Supplementary results

Molnupiravir versus control

Non-serious adverse events

Meta-analysis showed no evidence of a difference between molnupiravir versus control on non-serious adverse events (RR 0.97, 95% CI 0.86 to 1.09; t² = 0.0, I² = 0.0%; P = 0.6104) (S17 Fig). Visual inspection of the forest plot and measures to quantify heterogeneity (t² = 0.0, I² = 0.0%) indicated no heterogeneity. Trial Sequential Analysis showed that we had enough information to reject that molnupiravir versus control reduced the risk of non-serious adverse events with a relative risk reduction of 20% (S18 Fig). The time points of assessments were unclear, 14 days, 19 days, 28 days, 29 days, or 31 days after randomisation. This outcome result was assessed at high risk of bias (S3 Table).

Ritonavir-boosted nirmatrelvir versus placebo

Non-serious adverse events

251 out of 1109 participants (22.3%) had a non-serious adverse event in the ritonavir-boosted nirmatrelvir group versus 266 out of 1115 participants (23.9%) in the placebo group (Fisher’s exact test: P = 0.5141). The time point of assessment was 34 days after randomisation. This outcome result was assessed at high risk of bias (S3 Table).

Bamlanivimab/etesevimab versus placebo

Serious adverse events

7 out of 518 participants (1.4%) had a serious adverse event in the bebtelovimab/etesevimab group versus 5 out of 517 participants (1.0%) in the placebo group (Fisher’s exact test: P = 0.7731).
time point of assessment was 29 days after randomisation. This outcome result was assessed at low risk of bias, and the certainty of the evidence was very low (S3 Table, S6 Table).

### Non-serious adverse events

69 out of 518 participants (13.3%) had a non-serious adverse event in the bebtelovimab/etesevimab group versus 60 out of 517 participants (11.6%) in the placebo group (Fisher’s exact test: P = 0.4517). The time point of assessment was 29 days after randomisation. This outcome result was assessed at low risk of bias (S3 Table).

### Sotrovimab versus placebo

#### All-cause mortality

0 out of 528 participants (0.0%) died in the sotrovimab group versus 2 out of 529 participants (0.4%) in the placebo group (Fisher’s exact test: P = 0.4995). This outcome result was assessed at low risk of bias, and the certainty of the evidence was very low (S3 Table, S7 Table).

#### Non-serious adverse events

73 out of 430 participants (0.0%) had a non-serious adverse event in the sotrovimab group versus 85 out of 438 participants (0.4%) in the placebo group (Fisher’s exact test: P = 0.3795). The time point of assessment was 29 days after randomisation. This outcome result was assessed at low risk of bias (S3 Table).
Casirivimab/imdevimab versus placebo

All-cause mortality

It was not possible to perform any meta-analysis on casirivimab/imdevimab versus placebo on all-cause mortality due to insufficient data. Two trials reported data on all-cause mortality.\textsuperscript{39,40} Weinreich et al. reported that 2 out of 2716 participants (0.1%) died in the casirivimab/imdevimab group versus 3 out of 1342 participants (0.2%) in the placebo group (Fisher’s exact test: $P = 0.3400$).\textsuperscript{39} The time point of assessment was 29 days after randomisation.\textsuperscript{39} This outcome result was assessed at high risk of bias (S3 Table). O’Brien et al. reported that 0 out of 155 participants (0.0%) died in the casirivimab/imdevimab group versus 0 out of 156 participants (0.0%) in the placebo group.\textsuperscript{40} The time point of assessment was until March 11, 2021.\textsuperscript{40} This outcome result was assessed at high risk of bias, and the certainty of the evidence was very low (S3 Table, S8 Table).

It was not possible to perform any predefined subgroup analyses due to lack of relevant data.

Mechanical ventilation

It was not possible to perform any meta-analysis on casirivimab/imdevimab versus placebo on mechanical ventilation due to insufficient data. Two trials reported data on mechanical ventilation.\textsuperscript{39,40} Weinreich et al reported that 2 out of 2091 participants (0.1%) received mechanical ventilation in the casirivimab/imdevimab group versus 6 out of 1341 participants (0.4%) in the placebo group (Fisher’s exact test: $P = 0.0630$).\textsuperscript{39} The time point of assessment was 29 days after randomisation.\textsuperscript{39} This outcome result was assessed at high risk of bias (S3 Table). O’Brien et al. reported that 0 out of 100 participants (0.0%) received mechanical ventilation in the casirivimab/imdevimab group versus 0 out of 104 participants (0.0%) in the placebo group.\textsuperscript{40} The time point of assessment was 60 days after randomisation.\textsuperscript{40} This outcome result was assessed at high risk of bias (S3 Table).
Remdesivir versus placebo

All-cause mortality

0 out of 279 participants (0.0%) died in the remdesivir group versus 0 out of 283 participants (0.0%) in the placebo group. This outcome result was assessed at high risk of bias, and the certainty of the evidence was very low (S3 Table, S9 Table).

Non-serious adverse events

118 out of 279 participants (42.3%) had a non-serious adverse event in the remdesivir group versus 131 out of 283 participants (46.3%) in the placebo group (Fisher’s exact test: P = 0.3513). The time point of assessment was 28 days after randomisation. This outcome result was assessed at high risk of bias (S3 Table).

Regdanvimab versus placebo

We identified two trials randomising 345 participants to regdanvimab versus placebo.

