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MAJOR ARTICLE

Bamlanivimab and Etesevimab Improve Symptoms and Associated Outcomes in Ambulatory Patients at Increased Risk for Severe Coronavirus Disease 2019: Results From the Placebo-Controlled Double-Blind Phase 3 BLAZE-1 Trial

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Background. In the phase 2/3 BLAZE-1 trial, bamlanivimab and etesevimab together reduced coronavirus disease 2019 (COVID-19)–related hospitalizations and any-cause mortality in ambulatory patients. Herein, we assess the impact of bamlanivimab and etesevimab treatment on the severity and length of symptoms and health outcomes among patients at increased risk for severe COVID-19.

Methods. In the phase 3 portion of BLAZE-1 (NCT04427501), symptomatic patients with increased risk for severe COVID-19 were randomized (2:1) to a single infusion of 700 mg bamlanivimab and 1400 mg etesevimab or placebo. Hospitalization events, vital signs, and symptomatology were monitored throughout the trial.

Results. Overall, 769 patients were randomized to bamlanivimab and etesevimab together (n = 511) or placebo (n = 258). The time to sustained symptom resolution was significantly shorter among patients who received bamlanivimab and etesevimab compared with placebo (8 vs 10 days; $P < .01$). The median time to first sustained symptom resolution of body aches and pain, chills, fatigue, feeling feverish, headache, and shortness of breath was significantly different in patients receiving bamlanivimab and etesevimab compared to placebo ($P < .05$). The proportion of patients who experienced COVID-19–related hospitalization by day 29 was significantly reduced among the bamlanivimab and etesevimab group compared with placebo (0.8% vs 5.4%; $P < .01$). The mean duration of hospital stay was numerically shorter among patients who received bamlanivimab and etesevimab (7.3 vs 13.5 days; $P = .16$), with fewer intensive care admissions.

Conclusions. Patients receiving bamlanivimab and etesevimab together resolved their symptoms more rapidly than those receiving placebo. Bamlanivimab and etesevimab treatment was associated with reduced rates of hospitalizations and shorter hospital stays.

Clinical Trials Registration. NCT04427501.

Keywords. bamlanivimab; COVID-19; etesevimab; symptomatology; treatment.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) continues to spread globally, resulting in coronavirus disease 2019 (COVID-19) of varying illness severity, placing enormous strain on healthcare systems. As of March 2022, >5.9 million COVID-19–related deaths have been reported worldwide [1]. Signs and symptoms of COVID-19 include fever or chills, cough, shortness of breath or difficulty breathing, fatigue, muscle or body aches, headache, new loss of taste or smell, sore throat, and loss of appetite [2]. While the majority of patients with COVID-19 experience mild or moderate illness and do not require medical treatment, a subset of patients is particularly vulnerable to poor outcomes and develop severe illness that requires hospitalization [3–5]. Older adults and those with underlying comorbidities such as cardiovascular disease, obesity, diabetes, chronic kidney disease, or immunosuppressive conditions have a higher risk of progression to severe illness and COVID-19–associated hospitalizations [3, 6].

Once hospitalized, clinical management and treatment depend on disease severity. Care may comprise supplemental

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oxygen through a high-flow device or noninvasive ventilation; in more severe cases, patients require intensive care unit (ICU) admission, invasive mechanical ventilation, or extracorporeal membrane oxygenation [7, 8]. Furthermore, great uncertainty remains surrounding potential long-term health sequelae following recovery from COVID-19. A recent 1-year follow-up study revealed that only 22.9% of patients were completely free of COVID-19–related symptoms at month 12 [9].

Maintaining hospital treatment capacity, particularly the availability of ICU beds and mechanical ventilation equipment, is vital to mitigate the negative health impact of COVID-19. Therefore, preventing progression to severe COVID-19 and hospitalization and shortening the recovery time of hospitalized patients are crucial to ensuring that healthcare systems do not become overwhelmed.

