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Received 5 January 2022

https://doi.org/10.1016/j.reumae.2022.06.001
2173-5743/

Use of anakinra in the treatment of SARS-CoV-2 severe respiratory infection☆

Uso de anakinra en el tratamiento de la infección respiratoria grave por SARS-CoV-2

Dear Editor,

We would first like to thank Aomar-Millán et al.[1] for their response to our article in which we suggested the potential benefit of anakinra in the treatment of SARS-CoV-2 infection refractory to tocilizumab treatment.[2]

The "cytokine storm" secondary to SARS-CoV-2 infection leads to severe COVID-19 disease. Excessive activation of the immune system produces a picture like that of HLH.[3] Increased levels of proinflammatory cytokines (IL-1, IL-6, or TNF-alpha), procoagulant factors and lymphopenia play a major role in its pathogenesis.

The use of immunosuppressants such as dexamethasone and anti-IL-6 (tocilizumab) and anti-IL-1 (anakinra) antibodies are the mainstay of treatment of the inflammatory phase of SARS-CoV-2 infection.[4]

As reported by Aomar-Millán et al., anakinra has recently been approved by the EMA for the treatment of patients with SARS-CoV-2 pneumonia who require supplemental oxygen therapy and who are at risk of progressing to severe respiratory failure as determined by a plasma concentration of soluble urokinase-type plasminogen activator receptor (suPAR) ≥6 ng/mL. This approval was based on the SAVE MORE study,[5] which demonstrated a decrease in mortality and hospital stay in patients treated early with anakinra.

Interestingly, the retrospective study by Aomar-Millán et al.[6] analysed 143 patients with SARS-CoV-2 pneumonia. Patients refractory to treatment with corticosteroids and tocilizumab were treated with anakinra at a dose of 100 mg/every 8–12 h between day 2 and 6. Administration of anakinra was associated with a reduced risk of mortality (HR: .518; 95% CI: .265 – .910; p = .0437).

The patient described in our article[2] received 2 doses of tocilizumab (8 mg/kg, subcutaneously) and, given the absence of respiratory and analytical improvement 48 h after tocilizumab administration, it was decided to administer anakinra (100 mg single total dose, subcutaneously). At the time the patient was admitted to hospital (April 2020), the use of anakinra in the inflammatory phase of SARS-CoV-2 pneumonia was under study. Therefore, no recommended dose had been described in the literature at that time. Currently, although there is still no consensus, higher doses and several days of continuous treatment are recommended.[5–7] Like Aomar-Millán et al. in their response, we considered in the discussion of our article that the clinical improvement of the patient could not be explained solely by the effect of treatment with anakinra, and that a late benefit of tocilizumab should not be ruled out.

Conflict of interests

JJC-H: Consulting or Advisory Role: MSD Oncology, Bristol-Myers Squibb, Merck Speakers' Bureau: MSD Oncology, Bristol-Myers Squibb, Merck, Roche, Janssen Oncology, AstraZeneca Travel, Accommodations, Expenses: MSD Oncology; the remaining authors have no conflict of interests to declare.

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Received 1 February 2022

https://doi.org/10.1016/j.reumae.2022.02.001
2173-5743/

☆ Please cite this article as: Figuero-Pérez L, Olivares-Hernández A, Escala-Cornejo RA, Cruz-Hernández JJ. Uso de anakinra en el tratamiento de la infección respiratoria grave por SARS-CoV-2. Reumatol Clin. 2023;19:122.