Real-World Clinical Outcomes of Bamlanivimab and Casirivimab-Imdevimab among High-Risk Patients with Mild to Moderate Coronavirus Disease 2019

Ravindra Ganesh,*[1] Lindsey M. Philpot,*[1] Dennis M. Bierle,[1] Ryan J. Anderson,[1] Lori L. Arndt,[2] Richard F. Arndt,[2] Tracy L. Culbertson,[3] Molly J. Destro Borgen,[1] Sara N. Hanson,[3] Brian D. Kennedy,[4] Brian B. Kottke,[3] Jennifer J. Larsen,[1] Priya Ramar,[1] Jordan K. Rosedahl,[1] Maria Teresa Seville,[5] Leigh L. Speicher,[6] Sidna M. Tulledge-Scheitel,[1] Caroline G. Wilker,[7] and Raymund R Razonable[1] for the Monoclonal Antibody Treatment Program

[1]Mayo Clinic, Rochester, Minnesota, USA; [2]Mayo Clinic Health System – Eau Claire, Wisconsin, USA; [3]Mayo Clinic Health System – Mankato, Minnesota, USA; [4]Mayo Clinic Health System – Lake City, Minnesota, USA; [5]Mayo Clinic Arizona – Phoenix, Arizona, USA; [6]Mayo Clinic, Jacksonville, Florida, USA; [7]Mayo Clinic Health System – Franciscan Healthcare, La Crosse, Wisconsin, USA

*Contributed equally to the work

Correspondence:

Raymund R Razonable, MD

Division of Infectious Diseases

Mayo Clinic

200 First Street SW, Rochester, Minnesota 55905, USA

Razonable.raymund@mayo.edu; @RazonableMD

Telephone: 507-2843747

40-word summary

This real-world cohort study of 3596 high-risk patients with mild to moderate coronavirus disease-2019 demonstrates similarly low rates of hospitalization after bamlanivimab or casirivimab-imdevimab infusion. The number and type of medical comorbidities influence the risk of hospitalizations after antibody treatment.

Footnote Page:

Dr. Raymund Razonable is principal investigator of clinical trials on casirivimab and imdevimab (Regeneron), sarilumab (Regeneron), tocilizumab (Roche), and remdesivir (Gilead) with research funds all given to the Mayo Clinic. These industry sponsors did not provide any support for the conduct of the submitted research.

This study was funded by an intramural research grant from the Mayo Clinic to Dr. Raymund Razonable. Mayo Clinic did not have control in data analysis and the decision to submit the paper for publication.

All other no conflicts.

Abstract

Background: Bamlanivimab and casirivimab-imdevimab are authorized for treatment of high-risk patients with mild to moderate coronavirus disease-2019 (COVID-19). We compared the outcomes of patients who received these therapies to identify factors associated with hospitalization and other clinical outcomes.

Methods: Adult patients who received monoclonal antibody from November 19, 2020 to February 11, 2021 were selected and divided into those who received bamlanivimab (n=2747) and casirivimab-imdevimab (n=849). The 28-day all-cause and COVID-19-related hospitalizations were compared between the groups.

Results: The population included 3596 patients; median age was 62 years; and 50% were female. All had ≥1 medical comorbidity; 55% had multiple comorbidities. All cause- and COVID-19-related hospitalization rates at 28 days were 3.98% and 2.56%, respectively. After adjusting for medical comorbidities, there was no significant difference in all cause- and COVID-19-related hospitalization rates between bamlanivimab and casirivimab-imdevimab (adjusted HR, 1.4, 95% CI 0.9-2.2 and 1.6, 95% CI 0.8-2.7, respectively). Chronic kidney, respiratory and cardiovascular diseases, and immunocompromised status were associated with higher likelihood of hospitalization.

Conclusion: This observational study on the use of bamlanivimab and casirivimab-imdevimab in high-risk patients showed similarly low rates of hospitalization. The number and type of medical comorbidities are associated with hospitalizations after monoclonal antibody treatment.

Keywords: bamlanivimab, casirivimab, covid-19, hospitalization, outcomes

Introduction

Neutralizing monoclonal antibodies against the spike protein of Severe Acute Respiratory Syndrome-Coronavirus-2 (SARS-CoV-2) have been authorized by the United States (US) Food and Drug Administration (FDA) for treatment of high-risk individuals with mild to moderate coronavirus disease-2019 (COVID-19).[1-3] The emergency use authorizations (EUA) were based on early phase clinical trials that demonstrated reductions in viral load among patients who received monoclonal antibodies compared to placebo.[1-3] In a randomized clinical trial of 452 patients, there was a significantly lower viral load at day 11 after bamlanivimab infusion compared to placebo.[1] In another randomized clinical trial of 275 patients, a significantly lower viral load at day 7 after infusion was observed among patients who received casirivimab-imdevimab compared to placebo.[3] These early phase trials also showed lower numbers of hospitalizations, emergency department (ED) and medically attended visits among patients who received monoclonal antibodies compared to placebo.[1,3] The US FDA issued an EUA for bamlanivimab on November 9, 2020 and casirivimab-imdevimab on November 21, 2020.[4,5]

While the results of randomized placebo-controlled clinical trials of the two monoclonal antibody preparations appear similar, they have not been directly compared in cohorts of exclusively high-risk populations. In this retrospective study, we aimed to compare the outcomes of high-risk patients with mild to moderate COVID-19 treated with bamlanivimab monotherapy and those who received casirivimab-imdevimab therapy. The primary aim was to determine if there were differences in outcomes based on the administered monoclonal antibody therapy. In addition, we investigated whether patient-level factors were predictive of clinical outcomes.