All-cause mortality

It was not possible to perform any meta-analysis on regdanvimab versus placebo on all-cause mortality due to insufficient data. Two trials reported data on all-cause mortality. Eom et al. reported that 0 out of 215 participants (0.0%) died in the regdanvimab group versus 0 out of 110 participants (0.0%) in the placebo group. The time point of assessment was 28 days after randomisation. This outcome result was assessed at high risk of bias (S3 Table). Kim et al. reported that 0 out of 15 participants (0.0%) died in the regdanvimab group versus 0 out of 3 participants (0.0%) in the placebo group. The time point of assessment was 14 days after
randomisation. This outcome result was assessed at high risk of bias, and the certainty of the evidence was very low (S3 Table, S10 Table).

Serious adverse events

It was not possible to perform any meta-analysis on regdanvimab versus placebo on serious adverse events due to insufficient data. Two trials reported data on serious adverse events. Eom et al. reported that 0 out of 215 participants (0.0%) had a serious adverse event in the regdanvimab group versus 0 out of 110 participants (0.0%) in the placebo group. The time point of assessment was 28 days after randomisation. This outcome result was assessed at high risk of bias (S3 Table). Kim et al reported that 3 out of 15 participants (20.0%) had a serious adverse event in the regdanvimab group versus 1 out of 3 participants (33.3%) in the placebo group (Fisher’s exact test: P = 1.0000). The time point of assessment was 14 days after randomisation. This outcome result was assessed at high risk of bias, and the certainty of the evidence was very low (S3 Table, S10 Table).

Hospitalisations

9 out of 204 participants (4.4%) were hospitalised in the regdanvimab group versus 9 out of 103 participants (8.7%) in the placebo group (Fisher’s exact test: P = 0.1962). The time point of assessment was 28 days after randomisation. This outcome result was assessed at high risk of bias (S3 Table).

Mechanical ventilation

1 out of 204 participants (0.5%) received mechanical ventilation in the regdanvimab group versus 0 out of 103 participants (0.0%) in the placebo group (Fisher’s exact test: P = 1.0000). The time
point of assessment was 28 days after randomisation. This outcome result was assessed at high risk of bias (S3 Table).

### Intensive care

0 out of 204 participants (0.0%) were admitted to intensive care in the regdanvimab group versus 0 out of 103 participants (0.0%) in the placebo group (Fisher’s exact test: P = 1.0000). The time point of assessment was 28 days after randomisation. This outcome result was assessed at high risk of bias (S3 Table).

### Non-serious adverse events

Meta-analysis showed no evidence of a difference between regdanvimab versus placebo on non-serious adverse events (RR 0.92, 95% CI 0.65 to 1.30; $t^2 = 0.0$, $I^2 = 0.0\%$; $P = 0.6455$) (S19 Fig). Visual inspection of the forest plot and measures to quantify heterogeneity ($t^2 = 0.0$, $I^2 = 0.0\%$) indicated no heterogeneity. Trial Sequential Analysis showed that we did not have enough information to confirm or reject that regdanvimab versus placebo reduced the risk of non-serious adverse events with a relative risk reduction of 20% (no graph produced). The time points of assessment were 14 days or 28 days days after randomisation. This outcome result was assessed at high risk of bias (S3 Table).

### Bebtelovimab versus placebo

We identified one phase ½ trial randomising 287 participants to bebtelovimab versus placebo. Phase 1 randomised 34 participants, while phase 2 randomised 253 participants. This trial randomised participants with low risk for COVID-19 progression to 175 mg bebtelovimab, 175mg bebtelovimab/700 mg bamlanivimab/1400 mg etesevimab, or placebo. Since the combination of
bentelovimab/bamlanivimab/etesevimab has not been authorised by the FDA or EMA, only the results of bentelovimab versus placebo will be presented. It was not possible to perform meta-analyses or subgroup analyses due to lack of relevant data.

**All-cause mortality**

This trial only reported COVID-19 related mortality. 0 out of 24 participants (0.0%) died related to COVID-19 in the bentelovimab group versus 0 out of 10 participants (0.0%) in the placebo group in the phase 1 trial (Fisher’s exact test: \( P = 1.0000 \)). 48 0 out of 125 participants (0.0%) died related to COVID-19 in the bentelovimab group versus 0 out of 128 participants (0.0%) in the placebo group in the phase 2 trial (Fisher’s exact test: \( P = 1.0000 \)). The time point of assessment was unclear for phase 1 and 85 days after randomisation for phase 2. This outcome result was assessed at high risk of bias, and the certainty of the evidence was very low (S3 Table, S11 Table).

**Serious adverse events**

0 out of 24 participants (0.0%) had a serious adverse event in the bentelovimab group versus 0 out of 10 participants (0.0%) in the placebo group in the phase 1 trial (Fisher’s exact test: \( P = 1.0000 \)). 48 2 out of 125 participants (1.6%) had a serious adverse event in the bentelovimab group versus 2 out of 128 participants (1.6%) in the placebo group in the phase 2 trial (Fisher’s exact test: \( P = 1.0000 \)). The time point of assessment was unclear for phase 1 and 85 days after randomisation for phase 2. This outcome result was assessed at high risk of bias, and the certainty of the evidence was very low (S3 Table, S11 Table).
Non-serious adverse events

3 out of 24 participants (12.5%) had a non-serious adverse event in the bebtelovimab group versus 1 out of 10 participants (10.0%) in the placebo group in the phase 1 trial (Fisher’s exact test: \( P = 1.0000 \)). \(^{48}\) 11 out of 125 participants (8.8%) had a non-serious adverse event in the bebtelovimab group versus 10 out of 128 participants (7.8%) in the placebo group in the phase 2 trial (Fisher’s exact test: \( P = 0.8228 \)).\(^{46}\) The time point of assessment was unclear for phase 1 and 85 days after randomisation for phase 2.\(^{48}\) This outcome result was assessed at high risk of bias (\textbf{S3 Table}).