**Philippine COVID-19 Living Clinical Practice Guidelines**
*Institute of Clinical Epidemiology, National Institutes of Health, UP Manila*
*In cooperation with the Philippine Society for Microbiology and Infectious Diseases*
*Funded by the DOH AHEAD Program through the PCHRD*

# EVIDENCE SUMMARY

## Among COVID-19 patients, should bamlanivimab in combination with etesevimab be used for treatment?

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## RECOMMENDATION

**We suggest the use of bamlanivimab and etesevimab combination therapy as treatment for mild to moderate, non-hospitalized COVID-19 patients with at least 1 risk factor* for progression to severe disease**. *(Low quality of evidence; Weak recommendation)*

*Risk factors for severe COVID-19: age ≥65 years, body-mass index ≥35 kg/m$^2$, cardiovascular disease (including hypertension), chronic lung disease (including asthma), chronic metabolic disease (including diabetes), chronic kidney disease (including receipt of dialysis), chronic liver disease, and immunocompromised conditions

*Consensus Issues*
The panel favoured the use of bamlanivimab and etesevimab among non-hospitalized COVID-19 patients who are at risk for severe disease, based on the results of 2 randomized controlled trials that showed net potential benefit in terms of COVID-19 related hospitalizations and all-cause mortality, reduction in total symptom score, and number of days to symptom resolution, with no significant difference in terms of adverse events. Concern regarding the drug's effectivity against variants was raised by one of the panelists. As of writing, the drug has no emergency use authorization from the Philippine FDA, thus may only be used in the context of clinical trials.

## PREVIOUS RECOMMENDATIONS

We recommend against the use of bamlanivimab monotherapy as treatment for COVID-19 infection *(Very low quality of evidence; Strong recommendation)*

We suggest against the use of bamlanivimab/etesevimab in the treatment of non-hospitalized COVID-19 patients with mild-to-moderate COVID-19 at high risk of progression to severe disease *(Low quality of evidence; Conditional recommendation)*

*Previous Consensus Issues*
Bamlanivimab as monotherapy or in combination with etesevimab showed no significant benefit as treatment for COVID-19. Further studies are needed to show the effectiveness of bamlanivimab in the treatment of COVID-19 infection. In addition, the current cost of bamlanivimab remains high with an approximate cost of Php 60,000 to 120,000 per dose. Recommending its use will possibly promote inequity especially in remote areas. Its local availability should also be considered.

## What's new in this version?

This version includes one (1) new study (results of a phase 3 randomized controlled trial).

## Key Findings

The evidence on the use of bamlanivimab + etesevimab combination comes from two (2) randomized controlled trials (RCT) among non-hospitalized patients with COVID-19. Both studies found that there was a significant reduction in COVID-19 related hospitalizations, all-cause mortalities, symptom resolution, and reduction in viral load among the participants who received the bamlanivimab + etesevimab cocktail compared to placebo. There was no significant difference in adverse events between the two groups.

## Introduction

Neutralizing monoclonal antibodies are being studied as a way to boost the immune response to SARS-CoV-2. The investigational neutralizing IgG1 monoclonal antibody bamlanivimab (LY-CoV555; Lilly) was shown to bind to the receptor binding domain of the spike protein of SARS-CoV-2 viruses, which blocks attachment of the virus to the human ACE2 receptor.[1] Etesevimab (LY3832479 or LU-CoV016) is another potent monoclonal antibody that binds to a different epitope of the spike protein of SARS-CoV-2 viruses. Preclinical studies have shown that etesevimab may be able to neutralize even the emerging variants thus, the combination of the 2 drugs may prove to be an effective treatment against COVID-19 and the predominant variants. [2,3]

## Review Methods

A systematic search was done from the date of the last search April 7, 2021 until September 3, 2021 using Medline, CENTRAL, and Google Scholar with a combined MeSH and free text search using the terms coronavirus infections, COVID-19, severe acute respiratory syndrome coronavirus 2 or SARS-CoV-2, and bamlanivimab or etesevimab. We also looked at the COVID-NMA Living Data and searched for ongoing studies in the NIH *clinicaltrials.gov* and various trial registries. Preprints were also searched using medrxiv, chinaxiv and biorxiv. Only randomized controlled trials that compared a combination of bamlanivimab and etesevimab against placebo or standard care were included in this review. No limits were placed on age, COVID-19 severity, and dosing.

