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BRIEF REPORT

Infectious Disease

Use of sotrovimab in vaccinated versus unvaccinated COVID-19 patients in a resource-limited emergency department during the omicron surge

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Abstract

Objective: The treatment of outpatient COVID-19 patients at high risk of disease progression has been challenging, as both the virus and available therapeutics change. Here, we sought to evaluate the effect of vaccination status on the use of sotrovimab during the early phase of the Omicron surge.

Methods: This was a retrospective observational study performed at El Centro Regional Medical Center, a rural hospital on the southern Californian border. The electronic medical record was queried for all emergency department (ED) patients who received an infusion of sotrovimab between January 6 and February 6, 2022. We obtained patient demographics, COVID-19 vaccination status, medical comorbidities, and whether patients returned to the ED within 30 days. We stratified our cohort according to vaccination status and performed a multivariable logistic regression model to evaluate the relationship between these factors.

Results: One hundred seventy patients received an infusion of sotrovimab in the ED. The patient cohort had a median age of 65 years, 78.2% were Hispanic, and obesity (63.5%) was the most common comorbidity. A total of 73.5% of patients were vaccinated against COVID-19. A total of 12/125 (9.6%) of vaccinated patients returned to the ED within 30 days, versus 10/45 (22.2%) in the unvaccinated cohort, which was statically significant ($P = 0.03$). The presence of medical comorbidities was not associated with the primary outcome.

Conclusion: Of patients who received sotrovimab, those who were vaccinated were less likely to return to the ED within 30 days compared to those who were unvaccinated. Given the effectiveness of the COVID-19 vaccination campaign, and with the emergence of new variants, it is unclear what role monoclonal antibody therapy should play in the treatment of outpatient COVID-19 patients.

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1 | INTRODUCTION

1.1 | Background

The COVID-19 pandemic has had a severe impact throughout the United States, with the death toll crossing the 1 million mark on May 17, 2022.[1] This strain on the US health care system has been especially challenging for rural, resource-limited settings, where hospitals with limited numbers of beds quickly became overwhelmed.[2] It is hoped that vaccination and administration of therapeutics, such as monoclonal antibodies and antiviral therapies, in non-hospitalized patients can reduce the burden on these hospitals by limiting the progression of the disease.[3] Monoclonal antibodies function by binding the SARS-CoV-2 spike protein, thereby neutralizing the virus and its ability to enter cells.[4]

1.2 | Importance

Multiple different monoclonal antibody therapies have been developed, which when administered in outpatients with a high risk of progression of disease, likely demonstrate a decrease in disease progression and need for hospitalization.[5–8] However, a significant challenge to this strategy has been the emergence of SARS-CoV-2 variants, where mutations in the spike protein render the virus resistant to these monoclonal antibodies.[9] In January 2022, Omicron (BA.1) became the dominant variant, and based on the results of in vitro assays of antibody binding to the spike protein, sotrovimab was the only monoclonal therapy that was recommended by the Centers for Disease Control and Prevention.[10]

1.3 | Goal of this investigation

Here, we sought to describe our experience with using sotrovimab at a rural-situated hospital with limited resources. El Centro Regional Medical Center (ECRMC)is located on the Southern California border, 120 miles east of San Diego. The county had one of the highest rates of COVID-19 infection in the country,[11] which placed significant strain on hospital resources.[12] Our patient population is predominantly Hispanic, with high rates of comorbidities that place patients at increased risk of progression of disease, especially obesity, diabetes, and heart disease [13]. Our patient population also had a good response to the COVID-19 vaccination campaign, with over 80% of eligible patients fully vaccinated by the end of 2021.[14] The purpose of our study was to evaluate the association of vaccination status and return to the emergency department (ED) among patients who received sotrovimab.

2 | METHODS

Study design and setting: This was a cross-sectional retrospective observational study. The electronic medical record (EMR) at ECRMC was queried for all patients who received sotrovimab in the ED between January 6, 2022 and February 6, 2022.

The Bottom Line

Monoclonal antibodies are often used for treating COVID-19 syndrome, but their effectiveness in previously unvaccinated patients is unclear. In this series of 170 emergency department COVID-19 patients receiving sotrovimab (a dual function monoclonal SARS-CoV-2 neutralizing antibody), patients previously vaccinated against COVID-19 were over 3 times less likely to return to the ED within 30 days than those who were unvaccinated.

