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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Commentary

Tocilizumab in severe COVID-19: A promise fulfilled

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A proportion of patients who are infected with SARS-CoV-2 develop severe disease. Apart from a serious bilateral pneumonia organs other than the lungs may become involved as well. The clinical picture of severe coronavirus disease 2019 (COVID-19) has led to the concept that it is a generalised disease, i.e. a viral sepsis.

It has become clear that pro-inflammatory cytokines, including tumor necrosis factor-α (TNF-α) and several interleukins (IL), as well as other chemokines, inflammatory mediators, and damage-associated molecular patterns (DAMPs) play pivotal roles in the development of the systemic inflammatory response in severe COVID-19 [1]. In particular plasma levels of IL-6 are remarkably elevated in severe COVID-19. High levels of IL-6 levels are a strong predictor of a bad outcome in COVID-19 and have been associated with more severe lung injury [2]. For this reason therapeutic strategies targeting this cytokine have attracted a lot of attention.

Already early in 2020 tocilizumab (a monoclonal anti-soluble IL-6 receptor antibody licensed for the treatment of rheumatoid arthritis, and other forms of arthritis and systemic hyperinflammation) was seen as a candidate to modify the inflammatory response in severe COVID-19 [3, 4]. Initial case studies from China showed promising results and successively several retrospective cohort studies demonstrated efficacy and safety of this treatment [5–7]. Obviously, the drawback from these studies was that a retrospective non-randomised study design does not provide the highest degree of confidence in efficacy. Nevertheless, the results were sufficiently encouraging to classify tocilizumab as a 'promising' treatment in severe COVID-19[8] and prompted the execution of larger randomized controlled trials. Employing the REMAP/CAP-RECOVERY trial platform in patients with addition of tocilizumab to standard dexamethasone treatment was superior to treatment with dexamethasone alone [9]. Tocilizumab resulted in a significant increase in organ support-free days and a 1.6-fold increase in chance of survival compared to control. A subsequent meta-analysis of all studies with tocilizumab confirmed the positive effect of the drug [10]. In this issue of the European Journal of Internal Medicine, Campochiaro et al. summarize the available evidence that has been gathered with tocilizumab for severe COVID-19 in the past year [11].

One of the reasons tocilizumab is more effective than general anti-inflammatory interventions, such as corticosteroids or other cytokine blockers may be that the drug has additional beneficial effects. It has been speculated that next to the significant role in regulating IL-6 in the host-defense response in severe COVID19, modulation of this cytokine may also be important in reducing the activation of coagulation in this disease [8]. In fact, coagulopathy and the ensuing high incidence of thromboembolic complications are strong risk factors for an adverse outcome in severe COVID-19 [12].

Interestingly, a prospective cohort study of patients with severe COVID-19 treated with tocilizumab indeed demonstrated that this treatment was associated with a significant improvement of blood coagulation parameters independently of the use of anticoagulants for thrombosis prophylaxis [13]. These findings were recently confirmed in a study focusing on the incidence of thromboembolic events in COVID-19 patients receiving tocilizumab [14].

Taken together, it may be concluded that the promise represented by tocilizumab as important adjunctive agent in the management of severe COVID-19 seems to be fulfilled. The available evidence also suggests that modulation of downstream consequences of systemic inflammation, such as activation of coagulation, may also be beneficial in patients with severe COVID-19.

Declaration of Competing Interest

None.

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