## Results

The initial search yielded 66 articles. After review of search output, we retrieved 2 published studies that evaluated the use of combination bamlanivimab + etesevimab in COVID-19. One was a Phase 2/3 trial [4], while the more recently published trial was a Phase 3 trial.[5] The dose used in both studies was a single dose of bamlanivimab 2800mg + etesevimab 2800mg administered intravenously.

These 2 studies had a total of 1,303 participants. Both studies included non-hospitalized COVID-19 confirmed participants.[4,5] One study included non-hospitalized COVID-19 patients with ≥1 risk factor for severe COVID-19, including age ≥65 years, body-mass index ≥35 kg/m$^2$, cardiovascular disease (including hypertension), chronic lung disease (including asthma), chronic metabolic disease (including diabetes), chronic kidney disease (including receipt of dialysis), chronic liver disease, and immunocompromised conditions.[5] Both studies reported the following outcomes: COVID-19 related hospitalization and all-cause mortalities, resolution of COVID-19 symptoms, and adverse events. The characteristics of the included studies are summarized in Appendix 3.

The overall quality of evidence was rated low because of serious imprecision and inconsistency in one important outcome (adverse events). Appraisal of study quality showed no serious risk of bias in the included studies. The risk of bias summary is in Appendix 4. The GRADE evidence profile is in Appendix 5.

Pooled analysis showed significant decrease in the COVID-19 related hospitalizations and all-cause mortalities (combined endpoint) among COVID-19 patients who received the combination bamlanivimab + etesevimab compared to placebo (RR 0.28, 95% CI 0.15-0.53; $I^2$=0%). One study reported a reduction in mean total symptom score from baseline to day 11 in the bamlanivimab + etesevimab group compared to placebo (MD -0.6 points, 95% CI -1.18 to -0.03). The total symptom score ranges from 0 to 24 points based on 8 symptom domains (cough, shortness of breath, feeling feverish, fatigue, body aches and pain, sore throat, chills, and headache), with higher points correlating with more severe symptoms.[4] The other study recorded a 1-day decrease in the number of days to symptom resolution also in the bamlanivimab + etesevimab group compared to the control group (experimental group median 8 days, 95% CI 7-8 days vs. control group 9 days, 95% CI 8-10 days; p=0.007).[5]

**Safety**

There was no significant difference in adverse events (RR 0.87, 95% CI 0.49-1.57; $I^2$=75%) and serious adverse events (RR 1.09, 95% CI 0.40-2.93; $I^2$=0%) in the experimental group compared to placebo. The most common adverse effects mentioned were nausea, rash/pruritus [4,5], dizziness [5], diarrhea [5], and hypertension.[5] The serious adverse event noted in the combination bamlanivimab + etesevimab group for one study was a urinary tract infection, deemed unrelated to COVID-19 by the investigators.[4] The other study did not mention the serious adverse events encountered.[5]

## Recommendations from Other Groups

Table 1. Summary of Recommendations from other Groups

| Regulatory Agency | Recommendation |
|---|---|
| US Food and Drug Administration (FDA)<br>(as of September 2, 2021) | Revoked the Emergency Use Authorization (EUA) of bamlanivimab monotherapy as treatment for mild-to-moderate COVID-19 due to the emergence of Gamma (P.1), Beta (B.1351) and Delta (B.1.617.2) variants that have shown resistance to this drug, resulting in treatment failure.[7] Etesevimab remains active in neutralizing the Alpha, Beta and Delta variants.[8]<br><br>Maintained the EUA for the bamlanivimab + etesevimab cocktail for states in which the combined frequency of the variants resistant to the cocktail is less than 5%. The resistance rates are being closely monitored by the CDC. The cocktail is approved for use in all 50 states at a dose of bamlanivimab 700mg + etesevimab 1400mg.[9,10] |
| National Institutes of Health (NIH)<br>(as of September 15, 2021) | Recommends bamlanivimab 700mg + etesevimab 1400mg for treating non-hospitalized mild-to-moderate COVID-19 patients who are at high risk for progression to severe |