While vaccines have been shown to be highly effective in preventing clinically significant COVID-19 [10–12], treatments are necessary to prevent disease progression among unvaccinated individuals, immunocompromised individuals who may not respond to vaccines, and vaccine recipients who experience breakthrough infection. Thus, it is vital that individuals presenting with mild or moderate COVID-19 symptoms at high risk of disease progression receive treatment early in outpatient settings. Treatment options for mild to moderate ambulatory patients with COVID-19 include neutralizing anti–SARS-CoV-2 monoclonal antibody (mAb) treatment [13]. Bamlanivimab and etesevimab are 2 such mAbs that bind to the receptor-binding domain of the SARS-CoV-2 spike protein, thereby neutralizing further viral activity. In February 2021, the combination of 700 mg bamlanivimab and 1400 mg etesevimab received emergency use authorization (EUA) for the treatment of mild to moderate COVID-19 in adults and adolescent patients who are at high risk for progression to severe COVID-19 [14]. Findings from the phase 2/3 BLAZE-1 trial (A Randomized, Double-Blind, Placebo-Controlled, Phase 2/3 Study to Evaluate the Efficacy and Safety of LY3819253 and LY3832479 in Participants With Mild to Moderate COVID-19 Illness) evaluating the efficacy and safety of bamlanivimab and etesevimab at different doses showed that treatment with bamlanivimab and etesevimab together reduced viral load, COVID-19–related hospitalization, and any-cause mortality compared with placebo [15, 16]. In the phase 3 portion of BLAZE-1, the median time to sustained symptom resolution was significantly decreased among recipients of bamlanivimab and etesevimab [16, 17].

Herein, we extend upon these previously presented findings and report on study symptom endpoints, individual symptom scores, and a general overview on hospitalization details.

METHODS

Study Design and Patients

BLAZE-1 is an ongoing, phase 2/3, randomized, double-blind, placebo-controlled, single-dose study in patients with mild to moderate COVID-19 in the outpatient setting (ClinicalTrials.gov identifier NCT04427501). This report focuses on results from the phase 3 portion of the trial enrolling adolescent (12–17 years of age inclusive) and adult (≥18 years of age) patients with ≥1 risk factor for progression to severe COVID-19 and randomized to receive either a single intravenous infusion of 700 mg bamlanivimab and 1400 mg etesevimab together or placebo. Patients who had received at least 1 dose of a COVID-19 vaccine were excluded from enrollment. Patients were enrolled between 9 December 2020 and 7 January 2021 at 104 sites in the United States. Details on randomization and intervention have been described previously [17]. In brief, patients were administered treatment on study day 1 (baseline) and were monitored during the treatment period on study days 2–11, 22, and 29. The follow-up period consisted of monitoring at days 60 and 85.

The primary endpoint was the proportion of patients who experienced a COVID-19–related hospitalization (defined as ≥24 hours of acute care) or death from any cause by day 29. A previous report presented the primary and key secondary results [17].

This study was conducted in accordance with the Declaration of Helsinki and Council for International Organizations of Medical Sciences International Ethical Guidelines, and applicable International Council for Harmonisation Good Clinical Practice Guidelines, laws, and regulations. All participants or their legally authorized representative provided written informed consent or child/adolescent assent prior to study initiation.

Symptom Severity, Clinical Status, and Monitoring

On study days 1–11, 22, 29, 60, and 85, patients completed a daily questionnaire [17] assessing symptom severity experienced during the past 24 hours. The following symptoms were included in the questionnaire: cough, shortness of breath, feeling feverish, fatigue, body aches and pain, sore throat, chills, headache, loss of appetite, loss of taste, and loss of smell. Symptoms were scored as 0 (none or absent), 1 (mild), 2 (moderate), or 3 (severe), except loss of taste and loss of smell, which were answered with yes/no.

For hospitalized patients, vital signs and oxygen support were recorded on all study days. Additionally, information regarding emergency room visits, ICU admittance, and extended-care facility admittance and discharge were recorded daily on days 2–11, 22, and 29; every 7 days until discharge or day 60; and day 85. The investigator determined if the hospitalization was related to COVID-19.

