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Letter to the Editor

'Early administration of tocilizumab in hospitalized COVID-19 patients with elevated inflammatory markers; COVIDSTORM' — Author's reply

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To the Editor,

We thank Klopfenstein et al. [1] for their interest on our COVIDSTORM study results [2]. They ask for more details concerning the amount of oxygen support at randomization. As reported in the original article, an oxygen saturation <93% or a respiratory rate above 30/min was required for randomization.

With re-assessment of data, we noticed two minor errors in baseline supplemental oxygen data in the original study report. The original article mentions 21 instead of 22 standard of care (SoC) patients with supplemental oxygen <15 L/min. Also, one patient in the tocilizumab (TCZ) group with respiratory flow <15 L/min was mistakenly placed in the high flow (>15 L/min) group. We have now carefully checked baseline respiratory support data of all patients again and present the corrected and, as requested, more detailed data in Table 1. The errors and corrections have no effect on study outcomes.

Nine patients in the TCZ group (16%) and 2 in the SoC group (7%) did not receive any respiratory support at randomization. A majority of 33 (58%) patients in the TCZ group and 22 (76%) in the SoC group needed supplementary oxygen ≤15 L/min. This group includes patients with low flow (1–6 L/min) nasal oxygen supply as well as patients receiving supplemental oxygen by venturi mask. Eleven patients (19%) in the TCZ group and 4 (14%) in SoC group received high-flow oxygen treatment at randomization, which was defined as flow of >15 L/min in our study. Four patients (7%) in TCZ group and none in the SoC group received noninvasive ventilation. None in the TCZ group and one patient in SoC group (3%) at randomization was on invasive mechanical ventilation at randomization.

As pointed out in the discussion of the original report, our study differs from most other studies by the selection of patients eligible for randomization by the use of a set of inflammation markers. Our study was not powered for subgroup analysis according to the level of supplementary oxygen flow or other respiratory support. Therefore, we think that such a sub-analysis is not justified, as this may lead to false conclusions. However, we agree that from large studies or meta-analysis, such subgroup analyses may be helpful to identify which patients benefit most from TCZ use. Therefore, we will provide more detailed data linked to outcome for any meta-analysis upon request.

Table 1
Respiratory support in all COVIDSTORM study patients

	Tocilizumab		Standard of care	
None	9	16%	2	7%
Nasal flow 1–6 L/min	16	28%	8	28%
Venturi mask 28%	6	11%	5	17%
Venturi mask 40%	7	12%	4	14%
Venturi mask 60%	4	7%	5	17%
High flow >15 L/min	11	19%	4	14%
NIV	4	7%	0	0%
IMV	0	0%	1	3%
Total	57		29	

IMV, Invasive mechanical ventilation; NIV, Non-invasive ventilation.

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Author contributions

NB and TF were responsible for analysis and interpretation of data. NB, TF, and JO drafted the text and table.

References

[1] Klopfenstein T, Gendrin V, Zayet S. Re: 'Early administration of tocilizumab in hospitalized COVID-19 patients with elevated inflammatory markers; COVIDSTORM-a prospective, randomized, single-centre, open-label study' by Broman et al. Clin Microbiol Infect 2022 [Epub ahead of print].

[2] Broman N, Feuth T, Vuorinen T, Valtonen M, Hohenthal U, Löyttyniemi E, et al. Early administration of tocilizumab in hospitalized COVID-19 patients with elevated inflammatory markers; COVIDSTORM-a prospective, randomized, single-centre, open-label study. Clin Microbiol Infect 2022;28:844–51.