| | |
|---|---|
| | disease in regions where the combined frequency of potentially resistant variants is low.[11] |
| Infectious Diseases Society of America (IDSA)<br>(as of August 25, 2021) | Recommends the administration of a lower dose than the clinical trials of bamlanivimab 700mg + etesevimab 1400mg for those with mild-to-moderate COVID-19 symptoms who are at risk for progression to severe disease (*Moderate certainty of evidence; Conditional recommendation).*[12] |
| Australian Guidelines<br>(as of August 26, 2021) | Recommends against the use of bamlanivimab + etesevimab combination therapy due to the resistance of several variants against bamlanivimab.[13] |
| World Health Organization (WHO) | No recommendation on the use of bamlanivimab + etesevimab combination in the treatment of COVID-19.[14] |

## Research Gaps

There are currently six (6) ongoing randomized clinical trials on bamlanivimab + etesevimab as treatment for COVID-19 (Appendix 7).

## References


[1] An EUA for bamlanivimab - a monoclonal antibody for COVID-19. *Med Lett Drugs Ther*. [Internet]. 2020;62(1612):185-186. Available from: http://www.ncbi.nlm.nih.gov/pubmed/33443490.

[2] Shi R, Shan C, Duan X, et al. A human neutralizing antibody targets the receptor-binding site of SARS-CoV-2. *Nature.* [Internet]. 2020;584(7819):120-124. Available from: doi:10.1038/s41586-020-2381-y.

[3] Baum A, Fulto BO, Wloga E et al. Antibody cocktail to SARS-CoV-2 spike protein prevents rapid mutational escape seen with individual antibodies. *Science*. [Internet]. 2020;369(6506):1014-1018. Available from: doi:10.1126/science.abd0831.

[4] Gottlieb RL, Nirula A, Chen P, et al. 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. *JAMA - J Am Med Assoc*. [Internet]. 2021;325(7):632-644. Available from: doi:10.1001/jama.2021.0202

[5] Dougan M, Nirula, Azizad M et al. Bamlanivimab plus Etesevimab in Mild or Moderate COVID-19. *N Engl J Med.* 2021. [Internet]. Available from: doi:10.1056/NEJMoa2102685.

[6] Buntz B. Drug, Discovery and Development. [Internet]. Lilly's bamlanivimab and etesevimab cut COVID-19 hospitalization and deaths in study. [updated 2021 Mar 10; cited 2021 Sept 8]. Available from: https://www.drugdiscoverytrends.com/lillys-bamlanivimab-and-etesevimab-cut-covid-19-hospitalization-and-deaths-in-study/.

[7] FDA.gov. [Internet]. Coronavirus (COVID-19) Update: FDA revokes emergency use authorization for monoclonal antibody bamlanivimab. [updated 2021 Apr 16; cited 2021 Sept 7]. Available from: https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-revokes-emergency-use-authorization-monoclonal-antibody-bamlanivimab

[8] lanas D, Veyer D, Baidaliuk A et al. Reduced sensitivity of SARS-CoV-2 variant Delta to antibody neutralization. *Nature.* [Internet]. 2021;596:276-280. Available from: https://doi.org/10.1038/s41586-021-03777-9

[9] FDA.gov. [Internet]. Bamlanivimab and Etesevimab Authorized States, Territories and U.S. Jurisdictions. [updated 2021 2 Sept; cited 2021 Sept 9]. Available from: https://www.fda.gov/media/151719/download

[10] FDA.gov. [Internet]. Fact sheet for health care providers emergency use authorization (EUA) of bamlanivimab and etesevimab. [updated 2021 Aug; cited 2021 Sept 9]. Available from: https://www.fda.gov/media/145802/download

[11] National Institutes of Health. [Internet]. COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. 2021. [cited 2021 Sept 9]. Available from: https://www.COVID19treatmentguidelines.nih.gov/.

