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BRIEF REPORT

The Efficacy of Bamlanivimab in Reducing Emergency Department Visits and Hospitalizations in a Real-world Setting

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Bamlanivimab, a monoclonal antibody targeting the spike protein of severe acute respiratory syndrome coronavirus 2, is available for ambulatory treatment of coronavirus disease 2019 (COVID-19). This real-world study confirms the efficacy of bamlanivimab in reducing hospital admissions and emergency department visits among high-risk outpatients with mild to moderate COVID-19 illness and reveals a trend toward improved mortality.

Keywords. bamlanivimab; COVID-19; treatment; outcomes.

Limited ambulatory treatment options exist for coronavirus disease 2019 (COVID-19), the syndrome caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which contributes to the profound morbidity and mortality associated with this illness [1, 2]. The striking number of people afflicted with COVID-19 has resulted in a dramatic increase in health care resource requirements. More than a third of Americans live in locations with a critical bed shortage during a surge of cases of COVID-19, including metropolitan areas in the Middle Atlantic and Northeastern States [3]. This high degree of health care utilization has led to concerns about the quantity of resources available and ability to maintain a proper standard of care.

In November 2020, bamlanivimab (LY-CoV555; Lilly), an IgG1 monoclonal antibody that binds to the receptor-binding domain of the spike protein of SARS-CoV-2, inhibiting binding to the human ACE2 receptor, was granted Emergency Use Authorization (EUA) by the Food and Drug Administration (FDA) for ambulatory treatment of mild to moderate COVID-19. The BLAZE-1 trial revealed that the use of bamlanivimab resulted in a decrease in emergency department visits and hospital admission [4]. Granting of the authorization was at least partly based on an interim post hoc analysis of a small number of very high-risk patients (body mass index [BMI] ≥35 and/or ≥65 years old) in the BLAZE-1 trial showing that treatment with bamlanivimab led to a 10.4% absolute reduction in COVID-related hospitalization or emergency department visits within 29 days [5].

This study examines the efficacy of bamlanivimab in patients diagnosed with COVID-19 who have a BMI ≥35 and/or are age ≥65 years old and assesses the safety profile after administration in a real-world setting.

METHODS

St. Luke's University Health Network (SLUHN) includes 12 hospitals, 76 primary care sites, and 18 urgent care centers in Eastern Pennsylvania and Western New Jersey. Testing for COVID-19 occurred at dedicated outpatient testing sites and emergency departments within the St. Luke's Network. The analysis included patients treated with a single dose of 700 mg of bamlanivimab infused over 60 minutes from November 23, 2020, until January 17, 2021. Due to limited seat availability for infusion, in the setting of a large surge of patients in the region, only patients who were ≥65 years of age and/or had a BMI ≥35 with a positive COVID-19 test by polymerase chain reaction (PCR) within 7 days of symptoms received bamlanivimab treatment. One bamlanivimab infusion center is in Eastern Pennsylvania, and the other is in Western New Jersey. Referral for treatment was at the discretion of the primary care physician (PCP). A follow-up visit occurred 48 hours after the infusion with a PCP within SLUHN to monitor for any infusion related side effects and then on an as-needed basis. Patients were also monitored for all-cause hospital admission, emergency department visits, death, and side effects within 29 days through chart review. Treatment and control subjects in this analysis were restricted to those receiving primary care through SLUHN. A cohort of patients testing positive for COVID-19 and meeting the above criteria for the bamlanivimab infusion during the same time frame but not receiving the infusion were used as the control group.

Statistical Analysis

R, version 4.0.3 (R Core Team), and the Tidyverse package suite were used for data analysis [6]. Separate bivariate analyses

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using Student *t* tests and chi-square tests were used as appropriate to determine suitable covariates for multivariate modeling ($P < .25$). In addition to bamlanivimab infusion, potential covariates were age, BMI, sex, White race, Hispanic ethnicity, never-tobacco use, and the following comorbidities: diabetes, hypertension, congestive heart failure (CHF), coronary artery disease (CAD), and chronic obstructive pulmonary disease (COPD).

