

SHORT PAPER

COVID-19 patients with psoriasis and psoriatic arthritis on biologic immunosuppressant therapy vs apremilast in North Spain

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Abstract

Immunosuppressive and immunomodulatory treatments are critical for the management of inflammatory and autoimmune conditions such as psoriasis or psoriatic arthritis. Similar to those illnesses, the lung injury and acute respiratory distress shown in coronavirus disease 2019 (COVID-19) patients are the result of a disruption in the balance of pro- and anti-inflammatory cytokines. This hyperinflammatory response to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), associated with the severity of the coronavirus disease, is called the cytokine storm. There is a growing concern regarding how patients on immunosuppressant biologic therapies might be at higher risk of being infected and whether they need to discontinue their treatment preemptively. Clinical data on COVID-19-infected patients with psoriasis or psoriatic arthritis are still scarce. Here, we presented seven cases of these type of patients. The patient infected with COVID-19 on apremilast and the one on apremilast with infected spouse showed the best safety profile and mildest symptoms. One of the secukinumab patients also presented a relatively good outcome. Infliximab patients and the one with serious comorbidities showed the worst outcome. Even though more clinical data are yet needed to draw strong conclusions, apremilast could be a safer alternative for dermatology and rheumatology patients in case of clinically important active infection.

KEYWORDS

apremilast, COVID-19, cytokines, psoriasis, psoriatic arthritis

1 | INTRODUCTION

Coronavirus disease 2019 (COVID-19) pneumonia is characterized in some patients by an exaggerated immune hyperinflammatory response, with fast activation of innate immune cells and increased plasma concentration of interleukins (ILs) and tumor necrosis factor alpha (TNF α). It is the so-called “cytokine storm,” associated with the severity of the disease.^{1,2} This response comprise a series of

mediators that are pharmacologically targeted in immune-mediated inflammatory diseases such as psoriasis and psoriatic arthritis.^{2,3} Therefore, it might be considered that immunosuppressant drugs can be harmful by making these patients more susceptible to infection and to develop a more severe coronavirus syndrome.^{2,4}

With daily media warnings and dozens of articles published on the pandemic, patients and physicians are concerned on the possible higher risk of being infected, and whether they need to discontinue their biologic treatment preemptively.^{1,2,4-7} Moreover, these patients are often at greater risk of developing cardiovascular disease,

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depression, and other health conditions, which might increase the severity of the COVID-19 infection.^{8,9} Aggravation of previous skin diseases, such as rosacea, eczema, atopic dermatitis, and neurodermatitis, has been observed in some COVID-19 patients.⁸ It has been documented in psoriasis exacerbation following established respiratory virus infection¹⁰ and in a case of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.¹¹ In our facilities, one COVID-19 patient developed psoriasis without previous personal or family history.

Most current recommendations refer to guidelines and package inserts suggesting that biologics are contraindicated in case of clinically important active infection. It is not yet known if biologic therapies render patients more susceptible to coronavirus infection.^{1,3,6,9} On the other hand, discontinuing biologics can result in loss of response when treatments are reintroduced, or even result in the formation of antibodies to the discontinued biologic.⁶ Some physicians consider that immunosuppressant therapies should be suspended or reassessed until the infection is solved,^{4,7,9} while others argue that this might be a premature decision considering the available evidence.^{1,2,5}

2 | CASE PRESENTATION

At present, clinical data on COVID-19 patients with psoriasis or psoriatic arthritis on biologic therapies are scarce. Nonetheless, slowly but surely, new cases are emerging that allow us to shed some light on this issue. In our facilities, we have had seven cases of patients with COVID-19 on different biologic therapies that we describe below. Main clinical features are summarized in Table 1. Percentages of COVID-19-infected individuals among our psoriasis patients are shown in Table 2.

1. A 55-year-old woman with palmoplantar psoriasis on apremilast therapy for the last 6 months was diagnosed of bilateral

pneumonia and admitted to hospital during 3 days for COVID-19 treatment. Apremilast was maintained during hospitalization. A month later, COVID-19 tests were negative.

2. A 42-year-old man with psoriasis and psoriatic arthritis was treated with apremilast in outpatient confinement due to infected spouse with moderate COVID-19 symptoms. After quarantine period, both showed no respiratory affections. Apremilast was maintained during the confinement.
3. A 55-year-old man with plaque and nail psoriasis and psoriatic arthritis was treated with methotrexate and infliximab, and later switched to apremilast due to recurrent infections and cyclic neutropenia. He was recently diagnosed with hairy cell leukemia. The patient needed admission to intensive care unit (ICU) due to severe COVID-19 symptoms. After 50 days at the ICU and multiple complications (bacteremia, kidney deterioration, digestive hemorrhages, and so on), the patient remains currently hospitalized as a bed patient being treated for secondary effects of the disease. Apremilast was withdrawn in the ICU without prior dermatology consultation. The patient is currently on topical treatment for psoriasis.
4. A 37-year-old man with chronic plaque psoriasis under secukinumab therapy for years was admitted to hospital due to a right atypical pneumonia with negative COVID-19 tests. The infection process occurs just before the monthly secukinumab therapy. Currently, the patient is again under secukinumab treatment.
5. A 48-year-old woman with psoriasis under secukinumab treatment self-confined at home for meeting the COVID-19 infection criteria approve by the Ministry of Health. She did not receive treatment during the confinement period but did not meet the washout period. With good lung evolution, the patient received the corresponding secukinumab dose after confinement.
6. A 56-year-old man with psoriatic arthritis was in treatment with infliximab every 6 weeks and good disease control. Twenty days after the last infliximab dose, the patient was diagnosed with bilateral pneumonia and acute respiratory distress. Symptoms were severe and the patient was admitted to the ICU for 15 days.