[12] Bhimraj A, Morgan RL, Shumaker AH, et al. Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients with COVID-19. *Clin Infect Dis*. [Internet]. 2020:0-137. Available from: doi:10.1093/cid/ciaa478

[13] National COVID-19 Clinical Evidence Task Force. [Internet]. Australian guidelines for the clinical care of people with COVID-19. *Aust Gov*. 2020:215. [cited 2021 Sept 9]. Available from: www.COVID19evidence.net.au.

[14] World Health Organization. [Internet]. Therapeutics and COVID-19 Living Guidelines. [updated 2021 Jul 6; cited 2021 Sept 7]. Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-therapeutics-2021.2.

# Appendix 1. Evidence to Decision

Table 1. Summary of initial judgements prior to the panel discussion (N = 10)

| FACTORS | JUDGEMENT | | | | | | RESEARCH EVIDENCE/ADDITIONAL CONSIDERATIONS |
|---|---|---|---|---|---|---|---|
| **Problem** | No | Yes (10) | | | | | • COVID-19 has affected millions of people worldwide and has caused substantial mortality and morbidity. |
| **Benefits** | Large (2) | Moderate (6) | Small (2) | Uncertain | | | • Pooled analysis of the 2 RCTs showed significant decrease in the COVID-19 related hospitalizations and all-cause mortalities (combined endpoint) (RR 0.28, 95% CI 0.15-0.53, I2=0%). |
| **Harm** | Large (1) | Small (8) | Uncertain (1) | | | | • No significant difference in adverse events (RR 0.87, [0.49-1.57]) and serious adverse events ((RR 1.09, [0.40-2.93]) vs placebo |
| **Certainty of Evidence** | High | Moderate (2) | Low (8) | Very low | | | • Low because of serious imprecision and inconsistency in one important outcome (adverse events). |
| **Balance of effects** | Favors drug (9) | Does not favor drug (1) | Uncertain | | | | • There is net potential benefit in terms of COVID-19 related hospitalizations and all-cause mortalities, reduction in total symptom score and number of days to symptom resolution, with no significant difference in terms of adverse events.<br>• 1 panelist believed that there is still inadequate evidence to favor the drug, particularly with regards to its effectivity against variants. |
| **Values** | Important uncertainty or variability (2) | Possibly important uncertainty or variability (3) | Possibly NO important uncertainty or variability (5) | No important uncertainty or variability | | | |
| **Resources Required** | Uncertain | Large cost (10) | Moderate Cost | Negligible cost | Moderate savings | Large savings | • $2,100 or PHP 105,000 for a single course (1 dose bamlanivimab + etesevimab IV) |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Certainty of evidence of required resources** | No included studies (1) | Very low | Low (7) | Moderate | High (2) | | • There is low certainty of evidence on the cost of bamlanivimab + etesevimab treatment.<br>• The cost was derived from foreign news websites (Forbes, PMLive). |
| **Cost effectiveness** | No included studies (6) | Favors the comparison | Does not favor either the intervention or the comparison (1) | Favors the intervention (3) | | | • None of the included trials assessed cost effectiveness. |
| **Equity** | Uncertain (3) | Reduced (3) | Probably no impact | Increased (4) | | | |
| **Acceptability** | Uncertain (7) | No | Yes (3) | | | | |
| **Feasibility** | Uncertain (6) | No (1) | Yes (3) | | | | |

**Additional Considerations / Comments:**

- The drug currently has no emergency use authorization from the Philippine FDA, thus may only be used in the context of clinical trials.
- There is need for more data on the drug's effectivity against variants

