

## Introduction

This is the 3<sup>rd</sup> Summary of Main Results report from the [COVID-NMA initiative](#). It provides an overview of the results as of **June 3<sup>rd</sup>, 2022** and any notable changes since the previous report are highlighted in a section below. As mentioned in the previous update, the scope of the project has been reduced to vaccines, immunomodulators, and antivirals, which is reflected in this summary.

As before, the most up to date results are available on [covid-nma.com](https://covid-nma.com), and any studies pending data extraction are available [here](#). Feel free to get in touch with us using our [contact form](#) and to disseminate this document on twitter ([@Covid-NMA](#)).

## Updates since the previous report

Since the previous report (updated on May 4<sup>th</sup>) there have been the following changes:

- There is one new comparison, **Auxora** vs standard care/placebo, for which the certainty of evidence for adverse events and serious adverse events is moderate. This intervention probably results in little to no difference in the risk of adverse events and probably decreases the risk of serious adverse events.
- The following pharmacologic interventions have been removed from this summary, as they are not being updated anymore: **Aspirin** (acetylsalicylic acid), **Azithromycin** (an antimicrobial), **Hydroxychloroquine** (an antimalarial), **Colchicine** (an anti-inflammatory), and **Umbilical cord mesenchymal stem cell infusion**. Based on the evidence last updated on February 28<sup>th</sup> 2022, for all these outcomes there was moderate or high certainty indicating no evidence of beneficial effects (e.g. clinical improvement or reduction in mortality) or an increase in the risks of negative effects (e.g. serious adverse events) compared with placebo or standard care. Details of these results can still be found on the [project's website](#).
- Non-pharmacologic treatments are not being updated anymore either. Based on the evidence last updated on February 28<sup>th</sup> 2022, the only intervention with moderate certainty was **prone position vs standard care**, which probably slightly reduces the risk of requiring mechanical ventilation or death (WHO progression score level 7 or above) around 28 days in hospitalized patients. Details of these results can still be found on the [project's website](#).
- Additional studies and data updates have resulted in minimal changes in results for [Bamlanivimab \(LY-CoV555\)](#), [Convalescent plasma](#), [Corticosteroids](#), [Remdesivir](#), and [Ruxolitinib](#). The certainty and interpretation of these results did not change.

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# What is the current evidence regarding treatment of hospitalized Covid-19 patients?

Updated on June 3<sup>rd</sup>, 2022

## Pharmacologic treatments in hospitalized patients

*Critical outcomes of interest: Clinical improvement (around day 28 or day 60), WHO Clinical Progression Score  $\geq 7$  (around day 28 or day 60), all-cause mortality (around day 28 or day 60), viral negative conversion (around day 7), adverse events and serious adverse events.*

For most pharmacological treatments in hospitalized patients, the certainty of the evidence is still low or very low. Below is a summary of pharmacological interventions that have **results in favor of a beneficial effect** so far compared with placebo or standard care. We only highlight outcomes of moderate and high certainty; other outcomes are of low or very low certainty.

- **Anakinra** (a monoclonal antibody) probably reduces the risk of WHO score  $\geq 7$  (i.e. mechanical ventilation or death, around 28 days) in hospitalized patients, as well as slightly increases the likelihood of clinical improvement around 28 days. The risk of adverse events probably does not increase. It is one of the interventions that have been authorized in the EU to treat Covid-19.
- **Baricitinib** (a kinase inhibitor) reduces the risk of WHO score  $\geq 7$  (i.e. mechanical ventilation or death, around 28 days) in hospitalized patients, although it results in little to no difference in clinical improvement around 28 days. It is likely to reduce the risk of all-cause mortality (around 28 days and around 60 days). It probably does not increase the risk of adverse events but probably decreases the risk of serious adverse events.
- **Casirivimab + Imdevimab (REGN-COV2)** (Monoclonal antibody combination) probably reduces the risk of all-cause mortality (around 28 days), although the likelihood of clinical improvement around 28 days and around 60 days probably is not improved. It is one of the interventions that have been authorized in the EU to treat Covid-19.
- **Corticosteroids** probably increase clinical improvement (around 28 days) slightly and reduce the risk of all-cause mortality (around 28 days) in hospitalized patients. We pooled together oral and intravenous corticosteroids of participants with various disease severity. Of note, the largest study (the RECOVERY trial) found in subgroup analysis that “differences in mortality varied considerably according to the level of respiratory support that the patients were receiving at the time of randomization”, and that “the use dexamethasone resulted in lower 28-day mortality among those who were receiving either invasive mechanical ventilation or oxygen alone at randomization but not among those receiving no respiratory support.”
- **Tocilizumab** (a monoclonal antibody) is likely to reduce the risk of all-cause mortality (around 28 days) in hospitalized patients, although it probably results in little to no difference on clinical improvement around 28 days. It is one of the interventions that have been authorized in the EU to treat Covid-19.

For the treatments below there are outcomes with moderate or high certainty indicating **uncertainty of benefit or harm**

- **Remdesivir** (an anti-viral), which is one of the interventions recommended by the NIH and which has been authorized in the EU to treat COVID-19, we found that the risk estimate for all-cause mortality (around 28 days) and its wide confidence interval (RR 0.91, 95% CI 0.74 to 1.11) point to uncertainty of benefit or harm.

