**INTRODUCTION**

- Extensive efforts have been invested toward discovering effective COVID-19 therapeutics.
- SARS-CoV-2 spike glycoproteins bind the ACE2 receptor on the host's cell surface.
- Receptor recognition and fusion are critical steps for viral infection and transmission. Therefore, neutralizing anti-spike antibodies are potential treatment options for COVID-19.
- Bamlanivimab and Etesevimab are potent anti-spike neutralizing monoclonal antibodies that were derived from two separate patients who recovered from COVID-19.
- In preclinical experiments, Etesevimab binds to a different epitope from Bamlanivimab and neutralizes resistant variants with mutations in the epitope bound by Bamlanivimab. Hence, combining these two neutralizing monoclonal antibodies in clinical use may enhance viral load reduction and decrease treatment emergent resistant variants.

![Figure 1: Anti-spike proteins binding to the ACE2 receptor to block Viral Entry](image)

- In addition to anti-spike neutralizing antibodies, Molnupiravir, a potent ribonucleoside analog that inhibits the replication of RNA viruses including SARS-CoV-2 is currently being evaluated in phase 3 clinical trial for the treatment of non-hospitalized patients with laboratory-confirmed COVID-19.

**MATERIALS & METHODS**

**Eli- Lilly Study**

- **Study Design**: A randomized, double-blind, placebo-controlled, phase 2/3 clinical trial study.
- **Patient Population**: Adult patients with early mild to moderate symptoms of COVID-19.
  - Arm A: Experimental: LY3819253 (Bamlanivimab) + LY3819253 administered intravenously (IV)
  - Arm B: Experimental: LY3819253 + LY3832479 (Bamlanivimab and Etesevimab) + LY3819253 + LY3832479 administered IV or subcutaneously (SQ)
  - Arm C: Placebo Comparator: Placebo

**MERCK Study**

- **Study Design**: A randomized, double-blind, placebo-controlled, phase 2A clinical trial study.
- **Patient Population**: Adult patients who have tested positive for severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) infection within 144 hours of polymerase chain reaction (PCR) confirmation and are hospitalized with a diagnosis of COVID-19.
  - Arm A: Experimental: Oral Molnupiravir twice daily for 5 days
  - Arm B: Placebo Oral placebo capsule

**RESULTS**

**Eli- Lilly Study**

- Among non-hospitalized patients with mild to moderate COVID-19 illness, treatment with Bamlanivimab and Etesevimab, compared with placebo, was associated with a statistically significant reduction in SARS-CoV-2 viral load at day 11; no significant difference in viral load reduction was observed for Bamlanivimab monotherapy.
- Further ongoing clinical trials will focus on assessing the clinical benefit of anti-spike neutralizing antibodies in patients with COVID-19 as a primary end-point therapy.

**MERCK Study**

- Achievement of undetectable SARS-CoV-2 RNA by Day 5 in nasopharyngeal swabs by quantitative reverse transcription polymerase chain reaction (qPCR) after administration of Molnupiravir.

**REFERENCES**

- A Study of LY3819253 (LY-CoV555) and LY3832479 (LY-CoV016) in Participants with Mild to Moderate COVID-19 Illness - Full Text View - ClinicalTrials.gov, clinicaltrials.gov/ct2/show/NCT04427501.

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