Patients and Methods

Setting and the Monoclonal Antibody Program

Mayo Clinic is an integrated healthcare delivery network serving over 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 facilitate administration of monoclonal antibody therapies. The program started infusing bamlanivimab on November 19, 2020 and casirivimab-imdevimab on December 1, 2020. The MATRx program, protocols and procedures have been described.[6]

Study Design and Patient Population

This retrospective study was conducted among adult patients, ≥18 years, who were identified from the Mayo Clinic electronic health records (EHR) during the first 12-weeks of the MATRx program between November 19, 2020 and February 11, 2021. During this period, patients received bamlanivimab monotherapy or casirivimab-imdevimab combination based on the available supply at infusion facilities. For this study, all infused patients were divided into two cohorts based on the specific monoclonal antibody received. Informed consent was waived. Only patients with research authorization were included. This study was approved by the Mayo Clinic Institutional Review Board.

Patient Eligibility Criteria and the Monoclonal Allocation Screening Score

Under the FDA EUA directive, patients were eligible to receive monoclonal antibodies if they had a positive SARS-CoV-2 PCR or antigen test, had mild to moderate symptoms of COVID-19, were within 10 days of symptom onset, and had at least one of the following criteria: age ≥65 years, body

mass index (BMI) ≥35, diabetes, chronic kidney disease, immunosuppressive drug use, or an immunocompromising condition. Patients who are 55 years and older also qualified if they had hypertension, cardiovascular disease, or chronic lung disease.[4,5,7]

The MATRx Program developed a Monoclonal Allocation Screening Score (MASS) that stratified patients based on risk profile.[6] Developed using internal outcomes data, MASS assigned a score to each of the EUA criteria, as follows: age ≥65 (2), BMI ≥35 (2), diabetes mellitus (2), chronic kidney disease (3), cardiovascular disease in a patient ≥55 years (2), chronic respiratory disease in a patient ≥55 years (3), hypertension in a patient ≥55 years (1), and immunocompromised status (3). In an initial analysis, the rate of all-cause hospitalization among untreated high-risk patients correlated directly with MASS; higher rates of hospitalization were observed among patients with higher MASS.[8] MASS was originally intended to serve as an allocation mechanism during periods of resource scarcity. However, since there was sufficient supply of monoclonal antibody products and the capacity to infuse these therapies, MASS was used only to screen patients for eligibility for infusion.

Any patient with a MASS ≥1 was eligible for monoclonal antibody treatment and was contacted for medication education and consenting for infusion. During the first 6 weeks of the MATRx program in the Midwest, 59% of eligible patients consented for infusion while 41% declined the offer for treatment. Factors associated with the decision to consent for monoclonal antibodies have been reported.[8] Eligible patients received the monoclonal antibody that was available at the site on the day of infusion. The products that were available during this study were bamlanivimab (700-mg dose as one-time infusion) and the combination of casirivimab-imdevimab (1200-mg dose / 1200-mg dose, as one-time infusion). Sotrovimab and the combination of bamlanivimab-etesevimab were not yet authorized during this study.[2]

Outcome Measures

The primary outcome of this study was all-cause hospitalization within 28-days of receipt of monoclonal antibody therapy. The causes of hospitalization were also reviewed to determine the rates of COVID-19-related hospitalization. In addition, ED visits, intensive care unit (ICU) admission, and use of a mechanical ventilator within 28 days of receipt of monoclonal antibody therapy were evaluated.

The relationship of the outcomes with demographic and clinical characteristics, the type of monoclonal antibody therapy received, and the number of days from onset of COVID-19 symptoms to receipt of monoclonal therapy were also assessed. The demographic and clinical information evaluated included age, gender, ethnicity, race, need for language interpreter services, and individual medical comorbidity indications which qualified patients to receive monoclonal antibody therapy.