Outcomes

In this report, we summarize symptom endpoints and report on endpoints related to symptom resolution and symptom improvement. Time to first sustained resolution for each symptom is also presented (excluding loss of appetite, loss of taste, and loss of smell). Symptom resolution was defined as a score of 0

(absent) for shortness of breath, feeling feverish, body aches and pains, sore throat, chills, and headache; and a score of 0 or 1 (absent or mild) for cough and fatigue on the symptom questionnaire. Complete symptom resolution was defined as all symptoms (shortness of breath, feeling feverish, body aches and pains, sore throat, chills, headache, cough, and fatigue) on the symptom questionnaire scored as absent (0). Symptom improvement was defined as symptoms on the symptom questionnaire scored as moderate or severe (2 or 3) at baseline being subsequently scored as mild or absent (1 or 0), and symptoms on the symptom questionnaire scored as mild or absent (1 or 0) at baseline being subsequently scored as absent (0). First symptom improvement was defined as the time the patient first satisfied the definition of symptom improvement. Sustained symptom resolution was defined as the first of 2 consecutive assessments with the following improvements in symptoms: (1) absence of any shortness of breath, feeling feverish, body aches and pain, sore throat, chills, and headache; and (2) absence or mild symptoms of cough and fatigue. COVID-19–related hospitalization was defined as ≥24 hours of acute care.

Statistical Analysis

Statistical analyses for demographics and hospitalization outcomes included patients in the safety population. The safety population is defined as patients randomized to either 700 mg bamlanivimab and 1400 mg etesevimab together or concurrent placebo, and who received study intervention. Patients were analyzed according to randomization.

Statistical analyses for all other outcomes included patients in the efficacy population who also had a baseline score for the symptom/s of interest. The efficacy population is defined as patients included in the safety population and who had at least 1 nonmissing postbaseline viral load measurement. Patients were analyzed according to the intervention to which they were randomized.

Analyses for binary outcomes were adjusted for the stratification factor, duration from the onset of symptoms to randomization (≤8 days vs >8 days). Treatment group comparisons were conducted using a logistic regression model. The proportion, difference in treatment groups, relative risk, odds ratio, and *P* value are reported for hospitalization-related outcomes; otherwise, the proportion and *P* value are reported. Analyses for symptom resolution and symptom improvement used a nonresponder imputation method to handle missing data.

Analyses for the change from baseline in individual symptom scores were adjusted for the baseline symptom score. The least squares means, standard error, and *P* value are reported. Treatment group comparisons were performed using a mixed model for repeated measurement analysis.

The time-to-event analyses were conducted using a stratified log-rank test. Kaplan-Meier product limit curves were also produced. The proportion of patients experiencing the event, median days to the event, the hazard ratio, and *P* value are reported. Patients who reported a baseline symptom score of at least "mild" (score of 1) were included in the individual symptom analyses.

The percentage of patients and analyses for the mean duration of hospitalization (in days) were conducted using a nonparametric exact Mann-Whitney *U* test. The mean, standard deviation, and *P* value are reported.

Data used for analyses are from 2 separate interim database locks. The first interim database lock occurred when patients reached day 29 and the second interim database lock occurred when patients reached day 85. The day 85 database lock was used for analyses of individual symptom scores and pulmonary deterioration. The day 29 database lock was used for all other analyses.

RESULTS

The first interim database lock occurred when patients reached day 29 (safety population: placebo n = 258, bamlanivimab and etesevimab n = 511; efficacy population: placebo n = 258, bamlanivimab and etesevimab n = 510). The second interim database lock occurred when patients reached day 85 (efficacy population: placebo n = 258, bamlanivimab and etesevimab n = 513).

Baseline Patient Demographics and Clinical Characteristics

A total of 511 patients were randomized to receive bamlanivimab and etesevimab together whereas 258 patients were randomized to receive placebo. The median age of the patients was 56.0 years (range, 12–93 years), 408 patients (53.1%) were female, and 209 patients (27.2%) identified as Hispanic. Patient demographics and baseline characteristics were comparable among the treatment groups (Table 1). Cough was the most frequently reported COVID-19 symptom reported at baseline (81.1% and 80.9% of patients in the bamlanivimab and etesevimab group and the placebo group, respectively). Fatigue, loss of smell, and body aches and pain were also commonly reported (Table 2).

