Real-world evaluation of the impact of two anti-SARS-CoV-2 monoclonal antibody regimens on COVID-19 hospitalizations in older adults

Kristine A. Sobolewski1 | Steven M. Smoke1 | Alison Brophy1 | Andrew V. Vassallo2 | Brandon Chen3 | Patrick Hilden4 | Rebecca Patterson2 | Marina Pittiglio2 | Karan Raja3 | Eric Handler5 | Christopher Freer6

1Pharmacy Department, Saint Barnabas Medical Center, Livingston, New Jersey, USA
2Department of Pharmacy, Community Medical Center, Toms River, New Jersey, USA
3Pharmacy Department, Clara Maass Medical Center, Belleville, New Jersey, USA
4Biostatistics Department, Saint Barnabas Medical Center, Livingston, New Jersey, USA
5Emergency Department, Saint Barnabas Medical Center, Livingston, New Jersey, USA
6Emergency and Hospitalist Medicine Service Line, RWJBarnabas Health, West Orange, New Jersey, USA

Correspondence
Steven M. Smoke, Pharmacy Department, Saint Barnabas Medical Center, 94 Old Short Hills Rd, Livingston, NJ 07039, USA.
Email: Steven.smoke@rwjbh.org

Abstract
Evidence from clinical trials suggest anti-SARS-CoV-2 monoclonal antibodies (mABs) may reduce coronavirus disease 2019 (COVID-19)-related hospitalizations. The purpose of this study was to assess the real-world impact of mAB administration on COVID-19 hospitalization among patients 65 years or older. This was a retrospective, propensity-matched cohort study that included patients aged 65 years and older who presented to the emergency department (ED) within 10 days of symptom onset of mild to moderate COVID-19 infection. Outcomes were compared between those who did and did not receive mAB therapy. The primary endpoint was the rate of hospitalization for COVID-19 within 30 days of index ED visit. A total of 137 patients receiving mABs were matched to 137 controls. Hospitalization occurred in 2.9% of mAB-treated patients compared to 14.6% of patients of the standard of care (SOC) arm (odds ratio: 0.20 [95% CI: 0.07–0.59]). There were zero intubations and zero deaths compared to 3 (2.2%) and 2 (1.5%) in the SOC group. Among the 223 patients receiving mAB in the overall cohort, adverse drug events occurred in 10 (4.5%). Treatment with mAB therapy for mild to moderate COVID-19 was associated with a substantially reduced risk of hospitalization among patients at least 65 years of age.

Keywords
anti-SARS-CoV-2 monoclonal antibodies, bamlanivimab, casirivimab + imdevimab, COVID-19, older adults

1 | INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first identified in December 2019 and is the causative pathogen implicated in the development of coronavirus disease 2019 (COVID-19).1 The spread of this virus escalated to a global pandemic in the spring of 2020 and continues to impact public health. Patients infected with SARS-CoV-2 have variability in symptom presentation from asymptomatic disease to severe disease resultant in acute respiratory distress syndrome and death. The mortality rate for COVID-19 is approximately 1% and increases with additional patient risk factors, such as obesity, immunosuppression, and increasing age.1

The viral entry mechanism of SARS-CoV-2 is mediated by binding of the viral spike protein to receptors for angiotensin-converting enzyme 2 on target cells. This led to the development of potent anti-SARS-CoV-2 monoclonal antibody (mAB) therapies. Studies assessing
attenuation of disease progression have been conducted to evaluate the efficacy of anti-SARS-CoV-2 mABs as targeted antiviral therapies.\textsuperscript{2–4} In November of 2020, the United States Food and Drug Administration (FDA) granted the first Emergency Use Authorizations (EUA) for mABs for the treatment of mild to moderate COVID-19 among those at high risk for disease progression.

The first two therapies available through this EUA were bamlanivimab and the combination therapy, casirivimab + imdevimab. The Phase 2 portions of the BLAZE-1 trial and REGN-COV2 for non-hospitalized patients trial evaluated the impact of mABs on SARS-CoV-2 viral load reduction and associated patient outcomes.\textsuperscript{2–4} Use of these agents was associated with a decreased rate of hospitalization in high-risk patients presenting with COVID-19. Specifically, in a post hoc analysis of patients greater than or equal to 65 years of age or with body mass index (BMI) of greater than 35, hospitalization was required in 4% of patients in the bamlanivimab treated group compared to 15% in the placebo group.\textsuperscript{4} With increasing global use and emergency authorization of these agents, there is a growing need to review current use and resultant patient outcomes through a real-world analysis.

