

Letter to the Editor

Humoral and cellular immunity after mRNA COVID-19 vaccine in psoriatic patients on biological or immunosuppressive therapy: a real-life experience

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To the Editor

The COVID-19 pandemic has radically changed the way we manage dermatological patients, in particular those with psoriasis (1). In addition, psoriasis is a complex immune-mediated inflammatory disease associated with metabolic disorders (2, 3) with a higher risk of metabolic syndrome, diabetes mellitus, obesity, and cardiovascular diseases (4).

The introduction of mRNA vaccines (Pfizer-BioNTech, BNT162b2 vaccine, or Moderna, mRNA-1273 vaccine) is an important weapon against SARS-CoV2, but their real-life efficacy in psoriatic patients on biologic or immunosuppressive therapy has not yet been clearly defined (5, 6).

We report a case series of psoriatic patients from the Ancona Dermatological Clinic treated with the interleukin (IL)-17A inhibitor secukinumab (3), IL-17 receptor inhibitor brodalumab (1), IL-23 inhibitor risankizumab (1), and calcineurin inhibitor cyclosporine (1). Clinical features, treatments, antibody responses, and variations in the Psoriasis Area Severity Index (PASI) and Body Surface Area (BSA) before and after (6 weeks) vaccination are shown in Table 1.

In our clinical practice, a blood sample was collected 3 ± 1 weeks after the second dose of vaccine, assessing the anti-spike IgG antibody response (aSp, positive if > 7.10 IU/ml) and cellular immunity (interferon gamma [IFN- γ] production, positive if INF- γ

> 0.08 IU/ml). The results shown in Table 1 indicate that all subjects developed a satisfactory aSp response, and the INF- γ values produced after exposure to spike protein (S protein) also indicate a good cell-mediated immune response. No nucleocapsid antibodies were found in any of the patients, ruling out a previous recent SARS-CoV2 infection. In all subjects, the efficiency of cellular immunity was confirmed by positive and negative control tests. There were no vaccination-related adverse events.

Analyzing the data more specifically shows that the lowest results for the aSp titers are in patients treated with brodalumab (145.6 IU/ml) and cyclosporine (471.95 IU/ml), as well as for cellular immunity: 0.51 IU/ml and 0.23 IU/ml, respectively.

In the case of cyclosporine, this can be explained considering that the drug acts as an immunosuppressant and therefore may reduce the effectiveness of the adaptive immune response to the vaccine (7). On the other hand, a meta-analysis of transplant patients receiving cyclosporine does not show a reduction in humoral immune response to the influenza vaccine (8). Furthermore, because specific data are lacking in the literature, psoriatic patients treated with immunosuppressants, especially methotrexate, showed a lower frequency of aSp seroconversion after the first dose of BNT162b2 vaccine, but the cellular immune response was not lower than in healthy controls (5). After the second dose of vaccine, all subjects developed sufficient humoral and cellular immunity (6).

Table 1 | Clinical features, treatments, antibody responses, cell-mediated responses, and variations in the Psoriasis Area Severity Index (PASI) and Body Surface Area (BSA) before and after (6 weeks) vaccination.

Patient	Age (years)	Sex	Therapy	Vaccine	Time (weeks)	Anti-spike IgG (pos ≥ 7.1 IU/ml)	Interferon gamma	Clinical features before/after vaccination
1	40	M	Secukinumab	Pfizer BNT162b2	3	989	3.52 IU/ml	PASI 0/0 BSA (%) 0/0
2	70	M	Secukinumab	Pfizer BNT162b2	3	7,364	2.73 IU/ml	PASI 0/0 BSA (%) 0/0
3	62	F	Secukinumab	Pfizer BNT162b2	4	344.36	3.78 IU/ml	PASI 0/0 BSA (%) 0/0
4	78	M	Brodalumab	Pfizer BNT162b2	2	145.6	0.51 IU/ml	PASI 1/1 BSA (%) 1/1
5	23	M	Cyclosporine	Pfizer BNT162b2	2	471.95	0.23 IU/ml	PASI 3/2 BSA (%) 5/4
6	58	M	Risankizumab	Moderna mRNA-1273	3	4,888.8	9.77 IU/ml	PASI 3/3 BSA (%) 5/5

The Time column refers to weeks between the second dose of vaccination and blood sample. Dosing: cyclosporine 200 mg/day, secukinumab 150 mg every 4 weeks, brodalumab 210 mg every 2 weeks, risankizumab 150 mg every 12 weeks. No other concurrent therapy. M = male, F = female, pos = positive, PASI = Psoriasis Area Severity Index, BSA = Body Surface Area.

Regarding brodalumab, there are no specific data in the literature, but its mechanism of action blocks the IL-17 receptor, acting on all IL-17 isoforms, and could reduce the effectiveness of COVID-19 vaccination. In our case, the patient developed a sufficient humoral and cellular response. On the other hand, a protective role of IL-17 inhibitors against severe forms of SARS-CoV2 has also been proposed (9).

This is the first study to report efficacy after the second dose of BNT162b2 vaccine or mRNA-1273 vaccine in patients on biological therapy or immunosuppressive treatment with cyclosporine, evaluating both humoral and cellular immunity. We considered the aSp IgG titers because it is demonstrated in the literature to correlate with neutralizing activity in HIV patients (10). Cellular immunity was used because it is another crucial aspect of the immune response against SARS-CoV2 and may be an indicator of vaccination efficacy, especially in cases with low antibody titers (11).

From a clinical point of view, patients were in disease remission and no worsening of psoriasis occurred after vaccination. Although cases of psoriasis flare after COVID-19 vaccination with

Pfizer BNT162b2, AstraZeneca-Oxford AZD1222, and Moderna mRNA-1273 have been reported in the literature, even during biologic therapy, it appears that the use of systemic therapy may potentially reduce the risk of psoriasis worsening (12). While considering the limitations of our study, we can confirm that psoriasis flares after vaccination are a rare occurrence, and that biological therapies may play a protective role even if they do not remove the risk completely.

In conclusion, our real-life experience confirms what emerged in the study by Mahil et al., highlighting the efficacy of at least two doses of the COVID-19 vaccine even in psoriatic patients receiving immunomodulatory or immunosuppressive therapy (5, 6). The major limitations of this study are the very small number of patients, which limits the generalization of the results, the fact that only some biological therapies were investigated, and no comparison with methotrexate. Further research with a larger sample size is necessary for a complete definition not only of the efficacy but also of the durability of the immune response in this type of patient.

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