

Editorial letter

Trials of Low Dose Cytostatic Drugs in Severe Covid-19 Should Be Considered

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We three oncologists suggest that trials with low-dose cytostatic drugs be tested to counteract the severe lung and kidney reaction that patients may suffer from covid-19 infection.

It is now becoming a general notion that a hyperactive / dysregulated immune system, with an image that in an autoimmune response, is a significant factor behind the mortality of covid-19 disease [1]. The reaction often arrives late (1-3 weeks after illness) and rapidly in the course of the disease. So far, attempts to find effective drugs have had very limited success. Derivatives of anti-malaria drugs and anti-ebola drugs are under review, as is the supply of convalescent plasma from previously infected [1-3]. Autoimmune diseases and also autoimmune reactions in immune checkpoint inhibitors in tumor diseases are often treated with corticosteroids [4]. In severe autoimmune diseases, biological drugs such as TNF blockers, interleukin-1 and 6 inhibitors, and inhibitors of T and B cell surface markers have been used [5]. In very severe autoimmune disease, cytostatic drugs such as methotrexate and cyclophosphamide have been used successfully in, for example, rheumatoid arthritis or vasculitis [6-8]. We now propose that in more severe cases of covid-19 this possibility be tested for the following reasons:

- In our clinical everyday lives, with the treatment of thousands of cancer patients, we have noted that patients with treatment with low-dose cytostatic drugs rarely show signs of viral infection, including influenza. This is also the case during current flu epidemics and in both vaccinated and unvaccinated patients.
- Low dose cytostatics have few side effects and are a tried and tested treatment modality.
- Low dose cytostatic therapy is a therapy modality that even older individuals tolerate well.

We propose that, in trials, low dose cytostatic drugs be given to covid-19 patients admitted to the intensive care unit (both respiratory

and non-respiratory cases) either as a randomized study where admitted cases are allocated to +/- low dose cytostatic therapy or that therapy is given to everyone in an observational study with historical controls. The therapy program can be either by oral, intravenous, daily or at longer intervals eg. weekly. Outcome parameters are care time at intensive care units, need for respiratory care +/- and death in the disease. In analyzes comorbidity, gender, age and other experimental therapies are adjusted for. The proposal calls for increased cooperation between anesthesiologists, emergency care doctors, rheumatologists, infection disease doctors and oncologists. The attempts to limit the autoimmune response should, of course, not prevent / inhibit the possibility of combating the virus infection in general.

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