These treatment modalities received EUA specifically in high-risk patient groups, which was notably not the focus of the early portions of the trials but determined based on findings of the post hoc analysis. The clinical trials were not designed to detect differences in key clinical outcomes, including hospitalization. Considering that the Phase 3 portions of the underlying clinical trials were ongoing at the time of the emergency use authorization issuances, evidence from real-world settings will aid in validating the clinical trial results in parallel. The purpose of this study was to determine if use of either of the available mABs therapies, bamlanivimab monotherapy and casirivimab + imdevimab, for COVID-19 resulted in lower rates of hospitalization compared to the standard of care (SOC) outside the clinical trial environment in patients age 65 years or older.

2 | METHODS

2.1 | Study setting

RWJBarnabas Health consists of 11 hospitals in the state of New Jersey, and is one of the largest health care systems in the state. The emergency department (ED) served as the primary setting for which the mAB agents were administered. mAB treatment was available both for patients referred from the community and for those eligible for treatment without referrals. Three large, community hospitals within RWJBarnabas Health with a high portion of usage of these agents were selected for patient capture. These hospitals were selected due to the availability of data from a consistent electronic medical record. This multi-center retrospective cohort analysis was conducted from June 1, 2020 through December 31, 2020. Since mAB therapy was not available at the study sites before November 18, 2020 all patients in the mAB treatment cohort were seen between November 18, 2020, and December 31, 2020. The trial was reviewed and approved by the local institutional review boards at all participating centers. Investigators at each site reviewed charge codes for COVID-19 diagnosis and utilized the electronic medication record to access all key clinical data findings.

2.2 | Patients

Patients aged 65 years and older who presented to the ED for the first time, tested positive for SARS-CoV-2 by polymerase chain reaction or antigen test, and had one or more mild to moderate symptoms were assessed for inclusion. The COVID-19 symptoms assessed were consistent with those from the BLAZE-1 trial; patients must have reported one of the following: cough, fever, body aches/pain, sore throat, chills, loss of taste, diarrhea, shortness of breath, fatigue, loss of appetite, headache, or loss of smell. Patients with generalized upper respiratory symptoms identified in the provider documentation were also considered symptomatic and were included. Patients were excluded if they presented with symptoms for greater than 10 days, required hospitalization on the index visit, required supplemental oxygenation, or had previously presented to the ED for COVID-19. All high-risk criteria as determined by the EUA for the mABs were evaluated. Severity of disease was assessed according to the National Institute of Health (NIH) SARS-CoV-2 infection definitions: patients without shortness of breath, dyspnea, or abnormal chest imaging classified as mild and those with shortness of breath, dyspnea, or abnormal chest imaging and not requiring supplemental oxygen were considered moderate.\textsuperscript{5} Risk of disease progression was assessed using the CALL score.\textsuperscript{5} The CALL score uses four variables (presence of comorbidities, age, lymphocyte count, and lactate dehydrogenase) to calculate a risk for progression to severe COVID-19. Scores range from 4 to 13, with scores from 4 to 6 having low risk for progression, 7–9 having an intermediate risk for progression, and 10–13 having a high risk for progression. For patients without laboratory assessments, values were presumed to be within normal limits.

2.3 | Treatment groups

The mAB treatment cohort included patients who met inclusion criteria and received either of the available mAB therapies during the time of the study, bamlanivimab 700 mg or casirivimab 1200 mg/imdevimab 1200 mg. SOC patients included those who met criteria for the mAB agents but did not receive them (i.e., seeking care before mAB FDA EUA, patient refusal to mAB therapy, or other undocumented reasons).

2.4 | Primary and secondary outcomes

The primary outcome was hospitalization within the healthcare system for worsening COVID-19 within 30 days following index
presentation to the ED. Secondary outcomes included a composite evaluation of hospitalization and ED revisits with 30 days of initial ED presentation. Additionally, intubation, hospital mortality, and treatment emergent adverse events (TEAEs) were evaluated independently. Outcomes data were collected utilizing the electronic medical record of the index hospital and five other hospitals in the health care system. Insurance claim data, ED visit, or hospitalization data external to this health system were not available.

