Early Monoclonal Antibody Administration Can Reduce Both Hospitalizations and Mortality in High-Risk Outpatients with COVID-19

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Dear Editor:

We read with interest the article by Kumar and colleagues, who reported good experience with the neutralizing monoclonal antibody (mAb) bamlanivimab [1]. We developed a COVID-19 clinic during pandemic surge conditions and prioritized mAb infusion to high-risk patients, particularly with casirivimab/imdevimab, and would like to share our experience given limited data published on the efficacy of casirivimab/imdevimab.

We performed a retrospective review of medical records of patients referred to our clinic from 11/1/2020-2/28/2021 and included only those ≥18 years and considered high-risk. Patients were defined as high-risk (and assigned a risk score) if they met ≥1 criteria: age ≥65 years (3 points), body mass index ≥35 (3 points), age ≥55 years with hypertension, coronary artery disease or chronic lung disease (2 points), diabetes mellitus, chronic kidney disease, or immunosuppression (2 points each). One additional point was assigned for Black, Native American, and/or Hispanic/Latino ethnicity. Casirivimab/imdevimab or bamlanivimab was offered to all high-risk outpatients within 5 days of COVID-19 diagnosis via positive polymerase chain reaction. We extracted baseline demographics, medical co-morbidities, receipt of mAb, and 30-day outcomes including hospitalization and death related to COVID-19.

We performed unadjusted analyses used Fisher's exact test and t-test; and multivariate analysis using logistic regression controlling for risk score and local pandemic intensity. Sensitivity analyses did not find other significant predictors. Tests were 2-sided with an α level of .05 and performed using Stata version 12.1 (StataCorp) and R. The study was

approved by the Human Research Protections Program at the University of California San Diego.

Among 617 patients, 175 received mAb and 442 did not (control). The mAb group was older, had more men, more comorbidities, and a higher risk score. Casirivimab/imdevimab was given in 83.4% and bamlanivimab 16.6%. The majority (94%) received mAb within 5 days of symptom onset. There was a significant reduction in hospitalizations in the mAb group vs. control (1.7% vs. 24%, $p<0.005$) (**Table**), which was noted in the subset of patients only seen in our Telemedicine Clinic as well. Notably, there were no COVID-19-related deaths in the mAb group vs. 12 (2.7%) in controls ($p=0.024$). Mean length of stay for COVID-19-related hospitalization was shorter in those that received mAb, though not statistically significant. The number needed to treat (NNT) to prevent one hospitalization was 4.5. Hospitalization and mortality within 30 days were independently associated with receipt of mAb and the risk score via multivariate analysis.

Similar to the experience of Kumar and colleagues with bamlanivimab, we found that mAb receipt, primarily with casirivimab/imdevimab, was associated with a significant reduction in hospitalization. Unlike Kumar and colleagues, though, we found a lower mortality rate in the mAb group compared to controls and our NNT of 4.5 to prevent one hospitalization was lower than what they report. The significant reduction in COVID-19 related hospitalizations and death with early mAb administration should prompt more widespread use and development of dedicated outpatient COVID-19 centers to treat patients with COVID-19 infection, and this strategy may serve as a model in future infectious disease outbreaks.

NOTES

Author Contributions:

Drs Jenks, Aslam, Vaida and Ritter had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. All authors contributed to data collection.

Concept and design: All authors.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Jenks, Aslam, Ritter

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Aslam, Vaida.

Administrative, technical, or material support: Ritter

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Conflict of interest:

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SA: Grant funding by the Cystic Fibrosis Foundation. Received personal fees as a consultant for Merck and Gilead. Served as unpaid advisor for BioMx.

All others report no potential COI.

References

1. Kumar RN, Wu EL, Stosor V, et al. Real-World Experience of Bamlanivimab for COVID-19: A Case-Control Study. Clin Infect Dis **2021**.

Table. Outcomes of high-risk patients with COVID-19 based on whether they received monoclonal antibody (mAb group) or not (Control). Clinic cohort consists of the subset of the total cohort that was evaluated in the COVID-19 clinic.

Outcome	**mAb (N=174)**	**No mAb (N=442)**	**Bivariate Odds Ratio (95% CI)**	**p-value**	**Multivariate Odds Ratio (95% CI)**	**p-value**
Total Cohort						
Hospitalization due to COVID-19	3 (1.7%)	106 (24.0%)	0.055, (0.011, 0.170),	<0.0001	*0.0466, (0.0113, 0.128)	<0.0001
Mean days from symptom onset to hospitalization (SD)	4.67 (0.58)	9.37 (4.12)		0.052		
Mean number of days hospitalized (SD)	4.3 (1.15)	7.04 (7.18)		0.5		
Death from COVID-19	0	12 (2.71%)	0, (0, 0.897)	0.024	**0, 95% (0, 0)	0.0016.
Clinic Cohort	174	253				
Hospitalization due to COVID-19	3 (1.7%)	42 (16.6%)	0.088, (0.0172, 0.284)	<0.0001	***0.0693, (0.0162, 0.201)	< 0.0001
Death from COVID-19	0	1 (0.4%)	0, (0, 56.6),	1.0	-	-

COVID: coronavirus disease 2019; mAb: monoclonal antibody; SD: standard deviation

*Multivariate analysis included adjustment for risk score and local pandemic intensity (measured by rolling daily 7-day average of the number of daily cases in San Diego county, based on the NY Times github project) In this analysis, the risk score was statistically significant, OR = 1.121 per unit, 95% CI (1.016, 1.237), p-value = 0.023 as was the San Diego case rate, OR = 1.47 per 1000 daily cases, 95% CI (1.13, 1.93), p-value = 0.004.

** Multivariate analysis included adjustment for risk score The risk score was statistically significant, OR = 1.310 per unit, 95% CI (1.028, 1.661), p-value = 0.030. The San Diego case rate was not statistically significant at $p<0.15$, and not included in the model.

*** Multivariate analysis included adjustment for risk score. The risk score was statistically significant, OR = 1.254, 95% CI (1.094, 1.444), p-value = 0.0012. The San Diego case rate /1000 population was not statistically significant at $p<0.15$, and not included in the model.