

Anti-fibrotic therapy for the treatment of pulmonary sequelae in patients healed by COVID-19

Sir,

Severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2 or COVID-19) is the virus responsible for the current global pandemic. To date, 13.8 million people were infected and about 590,000 people died while 7.72 million were healed. The viral infection has been divided by scientific opinion into three phases: the first as asymptomatic or slightly symptomatic and the second and third with greater severity, characterized by a hyperinflammatory and fibrotic state, responsible for lung lesions, with in some cases being fatal.^[1-3]

Several studies have revealed clinical features at different stages of the ongoing viral infection^[4-6] however many pathophysiological aspects such as evolution and histological features of lung tissue during the convalescence period are not yet fully clear. Indeed, there is some evidence that residual lung lesions may be persistently present even years after recovery from SARS caused by SARS-CoV-2.^[7] Epidemiological studies show that during the post-COVID-19 convalescence period many patients still have lung lesions caused by the presence of fibrotic tissue and that the complete healing process may occur slowly.^[8] In addition, older patients need more time for complete resolution. Even if the virus is eradicated in patients who have recovered from COVID-19, total eradication of the virus, which causes lung lesions, does not completely exclude the development of a progressive and irreversible fibrotic interstitial lung disease.^[9] Furthermore, even a relatively small degree of residual, but not progressive, pulmonary fibrosis could cause significant long-term morbidity and

mortality, especially in the population of elderly patients who have had COVID-19.^[10]

At this stage described, pirfenidone, a drug used for the treatment of idiopathic pulmonary fibrosis, could be of clinical benefit for a faster resolution of lung complications after COVID-19 eradication, due to its pleiotropic effects. In fact, pirfenidone has both antifibrotic and anti-inflammatory properties; has been shown to reduce the accumulation of inflammatory cells;^[11] and is able to mitigate protein production and proliferation of fibroblasts and cytokines associated with fibrosis.^[12] In addition, evidence has already demonstrated the efficacy of antifibrotics in patients with pathogenic prophylactic pathways caused by immune/inflammatory dysregulation, which may be similar to those present in the convalescent period.^[13-15] For a possible relevance to the pulmonary outcomes of COVID-19, it should be noted that, recently, for pirfenidone, the revolutionary therapy status (which accelerates the drug approval process) for fibrous interstitial lung disease has been recognized by the Food and Drug Administration. It can be hypothesized that using antifibrotic therapy at the beginning of the convalescence period in patients with lung lesions could prevent further damage and accelerate full recovery.^[16]

However, given the huge number of individuals affected by COVID-19, post-eradication complications of COVID-19 should also be considered, and efforts should be made to understand the best treatment solutions. Interventional studies in this direction are needed to prevent a second

wave of late and “secondary” mortality and morbidity associated with this devastating pandemic.

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Conflicts of interest

There are no conflicts of interest.

Antonio Vitiello, Francesco Ferrara

Department of Pharmaceutical, Perugia Usl Umbria 1,
Perugia, Italy.

E-mail: francesco.ferrara@uslumbria1.it

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