Methods

**BLAZE-1**: Double-Blind RCT of Bamlanivimab 700 mg Plus Etesevimab 1,400 mg in Nonhospitalized Patients With Mild to Moderate COVID-19 in the United States and Puerto Rico

**Key Inclusion Criteria:**
- Aged ≥12 years
- At high risk for severe COVID-19 or hospitalization

**Interventions:**
- Within 3 days of a positive SARS-CoV-2 test result, single infusion of:
  - BAM 700 mg plus ETE 1,400 mg (n = 511)
  - Placebo (n = 258)

**Primary Endpoint:**
- 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 duration of symptoms was 4 days
- 76% with mild COVID-19, 24% with moderate COVID-19

**Primary Outcomes:**
- COVID-19-related hospitalizations or all-cause deaths 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)
- All-cause deaths 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 VOC

**Interpretation:**
- Compared to placebo, BAM plus ETE significantly reduced the number of COVID-19-related hospitalizations and all-cause deaths in high-risk patients.


**Key Inclusion Criteria:**
- Aged 18–64 years
- No risk factors for progression to severe COVID-19

**Key Exclusion Criteria:**
- ≥1 of the following:
  - SpO₂ ≤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 infusion of:

**Participant Characteristics:**
- Median age 35 years; 56% women
- 36% Hispanic/Latinx, 19% Black/African American
- Mean duration of symptoms prior to enrollment was 3.6 days

**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%)
  - 14% in BEB arm vs. 21% in placebo arm (P = 0.147), with a relative reduction of 34% (95% CI, -15% to 62%)

**Key Limitations:**
- Only low-risk patients included
- Not powered to assess hospitalizations and deaths
- Conducted before widespread circulation of the Omicron VOC

**Interpretations:**
- There were no differences in the proportion of patients with PHVL across the arms.
- Few COVID-19-related hospitalizations or deaths from any
### Methods

**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<sup>2</sup>, continued

- **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<sub>10</sub> by Day 7)

**Key Secondary Endpoints:**
- Mean change in VL from baseline to Days 3, 5, 7, and 11
- COVID-19-related hospitalization or death from any cause by Day 29
- Time to sustained symptom resolution

**Secondary Outcomes:**
- Mean decline in VL greater in mAb arms vs. placebo arm at Day 5 but not at Days 3, 7, or 11
- COVID-19-related hospitalizations or all-cause deaths 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 ($P = 0.003$)

**BLAZE-4, Treatment Arms 12 and 13**: Open-Label RCT of Bamlanivimab Plus Etesevimab Plus Bebtelovimab and Bebtelovimab Alone in High-Risk, Nonhospitalized Patients With Mild to Moderate COVID-19<sup>2</sup>

**Key Inclusion Criteria:**
- Aged ≥12 years
- Weight ≥40 kg
- ≥1 risk factor 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 infusion of:
  - BAM 700 mg plus ETE 1,400 mg plus BEB 175 mg (n = 50)
  - BEB 175 mg (n = 100)

**Participant Characteristics:**
- Median age 50 years; 52% women
- 18% Hispanic/Latinx, 18% Black/African American
- Mean duration of symptoms prior to enrollment was 4.7 days
- 21% had at least 1 dose of COVID-19 vaccine

**Efficacy Outcomes:**
- 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 greater in BAM plus ETE plus BEB arm vs. 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 VOC

**Interpretation:**
- There was no difference in the proportion of patients who were hospitalized or who died between the arms.
<table>
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| **BLAZE-4, Treatment Arms 12 and 13**: Open-Label RCT of Bamlanivimab Plus Etesevimab Plus Bebtelovimab and Bebtelovimab Alone in High-Risk, Nonhospitalized Patients With Mild to Moderate COVID-19<sup>2</sup>, continued | Efficacy Endpoints:  
• 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<sup>3</sup>** |

**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 factor 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:**  
• ≥1 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 duration of symptoms prior to enrollment was 3 days  

**Primary Outcomes:**  
• COVID-19-related hospitalizations or all-cause deaths through 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)  
• All-cause deaths:  
  • 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 VOC  

**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 hospitalizations or all-cause deaths in patients with mild to moderate COVID-19.
## Methods

**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

<table>
<thead>
<tr>
<th>Key Inclusion Criteria:</th>
<th>Participant Characteristics:</th>
<th>Key Limitation:</th>
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<tbody>
<tr>
<td>• Aged ≥18 years</td>
<td>• Median age 53 years; 20% aged ≥65 years; 54% women</td>
<td>• Conducted before widespread circulation of the Omicron VOC</td>
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<td>• ≥1 comorbidity or aged ≥55 years</td>
<td>• 65% Hispanic/Latinx, 8% Black/African American</td>
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<tr>
<td>• Positive SARS-CoV-2 RT-PCR or antigen test result</td>
<td>• 63% with obesity; 22% with DM; 17% with moderate to severe asthma</td>
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<td>• Symptom onset ≤5 days before enrollment</td>
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<td><strong>Key Exclusion Criteria:</strong></td>
<td><strong>Primary Outcome:</strong></td>
<td><strong>Interpretation:</strong></td>
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<td>• Hospitalized or required supplemental oxygen</td>
<td>• Hospitalizations or all-cause deaths 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 &lt; 0.001)</td>
<td>• Compared to placebo, SOT reduced the incidence of all-cause hospitalizations and deaths among patients with mild to moderate COVID-19.</td>
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<td>• Severely immunocompromised</td>
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<tr>
<td><strong>Interventions:</strong></td>
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<tr>
<td>• SOT 500 mg IV (n = 528)</td>
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<td>• Placebo (n = 529)</td>
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<td><strong>Primary Endpoint:</strong></td>
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<td>• Hospitalization or death from any cause by Day 29</td>
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</table>

**Key:** BAM = bamlanivimab; bpm = beats per minute; BEB = bebtelovimab; CAS = casirivimab; DM = diabetes mellitus; ETE = etesevimab; IMD = imdevimab; IV = intravenous; mAb = monoclonal antibody; PEP = post-exposure prophylaxis; PHVL = persistently high viral load; RCT = randomized controlled trial; RT-PCR = reverse transcription polymerase chain reaction; SOT = sotrovimab; SpO<sub>2</sub> = oxygen saturation; VL = viral load; VOC = variant of concern

## References