## Appendix 2. Characteristics of Included Studies

| DATABASE | SEARCH STRATEGY / SEARCH TERMS | DATE AND TIME OF SEARCH | RESULTS | |
|---|---|---|---|---|
| | | | Yield | Eligible |
| Medline | {"Coronavirus Infections"[Mesh] OR "Coronavirus"[Mesh] OR coronavirus OR novel coronavirus OR NCOV OR "COVID-19" [Supplementary Concept] OR COVID19 OR COVID 19 OR COVID-19 OR "severe acute respiratory syndrome coronavirus 2" [Supplementary Concept] OR severe acute respiratory syndrome coronavirus 2 OR SARS2 OR SARS 2 OR SARS COV2 OR SARS COV 2 OR SARS-COV-2} AND (Bamlanivimab)<br><br>Filters: from April 7, 2021 to September 1, 2021 | September 3, 2021 2PM | 66 | 1 |
| CENTRAL | MeSH descriptor: [Coronaviridae Infections] explode all trees OR MeSH descriptor: [Coronavirus] explode all trees OR coronavirus OR novel coronavirus OR NCOV OR COVID19 OR COVID 19 OR COVID-19 OR severe acute respiratory syndrome coronavirus 2 OR SARS2 OR SARS 2 OR SARS COV2 OR SARS COV 2 OR SARS-COV-2 AND (Bamlanivimab)<br><br>Filters: from April 7, 2021 to September 1, 2021 | September 3, 2021 830 PM | 6 | 1 |
| Google Scholar | Bamlanivimab AND etesevimab AND COVID AND randomized trial | September 3, 2021 840 PM | 369 | 2 |
| COVID-NMA initiative | Bamlanivimab and etesevimab | September 3, 2021 9 PM | 4 | 2 |
| | | | | |
| ClinicalTrials.gov | COVID19 AND bamlanivimab | September 3, 2021 915 PM | 14 | 0 |
| Chinese Clinical Trial Registry | Bamlanivimab | September 3, 2021 920 PM | 0 | 0 |
| EU Clinical Trials Register | Bamlanivimab | September 3, 2021 930 PM | 2 | 0 |
| Republic of Korea - Clinical Research Information Service | Bamlanivimab | September 3, 2021 940PM | 0 | 0 |
| Japan Primary Registries Network/ NIPH Clinical Trials Search | Bamlanivimab | September 3, 2021 945PM | 0 | 0 |
| CenterWatch | Bamlanivimab | September 3, 2021 950PM | 4 | 0 |

| | | | | |
|---|---|---|---|---|
| chinaxiv.org | Bamlanivimab | September 3, 2021 955PM | 0 | 0 |
| Medrxiv.org | Bamlanivimab<br><br>Filters: April 7, 2021 to September 3, 2021 | September 3, 2021 10PM | 2 | 0 |
| Biorxiv.org | Bamlanivimab<br><br>Filters: April 7, 2021 to September 3, 2021 | September 3, 2021 1010PM | 3 | 0 |

## Appendix 3. Characteristics of Included Studies

| Study ID | Patients (n) & Duration of Follow-Up | Interventions | Outcomes | Study Design |
|---|---|---|---|---|
| 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<br><br>*Gottlieb et al., USA* | Non-hospitalized confirmed COVID-19 patients with mild to moderate symptoms<br><br>(N = 268)*<br><br>Duration of follow-up:<br>29 days | EXPERIMENTAL:<br>Bamlanivimab 2800mg + Etesevimab 2800mg IV<br><br>CONTROL:<br>Placebo IV | PRIMARY:<br>Change in SARS-CoV-2 log viral load at day 11<br><br>SECONDARY:<br>Time to viral clearance, clinical recovery, COVID-19 related hospitalization or all-cause death, adverse events | Randomized, double-blind, placebo-controlled |
| Bamlanivimab plus Etesevimab in Mild or Moderate COVID-19<br><br>*Dougan et al., USA* | Ambulatory confirmed COVID-19 patients with ≥1 risk factor for severe COVID-19<br><br>(N = 1,035)<br><br>Duration of follow-up:<br>29 days | EXPERIMENTAL:<br>Bamlanivimab 2800mg + Etesevimab 2800mg IV<br><br>CONTROL:<br>Placebo IV | PRIMARY:<br>COVID-19 related hospitalization or all-cause death<br><br>SECONDARY:<br>Time to sustained patient-reported resolution of symptoms, reduction in viral load, time to viral clearance, adverse events | Randomized, double-blind, placebo-controlled |

