Table 4b. Anti-SARS-CoV-2 Monoclonal Antibodies: Selected Clinical Trial Data

Last Updated: February 29, 2024

This table describes the clinical trials that have evaluated anti-SARS-CoV-2 mAbs for the treatment of COVID-19.

Methods	Results	Limitations and Interpretation
BLAZE-1: Double-Blind RCT of Bamlanivimab Plus Etesevimab in Nonhospitalized Patients With Mild to Moderate COVID-19 in the United States and Puerto Rico[1]		

Key Inclusion Criteria
• Aged ≥12 years
• At high risk of severe COVID-19 or hospitalization
Interventions
• Within 3 days of a positive SARS-CoV-2 test result, single IV infusion of:
  • BAM 700 mg plus ETE 1,400 mg (n = 511)
  • Placebo (n = 258)
Primary Endpoint
• Composite of COVID-19–related hospitalization (defined as ≥24 hours of acute care) or death from any cause by Day 29
	Participant Characteristics
	• Median age 56 years; 30% aged ≥65 years; 53% women
	• 87% White, 27% Hispanic/Latinx, 8% Black/African American
	• Mean of 4 days of symptoms
	• 76% with mild COVID-19, 24% with moderate COVID-19
	Primary Outcomes
	• Composite of COVID-19–related hospitalization or death from any cause by Day 29: 4 (0.8%) in BAM plus ETE arm vs. 15 (5.8%) in placebo arm (change of -5.0%; 95% CI, -8.0% to -2.1%; $P < 0.001$)
	• Death from any cause by Day 29: 0 in BAM plus ETE arm vs. 4 (1.6%) in placebo arm
		Key Limitation
		• Conducted before widespread circulation of the Omicron variant
		Interpretation
		• Compared to placebo, BAM plus ETE significantly reduced the number of COVID-19–related hospitalizations and deaths from any cause in high-risk patients.

BLAZE-4, Treatment Arms 9–11: Double-Blind RCT of Bamlanivimab Plus Etesevimab Plus Bebtelovimab Versus Bebtelovimab Alone Versus Placebo in Low-Risk, Nonhospitalized Patients With Mild to Moderate COVID-19[2]		

Key Inclusion Criteria
• Aged 18–64 years
• No risk factors for progression to severe COVID-19
Key Exclusion Criteria
• ≥1 of the following:
  • SpO_2 ≤93% on room air
  • Respiratory rate ≥30 breaths/min
  • Heart rate ≥125 bpm
	Participant Characteristics
	• Median age 35 years; 56% women
	• 36% Hispanic/Latinx, 19% Black/African American
	• Mean of 3.6 days of symptoms prior to enrollment
	Primary Outcomes
	• Proportion with PHVL:
	  • 13% in BAM plus ETE plus BEB arm vs. 21% in placebo arm ($P = 0.098$), with a relative reduction of 38% (95% CI, -9% to 65%)
		Key Limitations
		• Only low-risk patients were included.
		• Not powered to assess hospitalizations and deaths
		• Conducted before widespread circulation of the Omicron variant
		Interpretations
		• There were no differences in the proportion of patients with PHVL across the arms.

Methods	Results	Limitations and Interpretation
BLAZE-4, Treatment Arms 9–11: Double-Blind RCT of Bamlanivimab Plus Etesevimab Plus Bebtelovimab Versus Bebtelovimab Alone Versus Placebo in Low-Risk, Nonhospitalized Patients With Mild to Moderate COVID-19[2], continued		