Symptom Endpoints

Patients treated with bamlanivimab and etesevimab together had a significantly shorter median time to sustained symptom resolution, symptom resolution, and sustained complete symptom resolution compared with placebo (*P* = .009, *P* = .016, and *P* = .01, respectively). Similarly, treatment with bamlanivimab and etesevimab together resulted in significant reductions in median time to symptom improvement compared with placebo (7 vs 9 days; *P* = .009). By day 11, the proportion of participants demonstrating sustained symptom resolution (57.8% vs 47.7%; *P* = .008), symptom resolution (61.8% vs 50.8%; *P* = .004), and symptom improvement (52.7% vs 40.7%; *P* = .002) was significantly higher among bamlanivimab and etesevimab recipients compared with placebo recipients (Figure 1).

Table 1. Patient Demographics and Baseline Clinical Characteristics[a]

Characteristic	Placebo (n = 258)	Bamlanivimab and Etesevimab (n = 511)
Age, y, median (min, max)	55 (13, 89)	57 (12, 93)
Male sex	114 (44.2)	247 (48.3)
Race, No.[b]	255	508
American Indian/Alaska Native	1 (0.4)	3 (0.6)
Asian	11 (4.3)	18 (3.5)
Black/African American	22 (8.6)	41 (8.1)
Native Hawaiian/other Pacific Islander	2 (0.8)	1 (0.2)
White	219 (85.9)	443 (87.2)
Multiracial	0 (0)	2 (0.4)
Missing	3	3
SpO_2 category		
<96%	56 (21.7)	88 (17.2)
≥96%	202 (78.3)	423 (82.8)
Duration of symptoms from symptom onset to randomization, d, median (min, max)	3 (1, 15)	4 (0, 19)
Baseline COVID-19 severity		
Mild	202 (78.3)	380 (74.4)
Moderate	56 (21.7)	131 (25.6)
Medical history and preexisting conditions		
Chronic kidney disease	3 (1.2)	6 (1.2)
Diabetes	59 (22.9)	139 (27.2)
Immunosuppressive disease	0	8 (1.6)
Immunosuppressive treatment	16 (6.2)	28 (5.5)
In adults aged ≥55 y, No.[b]	252	501
Cardiovascular disease	18 (7.1)	38 (7.6)
Hypertension	85 (33.7)	191 (38.1)
COPD	15 (6.0)	41 (8.2)

Data are presented as No. (%) unless otherwise indicated.

[a]Safety population of first interim database lock where patients reached day 29.

[b]No. of patients with nonmissing data used as the denominator.

Abbreviations: COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; SpO_2, saturation of peripheral oxygen.

Table 2. Coronavirus Disease 2019 Symptoms Reported at Baseline[a]

Characteristic	Placebo (n = 258)	Bamlanivimab and Etesevimab (n = 513)
Patients reporting each symptom at baseline, No. (%)[b]		
Body aches and pain	161 (62.6)	333 (65.1)
Chills	92 (35.8)	215 (42)
Cough	208 (80.9)	415 (81.1)
Fatigue	184 (71.7)	395 (77.1)
Feverish	108 (42)	191 (37.4)
Headache	151 (58.7)	322 (62.9)
Loss of appetite	97 (37.7)	237 (46.3)
Loss of taste	87 (33.9)	177 (34.6)
Loss of smell	83 (32.3)	182 (35.5)
Shortness of breath	92 (35.7)	225 (43.9)
Sore throat	91 (35.4)	201 (39.3)

[a]Efficacy population from second database lock.

[b]No. of patients with nonmissing data used as denominator.

Individual Symptom Scores

The symptom score change from baseline was calculated for each symptom at days 2–11. For the majority of symptoms, the bamlanivimab and etesevimab group showed greater changes in symptom scores compared to placebo (Figure 2), with statistically significant separation observed for cough, chills, fatigue, feeling feverish, headache, shortness of breath, and body aches and pain symptom scores. There was no significant difference in mean changes from baseline in sore throat symptom score between the 2 cohorts (Figure 2).

By day 29 and day 85, a higher proportion of patients in the bamlanivimab and etesevimab treatment group experienced sustained resolution of each symptom compared with the placebo group (Figure 3). At day 29 and day 85, the median time to first sustained symptom resolution was significantly decreased among the bamlanivimab and etesevimab group compared with placebo for body aches and pain ($P = .007$ and $P = .022$, respectively), chills ($P = .001$ and $P = .003$), fatigue ($P = .01$ and $P = .009$), feeling feverish ($P = .016$ and $P = .02$), headache ($P = .009$ and $P = .018$), and shortness of breath ($P = .016$ and $P = .022$).

