. Finally, this study had no control group of untreated patients, which made it impossible to measure treatment efficacy. Identifying a contemporaneous untreated cohort as a comparator during the Omicron surge was difficult due to the increasing widespread use of antiviral drugs (ritonavir-boosted nirmatrelvir, molnupiravir, remdesivir) for outpatient treatment. Hence, this study is purely descriptive and does not provide evidence of efficacy. These important limitations were counterbalanced by the large cohort of patients treated during the Omicron epoch, including the largest cohort of bebtelovimab-treated patients to date, and a standardized protocol for monoclonal antibody treatment that was coordinated by a single multidisciplinary team.

## CONCLUSIONS

This real-world retrospective analysis of a large cohort of high-risk patients demonstrates low rates of severe disease progression after treatment with sotrovimab during the era dominated by Omicron (B.1.1.529) and after treatment with bebtelovimab during the era dominated by BA.2 and Omicron subvariants. Our data support the FDA EUA of bebtelovimab for the treatment of high-risk patients with mild to moderate COVID-19 during the Omicron epoch. As the Omicron surge progresses with increasing proportions of BA.4 and BA.5 subvariants, we anticipate the continued use of bebtelovimab for outpatient treatment of mild to moderate COVID-19. Pseudovirus experiments suggest that bebtelovimab maintains activity against BA.4 and BA.5, and we strongly encourage real-time monitoring of its use in the clinical setting in order to determine its effectivity against emerging variants.

### 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.

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