Statistical Analysis

Descriptive statistics were calculated for patient-level factors by type of monoclonal antibody therapy received. The distributions of patient factors by therapy type were assessed using Chi Square test for independence for categorical variables or a *t*-test for continuous variables after ensuring testing parameters were met. To calculate the proportion of patients who experienced 28-day hospitalization, ED visit, ICU admission, or use of mechanical ventilator, each patient who experienced one of the outcomes was assigned to the numerator with the total population as the denominator. Simple proportions were then calculated by monoclonal antibody therapy medication, for the total population, and by patient-level factor. Differences in these proportions were assessed using Chi Square test for independence for categorical variables or a *t*-test for continuous variables after ensuring testing parameters were met. Fisher Exact test and the Wilcoxon Rank Sum test were

used if testing assumptions were not achieved. Crude odds ratios (OR) with 95% confidence intervals (CIs) were calculated to compare and further evaluate associations of patient characteristics with outcomes. The association between infusion therapy type and hospitalization within 28 days was assessed with proportional hazards regression, and with adjustment for MASS. Hazard ratios (HRs) and 95% CIs were calculated; $P < 0.05$ was deemed statistically significant. We also performed two models, one for overall hospitalization and one for COVID-19 related hospitalizations within 28 days. Furthermore, we investigated the opportunity to perform matched analyses, both via direct matching between the two therapies (bamlanivimab monotherapy or casirivimab-imdevimab combination) and via propensity score matching approaches. However, both methods introduced new imbalances between therapy groups by demographic factors, so the study team utilized an unmatched statistical approach. All data management and statistical analyses were performed using Statistical Analysis Software (SAS) version 9.4 (Cary, North Carolina, US).

Results

Patient Population

From November 19, 2020 to February 11, 2021, the MATRx Program identified and consented 3,596 adult patients to receive monoclonal antibody therapy for mild to moderate COVID-19 (**Table 1**). The average patient age was 62.0 years with a range of 18 to 100 years. The population was evenly split between males and females, was primarily of white race (93.2%), of non-Hispanic or Latin ethnicity (93.2%), and indicated that they were married or in a lifetime partnership (71.6%).

All 3,596 patients had at least one characteristic or medical comorbidity that categorized them as high risk for developing COVID-19 complications. The most common medical comorbidities were hypertension (52.1%), increased BMI (38.4%), diabetes mellitus (27.2%), and cardiovascular

disease (21.7%). The majority of patients (55.3%) had multiple medical comorbidities, as indicated by a MASS of 4 or higher.

Patient-level factors by monoclonal antibody therapy medication

The infused monoclonal antibody was dependent on the drug allocation to our sites by the government. In all our nine infusion facilities, the supply of bamlanivimab was more than casirivimab-imdevimab, and this was reflected by the more than three-fold higher number of patients who were infused with bamlanivimab (n=2747) compared to casirivimab-imdevimab (n=849). The median time to infusion was 2 days after diagnosis, and this was not significantly different between the two products.

Assessing the allocation of monoclonal antibody therapy by patient factors, the bamlanivimab cohort had a higher proportion of patients with hypertension than the cohort who received casirivimab-imdevimab (53.3% vs. 48.3%; p=0.01). There was also a significant difference between the two treatment cohorts based on the distribution of MASS (p=0.008; **Table 1**). For example, the proportion of patients with MASS ≥6 was higher in bamlanivimab-treated cohort when compared to casirivimab-imdevimab (28.4% versus 22.5%).

Clinical outcomes by monoclonal antibody therapy

The primary endpoint of 28-day all-cause hospitalization rate was 3.98% for the total population (**Table 2**). This rate was significantly higher among patients who received bamlanivimab monotherapy compared to those who received casirivimab-imdevimab combination (4.34% vs. 2.83%; p=0.05). The average follow-up period did not differ significantly by medication type (bamlanivimab, 27.2 days vs. casirivimab-imdevimab, 27.5 days), and there was no significant

difference in overall time to hospitalization within 28 days (**Figure 1, left panel**). Proportional hazards regression found that patients who received bamlanivimab were at increased likelihood of 28-day hospitalization compared to patients who received casirivimab-imdevimab (unadjusted HR=1.5, 95% CI 1.0- 2.4, p=0.05). However, this finding was no longer statistically significant after controlling for MASS (adjusted HR 1.4, 95% CI 0.9-2.2, p=0.12).

The majority of hospitalizations (64.3%) were related to COVID-19. The most common non-COVID-19 related hospitalizations (n=51) were due to cardiac (arrhythmia, congestive heart failure, myocardial infarction; n=10), orthopedic (fracture, inflammatory arthritis, osteomyelitis; n=9), other infectious (bacterial pneumonia, pyelonephritis, sepsis; n=9), pulmonary (COPD exacerbation, pulmonary embolism; n=6) and renal (acute or chronic kidney failure, dehydration; n=5) causes. Accordingly, the 28-day COVID-19-related hospitalization was 2.56%. COVID-19-related hospitalization rate was not statistically significant between the two groups (bamlanivimab, 2.84% vs. casirivimab-imdevimab, 1.65%, p=0.06; **Figure 1, right panel**). Proportional hazards regression found that patients who received bamlanivimab were at increased likelihood of COVID-19-related 28-day hospitalization compared to patients who received casirivimab-imdevimab (unadjusted HR=1.7, 95% CI 1.0- 3.1, p=0.05), but this finding was no longer significant following adjustment for MASS (adjusted HR 1.6, 95% CI 0.8-2.7, p=0.13).

