Received: 1 June 2020 | Revised: 10 June 2020 | Accepted: 12 June 2020

DOI: 10.1111/dth.13840

LETTER

DERMATOLOGIC THERAPY WILEY

Comment on "Psoriasis, COVID-19, and acute respiratory distress syndrome: Focusing on the risk of concomitant biological treatment"

Dear Editor,

We have read with great interest the review article published by Magnano et al which was recently published in *Dermatologic Therapy Journal*.[1] We found it interesting to expand the discussion in this regard that may be practically helpful for the dermatologists in the era of COVID19 pandemic. The authors pointed out the abrupt interruption of the biologics may increase the systemic inflammation, which may worsen the associated comorbidities and the prognosis of COVID-19. Herein, we agree with the authors and add more points that would be of interest for further interpretation in this critical time.

It is an area of debate whether it is advisable or not to stop biologic agents in the treatment of psoriasis during COVID-19 pandemic. Various scientific societies like American Academy of Dermatology (AAD) and International League of Dermatological Societies (ILDS) have issued guidelines to discontinue only in COVID-19 positive patients but can be carefully considered on a case-by-case basis if the patient is COVID-19 negative and with no symptoms by weighing risk vs benefit ratio. On the other hand, many of the published case series, retrospective studies have shown that although psoriasis patients have metabolic and cardiovascular comorbidities, there is no early sign of an increased hospitalization rate among these patients.[2,3] Moreover, the retrospective study conducted by Gisondi et al showed that there is no death due to COVID-19 and only one hospitalization, fully recovered among the patients with chronic plaque psoriasis receiving a biological treatment and renal transplant recipients who were under immunosuppressive therapies.[4] Various studies have suggested to discontinue biologics only in COVID-19 positive patients and consider biologics on case-by-case basis considering the severity of psoriasis and other comorbidities.[5,6]

Nuclear factor kappa B (NF-κB) is a protein transcription factor that orchestrates inflammation and other complex biological processes and is a key regulatory element in a variety of immune and inflammatory pathways, in cellular proliferation and differentiation and in apoptosis. Therefore NF-κB is a crucial mediator involved in the pathogenesis of psoriasis. Several anti-psoriatic therapies, including tumor necrosis factor-α blockers and glucocorticoids, reduce active NF-κB levels, and related down-stream elements, and other biologics currently in development, including interleukin-17 blockers, may also target this pathway. SARS-CoV-2 is known to be engulfed into the human cell along with the ACE2 receptor it had combined with. This reduces the number of ACE2 receptors on cells, leading to an increase of a polypeptide, called angiotensin II, in the blood. Angiotensin II triggers an inflammatory pathway involving NF-κB and IL-6-STAT3 particularly in nonimmune cells including endothelial cells and epithelial cells. This pathway forms a positive feedback cycle, named IL-6 amplifier, resulting in its excessive activation and therefore the cytokine storm and ARDS.[7]

It can be hypothesized that immunosuppressive/immunomodulator therapies using in psoriasis may suppress and/or control the "cytokine storm in COVID-19" and/or suppress viral activity in order to reach recovery. Zumla et al also hypothesized that blocking IL-17 could have the potential to improve COVID-19's aberrant immune response and acute respiratory distress syndrome-related mortality.[8] Moreover, previous studies have shown that biologic agents seem to have an acceptable safety profile and high effectiveness in the presence of immunocompromising such as HIV-positivity. Biologic agents had a positive effect on CD4 and viral counts when used in combined with highly active anti-retroviral therapies in these individuals.[9,10]

Since, we do not have much data on biologics in psoriasis patients effecting COVID-19 disease course, current data suggests that there is no increase morbidity/mortality among these patients. To reveal the relationship with immunomodulator therapies and its effects on COVID-19, further case-control studies are required.

CONFLICT OF INTEREST

The authors declared no potential conflict of interest.