Selection of participants: Per Bledsoe and Worster, we generated a complete list of every patient who received sotrovimab by reviewing the ED pharmacy database.[16] Patients had to be at least 18 years of age, have lab-confirmed infection with SARS-CoV-2, mild to moderate symptoms of COVID-19 (per definition of the National Institutes of Health)[15] with onset less than 10 days from presentation to the ED, no indications for admission to the hospital, and at least 1 medical condition associated with a high risk of progression to severe COVID-19 (ie, diabetes, hypertension, cardiac disease, obesity, underlying lung disease, or immunocomprise). Decision to prescribe sotrovimab was at the discretion of the treating physician. Patients received sotrovimab 500 mg intravenous as an infusion over 30 minutes in the ED and were monitored for at least 1 hour after the infusion for any signs of hypersensitivity reaction or infusion-related reactions, including fever, chills, nausea, headache, bronchospasm, hypotension, angioedema, throat irritation, urticaria, pruritus, myalgia, and dizziness.

Measurements: For each patient who received sotrovimab, the EMR was queried for patient demographics, including age, sex, ethnicity, COVID-19 vaccination status, and medical comorbidities. We evaluated if there was any documented adverse reaction to receiving the infusion. There were no patients who received sotrovimab who were excluded from this analysis. The data were abstracted by medical scribes who were already familiar with the EMR into a predefined abstraction form, with supervision from an emergency physician or ED pharmacist. Abstractors were not blinded to the study objectives.

Exposure: Vaccination status of each patient was evaluated by a combination of manual chart review as well as manual review of the paper ordering form from the ED pharmacy, which specified whether the patient was vaccinated, and if so, which vaccine they had received (Pfizer, Moderna, or Johnson & Johnson) and when they had received their last vaccination. Patients were considered vaccinated if they had completed a primary vaccination series.

Outcomes: We determined if the patient returned to the ED within 30 days of index visit and whether the patient subsequently required admission to the hospital, which was evaluated by a combination of reviewing the EMR and patient callbacks.

Data analysis: We stratified patients according to vaccination status. Adjusted odds ratios and 95% confidence intervals (CIs) were estimated using multivariable logistic regression models adjusting for age and the presence of comorbidities in predicting

TABLE 1 Descriptive statistics grouped by vaccinations status.

	Total		Unvaccinated		Vaccinated	
	(*n* = 170)		(*n* = 45)		(*n* = 125)	
Age, *n* (%)						
Median age, years	65	IQR:21	55	IQR:23	66	IQR:19
<65	84	(49.4)	31	(68.9)	53	(42.4)
65+	86	(50.6)	14	(31.1)	72	(57.6)
Sex, *n* (%)						
Female	95	(55.9)	23	(51.1)	72	(57.6)
Male	75	(44.1)	22	(48.9)	53	(42.4)
Ethnicity, *n* (%)						
Hispanic	133	(78.2)	28	(62.2)	105	(84.0)
Other	37	(21.8)	17	(37.8)	20	(16.0)
Comorbidities, *n* (%)						
Diabetes	67	(39.4)	10	(22.2)	57	(45.6)
CAD/HTN	93	(54.7)	20	(44.4)	73	(58.4)
Obesity	108	(63.5)	33	(73.3)	75	(60.0)
ED revisit, *n* (%)						(0.0)
No	148	(87.1)	35	(77.8)	113	(90.4)
Yes	22	(12.9)	10	(22.2)	12	(9.6)
Admitted, *n* (%)						
No	159	(93.5)	41	(91.1)	118	(94.4)
Yes	11	(6.5)	4	(8.9)	7	(5.6)

Abbreviations: CAD, coronary artery disease; ED, emergency department; HTN, hypertension; IQR, interquartile range.

30-day return to the ED. A *P* value less than 0.05 was used to indicate statistical significance. All data for variables of interest were complete and included in the logistic regression. All statistical analyses were performed using IBM SPSS statistical software, version 28.0.1.0 (Armonk, NY: IBM Corp.). This manuscript was developed and written in accordance with Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) criteria.[17] This study was judged exempt by our institutional review board (IRB #200558).

