Chapter 18
The Relationship Between Psoriasis, COVID-19 Infection and Vaccination During Treatment of Patients

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Abstract Since the outbreak of the COVID-19 pandemic in December 2019, scientists worldwide have been looking for a way to control this global threat. One of the most successful and practical solutions has been the development and worldwide distribution of the COVID-19 vaccines. However, in a small percentage of cases, vaccination can lead to de novo development or exacerbation of immune or inflammatory conditions such as psoriasis. Due to the immunomodulatory nature of this disease, people affected by psoriasis and other related skin conditions have been encouraged to receive COVID-19 vaccines, which are immunomodulatory by nature. As such, dermatological reactions are possible in these patients, and cases of onset, exacerbation or change in the type of psoriasis have been observed in patients

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administered with COVID-19 vaccines. Considering the rarity and minor nature of some of these cutaneous reactions to COVID-19 vaccination, there is a general consensus that the benefits of vaccination outweigh the potential risks of experiencing such side effects. Nevertheless, healthcare workers who administer vaccines should be made aware of the potential risks and advise recipients accordingly. Furthermore, we suggest careful monitoring for potentially deleterious autoimmune and hyperinflammatory responses using point-of-care biomarker monitoring.

Keywords COVID-19 · SARS-CoV-2 · Infection · Vaccination · Psoriasis

1 Introduction

The pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first reported in December 2019. This is the third coronavirus transmitted from zoonotic species to humans after the H1N1 influenza outbreak in 2016 [1]. COVID-19 is associated chiefly with self-limiting upper respiratory tract infections. However, a small but significant proportion of patients develop acute respiratory distress syndrome (ARDS), which cannot be treated effectively and may increase risk of death [2]. In cases of severe COVID-19, the host immune system appears to respond excessively, producing a damaging hyperinflammatory response known as a cytokine storm [3].

Potentially the most effective way of halting the spread of viral infections is through the development and deployment of approved vaccines. As of October 18, 2022, more than 68% of the world population have been administered at least one

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dose of an approved COVID-19 vaccine [4]. However, the rate of vaccination has declined [4], and there is still a significant proportion of populations around the world that show vaccine hesitancy [5]. One factor that may affect public confidence in vaccine uptake is the potential of long- and short-term adverse effects [6–8]. Although uncommon, some cases of new-onset psoriasis and exacerbation of existing ones have been reported around the world, following a COVID-19 vaccination [9–14]. However, it should be noted that both new psoriasis cases and exacerbation of existing ones were reported even before rollout of the COVID-19 vaccines [15–18]. This suggests the involvement of a common underlying mechanism in psoriasis, COVID-19 infection and vaccination. The most likely link is through immune and inflammatory pathway modulation as all of these work as a result of effects on these systems, including through activation of autoimmune mechanisms [19–23].

In this study, we have evaluated studies on the effect of various COVID-19 vaccines as a potential causative factor in the de novo appearance or exacerbation of psoriasis in the individuals who received these. We also make recommendations on how to deal with this potential issue while at the same time maintaining an effective vaccination approach.

2 Methods

Data were collected from papers published in PubMed, Scopus, Google Scholar and Cochrane library for Clinical Studies. This required that the papers were published in English up to January, 2022. Search terms included “psoriasis” OR “dermatological reactions” AND “COVID-19” OR “COVID-19 vaccines” AND “adverse reaction” OR “side effects” AND “immunological response.”

3 Psoriasis and Correlation with COVID-19

Psoriasis is an inflammatory skin disease that affects 0.09–11.43% of people in different countries around the world [24]. Psoriasis patients may be prescribed systemic immunomodulatory or immunosuppressive treatments depending on location and severity of the lesions or if they are resistant to topical treatments [25]. However, these therapies have been associated with the increased risk of infections, and there has been considerable controversy regarding the potential of increased susceptibility of psoriasis patients on such treatments to COVID-19 infections and/or a more serious disease course [26–31]. In this section, we review some of the relevant studies addressing this controversy.

Kara Polat et al. found no difference in the incidence, length of hospital stay, intensive care unit (ICU) admittance or death outcomes in psoriasis patients on immunosuppressive or biologic treatments with COVID-19 infections compared to those who had not been treated with these compounds [32]. None of the other tested potential risk factors that were assessed had an influence on COVID-19 disease trajectory apart from the presence of diabetes. However, there was an exacerbation of psoriasis with COVID-19 infections.

A retrospective multicentre study in Italy of 5206 patients with chronic plaque psoriasis on biological therapies found no deaths from COVID-19 and four hospitalizations for COVID-related interstitial pneumonia, which did not differ from the general population [33]. However, the authors acknowledged limitations due to the lack of standardization of the control group.

Carugno et al. evaluated 159 psoriasis patients during the first 45 days of the COVID-19 pandemic in the Lombardy region of Italy for SARS-CoV-2 infections [34]. They found no serious cases of COVID-19 and no difference in patients who continued or did not continue their psoriasis treatment.