**For the bamlanivimab + etesevimab + placebo groups only*

## Appendix 4. Study Appraisal

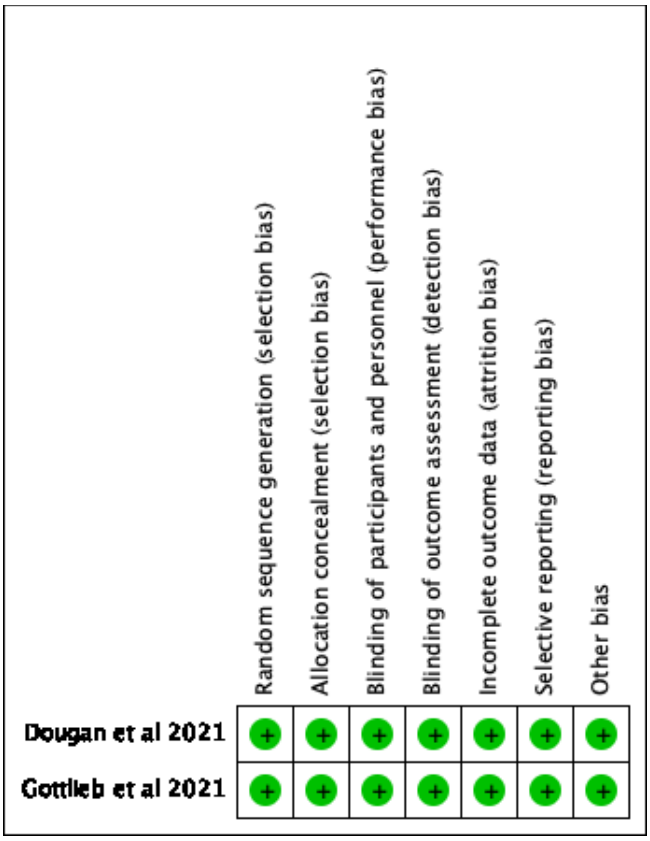


Figure 1. Risk of bias summary table

# Appendix 5. GRADE Evidence Profile

**Author(s)**: Isabella S. Ocampo, MD
**Question**: Bamlanivimab + Etesevimab compared to Placebo for COVID-19
**Setting**: Outpatient
**Bibliography**: 1. Gottlieb RL, Nirula A, Chen P, et al. 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. JAMA - J Am Med Assoc. 2021;325(7):632-644. doi:10.1001/jama.2021.0202 2. Dougan M, Nirula A, Azizad M et al. Bamlanivimab plus Eteseviman in Mild or Moderate Covid-19. N Engl J Med. 2021. doi:10.1056/NEJMoa2102685.

| Certainty assessment | | | | | | | № of patients | | Effect | | Certainty | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| № of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Bamlanivimab + Etesevimab | Placebo | Relative (95% CI) | Absolute (95% CI) | | |
| **Covid-19 related hospitalization and all-cause mortalities (follow up: 29 days)** | | | | | | | | | | | | |
| 2 | randomised trials | not serious | not serious | not serious | not serious | none | 12/630 (1.9%) | 45/673 (6.7%) | **RR 0.28** (0.15 to 0.53) | **48 fewer per 1,000** (from 57 fewer to 31 fewer) | ⊕⊕⊕⊕ HIGH | CRITICAL |
| **Number of days to sustained patient-reported Covid-19 symptom resolution (follow up: 29 days)** | | | | | | | | | | | | |
| 1 | randomised trials | not serious | not serious | not serious | not serious | none | There was a reduction in the number of days to symptom resolution (8 days in bamlanivimab + etesevimab group [95% CI: 7-8] vs 9 days in placebo group [95% CI: 8-10]; p=0.007). | | | | ⊕⊕⊕⊕ HIGH | CRITICAL |
| **Change in mean total symptom score from baseline (follow up: 11 days)** | | | | | | | | | | | | |
| 1 | randomised trials | not serious | not serious | not serious | serious [a] | none | 4.37 | 3.8 | - | MD **0.6 lower** (1.18 lower to 0.03 lower) | ⊕⊕⊕◯ MODERATE | CRITICAL |
| **Serious adverse events (follow up: 29 days)** | | | | | | | | | | | | |
| 2 | randomised trials | not serious | not serious | not serious | serious [c] | none | 8/630 (1.3%) | 8/673 (1.2%) | **RR 1.09** (0.40 to 2.93) | **1 more per 1,000** (from 7 fewer to 23 more) | ⊕⊕⊕◯ MODERATE | CRITICAL |
| **Adverse events (follow up: 29 days)** | | | | | | | | | | | | |
| 2 | randomised trials | not serious | serious [b] | not serious | serious [c] | none | 88/630 (14.0%) | 102/673 (15.2%) | **RR 0.87** (0.49 to 1.57) | **20 fewer per 1,000** (from 77 fewer to 86 more) | ⊕⊕◯◯ LOW | IMPORTANT |