The rates of ED visit within 28 days was 7.7% for the total population and this was similar between the two monoclonal antibody therapies. Admission to the ICU was uncommon and was similar between the two groups. Four patients needed mechanical ventilation, and all had received bamlanivimab monotherapy (**Table 2**).

There were total of 8 deaths (5 received bamlanivimab and 3 received casirivimab-imdevimab) at a median of 15.5 days after COVID-19 diagnosis (range, 4-28). The causes of death were progression of underlying medical comorbidities, including metastatic cancer, in patients under

hospice care (n=4), congestive heart failure (n=2), bacterial sepsis (n=1), and progression of COVID-19 pneumonia (n=1).

Demographic characteristics associated with clinical outcomes

Age, gender and marital status were associated with the risk of 28-day all-cause hospitalization and ED visits (**Table 3**). In our population, men were at increased odds of 28-day hospitalization (OR=1.49, 95% CI 1.06-2.10). Compared with individuals who were married or in a life partnership, those who indicated divorced as their marital status were at increased odds of 28-day hospitalization (OR=1.84, 95% CI 1.07-3.05). Patients who needed language interpretation services were at increased odds of visiting the ED within 28 days after monoclonal antibody infusion (OR=2.79, 95% CI 1.20-5.88). Race other than white had a significantly higher rate of being admitted to the ICU (**Table 3**).

Clinical characteristics associated with outcomes

MASS was significantly associated with 28-day all-cause hospitalization rate (**Table 4**). No patient with a score of 1 was admitted to the hospital, while 8.51% among those with MASS ≥6 was hospitalized. MASS was not associated with visits to the ED or admission to the ICU.

The individual medical comorbidities associated with 28-day all-cause hospitalization were chronic kidney disease (OR=6.10, 95% CI 3.06-11.5), an immunocompromised status (OR=2.78, 95% CI 1.91-4.00), cardiovascular disease (OR=2.20, 95% CI 1.55-3.12), chronic lung disease (OR=1.67, 95% CI 1.10-2.50), and hypertension (OR=1.67, 95% CI 1.10-2.50) (**Table 4**). Patients with an increased BMI were at decreased risk of 28-day hospitalization (OR=0.51, 95% CI 0.34-0.74).

Patients with chronic kidney disease (OR=2.30, 95% CI 1.10-4.06) and diabetes (OR=1.37, 95% CI 1.05-1.77) had significantly higher rates of ED visit by day 28. Chronic kidney disease (OR=10.8, 95% CI 3.10-30.4) and cardiovascular disease (OR=3.12, 95% CI 1.40-6.85) was associated with higher rate of admission to the ICU.

Discussion

This retrospective study of a large cohort of exclusively high-risk adult patients with mild to moderate COVID-19 demonstrates a similarly low rate of all-cause and COVID-19-related hospitalization after early treatment with bamlanivimab and casirivimab-imdevimab. The approximately 4% all-cause and 2.6% COVID-19-related hospitalization rates by day 28 is consistent with the reported rates in randomized clinical trials that compared monoclonal antibodies with placebo.[1-3] Our real-world clinical data confirms these observations of controlled clinical trials that monoclonal antibodies are associated with low rates of hospitalization if given early in the course of mild to moderate COVID-19.

On initial analysis, patients who received bamlanivimab monotherapy appeared to have higher rates of all-cause and COVID-19-related hospitalization when compared to patients who received casirivimab-imdevimab. It is possible that this difference may be due to the reported lack of activity of bamlanivimab against escape mutant variants.[9-11] However, this study was conducted between November 19, 2020 and February 11, 2021, when resistant variants were not yet known to circulate in our communities.[12] Alternatively, it is possible that the difference in all-cause hospitalization between the two monoclonal antibody products may be related to the imbalance in MASS distribution at baseline. Indeed, when adjusted for MASS, the difference in the all-cause and COVID-19-related hospitalization between the two products was not statistically significant.

Hospitalizations after the diagnosis of COVID-19 can be due to virus disease progression or from other unrelated conditions. In our study, the majority were attributed to COVID-19 progression, while cardiac, orthopedic, other infectious, pulmonary, and renal conditions accounted for the majority of hospitalizations unrelated to COVID-19. The likelihood of hospitalization after the diagnosis of COVID-19 was significantly associated with the type and number of medical comorbidities.[13,14] In this study, we observed that patients with MASS of 1 (comprised exclusively of patients with hypertension as a single risk factor) had significantly lower rates of worse outcomes when compared to groups with higher MASS. Indeed, patients who belonged to the highest risk group (MASS ≥6) had significantly highest rates of hospitalization. This observation is consistent with our prior report describing the correlation between MASS and rates of hospitalization in a cohort of high-risk patients with mild to moderate COVID-19 who did not receive monoclonal antibodies.[8] Collectively, these findings reflect the additive effect of comorbidities in defining the clinical outcomes of COVID-19, even in patients treated with monoclonal antibodies.

