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Title: The impact of COVID-19 infection on psoriatic patients treated with biologics: an Italian experience.

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Dear Editor,

COVID-19 pandemic had an important impact on daily dermatological practice, with several concerns raised by the effects of COVID-19 infection and its vaccination on different skin conditions.[1-3] In this scenario, we read with great interest the article by Bakirtzi et al.[4] evaluating the impact of SARS-CoV-2 infection on psoriatic patients treated with biologics. Particularly, the authors reported that 76.9% (n=432) of psoriasis patients affected by COVID-19 infection showed disease worsening, especially in those treated with anti-interleukin (IL)-23 and anti-IL-12/23, while patients treated with anti-IL-17 and anti-tumour necrosis factor (TNF), showed a higher sustained efficacy.[4] We are extremely surprised regarding this high rate of disease worsening in psoriasis subjects under biologics. Indeed, our experience highly differs from the one of Bakirtzi et al. Particularly, we retrospective analyzed psoriasis patients under biologics and reporting COVID-19 infection (confirmed by both molecular and/or antigenic nasopharyngeal swab) between October-2020 and May-2022 at our Clinic. A total of 205 (21.1%) (M/F: 116/89, with a mean age of 63.7±9.6 years) out of 970 patients treated with biologics experienced COVID-19 infection and were included in the study. We reported a psoriasis worsening in only 10.7% (n=22) (mean PASI increase of 2.8±3.2) of COVID-19 infected patients. Patients' characteristics and ongoing treatments were resumed in Table 1. The mean age of these patients resulted higher than those not reporting psoriasis exacerbation (68.6±4.2 vs 58.9±7.5), while no difference in sex and ongoing treatments were reported. Globally, COVID-19 induced disease worsening was mild, and only 3/22 patients (22%) required treatment switch (2 patients were under anti-TNF and 1 under secukinumab). No other treatment discontinuations were required, and patients recovered treatment response in all cases. Hence, in contrast with Bakirtzi et al,[4] we reported a COVID-19 induced psoriasis worsening in patients under biologics in a significantly lower rate of subjects (10.7% vs

76.9%). Furthermore, even if no significant differences among classes we also observed that treatment switching was more frequently required if patients were under anti-TNF when they contracted COVID-19. This results additionally differs from Bakirtzi et al who sustained that patients treated with anti-TNF, showed a higher sustained efficacy. It is hard to believe that anti-TNF may significantly protect from disease worsening compared to anti-ILs since the well-known superiority of anti-ILs vs anti-TNF in psoriasis clearance. Moreover, we also found that older patients may have a higher risk of psoriasis exacerbation in case of COVID-19 infection. This may be linked to the immunological aging (immunosenescence) in aged people, which has been linked to several diseases' complication in the elderly, as well as to higher mortality rates in case of COVID-19 infection.[5] Although the exact mechanism behind psoriasis burden during COVID-19 infection is still not well clarified, data reporting diseases exacerbations are increasing in literature.[6] COVID-19 seems to be linked to psoriasis onset/development,[7] while its exacerbation during biologics is less described. Our results confirm this trend, reporting the possibility of a generally mild psoriasis worsening in 10% of psoriasis patients under biologics, strongly contrasting with 76.9% reported by Bakirtzi et al. Honestly, it is very difficult to believe that up to 80% of psoriasis patients under biologics may experience a disease worsening induced by COVID-19 for different reasons such as i) the undergoing biologic therapy which strongly reduce disease relapse risk; ii) the lack of literature on this phenomenon which would have led to a significant increase of treatment switching; iii) the fact that other infections (e.g. upper respiratory tract infection which are also one of the most common adverse events of biologics) are not reported as significant in inducing such a frequent disease worsening in patients under biologics. Our data showed that COVID-19 infection in psoriasis patients under biologics may lead to a psoriasis burden only in a limited percentage of patients (10%), being usually mild, and showing the importance of avoiding treatment discontinuation or unnecessary therapy switch. Indeed, following COVID-19 or its vaccine, psoriasis burden risk is significantly higher in patients who are not under systemic treatment or who discontinue the treatment.[8,9] Study limitations include the delay or possibly long period between

COVID-19 infection and follow-up visits, and eventual unreported mild psoriasis worsening by patients, which may result in an underestimation of psoriasis exacerbations, as well as the lack of COVID-19 screening for the whole treated population, leading to the exclusion of asymptomatic infected patients not confirmed by a nasopharyngeal swab.

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Total patients treated with biologics (screened)	n=970
COVID-19 infected patients (swab confirmed)	21.1% (n=205)
Sex	
Male	56.5% (n=116)
Female	43.5% (n=89)
Patients experiencing a burden of psoriasis	10.7% (n=22)
Biological treatment	
TNF inhibitors	36.3% (n=8)
Adalimumab	18.2% (n=4)
Etanercept	18.2% (n=4)
Anti-IL-17	31.8% (n=7)
Secukinumab	13.6% (n=3)
Brodalumab	9.1% (n=2)
Ixekizumab	4.5% (n=1)
Anti IL-12/23	9.1% (n=2)
Ustekinumab	9.1% (n=2)
Anti-IL-23	27.2% (n=6)
Tildrakizumab	9.1% (n=2)
Guselkumab	9.1% (n=2)
Risankizumab	9.1% (n=2)

IL: Interleukin; TNF: Tumor Necrosis Factor

Table 1. Characteristics of the study population.