**CI:** Confidence interval; **RR:** Risk ratio; **MD:** Mean difference

## *Explanations*

a. The upper limit of the CI is clinically insignificant
b. There is considerable heterogeneity
c. There is a wide confidence interval

## Appendix 6. Forest Plots

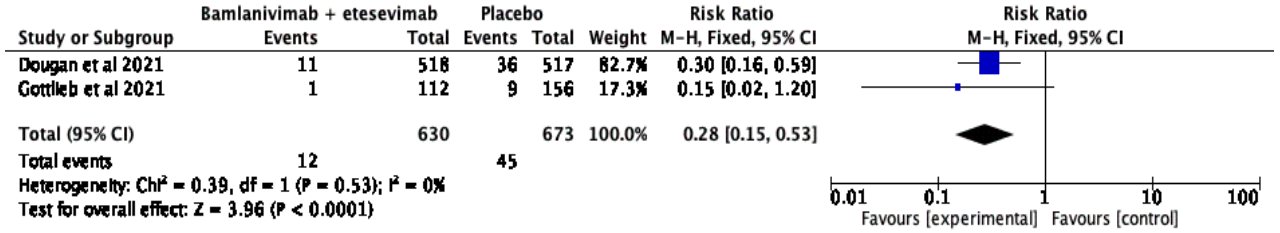


Figure 1. Effect of bamlanivimab + etesevimab compared to placebo on COVID-19 related hospitalizations and all-cause mortalities

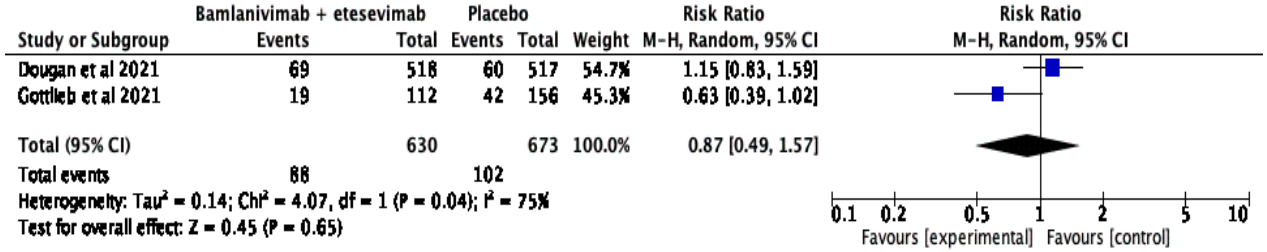


Figure 2. Effect of bamlanivimab + etesevimab compared to placebo on adverse events