Interventions
• Within 3 days of a positive SARS-CoV-2 test result, single IV infusion of:
  • BAM 700 mg plus ETE 1,400 mg plus BEB 175 mg (n = 127)
  • BEB 175 mg (n = 125)
  • Placebo (n = 128)
Primary Endpoint
• Proportion of patients with PHVL (defined as SARS-CoV-2 VL >5.82 $\log_{10}$ by Day 7)
Key Secondary Endpoints
• Mean change in VL from baseline to Days 3, 5, 7, and 11
• Composite of COVID-19–related hospitalization or death from any cause by Day 29
• Time to sustained symptom resolution
	• 14% in BEB arm vs. 21% in placebo arm ($P = 0.147$), with a relative reduction of 34% (95% CI, -15% to 62%)
	Secondary Outcomes
	• Mean decline in VL was greater in mAb arms than in placebo arm at Day 5 but not at Days 3, 7, or 11.
	• Composite of COVID-19–related hospitalization or death from any cause by Day 29:
	  • 3 (2.4%) in BAM plus ETE plus BEB arm, including 1 death
	  • 2 (1.6%) in BEB arm
	  • 2 (1.6%) in placebo arm
	• Median time to sustained symptom resolution:
	  • 7 days in BAM plus ETE plus BEB arm vs. 8 days in placebo arm ($P = 0.289$)
	  • 6 days in BEB arm vs. 8 days in placebo arm ($P = 0.003$)
		• Few COVID-19–related hospitalizations or deaths from any cause occurred by Day 29 across the arms, as is expected for a population of individuals who were at low risk of severe COVID-19.
		• The median time to sustained symptom resolution was shorter in the BEB arm than in the placebo arm.

BLAZE-4, Treatment Arms 12 and 13: Open-Label RCT of Bamlanivimab Plus Etesevimab Plus Bebtelovimab Versus Bebtelovimab Alone in High-Risk, Nonhospitalized Patients With Mild to Moderate COVID-19[2]		

Key Inclusion Criteria
• Aged ≥12 years
• Weight ≥40 kg
• ≥1 risk factors for progression to severe COVID-19
Key Exclusion Criteria
• ≥1 of the following:
  • SpO_2 ≤93% on room air
  • Respiratory rate ≥30 breaths/min
  • Heart rate ≥125 bpm
Interventions
• Within 3 days of a positive SARS-CoV-2 test result, single IV infusion of:
	Participant Characteristics
	• Median age 50 years; 52% women
	• 18% Hispanic/Latinx, 18% Black/African American
	• Mean of 4.7 days of symptoms prior to enrollment
	• 21% received ≥1 doses of a COVID-19 vaccine.
	Efficacy Outcomes
	• Composite of COVID-19–related hospitalization or death from any cause by Day 29: 2 (4%) in BAM plus ETE plus BEB arm vs. 3 (3%) in BEB arm
	• Mean decline in VL was greater in BAM plus ETE plus BEB arm than in BEB arm at Day 5 but not at Days 3, 7, or 11.
		Key Limitations
		• Open-label study
		• No placebo arm
		• Not powered to assess hospitalizations and deaths
		• Conducted before widespread circulation of the Omicron variant
		Interpretation
		• There was no difference between the arms in the proportion of patients who were hospitalized or who died.

Methods	Results	Limitations and Interpretation
BLAZE-4, Treatment Arms 12 and 13: Open-Label RCT of Bamlanivimab Plus Etesevimab Plus Bebtelovimab Versus Bebtelovimab Alone in High-Risk, Nonhospitalized Patients With Mild to Moderate COVID-19[2], continued		
• BAM 700 mg plus ETE 1,400 mg plus BEB 175 mg (n = 50) • BEB 175 mg (n = 100) **Efficacy Endpoints** • Composite of COVID-19–related hospitalization or death from any cause by Day 29 • Mean change in VL from baseline to Days 3, 5, 7, and 11		
Double-Blind RCT of Casirivimab Plus Imdevimab in Nonhospitalized Patients With Mild to Moderate COVID-19[3]		

