Targeting IL-6 in COVID-19. Response to: 'Rational use of tocilizumab in COVID-19' by Jain and Sharma

Dear Editor,

Siddharth and Sharma[1] suggest caution in using interleukin-6 (IL-6) receptor blocking agents, namely tocilizumab, in the treatment of patients with COVID-19 infection, particularly those requiring invasive mechanical ventilation because of the increased risk of infections and bowel perforation, possibly also masked by the anti-inflammatory activity of the agent.[1] Generally speaking, this is a fully acceptable principle to be observed as caution when using drugs is a common rule in the clinical setting. Thus, no doubt that the use of tocilizumab should be carefully evaluated in individual cases. Nevertheless, the same authors state that 'the efficacy data are promising (although preliminary)'.

Specifically regarding safety, Siddharth and Sharma quote that a 13% higher risk of new infections was seen with tocilizumab when added to standard of care.[2] Indeed, in the study by Guaraldi et al,[2] 24 (13%) of 179 patients treated with tocilizumab were diagnosed with new infections, versus 14 (4%) of 365 patients treated with standard of care alone (9% higher risk), and the overall conclusions of the authors were that 'tocilizumab might reduce the risk of invasive mechanical ventilation or death in patients with severe COVID-19 pneumonia'. Additionally, it should be noted that 13% is in the range of the reported concomitant bacterial infections (10%–20%) of COVID-19 cases.[3] Also, Toniati et al[4] conclude their report on an uncontrolled series of COVID-19 pneumonia patients with adult respiratory distress syndrome including two deaths due to septic shock that the response to tocilizumab was rapid, sustained and associated with significant clinical improvement. Finally, when considering cases of bowel perforation during tocilizumab treatment, the possible role of the concomitant treatment with steroids should also be considered.[4][5] Nevertheless, we acknowledge that data on the efficacy of tocilizumab are still preliminary and sometimes conflicting, particularly in terms of rate of adverse events.[6–8]

One should also consider the putative role of IL-6 blockade in reducing the occurrence of COVID-19-associated cardiovascular events, particularly arrhythmias,[9] which are increasingly reported in the literature.[10] In this regard, although the COVID-19-associated long QT syndrome as a real risk factor for arrhythmic cardiac death is under strong consideration,[11][12] studies regarding the possible protective effects of IL-6 blocking agents are still in progress and when concluded they might provide further support to the use of tocilizumab (figure 1).

In conclusion, we agree with Siddharth and Sharma that data on IL-6 antagonists in the treatment of COVID-19 infection are still preliminary and in some way unconclusive as yet and that controlled studies with a larger number of subjects are needed before treatment with these agents may achieve any level of recommendation. Nevertheless, we still remain convinced that the rationale for targeting IL-6 in COVID-19 infection is strong and to some extent supported by preliminary evidence.

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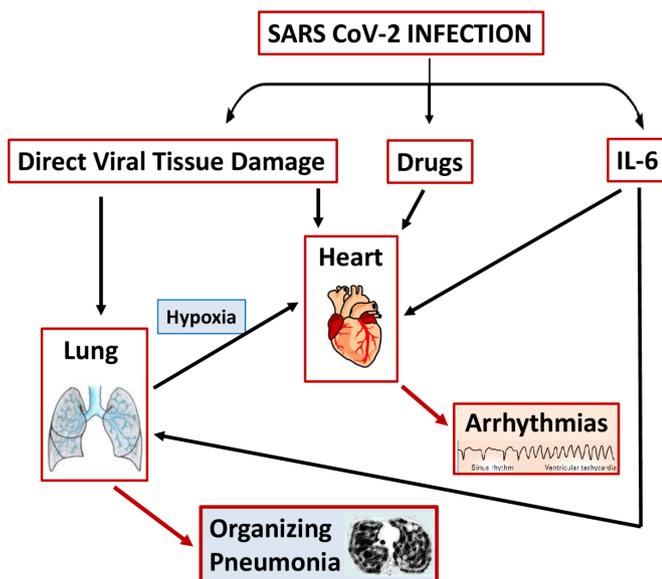
Figure 1 IL-6 in COVID-19. IL-6, interleukin-6.

Correspondence response

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