2.5 Statistical analysis

In the overall cohort, differences in patient and treatment characteristics between patients receiving mAB versus SOC were evaluated using the Wilcoxon rank-sum test for continuous characteristics and the χ² or Fisher’s exact test for categorical characteristics as appropriate. Due to potential confounding by indication or selection for mAB, we utilized a matched propensity score analysis to identify the odds ratio (OR) of hospitalization by mAB exposure. The propensity model included symptom onset to ED presentation (days), severity, age, sex, temperature, BMI, and CALL score (group). Patients were matched 1:1 from the mAB and SOC groups using a caliper of 0.2, with exact matching also performed by a specific site to control for facility-specific effects. Self-reported race or ethnicity was not included in the analysis due to inconsistent availability. Differences in patient and treatment characteristics, as well as outcomes in the matched cohort, were assessed using a conditional logistic regression model, which accounted for the matched pairs of patients. All significance tests were two-sided with p < 0.05 considered significant. Results were reported as median (range) and N(%) where appropriate. Analyses were completed in R 4.0.2.

3 RESULTS

Across the three study sites, 675 patients found to be positive for COVID-19 during ED visit were screened and 429 patients were included in the overall cohorts. The reasons for exclusion were asymptomatic presentation (n = 105), duration of symptoms greater than 10 days (n = 34), admitted from the ED (n = 30), COVID-19 negative (n = 25), severe COVID-19 (n = 22), non-index COVID-19 visit (n = 18), and index visit outside date range (n = 12). Baseline characteristics for both the overall and matched cohort are summarized in Table 1. In the overall analysis, there were 206 and 223 patients identified in the SOC and mAB groups, respectively. Differences between groups were identified in the distribution of ED location (p < 0.0001), duration of symptoms (3 [0, 10] vs. 4 [0, 10] days, p = 0.036), CALL score (9 [6, 13] vs. 9 [6, 12], p = 0.033), temperature (98.7 [96.5, 103.4] vs. 99 [97, 103.3], p = 0.004), and lowest oxygen saturation (96 [90, 100] vs. 96 [90, 100], p = 0.022). All other characteristics, including age, severity of illness, and BMI were similar between groups. Among those receiving mAB, 178 (79.8%) received bamlanivimab and 45 (20.2%) received casirivimab + imdevimab.

Of the 429 patients in the full cohort, 274 were propensity matched into 137 pairs and were included in the propensity-matched cohort. In this cohort, there were no significant differences between groups. The median symptom duration was 3 (0, 10) and 4 (1, 10) days in the SOC and mAB groups, respectively (p = 0.717). Severity of disease was mild in 62% and 59.9% of patients (p = 0.696). Median age was 71 (65, 97) and 73 (65, 100) years (p = 0.093). Median BMI was 27.9 in both groups (p = 0.346). Comorbidities, vital signs, and laboratory values were also similar between groups.

Outcomes are summarized in Table 2. In the propensity-matched cohort, the primary endpoint of hospitalization for COVID-19 within 30 days of the index visit occurred in 2.9% of patients treated with mAB compared with 14.6% of patients treated with SOC (OR: 0.20 [95% CI: 0.07–0.59], p = 0.003). When evaluating the composite rate of ED revisit or hospitalization, patients treated with mAB had a significantly decreased odds of experiencing the outcome at 30 days compared to those who did not receive mAB (5.8% vs. 16.8%, OR: 0.35 [0.16, 0.78]). Among patients treated with mAB, there were no intubations compared to three (2.2%) in the SOC group. There were no deaths in the mAB group compared to two (1.5%) in the SOC group.

In a post hoc analysis among those treated with mAB in the unmatched cohort, the primary outcome occurred in 10 of 178 (5.6%) patients receiving bamlanivimab and none (0%) of the 45 patients receiving casirivimab + imdevimab (p = 0.219). A greater number of patients receiving bamlanivimab (17 [9.6%]) experienced the composite outcome of ED revisit or hospitalization compared to those receiving casirivimab + imdevimab (0 [0%], p = 0.027). No difference was detected in the median timing from symptom onset to mAB administration among those who did and those who did not experience the primary outcome (4 [0, 10] vs. 4 [1, 5] days, p = 0.384).

TEAEs occurred in 10 (4.5%) of the 223 patients receiving mAB in the overall cohort. This included 4 (2.2%) TEAEs in patients receiving bamlanivimab and 6 (13.3%) TEAEs in patients receiving casirivimab + imdevimab. The TEAEs included hypoxia (3), headache (2), acute kidney injury (AKI) (1), chills (1), fever (1), hypertension (1), hypotension (1), nausea (1), shortness of breath (1), and syncope (1). All patients were discharged from the ED. The patient who experienced AKI subsequently returned to the ED and required hospitalization for further management.