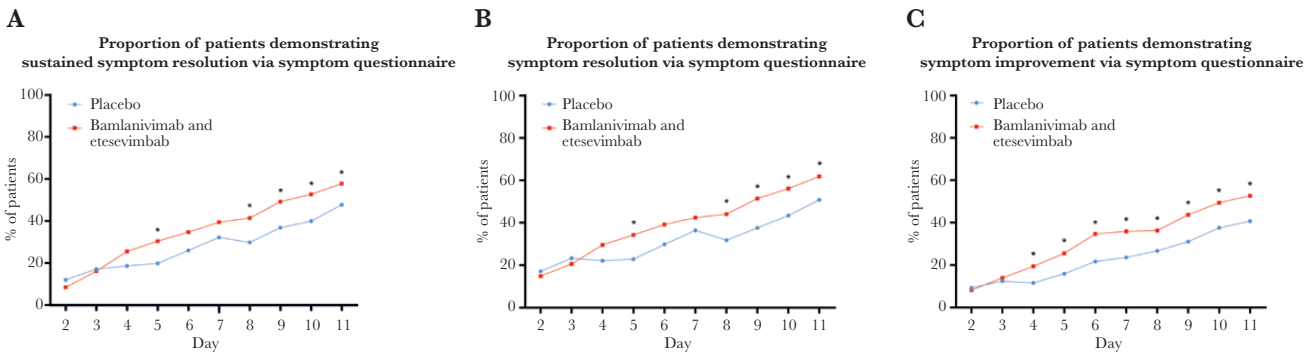

Figure 1. Proportion of participants demonstrating sustained symptom resolution (*A*), symptom resolution (*B*), and symptom improvement (*C*). Logistic regression analysis with duration of symptom onset category as factors. *$P < .05$. Efficacy population of first database lock: placebo, n = 258; bamlanivimab and etesevimab, n = 510.

