

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

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**Running head:** apremilast on COVID-19 patients

**Acknowledgements:** The authors have received writing and editorial support from José L. Ramírez, PhD, in the preparation of this manuscript.

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/dth.13961

## Abstract

Immunosuppressive and immunomodulatory treatments are critical for the management of inflammatory and autoimmune conditions such as psoriasis or psoriatic arthritis. Like in those illnesses, the lung injury and acute respiratory distress shown in COVID-19 patients are the result of a disruption in the balance of pro- and anti-inflammatory cytokines. This hyperinflammatory response to 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 this 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, psoriasis, psoriatic arthritis, cytokines, COVID-19

## Introduction

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 (IL) and tumor necrosis factor alpha (TNF $\alpha$ ). It is the so called “cytokine storm”, associated with the severity of the disease.<sup>1,2</sup> This response comprise a series of mediators that are pharmacologically targeted in immune-mediated inflammatory diseases such as psoriasis and psoriatic arthritis.<sup>2,3</sup> 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.<sup>2,4</sup>

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.<sup>1,2,4-7</sup> Moreover, these patients are often at greater risk of developing cardio-vascular disease, depression, and other health conditions which might increase the severity of the COVID-19 infection.<sup>8,9</sup> Aggravation of previous skin diseases, such as rosacea, eczema, atopic dermatitis, and neurodermatitis has been observed in some COVID-19 patients.<sup>8</sup> It has been documented psoriasis exacerbation following established respiratory virus infection<sup>10</sup> and in a case of SARS-CoV-2 infection.<sup>11</sup> 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.<sup>1,3,6,9</sup> 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.<sup>6</sup> Some physicians consider that immunosuppressant therapies should be suspended or reassessed until the infection is solved,<sup>4,7,9</sup> while others argue that this might be a premature decision considering the available evidence.<sup>1,2,5</sup>

### **Cases 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 years 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 years old man with psoriasis and psoriatic arthritis 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 years old man with plaque and nail psoriasis and psoriatic arthritis treated with methotrexate and infliximab, and later switched to apremilast due to recurrent infections and cyclic neutropenia. He was recently diagnosed with hairy cells leukemia. The patient needed admission to ICU (intensive care unit) due to severe COVID-19 symptoms. After 50 days at the ICU and multiple complications (bacteremia, kidney deterioration, digestive hemorrhages, etc.), 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. Currently on topical treatment for psoriasis.
- 4) A 37 years 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 patient is again under secukinumab treatment.
- 5) A 48 years 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 years old man with psoriatic arthritis in treatment with infliximab every 6 weeks and good disease control. Twenty days after the last infliximab dose, patient was diagnosis with bilateral pneumonia and acute respiratory distress. Symptoms were severe and the patient was admitted to the ICU for 15 days.

7) A 52 years old woman diagnose with peripheral spondyloarthritis and treated with infliximab for the last three 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 forces her to attend the emergency unit on several occasions, until disease recovery. Infliximab treatment was suspended during COVID-19 infection.

## 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.<sup>12</sup> Several studies have reported a good efficacy and an excellent safety profile for apremilast in the treatment of psoriasis and psoriatic arthritis.<sup>12,13</sup> Regarding virus infections, large studies have shown a significant decrease of serious infections rate in apremilast treated patients.<sup>14</sup> 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.<sup>15</sup>

Apremilast does not affect B cells, T cells, or IgG and IgM secretion, but partially inhibit TNF $\alpha$ , INF $\gamma$ , IL-17 and IL-23.<sup>16</sup> Given its immunomodulatory properties and its

specific mechanism of action,<sup>12,14,16</sup> apremilast does not favor neither the infections nor the cytokines storm, and it will not increase the risk of pulmonary fibrosis, one of COVID-19's mortality factors.<sup>9</sup> It has been reported that apremilast, as other systemic and biologic therapies, did not increase the risk of severe COVID-19 in psoriasis<sup>17</sup> and psoriatic arthritis<sup>9</sup> patients. Therefore, apremilast might offer a safe alternative, in the face of the ongoing pandemic, for those dermatology and rheumatology patients that present symptoms of COVID-19 infection. In this sense, Ricardo et al. 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.<sup>7</sup> Results in real-world settings have further reinforce the safety and efficacy of apremilast on psoriasis patients during COVID-19 pandemic.<sup>13</sup> 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 $\alpha$  inhibitors cautions is advised.<sup>4,7,8</sup>

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.

## References

1. Bashyam AM, Feldman SR. Should patients stop their biologic treatment during the COVID-19 pandemic. *J Dermatolog Treat* 2020;31(4):317-318.
2. Schett G, Sticherling M, Neurath MF. COVID-19: risk for cytokine targeting in chronic inflammatory diseases? *Nat Rev Immunol* 2020;20(5):271-272.
3. Price KN, Frew JW, Hsiao JL, Shi VY. COVID-19 and immunomodulator/immunosuppressant use in dermatology. *J Am Acad Dermatol* 2020;82(5):e173-e175.
4. Conforti C, Giuffrida R, Dianzani C, Di Meo N, Zalaudek I. COVID-19 and psoriasis: Is it time to limit treatment with immunosuppressants? A call for action [published online ahead of print, 2020 Mar 11]. *Dermatol Ther* 2020;e13298.
5. Abdelmaksoud A, Goldust M, Vestita M. Comment on "COVID-19 and psoriasis: Is it time to limit treatment with immunosuppressants? A call for action" [published online ahead of print, 2020 Apr 1]. *Dermatol Ther* 2020;e13360.
6. Lebwohl M, Rivera-Oyola R, Murrell DF. Should biologics for psoriasis be interrupted in the era of COVID-19? *J Am Acad Dermatol* 2020;82(5):1217-1218.