4 DISCUSSION

This retrospective cohort analysis evaluated the efficacy and safety of mAB therapy for older patients presenting to the ED with mild to moderate COVID-19. Propensity score matching was used to adjust for potential selection bias in those receiving mAB versus not. When compared to those who did not receive mAB, mAB therapy was associated with significantly less 30-day hospitalization due to worsening COVID-19. These findings are critical as there are currently no fully FDA-approved therapies available for the treatment of mild to moderate COVID-19. The ability to institute effective therapies early
| Characteristic                                      | Overall cohort, N (%)/median (range) | Propensity matched cohort, N (%)/median (range) | p value | p value |
|---------------------------------------------------|--------------------------------------|-------------------------------------------------|---------|---------|
| Facility                                          |                                      |                                                  |         |         |
| Emergency department 1                            | SOC (N = 206) 59 (28.6) 41 (18.4) | mAB (N = 223) 34 (24.8) 34 (24.8) | <0.001  |         |
| Emergency department 2                            | SOC (N = 206) 94 (45.6) 59 (26.5) | mAB (N = 223) 51 (37.2) 51 (37.2) |         |         |
| Emergency department 3                            | SOC (N = 206) 53 (25.7) 123 (55.2) | mAB (N = 223) 52 (38.0) 52 (38.0) |         |         |
| Symptom onset to ED presentation (days)           |                                      |                                                  | 0.036   | 0.717   |
| Severity                                          |                                      |                                                  | 0.091   | 0.696   |
| Mild                                             | 132 (64.1) 124 (55.6)               | 85 (62) 82 (59.9)                               |         |         |
| Moderate                                          | 74 (35.9) 99 (44.4)                 | 52 (38) 55 (40.1)                               |         |         |
| Age (years)                                       | 72 (65, 97) 73 (65, 100)            | 71 (65, 97) 73 (65, 100)                        | 0.091   | 0.093   |
| Gender—male                                       | 86 (41.7) 112 (50.2)                | 61 (44.5) 60 (43.8)                            | 0.096   | 0.898   |
| BMI (kg/m²)                                       | 28.1 (17.9, 54.6) 27.6 (17.3, 46.9) | 27.9 (18.1, 54.6) 27.9 (17.3, 46.9)            | 0.122   | 0.346   |
| Comorbidities                                     |                                      |                                                  |         |         |
| Chronic kidney disease                            | 11 (5.3) 12 (5.4)                   | 8 (5.8) 8 (5.8)                                 | >0.999  | >0.999  |
| Immunosuppression                                 | 14 (6.8) 17 (7.6)                   | 8 (5.8) 12 (8.8)                                | 0.886   | 0.369   |
| Hypertension                                      | 117 (56.8) 139 (62.3)               | 83 (60.6) 82 (59.9)                             | 0.285   | 0.908   |
| Diabetes                                          | 50 (24.3) 60 (26.9)                 | 40 (29.2) 42 (30.7)                             | 0.608   | 0.789   |
| Cardiovascular disease                            | 48 (23.3) 57 (25.6)                 | 37 (27) 35 (25.5)                               | 0.666   | 0.793   |
| Chronic lung disease                              | 21 (10.2) 34 (15.2)                 | 14 (10.2) 23 (16.8)                             | 0.156   | 0.126   |
| CALL score                                        | 9 (6, 13) 9 (6, 12)                 | 9 (6, 12) 9 (6, 12)                             | 0.033   | 0.472   |
| CALL score (group)                                |                                      |                                                  | 0.196   | 0.400   |
| 4–6                                               | 49 (23.8) 38 (17.0)                 | 23 (16.8) 25 (18.2)                             |         |         |
| 7–9                                               | 115 (55.8) 131 (58.7)               | 83 (60.6) 72 (52.6)                             |         |         |
| 10–13                                             | 42 (20.4) 54 (24.2)                 | 31 (22.6) 40 (29.2)                             |         |         |
| Primary ED visit labs and vitals                  |                                      |                                                  |         |         |
| Temperature (F)                                   | 98.7 (96.5, 103.4) 99.0 (97.0, 103.3) | 98.9 (96.5, 103.4) 98.9 (97.0, 103.3)            | 0.004   | 0.991   |
| Mean arterial pressure (mmHg)                     | 96 (66, 128) 95 (71, 131)           | 96 (66, 128) 96 (71, 131)                       | 0.419   | 0.871   |
| Lowest O₂ saturation                              | 96 (90, 100) 96 (90, 100)           | 96 (90, 100) 96 (92, 100)                       | 0.022   | 0.763   |
| O₂ at discharge                                   | 97 (92, 100) 97 (93, 100)           | 97 (92, 100) 97 (93, 100)                       | 0.217   | 0.301   |
| Respiratory rate at discharge                     | 18 (14, 22) 18 (16, 26)             | 18 (14, 22) 18 (16, 22)                        | 0.097   | 0.302   |
| White blood cell count (k/mm³)                    | 5.1 (2.2, 17.5) 5.3 (1.9, 13.9)      | 5.0 (2.2, 17.5) 5.3 (2.7, 13.9)                | 0.271   | 0.394   |
| Absolute lymphocyte count (k/mm³)                 | 1.0 (0.3, 4.2) 0.9 (0.3, 5.6)       | 0.9 (0.3, 4.2) 0.9 (0.3, 5.6)                   |         |         |
| Serum creatinine (mg/dl)                          | 1.0 (0.4, 6.8) 1.0 (0.2, 2.7)       | 0.9 (0.4, 3.5) 1.0 (0.2, 2.7)                   | 0.519   | 0.749   |
| Chest imaging performed                           | 123 (59.7) 117 (52.5)               | 83 (60.6) 82 (59.9)                             | 0.158   | 0.903   |
| Abnormal chest imaging                            | 38 (30.9) 46 (39.3)                 | 27 (32.5) 32 (39)                               | 0.218   | 0.413   |

