LETTER

Letter to the Editor Regarding Combination of Tocilizumab and Steroids to Improve Mortality in Patients with Severe COVID-19 Infection: A Spanish, Multicenter, Cohort Study

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Key Summary Points

The baseline characteristic among the case (tocilizumab group) and control groups varied significantly in this retrospective study.

Patients in both groups were treated with several drugs other than tocilizumab (treatment of interest).

A subgroup analysis was reported only for patients taking steroids while more patients were treated with other drugs like hydroxychloroquine and lopinavir/ritonavir.

The median time taken from onset of symptoms to baseline (day 0) is not reported for the control group.

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DIGITAL FEATURES

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To the Editor,

We would like to comment on a recent article published in your journal authored by Ruiz-Antorán et al. regarding the mortality benefits of tocilizumab and steroids in severe coronavirus disease 2019 (COVID-19) patients [1].

In this study, the baseline characteristics among the tocilizumab group and the control group in the raw analysis varied significantly. On average, the patients in the control group (mean age 65.0 years) were 6.3 years older than the tocilizumab group (mean age 71.3 years). The patients in the control group had significantly higher rates of high blood pressure, cardiovascular disease, chronic kidney disease, and neurological diseases, all of which are considered to increase the risk of severe COVID-19 and mortality [2]. Hence, we feel that the higher mortality observed in the control group compared to the tocilizumab group (31.5% vs. 16.8%) might be the result of confounding effects from the baseline dissimilarities.

Although the authors attempted to balance these dissimilarities with a statistical technique, it is important to note that because something is not statistically significant does not reduce the risk of it being clinically significant.

Patients in both groups were treated with several drugs other than the treatments of interest (tocilizumab). Additionally, their treatment timeline (when in the course of treatment it was given) is also not reported. Moreover, a higher number of patients were treated with hydroxychloroquine and lopinavir/ritonavir than with steroids. A significant number of patients were also treated with azithromycin. However, the authors reported a subgroup analysis only for patients receiving steroids. It is not clear why the authors only reported a subgroup analysis for patients receiving steroids when just over 50% of patients received steroids but over 90% of them received hydroxychloroquine.

The baseline (day 0) was defined as the day the patient first received tocilizumab for the tocilizumab group and the day the patient fulfilled the inclusion criteria for the control group. The median time from the onset of symptoms of COVID-19 to the patient receiving

tocilizumab (day 0 for the tocilizumab group) was reported as 11 days. However, the median time from the onset of symptoms of COVID-19 to the inclusion of patients in the study (day 0 for the control group) is not reported. We are interested to know how the patients in both groups correspond to each other at baseline with regards to the number of days from onset of symptoms.

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Disclosures. Rajesh N. Janapala, Jigar Patel, Omar Belfaqeeh, Abdulla Alhashmi, and Ali Pourmand have nothing to disclose.

Compliance with Ethics Guidelines. This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

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