

# IL-6 inhibitors in patients with COVID-19 pneumonia: a systematic review and meta-analysis of multicenter, randomized trials

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## Background

COVID-19 is characterized by dysregulated immune response, resulting in severe respiratory failure and death. Interleukin-6 is involved in COVID-19-associated cytokine storm. Several trials investigated whether its inhibition could improve patients' outcome.

## Methods

We performed a meta-analysis of randomized trials. PubMed, Scopus, ClinicalTrials.gov and medRxiv were searched up to February 23<sup>rd</sup>, 2021.

Inclusion criteria: administration of tocilizumab or sarilumab; COVID-19 pneumonia; randomized controlled trials. Studies in settings other than adult human COVID-19 were excluded.

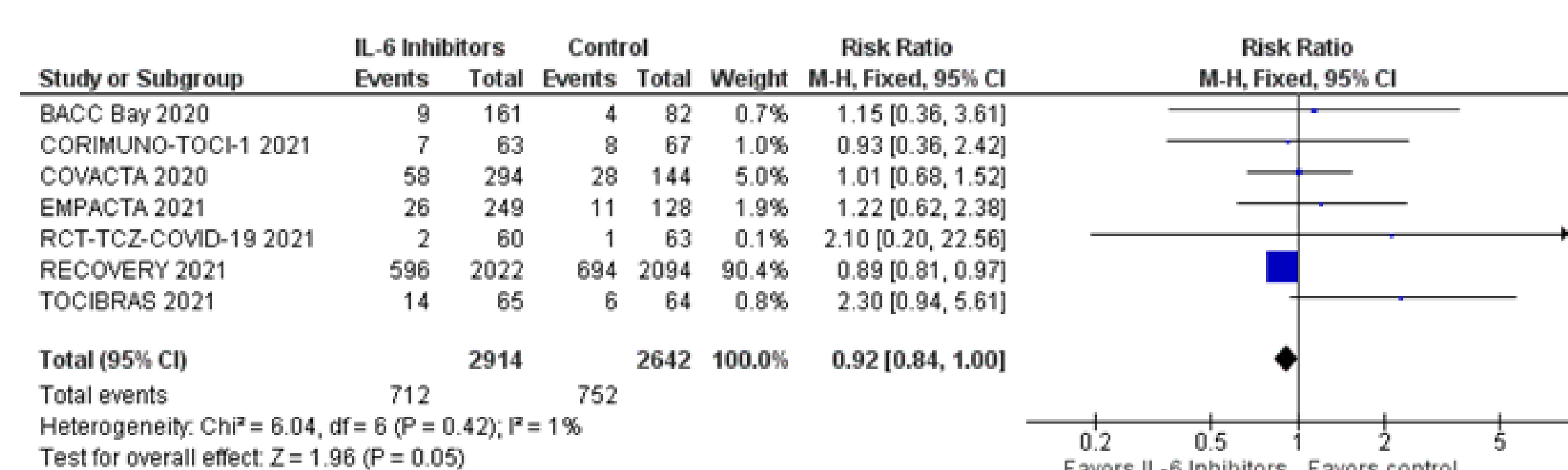
Data from eligible trials were extracted and quality-assessed according to PRISMA guidelines by two independent investigators. We calculated pooled risk ratio and corresponding 95% CI. We used fixed-effects model and random-effects model for  $I^2 < 25\%$  and  $I^2 \geq 25\%$ , respectively. Sensitivity analyses included analysis of trials with a low risk of bias only. The primary outcome was mortality at the longest follow-up available. Secondary outcomes included need for intubation and rate of adverse events.

## Results

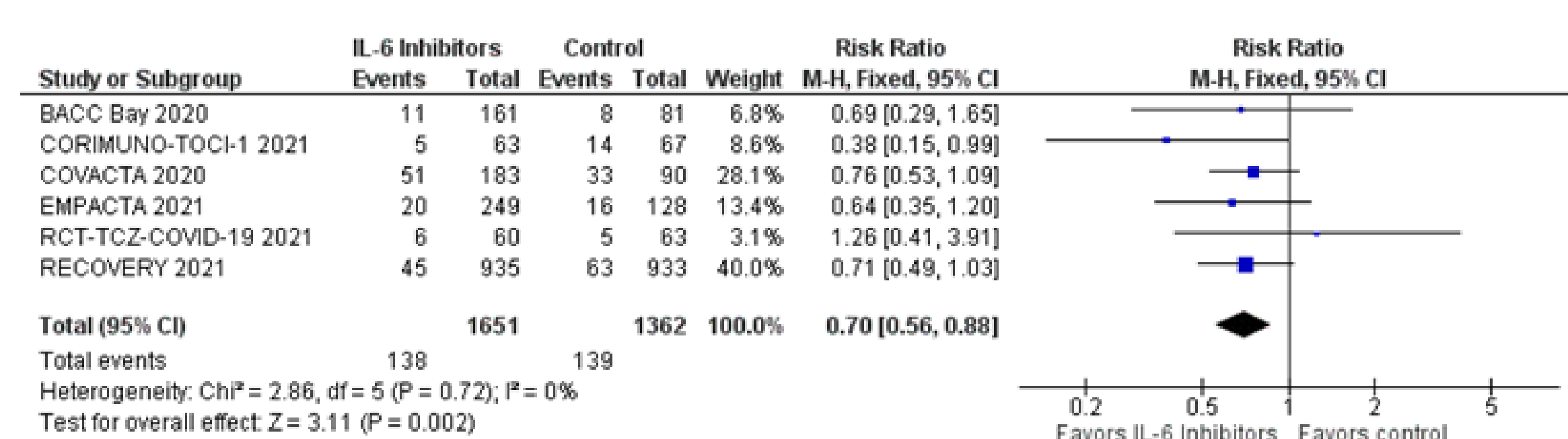
371 studies were assessed, and 10 studies were included in the meta-analysis. All trials were multicentre, the majority open-label vs standard treatment.

IL-6 inhibitors use was associated with lower all-cause mortality at the longest follow-up available (24.9% in the IL-6 inhibitors group versus 29.7% in the control group, RR=0.89;  $p=0.003$ ,  $I^2=6\%$ , eight studies included). Use of IL-6 inhibitors was associated with a significant reduction in need for intubation, while we found no difference in adverse events and secondary infections.

eFigure 2 – Forest plot for 28/30 days mortality



eFigure 4 – Forest plot for need for intubation



## Conclusions

Administration of IL-6 inhibitors may reduce mortality and need for intubation in COVID-19 patients, without increasing risk of adverse events.

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