Peer Review File

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Reviewer Comments

We thank all the reviewers for their constructive comments that have helped us improve our manuscript.

Comment 1: The main limitations of the paper were the small number of patients and it was a single center study.
Reply 1: Potential limitations of the study have been added from line 154 onward in the revised manuscript.
Changes in the text: Page 9, line 154.

Comment 2: The description of population studied should be improved:
- Were some patients admitted in intensive care unit?
- Which type of oxygen administration was necessary?
- Was Heparin administered at prophylactic or therapeutic doses and why this decision was made?
Reply 2: The details of the study population have been added in lines 108–109 in the revised manuscript. It has been reported that thrombotic events are strongly associated with mortality in patients with COVID-19, and heparin is recommended for the treatment for COVID-19 according to Japanese guideline. Furthermore, heparin reportedly blocks the SARS-CoV-2 viral spike protein from binding with endothelial cells. Hence, heparin was administered to the patients with COVID-19.
Changes in the text: Page 6, line 108–109.

Comment 3: Why was tocilizumab administered before day 7? Why was a second dose not administered in those patients with poor evolution?
Reply 3: According to the study protocol, tocilizumab was administered only for patients whose condition exacerbated during remdesivir and dexamethasone therapy. Likewise, the single-dose treatment was based on the study protocol.
Changes in the text: Page 5, line 80–85.

Comment 4: Were the levels of IL-6 correlated with a worse evolution?
Reply 4: The levels of IL-6 were not associated with the tocilizumab treatment sensitivity as stated in line 112 in the revised manuscript.
Changes in the text: Page 6, line 112.

Comment 5: The authors stated "obese patients had lower mortality compared with nonobese patients in tocilizumab treatment conditions". This is a risky statement because of the small number of patients and without an adequate statistical basis.

Reply 5: The sentence was modified as follows: “Obese patients effectively responded to tocilizumab treatment compared with patients who were not obese”.
Changes in the text: Page 6, line 114.

Comment 6: The authors stated “Therefore, severe obesity can diminish the effects of tocilizumab in patients with COVID-19". However, the sentence is confusing, contradictory and without bibliographic references. Please rephrase.
Reply 6: The sentence was modified as follows: “High doses of tocilizumab might be needed for the management of morbidly-obese patients with COVID-19”.
Changes in the text: Page 8, line 151.

Comment 7: The statement “In addition, a single-dose treatment of tocilizumab may release the maximum clinical benefit in mildly obese patients with COVID-19.” cannot be assured without dose comparison, or without bibliographic support. Therefore, it can be confusing, since depending on the evolution, patients may require a second dose.
Reply 7: The sentence was modified as follows: “The severity of obesity might be related to the anti-IL-6 treatment sensitivity in patients with COVID-19”.
Changes in the text: Page 9, line 162.

Comment 8: Tables should be better described.
Reply 8: Tables were modified and the details have been added from lines 97 to 103 of the revised manuscript.
Changes in the text: Page 6, line 97–103.