

## Therapies used in rheumatology with relevance to coronavirus disease 2019

Sirs,

With the ongoing coronavirus disease 2019 (COVID-19) pandemic and growing evidence suggesting a role for some drugs commonly used in the context of rheumatic diseases, both colleagues and patients are coming to us with questions about these claims. Despite the fact that evidence is still scarce, it is pertinent to be able to address these queries in light of our previous experience in handling these prescriptions and take part in the multidisciplinary care of COVID-19 patients.

Two of the most commented therapeutic options are chloroquine and hydroxychloroquine. A Chinese study demonstrated *in vitro* inhibition of SARS-CoV-2 by chloroquine (1). Multiple clinical trials are ongoing in China, with news briefing of interim results derived from more than 100 patients demonstrating chloroquine phosphate as superior to control in inhibiting the exacerbation of pneumonia, improving lung imaging findings, promoting a virus negative conversion and shortening the disease course (2). Accordingly, the Chinese Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia recommends chloroquine phosphate in its general treatment section (3). Concerning hydroxychloroquine, a Chinese study found it to be more potent than chloroquine *in vitro*, and a French open label non-randomised clinical trial reported a significant viral load reduction in COVID-19 patients treated with hydroxychloroquine, with this effect reinforced with the association of azithromycin (4, 5).

Another interesting option is tocilizumab, with the Chinese Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia introducing the possibility of its use in patients with extensive lung lesions and severe cases with increased levels of IL-6 (3). A preprint of a Chinese retrospective study evaluating treatment with tocilizumab in 21 patients with severe COVID-19 (chinaXiv:202003.00026), described symptoms, hypoxemia and imaging improvement in most patients, with no adverse drug reactions reported. An interesting correspondence in the *Lancet* emphasised the accumulating evidence suggesting a subgroup of severe COVID-19 patients that might have cytokine storm syndrome (6). The authors denote similitudes between the cytokine profile of these patients and patients with secondary haemophagocytic lymphohistiocytosis (sHLH), suggesting the possibility of using a score originally intended to recognise sHLH patients to identify the

subgroup of severe COVID-19 patients for whom immunosuppression could be beneficial (6). A trial evaluating the efficacy and safety of tocilizumab in COVID-19 is ongoing in China (ChiCTR2000029765).

Baricitinib also raised some attention after a correspondence published in the *Lancet* featured artificial intelligence predicting the possibility of this drug reducing the ability of the virus to infect lung cells (7). The rationale for this hypothesis is based on the fact that angiotensin-converting enzyme 2 might be used as a receptor by SARS-CoV-2 to enter cells, and one of the known regulators of this receptor-mediated endocytosis is the AP2-associated protein kinase 1 (AAK1), which is inhibited by baricitinib (7). To the best of our knowledge, however, there are no other publications on baricitinib in the context of COVID-19.

Lastly, corticosteroids, which, according to current guidance by CDC and WHO, should be avoided in the management of COVID-19 patients, based on the negative experience derived from SARS-Cov and MERS-Cov patients (no survival benefit, increased side effects and delayed viral clearance) (8, 9). If indicated for other reasons (such as chronic obstructive lung disease exacerbation, asthma or septic shock), administration should be evaluated on an individual basis. Nevertheless, the Chinese Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia includes the possibility of administering a corticosteroid course in patients with progressive deterioration of oxygenation, rapid imaging progression and excessive inflammatory response (3). Inclusively, a Chinese study reporting outcomes of COVID-19 patients describes, among those with acute respiratory distress syndrome, a decrease in the risk of death with methylprednisolone (10). Multiple clinical trials are ongoing in China to assess the safety and efficacy of corticosteroids in COVID-19.

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