Among medical comorbidities in this high-risk population, chronic kidney disease, cardiovascular disease, chronic lung disease and an immunocompromised status were significantly associated with higher rates of all-cause hospitalization. While these medical conditions predispose to severe COVID-19, it is also possible that SARS-CoV-2 infection exacerbated some of these underlying comorbidities. Indeed, having chronic kidney and cardiovascular diseases were also associated with subsequent admission to the ICU. These medical conditions should therefore be weighted more than the others if resource allocation is implemented during periods of scarcity. These findings confirm our initial programmatic decision to assign higher score for having an immunocompromised status, chronic lung disease and chronic kidney disease.[15-17] In contrast, our study did not identify diabetes as risk factor for hospitalization, and surprisingly showed that having a higher BMI had lower risk of hospitalization and need for ICU admission. Hypertension on its own does not appear to confer risk of hospitalization, since no person with MASS 1 was hospitalized.

However, hypertension appears to provide additive or synergistic effect with another medical comorbidity.

There were several non-clinical factors, such as older age and male gender, that were significantly associated with higher rates of hospitalization after monoclonal antibody infusion. Surprisingly, the time duration from the onset of symptoms and PCR diagnosis to monoclonal antibody infusion did not significantly correlate with the clinical outcomes. This is counterintuitive to the recommendation to treat eligible patients as early as possible. However, we emphasize that our strategy of encouraging early rapid testing and our pro-active approach of contacting all eligible patients led to the short time to infusion (median time, 2 days from PCR test), with the majority of patients infused within 5 days of symptom onset.

Limitations

This study had an observational and retrospective design that did not allow for a standardized data collection process. Relying on available information in our EHR system and databases may not have captured patients who subsequently obtained care in other facilities. This limitation is somewhat mitigated by an extensive institution-wide outpatient Remote Monitoring Program, a nurse-led program that follows enrolled patients with high risk characteristics using a telemedicine platform.[18,19] This Remote Monitoring Program involved daily conversations between enrolled patients and nurses to identify those needing to be evaluated due to worsening COVID-19 symptoms. Second, this study did not compare the outcomes with an untreated control population since our primary aim was only to compare the two monoclonal antibody products and to assess factors associated with hospitalizations in treated patients. In our analysis of untreated patients during the study period, the crude 28-day hospitalization rate was approximately 5%, which is higher than the rate for the antibody-treated patients. However, we caution against direct comparison of

these rates as it is likely biased; there are social, cultural, and medical factors that are significantly different between those who were infused monoclonal antibodies and those who declined treatment.[8] Indeed, the true measure of the efficacy of these monoclonal antibody therapies may be answered conclusively only by the ongoing randomized controlled trials. Third, the comparison between the two monoclonal antibody products was not based on randomized allocation. Random allocation was not possible or ethical because the program completely relied on the drug supplies allocated form our state health departments, and there was no existing data to support the superiority of one product over the other. This limitation is somewhat mitigated by the fact that the strict FDA EUA criteria homogenizes the patient population into an exclusively high-risk group. Despite the strict eligibility criteria, however, there was still a significant difference in the degree of baseline comorbidities between the two cohorts, as indicated by MASS distribution. To address this, we adjusted the analysis of clinical outcomes to account for this difference in comorbidity. Additionally, we assessed for the ability to adjust for these imbalances in demographic and clinical characteristics through direct and propensity matching statistical approaches. However, through evaluation of these methods, we noted the introduction of new imbalances, and were therefore unable to utilize a matched analytic approach. Fourth, the study population was predominantly Caucasian, and the clinical outcomes may not appropriately reflect those of non-Caucasian populations. Fifth, the overall rates of all-cause hospitalization were similarly low for both groups and these resulted in a small non-significant absolute difference in clinical outcomes between the two products. This limitation is mitigated by the large overall population, with over 3500 patients infused during the first 12 weeks of the program, which allowed for robust statistical analysis. Finally, this study was conducted on patients who received monoclonal antibody infusions during a period when potentially resistant variants are not yet known to be circulating in our communities. With their recent emergence, however, the knowledge of the infecting variant (at the patient level) or circulating variants (at the community level) will be helpful in the decision to use specific monoclonal antibody for treatment. Due to concerns of these resistant variants, the FDA has

revoked the EUA for bamlanivimab monotherapy, leaving bamlanivimab-etesevimab, casirivimab-imdevimab, and sotrovimab as current options for treatment.[20] More recently, the Department of Health and Human Services has advised against the use of bamlanivimab-etesevimab in communities where potentially resistant P.1 (gamma) and B.1.351 (beta) variants account for >10% of circulating virus.

Conclusion

This real-world analysis of a large cohort of high-risk patients with mild to moderate COVID-19 showed a low rate of all-cause hospitalization after treatment with anti-spike monoclonal antibody. The rates of 28-day all-cause and COVID-19-related hospitalization appeared higher among patients who received bamlanivimab monotherapy compared to casirivimab-imdevimab combination, although this did not reach statistical significance, and may be accounted for by the higher medical comorbidity in the bamlanivimab cohort. In this homogenous population of exclusively high-risk patients, there were a number of medical comorbidities that were more likely to be associated with all-cause 28-day hospitalization despite monoclonal antibody therapy. Moreover, there was a relationship between the total number of comorbidities, as measured by MASS, and the likelihood of all-cause hospitalization.