3 | RESULTS

During the study period, 170 patients presented to the ED with mild to moderate COVID-19 symptoms and were administered sotrovimab. This patient population had a median age in the 60s, was majority Hispanic, and had multiple medical comorbidities, with obesity being the most common (Table 1). Of the 170 patients, 22 (12.9%) had an ED return within 30 days for any reason (Table S1). Of those who returned, 20/22 presented for reassessment of their COVID-19 symptoms, 1 patient presented with new-onset hemiparesis and 1 presented with abdominal pain. Of those 22, 11 (50%) required admission to the hospital; 6 patients were admitted for progression of COVID-19 symptoms and 5 were admitted with a primary non-COVID-19 diagnosis (transient ischemic attack, hyponatremia, new onset atrial flutter, small bowel obstruction, and heart failure exacerbation). Of the 6 patients admitted for progression of COVID-19 disease, 4 (67%) were unvaccinated. There were 0 deaths. There were 2 documented adverse drug reactions to sotrovimab: 1 patient had a near syncopal event, and 1 patient developed an episode of sinus tachycardia; both were discharged home after a brief period of observation.

We stratified our cohort according to vaccination status. Demographics were similar between each of these groups; the unvaccinated cohort skewed to younger with fewer comorbidities; however, these did not reach statistical significance. Of those who were vaccinated, patients presented on average 5 months after their last vaccine, which included either completion of the primary vaccination series or a vaccine booster (median 4 months, interquartile range 2–8). We performed a logistic regression to further delineate the relationship between these factors (Table 2). Although age and comorbidity status were not significant in our univariate analysis, both were included in the logistic regression model for congruency with current literature.[7,18] When corrected for age and presence of medical comorbidities, vaccination status was still significantly associated with the primary outcome. Among patients who received sotrovimab, those who were vaccinated were less likely to return to the ED within 30 days (adjusted odds ratio 0.286, 95% CI 0.105– 0.778).

TABLE 2 Multivariable logistic regression analysis to examine association of vaccination status, medical comorbidities, and age on 30-day ED return.

	Unadjusted	95% CI			Adjusted	95% CI		
Effect	Odds ratio	LL	UL	*P* value	Odds ratio	LL	UL	*P* value
Vaccinated vs unvaccinated	0.37	0.15	0.93	0.04	0.29	0.11	0.78	0.01
Comorbidities vs none	0.81	0.32	2.07	0.67	0.85	0.32	2.30	0.76
65+ years vs <65 years	1.85	0.73	4.67	0.19	1.67	0.97	7.36	0.06

Abbreviations: CI, confidence interval; ED, emergency department; LL, lower limit; UL, upper limit.

4 | LIMITATIONS

We acknowledge that there are multiple limitations with this study. This was a retrospective observational study conducted at a single hospital and was heavily reliant on the fidelity and completeness of the EMR. There was no randomization, and the decision to administer sotrovimab was at the discretion of the treating physician. The 30-day follow-up was also reliant on the patients returning to our ED—although we are the only hospital in a 15-mile radius, it is possible patients may have sought additional care elsewhere. In an effort to address this limitation, we attempted to call back patients or their families to determine if they instead had a repeat visit or admission at an outside hospital. There may have also been additional confounding factors, such as the type of vaccine received, whether the patients had received a vaccination booster, and the recency of the last vaccination; the small size of these separate subgroups precluded any further rigorous statistical testing.

5 | DISCUSSION

In this retrospective cohort study, patients who presented to the ED with mild to moderate COVID-19 and received an infusion of sotrovimab were less likely to return to the ED or experience progression of disease if they were previously vaccinated against SARS-CoV-2. With a patient cohort that is primarily Hispanic, elderly, and with many medical comorbidities that put them at risk for progression to severe disease, it is important to identify interventions that improve the morbidity and mortality of this patient population. Furthermore, in a health care system with limited resources and few hospital and intensive care unit (ICU) beds, it is vital to identify outpatient interventions that prevent these patients from having to return to the hospital and potentially be admitted. In this study, surprisingly neither advanced age nor the presence of multiple medical comorbidities was associated with the primary outcome, though the study may have been underpowered to detect these differences.

A living systematic review and meta-analysis of available COVID-19 therapies published in the *British Medical Journal* concluded with low certainty that monoclonal antibody therapy in non-severe patients may reduce hospitalization,[8] and a *Cochrane Database Systematic Review* concluded there was insufficient evidence regarding the effectiveness of these therapies.[19] Furthermore, most of the published data on the use of these therapeutics come from phase 2 or phase 3 clinical trials, were often industry funded, and with little published from follow-up studies. Nevertheless, when available, monoclonal antibody therapy has been recommended for patients at high risk for disease progression by many major public health organizations, including the Centers for Disease Control and Prevention and the National Institutes of Health.