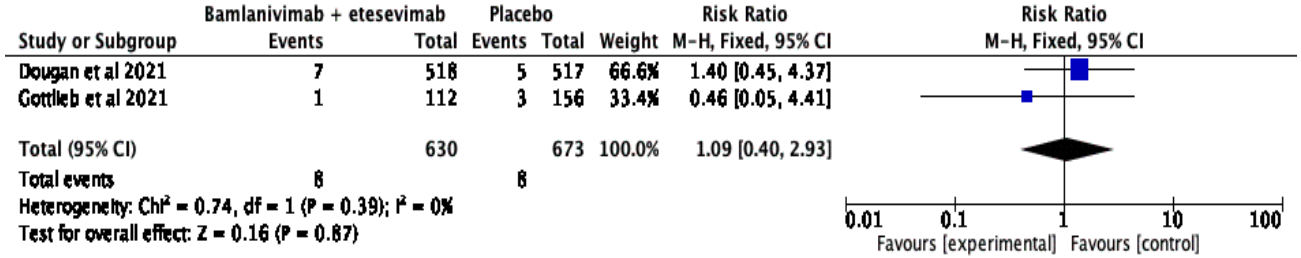


Figure 3. Effect of bamlanivimab + etesevimab compared to placebo on serious adverse events

## Appendix 7. Table of Ongoing Studies

| Clinical Trial Identifier/Title | Study Design | Population | Intervention | Outcome | Completion |
|---|---|---|---|---|---|
| NCT04790786<br>UPMC OPTIMISE-C19 Trial, a COVID-19 Study (OPTIMISE-C19) | Randomized, open-label, parallel assignment | COVID-19 confirmed patients | Bamlanivimab vs casirivimab + imdevimab vs. bamlanivimab + etesevimab | Alive and free from hospitalization 28 days after initial participation | December 2022 |
| NCT04427501<br>A Study of LY3819253 (LY-CoV555) and LY3832479 (LY-CoV016) in Participants With Mild to Moderate COVID-19 Illness (BLAZE-1) | Randomized, double blind, sequential assignment | Confirmed COVID-19, non-hospitalized with mild to moderate symptoms | Bamlanivimab vs. bamlanivimab + etesevimab vs. placebo | Percentage of patients who experience COVID-related hospitalization or death from any cause up to 29 days from baseline; change from baseline to day 11 in viral load; adverse events | June 24, 2022 |
| NCT04497987<br>A Study of LY3819253 (LY-CoV555) and LY3832479 (LY-CoV016) in Preventing SARS-CoV-2 Infection and COVID-19 in Nursing Home Residents and Staff | Randomized, double-blind, parallel assignment | Resident or facility staff in a skilled nursing or assisted living facility with at least one confirmed case of SARS-CoV-2 | Bamlanivimab vs. bamlanivimab + etesevimab vs. placebo | Percentage of participants with COVID-19 within 21 days of detection | May 20, 2021 |
| NCT04634409<br>A Study of Immune System Proteins in Participants With Mild to Moderate COVID-19 Illness | Randomized parallel assignment | Confirmed COVID-19, Not hospitalized with mild to moderate symptoms | Bamlanivimab + etesevimab vs. bamlanivimab vs. placebo | Percentage of participants with SARS-CoV-2 viral load greater than 5.27 | October 13, 2021 |
| EudraCT 2021-002612-31<br><br>Adaptive, randomized, placebo-controlled trial to evaluate the efficacy | Randomized, placebo-controlled trial | Adult patients with mild confirmed COVID-19 | Bamlanivimab + etesevimab vs. casirivimab + imdevimab vs. placebo | Prevention of disease progression (need for oxygen therapy supplementation | Not mentioned |

| | | | | | |
|---|---|---|---|---|---|
| of monoclonal antibodies in outpatients with mild or moderate COVID-19 | | | | , hospitalization and/or death) | |
| EudraCT 2021-004035-88<br><br>A randomized, open-label, active controlled, parallel group, multicenter phase 3 study to evaluate the efficacy and tolerability of bamlanivimab and etesevimab, casirivimab and imdevimab, and sotrovimab versus standard of care in patients with mild to moderate COVID-19 disease | Randomized, open-label, parallel assignment | Patients with mild to moderate confirmed COVID-19 infection | Bamlanivimab + etesevimab vs. casirivimab + imdevimab vs. sotrovimab vs. placebo | Prevention of disease progression (hospitalization in intensive care unit, peripheral oxygen saturation ≤92%, oxygen desaturation ≤4%) | Not mentioned |