Funding:

This study was funded by an intramural grant awarded to Raymund R Razonable from the Mayo Clinic.

Acknowledgments:

The authors would like to thank all the members of the Monoclonal Antibody Treatment (MATRx) Program of the Mayo Clinic.

REFERENCES:

1. Chen P, Nirula A, Heller B, et al. SARS-CoV-2 Neutralizing Antibody LY-CoV555 in Outpatients with Covid-19. *N Engl J Med.* 2021;384(3):229-237.
2. Gottlieb RL, Nirula A, Chen P, et al. Effect of Bamlanivimab as Monotherapy or in Combination With Etesevimab on Viral Load in Patients With Mild to Moderate COVID-19: A Randomized Clinical Trial. *JAMA.* 2021;325(7):632-644.
3. Weinreich DM, Sivapalasingam S, Norton T, et al. REGN-COV2, a Neutralizing Antibody Cocktail, in Outpatients with Covid-19. *N Engl J Med.* 2021;384(3):238-251.
4. An EUA for Bamlanivimab-A Monoclonal Antibody for COVID-19. *JAMA.* 2020.
5. An EUA for casirivimab and imdevimab for COVID-19. *Med Lett Drugs Ther.* 2020;62(1614):201-202.
6. Razonable RR, Aloia NCE, Anderson RJ, et al. A Framework for Outpatient Infusion of Anti-Spike Monoclonal Antibodies to High-Risk Patients with Mild to Moderate Coronavirus Disease-19: The Mayo Clinic Model. *Mayo Clinic Proceedings.*
7. An EUA for bamlanivimab and etesevimab for COVID-19. *Med Lett Drugs Ther.* 2021;63(1621):49-50.
8. Bierle DM, Ganesh R, Wilker CG, et al. Influence of Social and Cultural Factors on the Decision to Consent for Monoclonal Antibody Treatment among High-Risk Patients with Mild-Moderate COVID-19. *J Prim Care Community Health.* 2021;12:21501327211019282.
9. Dejnirattisai W, Zhou D, Supasa P, et al. Antibody evasion by the P.1 strain of SARS-CoV-2. *Cell.* 2021.
10. Weisblum Y, Schmidt F, Zhang F, et al. Escape from neutralizing antibodies by SARS-CoV-2 spike protein variants. *Elife.* 2020;9.
11. Wu A, Wang L, Zhou HY, et al. One year of SARS-CoV-2 evolution. *Cell Host Microbe.* 2021;29(4):503-507.
12. CDC. SARS-CoV-2 Variant Classifications and Definitions. https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/variant-surveillance/variant-info.html. Published 2021. Updated 3/24/21. Accessed 4/21/21, 2021.
13. Gold MS, Sehayek D, Gabrielli S, Zhang X, McCusker C, Ben-Shoshan M. COVID-19 and comorbidities: a systematic review and meta-analysis. *Postgrad Med.* 2020;132(8):749-755.
14. Yang J, Zheng Y, Gou X, et al. Prevalence of comorbidities and its effects in patients infected with SARS-CoV-2: a systematic review and meta-analysis. *Int J Infect Dis.* 2020;94:91-95.
15. Gosain R, Abdou Y, Singh A, Rana N, Puzanov I, Ernstoff MS. COVID-19 and Cancer: a Comprehensive Review. *Curr Oncol Rep.* 2020;22(5):53.
16. Nair V, Jandovitz N, Hirsch JS, et al. COVID-19 in kidney transplant recipients. *Am J Transplant.* 2020;20(7):1819-1825.
17. Gao YD, Ding M, Dong X, et al. Risk factors for severe and critically ill COVID-19 patients: A review. *Allergy.* 2021;76(2):428-455.
18. Ganesh R, Salonen BR, Bhuiyan MN, et al. Managing Patients in the COVID-19 Pandemic: A Virtual Multidisciplinary Approach. *Mayo Clin Proc Innov Qual Outcomes.* 2021;5(1):118-126.
19. O'Horo JC, Cerhan JR, Cahn EJ, et al. Outcomes of COVID-19 With the Mayo Clinic Model of Care and Research. *Mayo Clinic Proceedings.* 2020.
20. FDA. Coronavirus (COVID-19) Update: FDA Revokes Emergency Use Authorization for Monoclonal Antibody Bamlanivimab. FDA NEWS RELEASE Web site. https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-revokes-emergency-use-authorization-monoclonal-antibody-bamlanivimab. Published 2021. Accessed 4/21/21, 2021.

Table 1. Characteristics of patients who received outpatient anti-spike monoclonal antibody therapy for COVID-19, by medication and total population.

