

Review of: "Tocilizumab Plus Corticosteroid in Elderly Patients Hospitalized With COVID-19 Pneumonia: A Retrospective Cohort Study"

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Potential competing interests: No potential competing interests to declare.

The authors are to be commended for this well written, well designed, cohort study of the effects of tocilizumab plus steroids vs. the effect of steroids alone for the treatment of severe SARS COV2 infection in the population over 65 years of age. As the authors point out, previous trials and meta-analyses have been confounded in several ways as to the safety and efficacy of tocilizumab in patients over 65 years of age: by including data on patients with severe lung injury requiring mechanical ventilation at baseline prior to the administration of tocilizumab, by failures to analyze data on patients receiving both tocilizumab plus steroids versus those receiving steroids alone, and by failing to provide data specifically regarding the population over 65 years of age.

It is quite plausible that outcomes with tocilizumab plus steroids for SARS COV2 might be different in an older population compared to younger persons due to differences in tocilizumab metabolism and to less robust immune responses in older individuals.

However, I believe several changes in the manuscript can further strengthen the conclusions we can derive from this study.

In the BACKGROUND section, paragraph 2, third sentence, the manuscript reads that "tocilizumab is an IL-6 inhibitor". Tocilizumab is a IL-6 receptor blocker, not a direct IL-6 inhibitor and this statement should be changed.

Many readers will be concerned about the conclusions of the authors by the fact that the baseline characteristics of the two cohorts in terms of respiratory support were different, with a higher percentage of patients in the "corticosteroid alone" group receiving oxygen by nasal cannula alone; whereas, a higher percentage of those in the "tocilizumab plus corticosteroid" cohort were receiving some form of high flow oxygen or noninvasive mechanical ventilation. The reader's suspicion is that the worsened outcomes in the "tocilizumab plus corticosteroid" cohort were due to the fact that the severity of illness was greater in patients that received tocilizumab in comparison to those in "corticosteroid alone" cohort.

The inclusion of P values for Table 1 might lessen this concern for the reader. Additionally, the inclusion of other baseline characteristics known to be of prognostic significance in SARS COV2 in Table 1 including: CRP, D-dimer, ferritin, and lymphocyte counts might yield further information about the comparability of the 2 cohorts.

Additionally, the British Medical Journal has posted a final analysis of a living review of prognostic predictive models for

SARS COV 2 infection (BMJ. 2022;378:o2009. Epub 2022 Aug 22) with the conclusion that the QCOVID4, PRIEST, ISARIC4C, and the CARR's models are the least biased and best validated models available. Comparison of the two cohorts using one of these models would be ideal. If that is not practical for the authors, inclusion of more routinely available severity of illness scores like APACHE 2, SAPS, or SOFA for comparison between the cohorts would be helpful.

I believe these updates will further strengthen the quality and impact of this study. With these changes the study may raise the concerns for clinicians caring for patients suffering from severe SARS COV 2 regarding the benefits and side effects of tocilizumab plus corticosteroids in patients over 65 years of age. Clinicians should be cautious about using tocilizumab plus corticosteroids in older patients until further data from randomized, controlled, trials become available.