TABLE 1 Summary of main clinical features of COVID-19 patients on biologic therapies

Age	Sex	Disease	Ongoing treatment		COVID-19			Severity of disease
			Drug	Time	Clinic	Hospital admission	KT	
55	Woman	Palmoplantar psoriasis	Apremilast	6 mo	Bilateral pneumonia	3 d	Yes	Mild
42	Man	Psoriasis and psoriatic arthritis	Apremilast	12 mo	No symptoms (infected spouse)	Home confinement	Yes	None
55	Man	Psoriasis and psoriatic arthritis (leukemia)	Apremilast	6 mo	Bilateral pneumonia	ICU: 50 d	No	Severe
37	Man	Plaque psoriasis	Secukinumab	12 mo	Atypical bilateral pneumonia	9 d	No	Moderate
48	Woman	Psoriasis	Secukinumab	15 mo	Bilateral pneumonia	Home confinement	No	Mild
56	Man	Psoriatic arthritis	Infliximab	12 mo	Bilateral pneumonia	ICU: 15 d	No	Severe
52	Woman	Peripheral spondyloarthritis	Infliximab	3 y	Bilateral pneumonia	Home confinement: 12 d	No	Moderate

Abbreviations: COVID-19, coronavirus disease 2019; ICU, intensive care unit; KT, keep treatment during COVID-19 infection.

TABLE 2 Percentages of patients on biologic therapies for psoriasis infected with COVID-19 at the HUMV

Biologic	Target	Patients on current psoriasis treatment	COVID-19-infected patients	%
Apremilast	PDE4	303	3	0.99
Secukinumab	IL-17	209	2	0.96
Infliximab	TNF α	36	1	2.78

Abbreviations: COVID-19, coronavirus disease 2019; HUMV, Hospital Universitario Marques de Valdecilla; IL, interleukin; PDE4, phosphodiesterase 4; TNF α , tumor necrosis factor alpha.

7. A 52-year-old woman was diagnosed with peripheral spondyloarthritis and treated with infliximab for the last 3 years, after failure with adalimumab therapy. The disease was kept under control with moderate inflammatory symptoms. Even though self-confined at home, persistency of COVID-19 symptoms forced her to attend the emergency unit on several occasions, until disease recovery. Infliximab treatment was suspended during COVID-19 infection.

3 | DISCUSSION

Even though the number of patients presented here is still too low to draw strong conclusions, it is noteworthy that the patients on apremilast showed the best safety profile (Table 1) and, along with secukinumab, the lowest infection rate (Table 2).

We have already indicated that apremilast could be a safer alternative in the COVID-19 era.¹² Several studies have reported a good efficacy and an excellent safety profile for apremilast in the treatment of psoriasis and psoriatic arthritis.^{12,13} Regarding virus infections, large studies have shown a significant decrease of serious infection rate in apremilast-treated patients.¹⁴ In a prospective safety study on the long-term safety of different medications for psoriasis, authors reported that apremilast patients had a lower risk of infections and infestations.¹⁵

Apremilast does not affect B cells, T cells, or immunoglobulin (Ig) G and IgM secretion, but partially inhibits TNF α , interferon gamma, IL-17, and IL-23.¹⁶ Given its immunomodulatory properties and its specific mechanism of action,^{12,14,16} apremilast does not favor neither the infections nor the cytokines storm, and it will not increase the risk of pulmonary fibrosis, one of the COVID-19's mortality factors.⁹ It has been reported that apremilast, as other systemic and biologic therapies, did not increase the risk of severe COVID-19 in psoriasis¹⁷ and psoriatic arthritis⁹ patients. Therefore, apremilast might offer a safe alternative, in the face of the ongoing pandemic, for those dermatology and rheumatology patients who present symptoms of COVID-19 infection. In this sense, Ricardo and Lipner proposed an algorithm for the treatment of psoriasis during COVID-19 pandemic where apremilast and acitretin are the only two drugs proposed by the authors to continue or initiate psoriasis therapy.⁷ Results in real-world settings have further reinforced the safety and efficacy of apremilast on psoriasis patients during the COVID-19 pandemic.¹³ In

conclusion, apremilast does not seem to particularly increase susceptibility to infection and can be considered a safe alternative for both infected and uninfected COVID-19 patients. IL-17 inhibitors seem to have also a relatively safe profile, while with systemic agents and TNF α inhibitors cautions are advised.^{4,7,8}

At this point, there are no strong and sure recommendations that can be given for the treatment of patients on biologic therapies in case of COVID-19 infection. As clinical data are collected, evidence-based guidelines will emerge for the management of these patients. The current paradigm might change in light of the pandemic. Final decision must depend on the well-informed clinicians and the patient's idiosyncrasy. The most important goal is that patient's disease is kept under control and risks are being minimized.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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