A significant challenge in providing outpatient care to COVID-19 patients has been the rapidly evolving landscape, as both the virus and available therapies change. In January 2022, due to the high prevalence of the Omicron variant (BA.1), the Food and Drug Administration (FDA) withdrew authorization for the administration of bamlanivimab-etesevimab and REGEN-COV (casirivimab and imdevimab), leaving sotrovimab as the primary recommended therapy.[20] An additional complication is the trials that described these therapies were either performed before the wide availability of COVID-19 vaccines, excluded vaccinated patients, or made no mention about the vaccination status of the study cohort. Thus, we sought to evaluate the potential interaction between sotrovimab infusion and vaccination status.

Interestingly, we found that among patients receiving sotrovimab, those who were vaccinated were less likely to return to the ED or suffer progression of disease compared to unvaccinated patients. Subgroup analysis from the RECOVERY trial showed that REGEN-COV (casirivimab and imdevimab) was effective only in patients who were seronegative,[21] leading to some concern that monoclonal antibodies may be ineffective or even harmful in seropositive patients (ie, vaccinated or previously infected). Conversely, another explanation for our results would be that sotrovimab has little effect on progression of disease, and vaccination status is most important regardless of any other treatments, as has previously been demonstrated.[22,23] Alternatively, the benefit afforded to unvaccinated patients from receiving sotrovimab is less than that to fully vaccinated patients. Our study design does not allow us to comment directly on the effectiveness of sotrovimab; given all the available evidence and current treatment guidelines, we felt it was most appropriate to offer sotrovimab to all patients who qualified. However, since the completion of this study, additional Omicron subvariants have emerged that have marked resistance against sotrovimab,[24] and the FDA repealed its authorization for the use of sotrovimab on April 5, 2022.[25] Regardless, our data support the general conclusion that vaccination against COVID-19 continues to be the most protective factor against disease progression.

AUTHOR CONTRIBUTIONS

The study was designed by Rahul V. Nene, Bruce Balog, and Andrew LaFree. Data were collected by Bruce Balog, Hector Martinez, and

Elias Murillo and analyzed by Rahul V. Nene, Melodie A. Santodomingo, and Bruce Balog. Rahul V. Nene drafted the manuscript with assistance from Melodie A. Santodomingo, Bruce Balog, Christian A. Tomaszewski, and Andrew LaFree. All authors reviewed and assisted with revisions of the final manuscript. Rahul V. Nene takes responsibility for the manuscript as a whole.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