	Bamlanivimab (N=2747)	Casirivimab-Imdevimab (N=849)	Total Population (N=3596)	p value
Age group				0.9
<20	12 (0.4%)	6 (0.7%)	18 (0.5%)	
20-29	74 (2.7%)	17 (2.0%)	91 (2.5%)	
30-39	181 (6.6%)	56 (6.6%)	237 (6.6%)	
40-49	281 (10.2%)	91 (10.7%)	372 (10.3%)	
50-59	481 (17.5%)	156 (18.4%)	637 (17.7%)	
60-69	803 (29.2%)	244 (28.7%)	1047 (29.1%)	
70-79	617 (22.5%)	184 (21.7%)	801 (22.3%)	
80-89	248 (9.0%)	74 (8.7%)	322 (9.0%)	
90-99	49 (1.8%)	20 (2.4%)	69 (1.9%)	
100+	1 (0.0%)	1 (0.1%)	2 (0.1%)	
Gender				0.1
Female	1351 (49.2%)	446 (52.5%)	1797 (50.0%)	
Male	1396 (50.8%)	403 (47.5%)	1799 (50.0%)	
Ethnicity				0.3
Hispanic or Latino	137 (5.0%)	32 (3.8%)	169 (4.7%)	
Not Hispanic or Latino	2554 (93.0%)	798 (94.0%)	3352 (93.2%)	
Unknown	56 (2.0%)	19 (2.2%)	75 (2.1%)	
Race				0.3
Other	180 (6.6%)	64 (7.5%)	244 (6.8%)	
White	2567 (93.4%)	785 (92.5%)	3352 (93.2%)	
Marital status				0.3
Divorced	213 (7.8%)	63 (7.4%)	276 (7.7%)	
Married/Partner	1980 (72.1%)	596 (70.2%)	2576 (71.6%)	
Other	205 (7.5%)	80 (9.4%)	285 (7.9%)	
Single	349 (12.7%)	110 (13.0%)	459 (12.8%)	
Language Interpreter Needed	35 (1.3%)	8 (0.9%)	43 (1.2%)	0.4
Time to infusion, Mean (SD)	2.8 (1.5)	2.8 (1.5)	2.8 (1.5)	0.3
Most recent Body Mass Index, Mean (SD)	32.6 (8.3)	32.4 (8.8)	32.5 (8.4)	0.5
MASS Group				0.008
Missing	49	19	68	
1	56 (2.1%)	23 (2.8%)	79 (2.2%)	
2-3	1127 (41.8%)	370 (44.6%)	1497 (42.4%)	
4-5	750 (27.8%)	250 (30.1%)	1000 (28.3%)	
6+	765 (28.4%)	187 (22.5%)	952 (27.0%)	
Monoclonal Antibody Qualifying Condition				
Body Mass Index risk	1067 (38.8%)	313 (36.9%)	1380 (38.4%)	0.3
Chronic kidney disease risk	54 (2.0%)	9 (1.1%)	63 (1.8%)	0.1

Table 1. Characteristics of patients who received outpatient anti-spike monoclonal antibody therapy for COVID-19, by medication and total population.

	Bamlanivimab (N=2747)	Casirivimab-Imdevimab (N=849)	Total Population (N=3596)	p value
Cardiovascular disease risk	613 (22.3%)	168 (19.8%)	781 (21.7%)	0.1
Diabetes mellitus risk	761 (27.7%)	216 (25.4%)	977 (27.2%)	0.2
Hypertension risk	1463 (53.3%)	410 (48.3%)	1873 (52.1%)	0.01
Immunosuppression risk	413 (15.0%)	122 (14.4%)	535 (14.9%)	0.6
Respiratory disease risk	409 (14.9%)	112 (13.2%)	521 (14.5%)	0.2

MASS, monoclonal antibody screening score

Table 2. Rates of 28-day all-cause hospitalization, emergency department visit, intensive care unit admission, and use of mechanical ventilator for 3,596 patients following anti-spike monoclonal antibody therapy for COVID-19.

	Hospitalization*	Emergency Department Visits	Intensive Care Unit Admission	Ventilator Use
Bamlanivimab	119 (4.34%)	213 (7.76%)	21 (0.77%)	4 (0.15%)
Casirivimab-Imdevimab	24 (2.83%)	64 (7.54%)	5 (0.77%)	0 (0.00%)
Total Population	143 (3.98%)	277 (7.71%)	26 (0.72%)	4 (0.11%)

*Denotes significantly different proportions based on Chi Square test for differences or Fisher Exact Test based on necessary test assumptions. All others are not statistically significant.

Table 3. Rates of 28-day all-cause hospitalization, emergency department visit, intensive care unit admission, and use of mechanical ventilator for 3,596 patients who received monoclonal antibody therapy for COVID-19, stratified based on demographic and social factors.