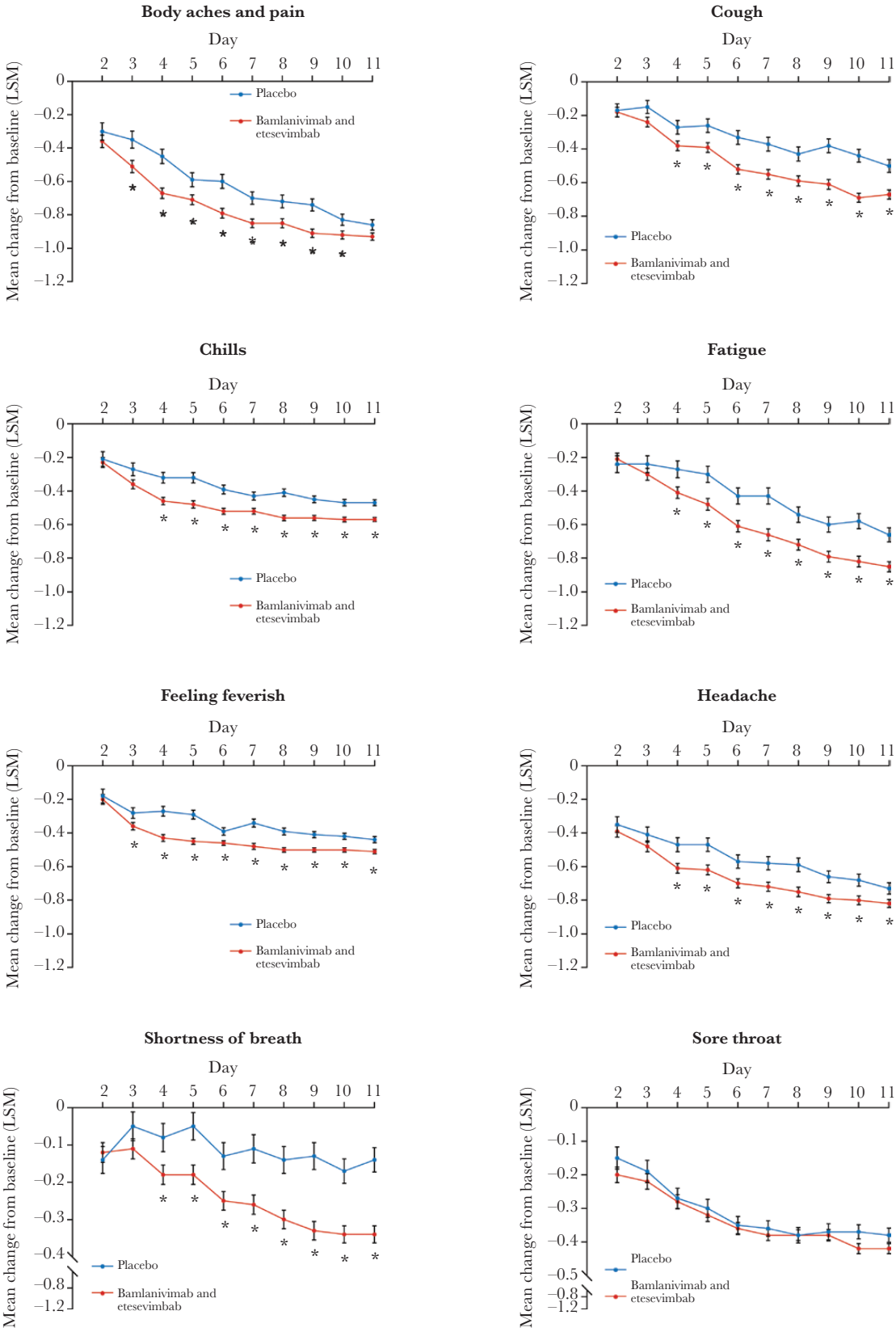

Figure 2. Symptom score change from baseline (least squares mean [LSM]) at days 2–11. Error bars represent standard error. *$P < .05$, comparison vs placebo hazard ratio.

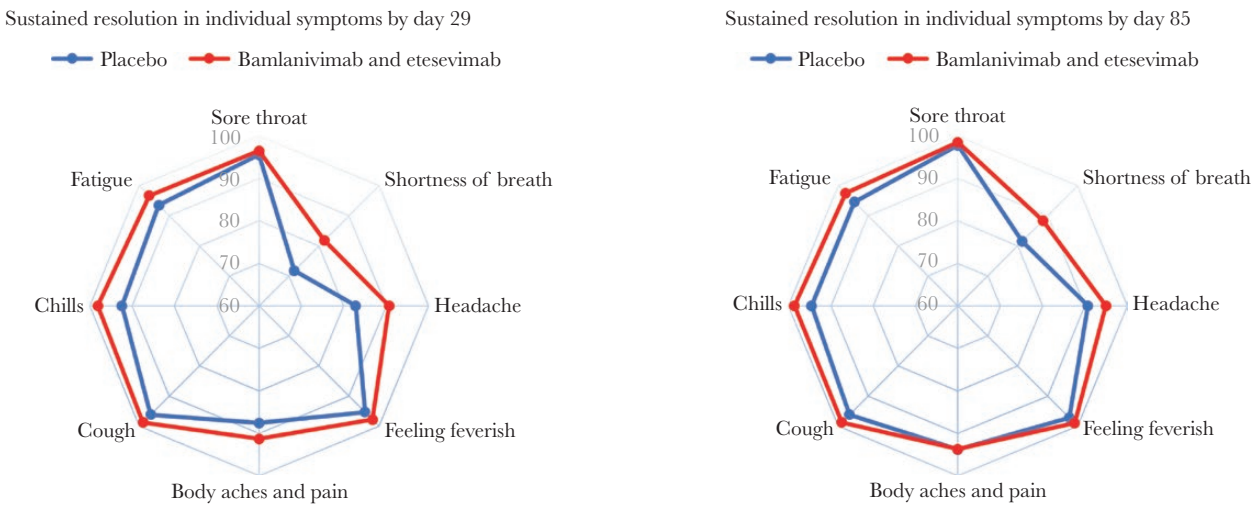

Figure 3. Spider plot showing percentage of patients with sustained resolution at days 29 and 85. Numbers (60–100) represent percentage of patients at day 29 or day 85 with sustained resolution of each symptom. Patients with a baseline symptom score of 1 (mild) or more were included. Numbers for each symptom are shown in Table 2.