For the treatments below there are outcomes with moderate or high certainty indicating **no evidence of beneficial effects** (e.g. clinical improvement or reduction in mortality) or an increase in the risks of negative effects (e.g. serious adverse events) compared with placebo or standard care:

- **Auxora** (an immunomodulator) probably results in little to no difference in the risk of adverse events and probably decreases the risk of serious adverse events.
- **Bamlanivimab** (a monoclonal antibody) probably results in little to no difference on clinical improvement around day 60.

- **Canakinumab** (a monoclonal antibody) probably results in little to no difference on clinical improvement around 28 days and in little to no difference in the risk of adverse events.
- **Convalescent plasma** probably results in little to no difference on clinical improvement around 28 days or all-cause mortality (around 28 days).
- **Lopinavir + Ritonavir** (an anti-viral) probably results in little to no difference on viral negative conversion (around day 7), clinical improvement (around 28 days) or all-cause mortality (around 28 days).
- **Ruxolitinib** (a kinase inhibitor) probably results in little to no difference in the risk of adverse events.
- **Sotrovimab** (a monoclonal antibody) probably results in little to no difference in clinical improvement around day 60. Furthermore, it probably increases the risk of serious adverse events. While the NIH recommends this intervention for outpatients, it has not been recommended for hospitalized patients. Similarly, this intervention has been authorized in the EU to treat COVID-19, but only in patients who do not require supplemental oxygen and are at increased risk of the disease becoming severe.

For another intervention authorized by the European Medicines Association (Ritonavir alone) we have not yet identified randomized controlled trials reporting its effectiveness.

*Summary table on next page...*

**Summary Table: Pharmacologic treatments in hospitalized patients**  
(Updated on June 3<sup>rd</sup>, 2022)

Legend:

Moderate/ <b>High</b> certainty of benefit
Moderate/ <b>High</b> certainty of little or no difference
Moderate/ <b>High</b> certainty of harm

Treatment (vs standard care or placebo)	Treatment effectiveness					Adverse events			
	Improvement			Covid-19 events				Adverse events	Serious adverse events
	Viral negative conversion (D7)	Clinical improvement (D28)	Clinical improvement (D60)	WHO progression score (level ≥7) (D28)	WHO progression score (level ≥7) (D60)	All-cause mortality (D28)	All-cause mortality (D60)		
<a href="#">Anakinra</a>	low certainty	1.10 (1.00-1.20)	very low certainty	0.64 (0.42 - 0.98)		low certainty	very low certainty	1.02 (0.94-1.10)	low certainty
<a href="#">Auxora</a>			very low certainty	very low certainty	very low certainty	very low certainty	very low certainty	1.04 (0.87 - 1.25)	0.68 (0.47 - 0.99)
<a href="#">Bamlanivimab (LY-CoV555)</a>			0.98 (0.90 - 1.07)	low certainty		low certainty	low certainty	low certainty	low certainty
<a href="#">Baricitinib</a>		1.02 (1.00 - 1.05)		0.87 (0.78 - 0.97)		0.75 (0.58 - 0.98)	0.69 (0.56 - 0.86)	0.96 (0.88 - 1.05)	0.77 (0.64 - 0.94)
<a href="#">Canakinumab</a>		1.05 (0.96-1.14)		low certainty		low certainty	very low certainty	1.02 (0.86-1.21)	low certainty
<a href="#">Casirivimab + Imdevimab (REGN-COV2)</a>		1.02 (0.99 - 1.04)	1.04 (0.97 - 1.12)	low certainty		0.93 (0.86 - 1.01)	low certainty		
<a href="#">Convalescent plasma</a>	very low certainty	1.00 (0.97-1.02)	low certainty	low certainty	very low certainty	0.97 (0.92 - 1.02)	very low certainty	low certainty	low certainty
<a href="#">Corticosteroids</a>	very low certainty	1.05 (1.02 – 1.09)		very low certainty		0.91 (0.85-0.98)	very low certainty	low certainty	very low certainty
<a href="#">Lopinavir + Ritonavir</a>	1.05 (0.88 - 1.25)	0.99 (0.90 - 1.09)		low certainty	very low certainty	1.02 (0.92-1.12)	low certainty	low certainty	very low certainty
<a href="#">Remdesivir</a>	low certainty	low certainty		low certainty		0.91 (0.74-1.11)	very low certainty	very low certainty	very low certainty
<a href="#">Ruxolitinib</a>		low certainty		low certainty		low certainty		1.01 (0.85 - 1.19)	low certainty
<a href="#">Sotrovimab</a>			1.05 (0.97 - 1.15)	low certainty		low certainty	low certainty	low certainty	2.03 (1.32 - 3.13)
<a href="#">Tocilizumab</a>		1.04 (1.00-1.09)	very low certainty	low certainty		0.88 (0.82-0.95)	low certainty	low certainty	very low certainty

All values are RR (95% CI). Bolded results have a high level of certainty, while non-bolded results have a moderate level of certainty. Last updated: June 3<sup>rd</sup> 2022. Click on the treatment to access the corresponding site at covid-nma.com.

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