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CE - LETTER TO THE EDITOR

Anakinra after treatment with corticosteroids alone or with tocilizumab in patients with severe COVID-19 pneumonia and moderate hyperinflammation. A retrospective cohort study: reply

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Dear Editor,

We thank Dr Yurttutan et al. [1] for sharing the beneficial effect of anakinra in an 8-year-old girl with COVID-19-related multisystem inflammatory syndrome refractory to vasopressors, anticoagulation, corticosteroids, and intravenous immunoglobulin. After anakinra was added to her treatment plan at a dose of 8 mg/kg/day administered s.c. for 4 days, her cardiac functions immediately improved. We would like to focus on the anakinra dose used in their patient. In contrast to other anticytokine therapies for COVID-19-related hyperinflammation, such as tocilizumab, with a well-defined dosage according to weight (8 mg/kg i.v.), anakinra dosage calculation is not standardized. Dosages of anakinra used in patients with severe forms of COVID-19 vary from intermediate (200 mg/d s.c.) to high (10 mg/kg/d i.v.) in different studies [2, 3], an important clue to its safety and effectiveness in controlling COVID-19-related hyperinflammation. High doses of anakinra were associated with a 24% rate of severe adverse effects and a 14% rate of infectious complications in one published study [2], with no adverse events reported by other authors with intermediate doses [3, 4]. Moreover, several clinical trials of high doses of anakinra in patients with COVID-19 have been stopped because of safety concerns. Accordingly, we believe that efforts to counterbalance the benefits and risks of anakinra for this condition should take three issues into consideration: first, adjustment of the dose of anakinra to the degree of hyperinflammation; second, the timing of anakinra administration; and last but not least, the duration and tapering of anakinra. All three factors are considered by Dr Yurttutan et al., who reported excellent clinical results in their patient. Our as yet unpublished clinical experience with more than 100 patients with COVID-19 pneumonia and moderate hyperinflammation (concentrations of C-reactive protein 90–150 mg/L) treated with intermediate doses of anakinra (100 mg/12 h s.c. until sustained improvement in respiratory parameters and serum C-reactive protein, then 100 mg/day s.c. for 5–7 days) suggests that this regimen is efficacious in controlling inflammation and reducing mortality without increasing adverse events in patients whose respiratory condition worsened within 24 h after receiving glucocorticoids (methylprednisolone 1 mg/kg/day i.v.). Regarding the use of intermediate doses, the duration and tapering of anakinra in patients with COVID-19-related moderate hyperinflammation are important issues since respiratory condition stabilizes for 48–72 h after starting anakinra and then steadily improves, making it necessary to taper the dose before stopping to avoid reactivating hyperinflammation. However, in patients with severe hyperinflammation, such as the girl described by Dr Yurttutan et al. [1], higher doses of anakinra are probably necessary to control SARS-CoV-2-related multisystem inflammatory syndrome and reduce mortality. In our opinion, the dose, timing of administration, duration, and tapering of anakinra for COVID-19-related hyperinflammation are essential considerations in reducing mortality and optimizing the safety/risk profile. Future studies to examine these issues in the use of anakinra for COVID-19-related hyperinflammation will shed light on this treatment in routine practice. Until then, clinical management decisions based on the experience and expertise, such as shown by Dr Yurttutan et al. will save lives.

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