Therapeutics for Patients with COVID-19 Illness: Clinical Trials in Progress

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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.**

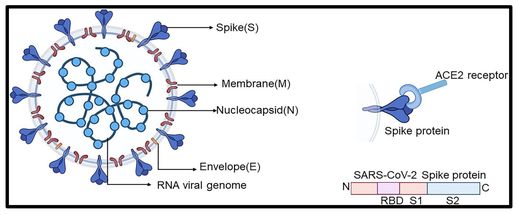

Figure 1: Ant-spike proteins binding to the ACE2 receptor to block Viral Entry

- 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**
- **Administered IV**

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

- "Effect of Bamlanivimab as Monotherapy or in Combination with Etesevimab on Viral Load in Patients with Mild to Moderate COVID-19: A Randomized Clinical Trial." *The Journal of the American Medical Association*, 21 Jan. 2021, pp. 632–644., doi:10.1001.
- *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.
- "The Safety OF MOLNUPIRAVIR (EIDD-2801) and Its Effect on Viral Shedding OF SARS-CoV-2 (End-Covid) - Full Text View." *ClinicalTrials.gov*, clinicaltrials.gov/ct2/show/NCT04405739.

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