For all 3 models, linearity in the logit was not satisfied based on the predicted probabilities; therefore, age and BMI were collapsed into ≥65 years of age and/or a BMI ≥35, matching the criteria for BAM eligibility. None of the models contained outliers or influential data points, based on normalized residuals, Cook's distance, and Bonferroni-corrected *P* values.

Model performance was assessed using omnibus chi-square, Hosmer Lemeshow goodness of fit, and C statistics. Mean with SD and adjusted odds ratio (aOR) with 95% CI are reported, with $P < .05$ denoting statistical significance.

Patient Consent

The Institutional Review Board of SLUHN approved the protocol and did not require patient consent.

RESULTS

From November 23, 2020, until January 17, 2021, a total of 6117 patients met criteria for bamlanivimab treatment. Seven hundred eighty (12.8%) patients received the bamlanivimab infusion, while 5337 (87.2%) did not despite being eligible. The bamlanivimab cohort was older, predominantly white, and majority female (Table 1). Comorbidities including diabetes, hypertension, CHF, COPD, and CAD were significantly more prevalent in the bamlanivimab group (Table 1). The mean durations from symptom onset and diagnosis to treatment (SD) were 5.6 (1.9) and 2.9 (1.6) days, respectively.

Table 1. Patient Demographic and Clinical Variables

	Bamlanivimab (n = 780)	No Bamlanivimab (n = 5337)	*P* Value
Age, mean + SD, y	62.6 + 15.6	56.7 + 2.0	<.001
BMI, mean + SD, kg/m^2	35.4 + 7.9	35.7 + 8.2	.413
Sex, No. (%)	Female 428 (54.9)	Female 3028 (56.7)	.009
Race, No. (%)	White 685 (87.8)	White 4491 (84.1)	.009
Ethnicity, No. (%)	Hispanic or Latino 76 (9.7)	Hispanic or Latino 769 (14.4)	.001
Ever smoking, No. (%)	350 (44.9)	2122 (39.8)	.007
Diabetes, No. (%)	236 (30.3)	1059 (19.8)	<.001
Hypertension, No. (%)	531 (68.1)	2515 (47.1)	<.001
Congestive heart failure, No. (%)	66 (8.5)	281 (5.3)	.001
Chronic obstructive pulmonary disease, No. (%)	70 (9.0)	279 (5.2)	.010
Coronary artery disease, No. (%)	121 (15.5)	521 (9.8)	.007

Abbreviations: BMI, body mass index

A lower percentage of patients receiving bamlanivimab required emergency department care, inpatient admission, or a composite of these 2 outcomes, but these differences were not statistically significant (Table 1). Multivariable logistic regression analysis revealed that those receiving bamlanivimab were less likely to experience any of the 3 outcomes after adjustment (Table 2). One (0.13%) patient death occurred in the treatment group, while 35 (0.66%) died in the control group (Table 2).

A total of 74 adverse events were reported by 42 patients (5.4%) receiving bamlanivimab, all within 48 hours of infusion. The most common events included chills, fevers, nausea, muscle aches, headaches, diarrhea, blurry vision, rash, and abnormal smell. No serious adverse events occurred, and no patients required admission for an infusion-related reaction.

DISCUSSION

In a real-world setting, treatment with bamlanivimab reduced the likelihood of inpatient admission and emergency department visits in patients with a BMI ≥35 and/or age ≥65 years. These results concur with the post hoc analysis from the BLAZE-1 trial that this treatment decreases resource utilization and improves outcomes. This analysis suggests a >40% decreased risk of admission and a >35% decreased risk of emergency department visit in this population.

While all study patients were required to meet a minimum age or BMI to receive therapy, the treatment group was older and had higher rates of diabetes, hypertension, CAD, and COPD. These cardiometabolic and pulmonary conditions are significant risk factors for complications of COVID-19 and account for most COVID-19 hospitalizations [7, 8]. Higher risk factors in the bamlanivimab group may explain the insignificant reduction in hospitalizations and emergency department visits seen with the unadjusted data.