Outcomes Related to Hospitalization and Pulmonary Deterioration

A total of 18 patients experienced COVID-19–related hospitalizations by day 29, with no additional hospitalizations reported through day 85 (Table 3). The proportion of patients with COVID-19–related hospitalizations was 0.8% (4 patients) for the bamlanivimab and etesevimab group and 5.4% (14 patients) for the placebo group. The difference vs placebo was −4.6 (95% confidence interval, −7.5 to −1.8; $P = .0004$). The mean duration of hospitalization stay was 7.3 and 13.5 days through day 29, and 7.3 and 14.5 days through day 85, for the bamlanivimab and etesevimab group and placebo group, respectively.

The number of patients requiring supplemental oxygen therapy was significantly lower among the bamlanivimab and etesevimab group compared with the placebo group at day 29 (1 vs 9 patients; $P = .003$) and day 85 (1 vs 10 patients; $P = .0019$). One patient in the placebo group required mechanical ventilation. A total of 5 patients were admitted to the ICU (1 from the bamlanivimab and etesevimab group and 4 from the placebo group). Treatment with bamlanivimab and etesevimab together significantly reduced the time to admission to ICU compared with placebo ($P = .027$).

DISCUSSION

Previous data from the phase 3 portion of the BLAZE-1 trial showed that the EUA dose of bamlanivimab and etesevimab together (700/1400 mg) reduced COVID-19–related hospitalizations and any-cause death, time to symptom improvement, time to symptom resolution, and accelerated viral clearance as compared with placebo. Herein, the symptomatology and outcomes data presented provide further support that bamlanivimab and etesevimab improve health outcomes for patients with mild to moderate COVID-19 with 1 or more risk factors for progressing to severe COVID-19.

This study reports that treatment with bamlanivimab and etesevimab together reduced the time to symptom improvement and resolution, showing that mAb treatment speeds up the time to recovery from COVID-19. Analysis of symptom questionnaires revealed greater changes from baseline symptom scores among the bamlanivimab and etesevimab group for the majority of symptoms (all except sore throat), highlighting the improvements in patient outcomes as a result of antibody treatment.

In both the bamlanivimab and etesevimab group and placebo group, the incidences of sustained resolution of shortness of breath and headache at days 29 and 85 were lower than the incidences of sustained resolution of other symptoms; however, reporting of sustained resolution in shortness of breath and headache was numerically higher among recipients of bamlanivimab and etesevimab. Studies have reported that patients with COVID-19 may experience prolonged symptoms; a recent study revealed that the persistence of shortness of breath and headache were common among individuals with continued symptoms at 6 months [18], highlighting the need to resolve such symptoms. While suggestive that treatment with bamlanivimab and etesevimab may decrease to some extent the potential proportion of patients with persistent symptoms, our study was not designed to directly address this unmet medical need.

The primary endpoint previously reported was the proportion of patients who experienced a COVID-19–related hospitalization (≥24 hours of acute care) or any-cause death by day 29 [17]. Here, we report the proportion of patients who experienced a COVID-19–related hospitalization (≥24 hours of acute care) by day 29 and day 85. We found that incidences