Abbreviations: BMI, body mass index; ED, emergency department; mAB, monoclonal antibody; SOC, standard of care.

aMissing data for 198/429.

bAny chest imaging consistent with lower respiratory tract disease.
on in the disease course is needed to prevent morbidity and mortality in the ongoing COVID-19 pandemic.

Recently, several studies have reported on the real-world experience and efficacy of anti-SARS-CoV-2 mABs in mild to moderate COVID-19.\(^6\)–\(^8\) Results from all three studies show consistent benefit with mAB therapy. Webb et al. found that treatment with mAB was associated with fewer ED visits or hospitalization within 14 days (OR: 0.69 [0.6–0.79]). Substantially reduced odds of hospitalization were found by Bariola et al. (OR: 0.31 [0.17–0.56], \(p = 0.00001\)) and in Kumar et al. the 30-day rate of hospitalization was found to be lower with the mAB group (RR: 0.37 [0.21–0.64], \(p < 0.001\)). These findings align with those in our study which identified a lower rate of 30-day rehospitalization in the mAB treated cohort (OR: 0.20 [0.07, 0.59], \(p < 0.001\)). Our study population included 100% of patients with at least one pre-defined risk factor per the EUA criteria.\(^2\)–\(^4\) Our results also identified that a total of nine patients with mild to moderate COVID-19 would need to be treated to prevent one hospitalization, which is similar to the post hoc analysis number needed to treat of 10 in the BLAZE-1 trial.\(^2\) These results further support mAB therapy as a key component in the management of mild to moderate COVID-19 among those at high risk for progression to severe disease.

Several notable differences exist between these recent studies and ours. First, our study only included patients with age 65 or greater, which resulted in an older patient population than that seen in the other studies. The other real-world experiences published utilized broad inclusion and exclusion criteria resulting in a heterogeneous population of patients at high risk for progression to severe disease. Benefits from this therapy may vary among sub-populations. Our study design allowed the identification of a treatment effect estimate specific for this older adult population.

Second, our study describes the use of mAB exclusively within the ED setting. The decrease in overall ED volume during the pandemic allowed for the launch of the mAB therapy in this setting with over 6000 patients treated across this New Jersey-based healthcare system. This has several important implications. Our patient population included walk-ins and provider referrals in both study groups, which may be a fundamentally different population than those seen exclusively in other outpatient settings. The ED setting also allowed collection of vital signs, as well as laboratory and radiographic data which enabled robust assessments of disease severity and prognosis. Advantages of mAB administration in the ED include highly trained and experienced staff, 24/7 availability, and ease of access for patients. The primary disadvantage of the ED setting is throughput challenges for the patients and the department. This experience demonstrates the feasibility of the deployment of intravenous therapy for outpatients in the ED during a pandemic.