Patients receiving bamlanivimab strongly trended toward decreased mortality. As the treatment group had several more risk factors for death from COVID-19, bamlanivimab may offer a mortality benefit. The only patient in the treatment group to expire suffered from superior mesenteric artery obstruction and had numerous comorbidities associated with peripheral arterial disease.

High patient volumes in the acute care setting from COVID-19 strain resources and supplies. Treatments administered in the prehospital setting may preserve hospital supplies and reduce overcrowding. Overtaxing health care capacity appears critical during the ongoing COVID-19 pandemic as inadequate staffing has been associated with worse outcomes in hospital settings [9, 10]. Shortages of personal protective equipment and airborne isolation rooms have also placed health care workers at greater risk [11]. The use of bamlanivimab to limit hospitalization and

Table 2. Bamlanivimab Treatment Outcomes

Outcome	Total (n = 6117)	BAM (n = 780)	No BAM (n = 5337)	Infusion Outcome, No. (%)	Control Group Outcome, No. (%)	Unadjusted Odds Ratio	*P* Value	Adjusted[a] Odds Ratio (95% CI)	*P* Value
Admission	547	57	490	57 (7.3)	490 (9.2)	0.79	.081	0.583 (0.431–0.776)	<.001
ED visit	352	41	311	41 (5.3)	311 (5.8)	0.91	.577	0.635 (0.458–0.861)	.005
Combined	899	98	801	98 (12.6)	801 (15.0)	0.84	.156	0.663 (0.524–0.831)	<.001
Death	36	1	35	1 (0.13)	35 (0.66)	0.20	.079		

Abbreviations: BAM, bamlanivimab; BMI, body mass index; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; ED, emergency department.

[a]Unadjusted odds ratios and resulting *P* values were calculated with chi-square and Fisher exact tests. Each of the multivariable logistic regressions had an omnibus chi-square *P* value <.0001 and a Hosmer-Lemeshow goodness-of-fit *P* value of >.05. The inpatient admission model was adjusted for: age ≥65, BMI ≥35, gender, race, ethnicity, ever-smoker status, diabetes, hypertension, CHF, and COPD. The ED visit model was adjusted for: age group, gender, race, ethnicity, ever-smoker status, and diabetes. The composite model was adjusted for: age group, BMI group, ever-smoker status, and all the comorbidities.

emergency department visits can preserve limited supplies and the need for airborne isolation rooms.

No serious or lasting side effects were identified with bamlanivimab infusion. While a small number of patients required medical care for infusion-related side effects, these complications were brief and easily managed, and none required hospitalization.

The limitations of the study should be recognized. Those in the control population may have presented later for care, resulting in immediate admission at the time of diagnosis, which would bias the data. However, an identical analysis after elimination of study subjects hospitalized or requiring emergency department visit within 48 hours of a positive test did not reveal any change in the results (data not shown). While logistic regression was used to control for confounders, only a well-done randomized trial can most effectively control for confounders. Some study subjects may have received emergency department care or hospitalization outside of SLUHN, resulting in incomplete capture of data. However, our study group was limited to those receiving Primary Care within SLUHN. The comorbidities used as covariates in our regression analyses were limited to the variables coded in the EMR data warehouse. The study population was primarily White; therefore, the results may not apply to communities with more diverse racial/ethnic backgrounds.

With variants becoming more prevalent in the United States, the efficacy of single-agent monoclonal antibody therapy may be compromised [12–14]. Because of this concern and the more robust data available for dual monoclonal treatment for COVID-19, the FDA has rescinded the EUA for bamlanivimab monotherapy [12, 15]. While dual therapy is now the standard of care, this analysis supports monoclonal antibody treatment to improve outcomes.

This real-world study confirms the efficacy of bamlanivimab in reducing hospital admissions and emergency department visits among high-risk outpatients with mild to moderate COVID-19 illness. Only mild to moderate side effects were observed with this intervention. The use of bamlanivimab infusion early in COVID-19 illness may mitigate hospital strain and preserve resources, thus leading to improved inpatient outcomes.

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