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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Tocilizumab: A new opportunity in the possible therapeutic arsenal against COVID-19

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To the Editor,

In a recent review, the authors synthesized the current evidence for one of the possible therapeutic options for the treatment of SARS-CoV-2 infection [1], in the context of the urgent need for effective therapies in the current pandemic, particularly in severe cases. However, there is no systematically recommended treatment for COVID-19.

Tocilizumab is a humanized monoclonal antibody against the interleukin-6 receptor (IL-6R) and is FDA-approved for the treatment of rheumatoid arthritis, systemic juvenile idiopathic arthritis, giant cell arteritis, cytokine release syndrome and recently, has been administered intravenous experimentally in the treatment of severe COVID-19 pneumonia in China and Italy with promising results [2].

The therapeutic mechanism of this drug dates back to the pathophysiology of SARS-CoV-2-induced lung damage. In the alveolar epithelial cells, the virus activates innate immune and adaptive immune systems, resulting in the release of a large number of cytokines, including IL-6, IL-2, IL-7, IL-10, granulocyte-colony stimulating factor (G-CSF), interferon-γ-inducible protein (IP10), monocyte chemoattractant protein (MCP1), macrophage inflammatory protein 1 alpha (MIP1A), inducing a cytokine storm [2], that occurs in a large number of patients with severe COVID-19 [3]. G-CSF and IL-6 are the key cytokines leading to inflammatory storm which may result in impaired oxygen diffusion and eventually lead to respiratory failure. Therefore, some authors have suggested that interfering of IL-6 might be a potentially beneficial for severe and critical COVID-19 [2].

A study in two hospitals of Anhui, China that included 21 patients with severe COVID-19 infection treated with Tocilizumab in addition to routine therapy, showed as results a high rate of absorption of lung lesions, decreased C-reactive protein, lymphocytes count in peripheral blood and oxygen requirement and early hospital discharge (13.5 days on average), suggesting that Tocilizumab could be an effective therapy in patients with severe infection, effectively improve clinical symptoms and repress the deterioration of critical patients [4]. More recently, favorable changes of CT findings (size reduction of consolidations and ground glass opacities) were reported in a 64-year-old man 14 days after the administration of tocilizumab as a treatment of COVID-19 pneumonia in Milan, Italy [5]. Moreover, a 57-year-old patient in Switzerland with insulin-dependent type 2 diabetes mellitus and interstitial lung disease associated with systemic sclerosis treated with tocilizumab developed a mild form of COVID-19, suggesting that IL-6-blocking treatment given for chronic diseases may even prevent the development of severe COVID-19 [6].

The Italian Medicines Agency (AIFA) announced on March 19 the launch of TOCIVID-19, a single-arm phase 2 study and a parallel observational cohort study, with approximately 330 participants, with the aim to assess the efficacy and safety of two doses of Tocilizumab 8 mg/kg (up to a maximum of 800mg per dose), with an interval of 12 hours in the treatment of COVID-19 pneumonia, one-month mortality rate is the primary endpoint and secondary outcome measures included IL-6 levels, lymphocyte count, C-reactive protein level, change of SOFA (Sequential Organ Failure Assessment), PaO2 (partial pressure of oxygen)/FiO2 (fraction of inspired oxygen, FiO2) ratio, rate of adverse events, radiological response, duration of hospitalization and remission of respiratory symptoms [7]. Additionally, in the largest clinical trials database (clinicaltrials.gov) there are eleven ongoing studies registered in Italy, China, Belgium, Denmark and France.

The evolution of the current pandemic is putting strong pressure on health systems around the world in search for effective therapies against COVID-19 infection. Apparently, Tocilizumab provided a new therapeutic strategy for severe and critical cases, although the evidence strength needs to be enhanced, the results of further controlled trial studies will clarify the true clinical impact of this IL-6- blocking treatment on COVID-19 infection.

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Declaration of competing interest

None.

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