It is important to note that the mAB treatment used most frequently in these studies was bamlanivimab monotherapy. While our subgroup analysis comparing mAB therapies noted numerically lower rates of hospitalization among those receiving casirivimab + imdevimab, this study was not appropriately designed to determine optimal mAB therapy regimen. More importantly, evidence from

### Table 2: Study outcome measures

| Study outcome measures                                                                 | Overall cohort, N (%)/median (range) | Primary outcome | Secondary outcomes |
|----------------------------------------------------------------------------------------|--------------------------------------|-----------------|-------------------|
| Hospitalization within 30 days of initial presentation                                 |                                      | 33 (16)         | 10 (4.5)          |
| Composite ED revisit or hospitalization within 30 days of initial presentation         |                                      | 40 (19.4)       | 17 (7.6)          |
| Intubation                                                                             |                                      | 7 (3.4)         | 0 (0)             |
| Mortality                                                                              |                                      | 6 (2.9)         | 0 (0)             |
| Mortality                                                                              |                                      | 6 (2.9)         | 0 (0)             |

| Propensity-matched cohort, N (%)/median (range)                                        |                                      |                 |                   |
|--------------------------------------------------------------------------------------|--------------------------------------|-----------------|-------------------|
| Hospitalization within 30 days of initial presentation                               |                                      | 20 (14.6)       | 4 (2.9)           |
| Composite ED revisit or hospitalization within 30 days of initial presentation       |                                      | 23 (16.8)       | 8 (5.8)           |
| Intubation                                                                             |                                      | 3 (2.2)         | 0 (0)             |
| Mortality                                                                              |                                      | 2 (1.5)         | 0 (0)             |

| Abbreviations: ED, emergency department; mAB, monoclonal antibody; OR, odds ratio; SOC, standard of care. |
|-----------------------------------------------------------------------------------------------|-----------------|-----------------|-------------------|
| *Standard of care is the reference group.*                                                    |                 |                 |                   |
preliminary in vitro studies suggests that emerging variants may evade neutralization for some mAB treatments. Unfortunately, genomic sequencing for identification of SARS-CoV-2 variants in our study was not available. Data from the Centers for Disease Control and Prevention's National Genomic Surveillance Program collected at the end of our study period indicate that variants of concern potentially resistant to mAB therapy were <4% of all sequenced viruses in the United States.

Since the completion of this study, distribution of bamlanivimab monotherapy was replaced by bamlanivimab + etesevimab and subsequently, bamlanivimab + etesevimab distribution was paused June 25, 2021 and reinitiated September 15, 2021 in the United States. All of these decisions were driven by genomic surveillance indicating increasing prevalence of variants shown to evade these mAB treatments. Therefore, while the therapy used primarily in this study is not currently recommended in the United States, our results support the role of anti-SARS-CoV-2 mAB therapy for mild to moderate COVID-19. That is, these results show that anti-SARS-CoV-2 mAB therapy is effective when in vitro data suggests activity against currently circulating variants.

Evidence from clinical trials indicated that mABs were largely well tolerated. We similarly found low rates of TEAEs, most of which were minor in severity. Additional questions regarding the optimal use of mAB therapy remain. This includes the timing of therapy relative to onset of symptoms. Our subgroup analysis, while underpowered, found no difference in the timing of therapy from symptom onset between those who were hospitalized and those who were not.

To our knowledge, this is the first trial to report findings of mAB treatment efficacy in a targeted high-risk subgroup, patients over 65 years, which accounts for a significant amount of usage of this agent across real-world data demographics. Our study also delineated and matched for both disease severity and risk of progression to severe COVID-19 to account for significant variables that may have influenced the outcome results. This trial did have several limitations. The accuracy of the data capture is limited by the detail provided through chart documentation. Readmission and ED revisit data may be underestimated as our data set was restricted to encounters within the healthcare system. The unbalanced timeframe for each cohort may make this study vulnerable to maturation bias. However, propensity score matching likely minimized the impact of this limitation. This analysis described the impact of patients treated within the ED. mABs have been deployed in other settings, including outpatient clinics and infusion centers, with patient populations that may differ from those presenting to the ED. Therefore, the impact of these agents in different settings may vary. Additionally, despite our propensity score matching methods, residual unmeasured confounding may exist to explain the difference in hospitalization rates that we found. Additionally, our study timeline briefly overlapped with the initiation of vaccination efforts, primarily for healthcare workers. We did not collect COVID-19 vaccination status. While vaccination may now have an impact on efficacy and patient selection of mAB therapy, our results are unlikely to be affected. The CALL score, which we used to assess the risk of disease progression, was derived from patients in China with non-severe COVID-19 who were admitted to the hospital. This score has not been validated in the ED setting. Collectively, our findings contribute to the growing data showing the clinical benefit of these therapeutic agents for treatment of COVID-19 and help to generate increased confidence in their use in preventing COVID-19 hospitalizations.

