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Covid-19 infection in psoriasis patients treated with cyclosporin.

Running title: Covid-19 and cyclosporin

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Dear Editor,

the rapid dissemination of coronavirus disease 2019 (COVID-19) has raised concerns related to fragile patients. There is uncertainty concerning the outcome of COVID-19 infection in patients with chronic plaque psoriasis and atopic dermatitis receiving immunosuppressants. Indeed, it is debated whether such drugs should be stopped for preventing severe complications of the COVID-19 infection <sup>1-3</sup>.

Cyclosporin A (CsA) is a polypeptide immunosuppressant agent which suppresses T cell responses by preventing the transcription of genes encoding IL-2, which drives various lymphocyte subsets during differentiation, immune responses and homeostasis <sup>4</sup>. Due to its high efficacy and rapid onset of action, CsA has been widely used in dermatologic patients with psoriasis and atopic dermatitis, mostly in the short term. The primary molecular target of CsA is cyclophilin, a specific cytosolic binding protein, which is also required by many viruses for replication. Consequently, CsA is able to inhibit many viruses, among which influenza A virus, human immunodeficiency virus, hepatitis C virus, and coronaviruses <sup>5-6</sup>, including the two life-threatening Severe Acute Respiratory Syndrome-Coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) <sup>7</sup>. Consequently, a possible beneficial effect has been speculated in patients taking CsA during COVID-19 outbreak <sup>8-9</sup>.

A large number of individuals have been exposed to SARS-CoV2 so far, but currently, there are no data describing the benefits or risks of discontinuing CsA during the COVID-19 outbreak.

We have decided to advise patients treated with CsA not to spontaneously stop ongoing therapy, but to inform us in case of the onset of symptoms or close contact or contact history with COVID-19 patients. Therefore, we decided to evaluate the risk of COVID-19 infection and its severity in a group of adult patients treated with CsA for psoriasis (n=114) or atopic dermatitis (n=16).

Clinical data, including comorbidities, were obtained by consulting the electronic hospital records of each patient, and/or by directly contacting the patients by phone, email or performing dermatologic consultation in the hospital setting from 30 to 90 days after the beginning of the spread of the outbreak. Case series consisted of 71 males, 59 females, mean age  $48.4 \pm 14.2$  years, range 18-60 years.

There were no cases of deaths from COVID-related disease in our study, nor patients hospitalized for COVID-19 related interstitial pneumonia. Two psoriatic patients, respectively an otherwise healthy 48-year old female and a hypertense 56-year old female, had a COVID-19 infection confirmed with nasopharyngeal swab and/or serological tests. Both patients reported mild respiratory symptoms, such as mild cough, without fever in the first one patient and with low-grade fever in the second one, resolving in about five days. Neither of them reported serious symptoms that required hospitalization. After onset of respiratory symptoms, a preventive transient CsA discontinuation until complete remission of symptoms and at least a week without fever was suggested by us. Additional two asymptomatic female patients, who did not show symptoms, had reported contact history with suspected COVID-19 patients. Both of them had two real-time polymerase chain reaction nasal swabs for SARS-CoV-2 detection with negative result.

This is the first study evaluating the frequency and severity of COVID-19 in patients treated with CsA. This analysis has many limitations, since the number of patients with COVID-19 infection is too small to provide definitive conclusions. A particular susceptibility and severity of COVID-19 in patients treated with CsA was not observed. On the basis of our observation, there are not evidences that support a preventative discontinuation of CsA during COVID-19 outbreak in patients with psoriasis and atopic dermatitis. In addition to support advise and empowerment on activities to limit the risk of infection (hand hygiene, social distancing, use of protective devices), a telephone counselling may reassurance to the patients who spend at home the period of illness. Further observations or larger studies need to be done to confirm such approach.

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