Table 3. Descriptive Outcomes Related to Hospitalization/Pulmonary Deterioration

Outcome	Placebo (n = 258)	Bamlanivimab and Etesevimab (n = 511)	Difference (95% CI)	RR (95% CI)	OR (95% CI)	*P* Value
No. of patients with COVID-19–related hospitalization[a,b]	14 (5.4)	4 (0.8)	–4.6 (–7.5 to –1.8)	0.14 (.05–.43)	0.15 (.05–.43)	.0004
Duration of COVID-19–related hospitalization[a], d, mean (SD)						
Day 29	13.5 (7.5)	7.3 (3.3)	…	…	…	.161
Day 85	14.5 (9.1)	7.3 (3.3)	…	…	…	.165
No. of patients admitted to ICU[a]	4 (1.6)	1 (0.2)	–1.4 (–2.9 to .2)	0.13 (.01–1.12)	0.17 (.03–.99)	.049
Proportion of patients with SpO_2 <92% vs ≥92%[c]						
Day 11	12 (4.7)	14 (2.7)	–1.9 (–4.9 to 1.0)	0.59 (.28–1.25)	0.57 (.26–1.24)	.157
Day 29	18 (7.0)	15 (2.9)	–4.1 (–7.5 to –.6)	0.42 (.21–.82)	0.40 (.20–.81)	.010
Proportion of patients with SpO_2 <96% vs ≥96%[c]						
Day 11	135 (52.3)	228 (44.4)	–7.9 (–15.3 to –.4)	0.85 (.73–.99)	0.73 (.54–.98)	.039
Day 29	141 (54.7)	244 (47.6)	–7.1 (–14.5 to .4)	0.87 (.75–1.00)	0.75 (.56–1.02)	.064
No. of patients requiring supplemental oxygen therapy[c]						
Day 29	9 (3.5)	1 (0.2)	–3.3 (–5.6 to –1.0)	0.06 (.01–.44)	0.08 (.01–.42)	.003
Day 85	10 (3.9)	1 (0.2)	–3.7 (–6.1 to –1.3)	0.05 (.01–.39)	0.07 (.01–.37)	.002
No. of patients requiring MV[c]	1 (0.4)	0 (0.0)	–0.4 (–1.1 to .4)	0.00 (0–0)	0.17 (<.01–3.11)	.233

Data are presented as No. (%) unless otherwise indicated.

Abbreviations: CI, confidence interval; COVID-19, coronavirus disease 2019; ICU, intensive care unit; MV, mechanical ventilation; OR, odds ratio; RR, relative risk; SD, standard deviation; SpO_2, saturation of peripheral oxygen.

[a]Analysis uses the safety population of first database lock (placebo, n = 258; bamlanivimab and etesevimab, n = 511).

[b]No. of patients hospitalized (defined as ≥24 hours of acute care).

[c]Analysis uses the efficacy population of second database lock (placebo, n = 258; bamlanivimab and etesevimab, n = 513).

of COVID-19–related hospitalizations were lower among the bamlanivimab and etesevimab group and, importantly, the mean length of stay was shorter among bamlanivimab and etesevimab recipients. Furthermore, among those hospitalized, ICU admissions and supplemental oxygen requirements were reduced among the bamlanivimab and etesevimab group. These clinical benefits are particularly noteworthy as, although prevention of hospitalization is a highly relevant clinical metric, reductions in the ICU admissions and supplemental oxygen requirements further emphasize the impact of bamlanivimab and etesevimab treatment on halting progression to severe or critical disease. Additionally, such reductions in medical resources considerably alleviates the burden placed on healthcare systems.

While morbidity and mortality associated with COVID-19 persist, reports have indicated that widespread uptake of mAb treatments among patients with COVID-19 have been low [19]. Additionally, setting up infusion sites can be challenging; however, clinical results show that mAb treatment, including the results presented herein, are effective outpatient strategies and reduce COVID-19 disease burden [20–22]. By administering these therapies to ambulatory patients with mild to moderate COVID-19 early in the disease course, faster control of symptoms, prevention of severe disease, and return to normal health status (pre–COVID-19) can be achieved in a higher proportion of patients than just using standard-of-care approaches. This might also help prevent "long COVID" consequences [23], although no studies investigating currently authorized or approved neutralizing mAbs have specifically addressed this question yet.

There are several limitations of our study. First, there was very little racial diversity in the participant population, and participant enrollment was limited to the United States only. Second, the results are limited to patients aged ≥12 years who are at high risk for severe disease. Third, patients reported loss of appetite, loss of smell, and loss of taste; however, this was not included in this analysis of the symptom questionnaire as these were exploratory items. Fourth, the overall number of patients requiring hospitalization in this study was low, so we were unable to determine relationships between symptoms and the need for hospitalizations. Finally, patients were randomized between December 2020 and January 2021 when the ancestral SARS-CoV-2 was prevalent. Since this time, a number of viral variants of SARS-CoV-2 have emerged with varying degrees of infectivity, severity, and immune evasion. Per nonclinical studies, bamlanivimab and etesevimab are not expected to be efficacious against the current predominant variant, Omicron (as of March 2022); therefore, the EUA for bamlanivimab and etesevimab was modified in January 2022 to limit authorization in areas with a high prevalence of nonsusceptible variants as determined by the United States Food and Drug Administration.

Notes

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All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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