Our retrospective propensity-matched cohort study of patients at least 65 years of age with mild to moderate COVID-19 found that those who received mAB were significantly less likely than those who did not receive therapy to require hospitalization. These findings are consistent with data from clinical trials and other real-world reports. Treatment with mAB therapy should be considered a key component of the management of mild to moderate COVID-19 among those at least 65 years old.

ACKNOWLEDGMENTS
The authors would like to acknowledge Jennifer Sternbach, PharmD for her contribution to data acquisition.

CONFLICTS OF INTEREST
The authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS
Kristine A. Sobolewski contributed to study concept and design, data collection, interpretation and preparation of manuscript. Steven M. Smoke contributed to study design, data collection and preparation of manuscript. Andrew V. Vassallo, Brandon Chen, Rebecca Patterson, Marina Pittiglio, and Karan Raja contributed to data collection and preparation of manuscript. Patrick Hilden contributed to data analysis. Eric Handler and Christopher Freer contributed to preparation of manuscript.

DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID
Steven M. Smoke https://orcid.org/0000-0003-4847-3432
Karan Raja https://orcid.org/0000-0003-0173-3313

REFERENCES
1. COVID-19 Treatment Guidelines Panel. Coronavirus disease 2019 (COVID-19) treatment guidelines. National Institutes of Health. Accessed April 5, 2021. https://www.covid19treatmentguidelines.nih.gov/
2. 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. doi:10.1056/NEJMoa2029849
3. 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. doi:10.1001/jama.2021.0202
4. 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. doi:10.1056/NEJMoa2035002
5. Ji D, Zhang D, Xu J, et al. Prediction for progression risk in patients with COVID 19 pneumonia: the CALL score. Clin Inf Dis. 2020;71(6):1393-1399.

6. Webb BJ, Buckel W, Vento T, et al. Real-world effectiveness and tolerability of monoclonal antibody therapy for ambulatory patients with early COVID-19. Open Forum Infect Dis. 2021;8(7):ofab331. doi:10.1093/ofid/ofab331

7. Bariola JR, McCreary EK, Wadas RJ, et al. Impact of bamlanivimab monoclonal antibody treatment on hospitalization and mortality among non-hospitalized adults with SARS-CoV-2 infection. Open Forum Infect Dis. 2021:ofab254. doi:10.1093/ofid/ofab254

8. Kumar RN, Wu EL, Stosor V, et al. Real-world experience of bamlanivimab for COVID-19: a case-control study. Clin Infect Dis. 2021;13:ciab305. doi:10.1093/cid/ciab305

9. Wang P, Liu L, Iketani S, et al. Increased resistance of SARS-CoV-2 variants B.1.351 and B.1.1.7 to antibody neutralization. bioRxiv. 2021. doi:10.1101/2021.01.25.428137

10. Variant proportions in the U.S. National Center for Immunization and Respiratory Diseases, Division of Viral Diseases, Centers for Disease Control and Prevention. Accessed April 5, 2021. https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/variant-proportions.html

11. Assistant Secretary of Preparedness and Response. Pause in the distribution of bamlanivimab/etesevimab. U.S. Department of Health and Human Services. Accessed August 20, 2021. https://www.phe.gov/emergency/events/COVID19/investigation-MCM/Bamlanivimab-etesevimab/Pages/bamlanivimab-etesevimab-distribution-pause.aspx

**How to cite this article:** Sobolewski KA, Smoke SM, Brophy A, et al. Real-world evaluation of the impact of two anti-SARS-CoV-2 monoclonal antibody regimens on COVID-19 hospitalizations in older adults. J Med Virol. 2022;94:2493-2499. doi:10.1002/jmv.27668