AUTHOR CONTRIBUTIONS

Banu Farabi: conceived ideas, data analysis; Shashank Bhargava: data analysis and interpretation; Mohamad Goldust: revisions to scientific content of the manuscript; Mehmet Fatih Atak: conceived ideas and data analysis.

Banu Farabi[1,2]
Shashank Bhargava[3]
Mohamad Goldust[4]
Mehmet Fatih Atak[2]

[1]*Department of Dermatology, Robert Wood Johnson Medical Center, Rutgers University, New Brunswick, New Jersey*
[2]*Department of Dermatology, Ankara University School of Medicine, Ankara, Turkey*

[3]Department of Dermatology, R. D. Gardi Medical College, Ujjain, India
[4]Department of Dermatology, University Hospital Basel, Basel, Switzerland

Correspondence
Banu Farabi, Department of Dermatology, Robert Wood Johnson Medical Center, Rutgers University, New Brunswick, NJ, USA.
Email: banufarabi91@gmail.com

ORCID

Banu Farabi https://orcid.org/0000-0002-4748-1556
Shashank Bhargava https://orcid.org/0000-0003-4141-5520
Mohamad Goldust https://orcid.org/0000-0002-9615-1246

REFERENCES

1. Magnano M, Balestri R, Bardazzi F, Mazzatenta C, Girardelli CR, Rech G. Psoriasis, COVID-19 and acute respiratory distress syndrome: focusing on the risk of concomitant biological treatment. *Dermatol Ther*. 2020;30:e13706. https://doi.org/10.1111/dth.13706. [Epub ahead of print].
2. Conti A, Lasagni C, Bigi L, Pellacani G. Evolution of COVID-19 infection in 4 psoriatic patients treated with biological drugs. *J Eur Acad Dermatol Venereol*. 2020;7. https://doi.org/10.1111/jdv.16587. [Epub ahead of print].
3. Megna M, Ruggiero A, Marasca C, Fabbrocini G. Biologics for psoriasis patients in the COVID-19 era: more evidence, less fears [Published online ahead of print, 2020 Apr 27]. *J Dermatolog Treat*. 2020;31(4):328-329. https://doi.org/10.1080/09546634.2020.1757605.
4. Gisondi P, Zaza G, Del Giglio M, Rossi M, Iacono V, Girolomoni G. Risk of hospitalization and death from COVID-19 infection in patients with chronic plaque psoriasis receiving a biological treatment and renal transplanted recipients in maintenance immunosuppressive treatment. *J Am Acad Dermatol*. 2020;83:285-287.
5. 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. *Dermatol Ther*. 2020;e13298-e13490. https://doi.org/10.1111/dth.13490. [Epub ahead of print].
6. Di Lernia V. Antipsoriatic treatments during COVID-19 outbreak. *Dermatol Ther*. 2020;e13345. https://doi.org/10.1111/dth.13345. [Epub ahead of print].
7. Brownstone ND, Thibodeaux QG, Reddy VD, et al. Novel coronavirus disease (COVID-19) and biologic therapy in psoriasis: infection risk and patient counseling in uncertain times. *Dermatol Ther (Heidelb)*. 2020;10(3):1-11.
8. Zumla A, Hui DS, Azhar EI, Memish ZA, Maeurer M. Reducing mortality from 2019-nCoV: host-directed therapies should be an option. *Lancet*. 2020;395(10224):e35-e36.
9. Montes-Torres A, Aparicio G, Rivera R, et al. Safety and effectiveness of conventional systemic therapy and biological drugs in patients with moderate to severe psoriasis and HIV infection: a retrospective multicenter study. *J Dermatolog Treat*. 2019;30(5):461-465.
10. Nakamura M, Abrouk M, Farahnik B, Zhu TH, Bhutani T. Psoriasis treatment in HIV-positive patients: a systematic review of systemic immunosuppressive therapies. *Cutis*. 2018;101(1):38;42;56.