7. Ricardo JW, Lipner SR. Considerations for safety in the use of systemic medications for psoriasis and atopic dermatitis during the COVID-19 pandemic [published online ahead of print, 2020 May 27]. *Dermatol Ther* 2020;10.1111/dth.13687.
8. Zheng Y, Lai W. Dermatology staff participate in fight against Covid-19 in China. *J Eur Acad Dermatol Venereol* 2020;34(5):e210-e211.
9. Wollina U, Fioranelli M, Goldust M, Lotti T. Psoriatic Arthritis and COVID-19 Pandemic: Consequences in Medical Treatment? [published online ahead of print, 2020 Jun 1]. *Dermatol Ther*. 2020;e13743.
10. Sbidian E, Madrange M, Viguiet M, Salmona M, Duchatelet S, Hovnanian A, Smahi A, Le Goff J, Bachelez H. Respiratory virus infection triggers acute psoriasis flares across different clinical subtypes and genetic backgrounds. *Br J Dermatol* 2019;181(6):1304-1306.
11. Kutlu Ö, Metin A. A case of exacerbation of psoriasis after oseltamivir and hydroxychloroquine in a patient with COVID-19: Will cases of psoriasis increase after COVID-19 pandemic? [published online ahead of print, 2020 Apr 7]. *Dermatol Ther* 2020;e13383.
12. Armesto S, González Vela C, González López MA. Opportunistic virus infections in psoriasis patients: the safer alternative of apremilast in the COVID-19 era [published online ahead of print, 2020 May 18]. *Dermatol Ther* 2020;e13618.

13. Melis D, Mugheddu C, Sanna S, Atzori L, Rongioletti F. Clinical efficacy, speed of improvement and safety of apremilast for the treatment of adult Psoriasis during COVID-19 pandemic [published online ahead of print, 2020 May 30]. *Dermatol Ther* 2020;e13722.
14. Dommasch ED, Kim SC, Lee MP, Gagne JJ. Risk of serious infection in patients receiving systemic medications for the treatment of psoriasis [published online ahead of print, 2019 May 10] [published correction appears in *JAMA Dermatol*. 2019 Jul 1;155(7):865]. *JAMA Dermatol* 2019;155(10):1142-1152.
15. Daudén E, Carretero G, Rivera R, Ferrándiz C, Llamas-Velasco M, de la Cueva P, et al. Long term safety of nine systemic medications for psoriasis: a cohort study using the Biobadaderm Registry [published online ahead of print, 2020 Mar 22]. *J Am Acad Dermatol* 2020;S0190-9622(20)30451-5.
16. Schafer PH, Parton A, Capone L, et al. Apremilast is a selective PDE4 inhibitor with regulatory effects on innate immunity. *Cell Signal* 2014;26(9):2016-2029.
17. Fougousse AC, Perrussel M, Bécherel PA, Begon E, Pallure V, Zaraa I, et al. Systemic or biologic treatment in psoriasis patients does not increase the risk of a severe form of COVID-19 [published online ahead of print, 2020 Jun 21]. *J Eur Acad Dermatol Venereol*. 2020;10.1111/jdv.

## Tables

**Table 1.** Summary of main clinical features of COVID-19 patients on biologic therapies.

Age	Sex	Disease	Ongoing Treatment		COVID-19			
			Drug	Time	Clinic	Hospital Admission	KT	Severity of disease
55	woman	Palmoplantar psoriasis	Apremilast	6 months	Bilateral pneumonia	3 days	Yes	Mild
42	man	Psoriasis and psoriatic arthritis	Apremilast	12 months	No symptoms (infected spouse)	Home confinement	Yes	None
55	man	Psoriasis and psoriatic arthritis (leukemia)	Apremilast	6 months	Bilateral pneumonia	ICU 50 days	No	Severe
37	man	Plaque psoriasis	Secukinumab	12 months	Atypical bilateral pneumonia	9 days	No	Moderate
48	woman	Psoriasis	Secukinumab	15 months	Bilateral pneumonia	Home confinement	No	Mild
56	man	Psoriatic arthritis	Infliximab	12 months	Bilateral pneumonia	ICU 15 days	No	Severe

52	woman	Peripheral spondyloarthritis	Infliximab	3 years	Bilateral pneumonia	Home confinement 12 days	No	Moderate
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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.

<b>Biologic</b>	<b>Target</b>	<b>Patients on current psoriasis treatment</b>	<b>COVID-19 infected patients</b>	<b>%</b>
<b>Apremilast</b>	PDE4	303	3	0.99
<b>Secukinumab</b>	IL-17	209	2	0.96
<b>Infliximab</b>	TNF $\alpha$	36	1	2.78

COVID-19, coronavirus disease 2019; HUMV, Hospital Universitario Marques de Valdecilla; IL-17, interleukin 17; PDE4, phosphodiesterase 4; TNF $\alpha$ , tumor necrosis factor alpha