Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the Editor

Effect of tocilizumab versus standard of care in adults hospitalized with moderate-severe COVID-19 pneumonia

Efecto del tocilizumab frente a cuidado estándar en pacientes adultos hospitalizados con neumonía por COVID-19 moderada-grave

Dear Editor,

We have read with special interest Cardona-Pascual et al.'s[1] study on the effect of tocilizumab versus standard of care in patients hospitalized with moderate-severe pneumonia caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), in which no correlation was found between the use of tocilizumab and overall mortality (odds ratio [OR]: 1.03, 95% confidence interval [CI]: 0.63–1.68), and wish to make some comments.

Their study might seem of little clinical relevance following the publication of the Recovery-Tocilizumab study[2] in 2021, in which it was concluded that the use of tocilizumab in patients with hypoxia and systemic inflammation was beneficial in reducing mortality (31% vs. 35%) and mean hospital stay (57% vs. 50%). However, it should not be forgotten that Recovery-Tocilizumab is a platform trial that was carried out with patients who were not randomized at the same time, so it cannot be guaranteed that the patient populations included in the different treatment groups were equivalent, which is why it has not been added as an indication in the drug's summary of product characteristics.

In contrast, Cardona-Pascual et al.'s study was an observational, retrospective trial, with propensity score-matching aimed at reducing selection biases and an appropriate sample size, owing to which we believe that its results are relevant to clinical practice to attempt to adapt treatment protocols to different patient profiles. Our group published a retrospective cohort study[3] including patients with moderate-severe pneumonia who had been hospitalized between 15 March 2020 and 15 May 2020, a period equivalent to that covered by Cardona-Pascual et al.'s study, and who met at least two of the following criteria for hyperinflammation: CRP >100 mg/L, ferritin >500, or D-dimer >1 mg/L. In Cardona-Pascual et al.'s study, the administration of tocilizumab to the patients analyzed in their study required that they meet at least one of the following criteria: IL6 >40 μL/L, D-dimer >1500 μg/m, or persistently increased levels of this parameter. In line with the findings of our group, the use of tocilizumab was not linked to a reduction in mortality or mean hospital stay, not even among patients who received tocilizumab within the first 72 h following their admission. On the contrary, in their study they found a tendency toward a longer mean hospital stay. Similarly, in our study we also observed a greater mean hospital stay among the patients who received tocilizumab in monotherapy (23 days) versus those who received corticosteroids (15 days). Prior experience in the treatment of these patients demonstrates the existence of clinical phenotypes with different responses to immunomodulatory treatments. Therefore, it would be interesting to determine the percentage of patients reported by Cardona-Pascual et al. who had CRP levels above 75 mg/dL, as this was the serum level defined as indicative of inflammation in the Recovery-Tocilizumab study. Nevertheless, we believe that CRP values between 75 mg/dL and 100 mg/dL reflect "mild inflammation", which are far from the figures observed in macrophage activation syndrome or chimeric antigen receptor (CAR) T-cell toxicity, situations in which the early use of this drug would be indicated.[4] Finally, in line with these authors, we believe that the initial use of tocilizumab in patients with moderate-severe pneumonia secondary to SARS-CoV-2 must be limited to cases with initial data of severe hyperinflammation (CRP >150–200 mg/L and/or ferritin >1000) resembling those described in hemophagocytic syndrome. We currently believe that, in patients with data of moderate inflammation (CRP 50–100 mg/L and/or ferritin 400–600), there are other more appropriate inmunomodulatory treatments, such as anakinra, which has been granted this indication in its summary of product characteristics by demonstrating a reduction in mortality and ICU admission in patients at risk of progression to respiratory distress.[5]

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