Key Inclusion Criteria
• Aged ≥18 years
• Laboratory-confirmed SARS-CoV-2 infection
• Symptom onset within 7 days of randomization
• For patients included in the modified full analysis only:
  • ≥1 risk factors for severe COVID-19
  • Positive SARS-CoV-2 RT-PCR result at baseline
Interventions
• Single IV infusion of:
  • CAS 600 mg plus IMD 600 mg (n = 736) or placebo (n = 748)
  • CAS 1,200 mg plus IMD 1,200 mg (n = 1,355) or placebo (n = 1,341)
Primary Endpoint
• Composite of COVID-19–related hospitalization or death from any cause by Day 29
	Participant Characteristics
	• Median age 50 years
	• 35% Hispanic/Latinx, 5% Black/African American
	• Median of 3 days of symptoms prior to enrollment
	Primary Outcomes
	• COVID-19–related hospitalizations or deaths from any cause by Day 29:
	  • 7 (1.0%) in CAS 600 mg plus IMD 600 mg arm vs. 24 (3.2%) in placebo arm ($P = 0.002$)
	  • 18 (1.3%) in CAS 1,200 mg plus IMD 1,200 mg arm vs. 62 (4.6%) in placebo arm ($P < 0.001$)
	• Deaths from any cause by Day 29:
	  • 1 (0.1%) in CAS 600 mg plus IMD 600 mg arm vs. 1 (0.1%) in placebo arm
	  • 1 (<0.1%) in CAS 1,200 mg plus IMD 1,200 mg arm vs. 3 (0.2%) in placebo arm
		Key Limitation
		• Conducted before widespread circulation of the Omicron variant
		Interpretation
		• Compared to placebo, CAS 600 mg plus IMD 600 mg and CAS 1,200 mg plus IMD 1,200 mg reduced the risk of COVID-19–related hospitalization or death from any cause in patients with mild to moderate COVID-19.

Methods	Results	Limitations and Interpretation
COMET-ICE: Double-Blind RCT of Sotrovimab in Nonhospitalized Patients With Mild to Moderate COVID-19 in Brazil, Canada, Peru, Spain, and the United States[4]		
Key Inclusion Criteria • Aged ≥18 years • ≥1 comorbidities or aged ≥55 years • Positive SARS-CoV-2 RT-PCR or antigen test result • Symptom onset ≤5 days before enrollment **Key Exclusion Criteria** • Hospitalized or required supplemental oxygen • Severely immunocompromised **Interventions** • SOT 500 mg IV (n = 528) • Placebo (n = 529) **Primary Endpoint** • Composite of hospitalization or death from any cause by Day 29	**Participant Characteristics** • Median age 53 years; 20% aged ≥65 years; 54% women • 65% Hispanic/Latinx, 8% Black/African American • 63% with obesity; 22% with DM; 17% with moderate to severe asthma **Primary Outcome** • Composite of hospitalization or death from any cause by Day 29: 6 (1%) in SOT arm vs. 30 (6%) in placebo arm, including 2 deaths (adjusted relative risk 0.21; 95% CI, 0.09–0.50; absolute difference -4.53%; 95% CI, -6.70% to -2.37%; $P < 0.001$)	**Key Limitation** • Conducted before widespread circulation of the Omicron variant **Interpretation** • Compared to placebo, SOT reduced the incidence of hospitalization and death from any cause among patients with mild to moderate COVID-19.

Key: BAM = bamlanivimab; bpm = beats per minute; BEB = bebtelovimab; CAS = casirivimab; DM = diabetes mellitus; ETE = etesevimab; IMD = imdevimab; IV = intravenous; mAb = monoclonal antibody; PHVL = persistently high viral load; RCT = randomized controlled trial; RT-PCR = reverse transcription polymerase chain reaction; SOT = sotrovimab; SpO_2 = oxygen saturation; VL = viral load

References

1. Dougan M, Azizad M, Mocherla B, et al. A randomized, placebo-controlled clinical trial of bamlanivimab and etesevimab together in high-risk ambulatory patients with COVID-19 and validation of the prognostic value of persistently high viral load. *Clin Infect Dis*. 2022;75(1):e440-e449. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34718468.
2. Food and Drug Administration. Fact sheet for healthcare providers: Emergency Use Authorization for bebtelovimab. 2022. Available at: https://www.fda.gov/media/156152/download.
3. Weinreich DM, Sivapalasingam S, Norton T, et al. REGEN-COV antibody combination and outcomes in outpatients with COVID-19. *N Engl J Med*. 2021;385(23):e81. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34587383.
4. Gupta A, Gonzalez-Rojas Y, Juarez E, et al. Effect of sotrovimab on hospitalization or death among high-risk patients with mild to moderate COVID-19: a randomized clinical trial. *JAMA*. 2022;327(13):1236-1246. Available at: https://www.ncbi.nlm.nih.gov/pubmed/35285853.