Response to: 'High dosage of Methylprednisolone as a rescue, second-line treatment in COVID-19 patients who failed to respond to Tocilizumab' by Conticini *et al*

Conticini *et al* share with us their positive experience with immunosuppressive treatment in patients with severe COVID-19 pneumonia.[1] From the description we infer that the described patients suffered from COVID-19-associated cytokine storm syndrome (CSS). We would like to thank our colleagues for sharing their experience which aligns with ours[2] and for their insightful comments.

In our COVID-19 High-intensity Immunosuppression in Cytokine storm syndrome (CHIC) study we have used an immunosuppressive strategy composed by glucocorticoids in first-line treatment, followed, in case of insufficient response, by tocilizumab. Conticini *et al* have in turn used glucocorticoids in patients with insufficient response to tocilizumab.[1]

We share thus the experience of a positive effect of immunosuppressive treatment for COVID-19-associated CSS. The exact contribution of each specific part of the immunosuppressive strategy to the positive outcomes in patients with COVID-19-associated CSS is at the moment difficult to disentangle. The positive effect of glucocorticoids has also been recently shown in the RECOVERY trial.[3] The effect of tocilizumab is still under research with some reports of positive and negative results from trials, publications still have to follow.[4 5] Of note, the negative results are from a trial with unselected COVID-19 patients, meaning not specifically patients with CSS. We believe that the patient selection is crucial and the rationale for immunosuppressive treatment applies in patients with CSS and not so much in patients without CSS. Conticini *et al* describe several of the advantages of glucocorticoids as their wide spectrum of action and the parallel made with other life-threatening inflammatory conditions treated with glucocorticoids in the acute phase and only eventually later with other more selective cytokine inhibitors. Additionally, the safety of glucocorticoids, particularly in short-term use, their wide availability and low cost, make them an attractive first-line treatment for COVID-19-associated CSS. Still, future studies and ideally trials should inform us on the best immunosuppressive strategy for these patients. Head-to-head trials with different immunosuppressive strategies are, in our opinion, a next logic and relevant step. Nevertheless, early identification and intervention for patients with CSS ('window of opportunity hypothesis') may play a relevant role next to the selection of the immunosuppressive strategy.

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