REFERENCES

1. U.S. Officially Surpasses 1 Million COVID-19 Death. Johns Hopkins Coronavirus Resource Center. Accessed May 30, 2022. https://coronavirus.jhu.edu/from-our-experts/u-s-officially-surpasses-1-million-covid-19-deaths
2. Sharma S, Badami V, Rojas E, et al. ICU mortality in patients with coronavirus disease 2019 infection: highlighting healthcare disparities in rural Appalachia. *Crit Care Explor*. 2021;3(10):e547. doi:10.1097/CCE.0000000000000547
3. Gandhi RT, Malani PN, del Rio C. COVID-19 therapeutics for nonhospitalized patients. *JAMA*. 2022;327(7):617. doi:10.1001/jama.2022.0335
4. Deb P, Molla MMA, Saif-Ur-Rahman KM. An update to monoclonal antibody as therapeutic option against COVID-19. *Biosaf Heal*. 2021;3(2):87-91. doi:10.1016/j.bsheal.2021.02.001
5. Cohen MS, Nirula A, Mulligan MJ, et al. Effect of bamlanivimab vs placebo on incidence of COVID-19 among residents and staff of skilled nursing and assisted living facilities: a randomized clinical trial. *JAMA*. 2021;326(1):46-55. doi:10.1001/jama.2021.8828
6. O'Brien MP, Forleo-Neto E, Musser BJ, et al. Subcutaneous REGEN-COV antibody combination to prevent Covid-19. *N Engl J Med*. 2021;385(13):1184-1195. doi:10.1056/NEJMoa2109682
7. Gupta A, Gonzalez-Rojas Y, Juarez E, et al. Early treatment for Covid-19 with SARS-CoV-2 neutralizing antibody sotrovimab. *N Engl J Med*. 2021;385(21):1941-1950. doi:10.1056/NEJMoa2107934
8. Siemieniuk RA, Bartoszko JJ, Díaz Martinez JP, et al. Antibody and cellular therapies for treatment of Covid-19: a living systematic review and network meta-analysis. *BMJ*. 2021:n2231. doi:10.1136/bmj.n2231
9. Borio LL, Bright RA, Emanuel EJ. A national strategy for COVID-19 medical countermeasures. *JAMA*. 2022;327(3):215. doi:10.1001/jama.2021.24165
10. Hoffmann M, Krüger N, Schulz S, et al. The Omicron variant is highly resistant against antibody-mediated neutralization: implications for control of the COVID-19 pandemic. *Cell*. 2022;185(3):447-456.e11. doi:10.1016/j.cell.2021.12.032
11. Imperial County Health Department COVID-19 Data. Accessed June 3, 2022. https://www.icphd.org/health-information-and-resources/healthy-facts/covid-19/
12. Nene RV, Amidon N, Tomaszewski CA, Wardi G, Lafree A. Outcomes for in-hospital cardiac arrest for COVID-19 patients at a rural hospital in Southern California. *Am J Emerg Med*. 2021;47:244-247. doi:10.1016/j.ajem.2021.04.070
13. Macias GR, Marcelin JR, Zuniga-Blanco B, Marquez C, Mathew T, Piggott DA. COVID-19 pandemic: disparate health impact on the Hispanic/Latinx population in the United States. *J Infect Dis*. 2020;222(10):1592-1595. doi:10.1093/infdis/jiaa474
14. Statewide vaccination data. Accessed June 3, 2022. https://covid19.ca.gov/vaccination-progress-data/
15. National Institutes of Health. Clinical spectrum of SARS-CoV-2 infection. Accessed January 2, 2022. https://www.covid19treatmentguidelines.nih.gov/overview/clinical-spectrum/
16. Worster A, Bledsoe RD, Cleve P, Fernandes CM, Upadhye S, Eva K. Reassessing the methods of medical record review studies in emergency medicine research. *Ann Emerg Med*. 2005;45(4):448-451. doi:10.1016/j.annemergmed.2004.11.021
17. von Elm E, Altman DG, Egger M, et al. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *Ann Intern Med*. 2007;147(8):573-577. doi:10.7326/0003-4819-147-8-200710160-00010
18. Gupta S, Hayek SS, Wang W, et al. Factors associated with death in critically ill patients with coronavirus disease 2019 in the US. *JAMA Intern Med*. 2020;180(11):1436. doi:10.1001/jamainternmed.2020.3596
19. Kreuzberger N, Hirsch C, Chai KL, et al. SARS-CoV-2-neutralising monoclonal antibodies for treatment of COVID-19. *Cochrane Database Syst Rev*. 2021;9:CD013825. doi:10.1002/14651858.CD013825.pub2
20. COVID-19 Monoclonal Antibodies. Centers for Medicare and Medicaid services. Accessed June 1, 2022. https://www.cms.gov/monoclonal
21. RECOVERY Collaborative Group. Casirivimab and imdevimab in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial. *Lancet*. 2022;399(10325):665-676. doi:10.1016/S0140-6736(22)00163-5
22. Feikin DR, Higdon MM, Abu-Raddad LJ, et al. Duration of effectiveness of vaccines against SARS-CoV-2 infection and COVID-19 disease: results of a systematic review and meta-regression. *Lancet*. 2022;399(10328):924-944. doi:10.1016/S0140-6736 (22)00152-0
23. Thompson MG, Stenehjem E, Grannis S, et al. Effectiveness of Covid-19 vaccines in ambulatory and inpatient care settings. *N Engl J Med*. 2021;385(15):1355-1371. doi:10.1056/NEJMoa2110362
24. Iketani S, Liu L, Guo Y, et al. Antibody evasion properties of SARS-CoV-2 Omicron sublineages. *Nature*. 2022;604(7906):553-556. doi:10.1038/s41586-022-04594-4
25. US Food and Drug Administration. FDA updates Sotrovimab emergency use authorization. Accessed June 20, 2022. https://www.fda.gov/drugs/drug-safety-and-availability/fda-updates-sotrovimab-emergency-use-authorization

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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