	Hospitalization	Emergency Department Visit	Intensive Care Unit Admission	Ventilator Use
Age group, in years				
<20		2 (11.11%)*		
20-29	2 (2.20%)*	10 (10.99%)	1 (1.10%)	
30-39	3 (1.27%)	47 (19.83%)		
40-49	6 (1.62%)	40 (10.78%)	1 (0.27%)	
50-59	11 (1.73%)	95 (14.91%)	1 (0.16%)	
60-69	40 (3.82%)	113 (10.80%)	10 (0.96%)	
70-79	42 (5.24%)	130 (16.23%)	11 (1.37%)	
80-89	30 (9.32%)	70 (21.74%)	3 (0.93%)	
90-99	8 (11.59%)	14 (20.29%)		
100+		1 (50.00%)		
Gender				
Female	58 (3.23%)*	158 (8.80%)*	9 (0.50%)	2 (0.11%)
Male	85 (4.72%)	119 (6.61%)	17 (0.94%)	2 (0.11%)
Ethnicity				
Hispanic or Latino	6 (3.55%)	18 (10.65%)	1 (0.59%)	
Not Hispanic or Latino	137 (4.09%)	256 (7.64%)	25 (0.75%)	4 (0.12%)
Unknown		3 (4.00%)		
Race				
White	129 (3.85%)	252 (7.52%)	21 (0.63%)*	3 (0.09%)
Other	14 (5.74%)	25 (10.25%)	5 (2.05%)	1 (0.41%)
Marital status				
Married/Partner	94 (3.65%)*	176 (6.83%)*	19 (0.74%)	2 (0.08%)
Divorced	18 (6.55%)	26 (9.45%)	2 (0.73%)	1 (0.36%)
Single	10 (2.18%)	36 (7.84%)	2 (0.44%)	1 (0.22%)
Other	21 (7.39%)	39 (13.73%)	3 (1.06%)	
Days to infusion±				
0-1	23 (4.50%)	39 (7.63%)	2 (0.39%)	
2	49 (3.73%)	96 (7.32%)	11 (0.84%)	1 (0.08%)
3	38 (4.65%)	63 (7.70%)	7 (0.86%)	1 (0.12%)
4	17 (3.57%)	32 (6.72%)	3 (0.63%)	2 (0.42%)
5+	13 (2.96%)	43 (9.79%)	3 (0.68%)	
Language interpreter use				
No	141 (4.01%)	269 (7.60%)*	25 (0.71%)	4 (0.11%)
Yes	1 (2.22%)	8 (17.78%)	1 (2.22%)	

*Denotes significantly different ($p<0.05$) proportions based on Chi Square test for differences or Fisher Exact test. All others without asterisk are not statistically significant. ±Days to infusion is from symptom onset.

Table 4. Rates of 28-day all cause hospitalization, emergency department visit, intensive care unit admission, and use of mechanical ventilator for 3,596 patients who received monoclonal antibody therapy for COVID-19, stratified based on medical comorbidities.

	Hospitalization	Emergency Department Visit	Intensive Care Unit Admission	Ventilator Use
MASS Group				
1	0 (0.00%)*	4 (5.06%)	0 (0.00%)	
2 to 3	32 (2.14%)	102 (6.82%)	9 (0.60%)	1 (0.07%)
4 to 5	30 (3.00%)	80 (8.00%)	4 (0.40%)	
6+	81 (8.51%)	88 (9.24%)	13 (1.37%)	3 (0.32%)
Body Mass Index Risk				
No	108 (4.88%)*	177 (7.99%)	21 (0.95%)*	4 (0.18%)
Yes	35 (2.54%)	100 (7.25%)	5 (0.36%)	
Chronic Kidney Disease Risk				
No	131 (3.71%)*	267 (7.56%)*	22 (0.62%)*	3 (0.08%)
Yes	12 (19.05%)	10 (15.87%)	4 (6.35%)	1 (1.59%)
Chronic Respiratory Disease Risk				
No	112 (3.64%)*	233 (7.58%)	19 (0.62%)	3 (0.10%)
Yes	31 (5.95%)	44 (8.45%)	7 (1.34%)	1 (0.19%)
Diabetes mellitus Risk				
No	100 (3.82%)	185 (7.07%)*	18 (0.69%)	1 (0.04%)
Yes	43 (4.40%)	92 (9.42%)	8 (0.82%)	3 (0.31%)
Hypertension Risk				
No	41 (2.38%)*	114 (6.62%)*	8 (0.46%)	
Yes	102 (5.45%)	163 (8.70%)	18 (0.96%)	4 (0.21%)
Immunosuppressed Status Risk				
No	98 (3.20%)*	231 (7.55%)	21 (0.69%)	3 (0.10%)
Yes	45 (8.41%)	46 (8.60%)	5 (0.93%)	1 (0.19%)
Cardiovascular Disease Risk				
No	90 (3.20%)*	209 (7.43%)	14 (0.50%)*	2 (0.07%)
Yes	53 (6.79%)	68 (8.71%)	12 (1.54%)	2 (0.26%)

*Denotes significantly different ($p<0.05$) proportions based on Chi Square test for differences or Fisher Exact test. All others without an asterisk are not statistically significant. MASS, Monoclonal Antibody Screening Score

Figure Legends

Figure 1. Proportional hazards of all-cause and COVID-19-related hospitalizations within 28 days for Bamlanivimab and Casirivimab-Imdevimab-treated groups, with adjustment for Monoclonal Allocation Screening Score.

Figure 1