A case–control study performed in 2020 by Damiani et al. of 1193 psoriasis patients in Lombardy receiving small molecules or biological drugs found that 22 of these tested positive for COVID-19, with 5 of these being hospitalized and none admitted to the ICU or who died [35]. In comparison to the general population, the researchers found that patients were at higher risk to test positive for COVID-19 and hospitalized. These findings suggested that treatment with biologic or immunosuppressive therapeutics may increase the risk of contracting mild forms of COVID-19 disease.

Other studies showed de novo or exacerbation of psoriasis in COVID-19 cases who were not on immunosuppressive therapies. A case study of a 38-year-old man with a single psoriatic plaque but who had received no treatment for this condition was diagnosed with COVID-19 infection after a nasopharyngeal test [36]. Six days after the onset of COVID-19 symptoms, several psoriatic lesions formed on his knee with no improvement after 22 days. After this, treatment with topical betamethasone cream led to significant clinical improvement after 2 weeks. Another case report of a 25-year-old male diagnosed with a COVID-19 infection developed multiple psoriatic lesions 15 days later [37]. As above, treatment with topical betamethasone led to recovery.

Taken together, these studies provide no evidence that biologic or immunosuppressive treatments increase the risk of COVID-19 infection or severity of disease course. However, they do suggest that COVID-19 disease can lead to de novo eruptions or exacerbations of existing psoriatic lesions. This was supported by a study covering the first (February 15, 2020 to June 30, 2020) and second (October 1, 2020 to January 31, 2021) waves of the pandemic in France [38]. This investigation found that COVID-19 patients who had received systemic treatments for psoriasis did not show an increased risk of in-hospital mortality due to COVID-19 infection.

4 Efficacy and Safety of COVID-19 Vaccines in Patients with Psoriasis

Wack et al. reviewed the evidence related to COVID-19 vaccine safety and efficacy in patients with immune-mediated inflammatory diseases [39]. They found no evidence to support the point that these patients are at a higher risk of harmful side effects from a COVID-19 vaccination compared to healthy controls. However, they could not determine if patients on biologics or immunosuppresants produce a sufficient immune response to the vaccine, as this may depend on the specific indication and therapeutic employed.

A study conducted by Geisen et al. showed that SARS-CoV-2 mRNA vaccines produce antibodies with neutralizing activity in healthy controls as well as in patients who were on immunosuppressant therapies for chronic inflammatory conditions [40]. However, the immunoglobulin G (IgG) titres were significantly lower in the immunosuppressant-treated patients compared to controls. It should be noted that vaccination did not lead to significant side effects or disease flare-ups in the immunosuppressed group.

Along the same lines, another study found that patients with immune-mediated inflammatory diseases who received the Pfizer-BioNTech mRNA vaccine produced slower antibody responses compared to the control group, and a higher proportion of these patients showed no detectable response [41]. Furthermore, those patients with immune-mediated inflammatory diseases who had not been treated showed a similar diminished response, suggesting that this effect may be linked to the disease rather than to a treatment effect.

Skroza et al. evaluated the safety of COVID-19 vaccination in psioriasis patients who had received biological or immunosuppressive treatment for at least 24 weeks [42]. The study found that all patients showed a similar reduction in their psoriasis area severity index scores, and this did not differ between vaccinated and non-vaccinated individuals. In addition, no adverse effects were detected in either group.

In another study, Damiani et al. evaluated four psoriatic cases who took biological or immunomodulatory medications and received two doses of the Pfizer-BioNTech vaccine [43]. This showed that none of the patients showed changes in cutaneous manifestations or a psoriasis flare up. Furthermore, all patients showed an effective response to the vaccine.

In order to promote optimal treatment of patients with psoriasis during the pandemic, the National Psoriasis Foundation COVID-19 Task Force guideline has proposed that patients with psoriasis should receive their COVID-19 vaccine in the shortest possible time while continuing with their biological or immunomodulatory treatments drugs [44]. However, this proposal stipulates that the ultimate judgement should be made by the treating clinician and the patient due to variability of psoriatic diseases and the medications used to treat them.

5 Psoriasis After COVID-19 Vaccination

5.1 COVID-19 Vaccination Leading to De Novo Psoriasis

A number of studies have reported on cases of individuals who developed different forms of psoriasis for the first time after receiving a COVID-19 vaccine (see Table 18.1). This includes de novo psoriasis cases following the first [46, 46] or second [46] dose of Oxford-AstraZeneca vaccine. In addition, there have been reports of new psoriasis eruptions following the first [47, 48] or second [49] dose of the Pfizer-BioNTech vaccine. Although the mechanism for these spontaneous eruptions is not clear, it is possible that it is linked to dysregulation of immune system due to the virus or vaccine components, as proposed by Gunes et all for other vaccines such as influenza, BCG and tetanus-diphtheria vaccines [50]. In addition, mRNA vaccines such as Pfizer-BioNTech vaccine can lead to increased levels of interleukin 6 (IL-6) and Th17 cell activation, which are known to be involved in the pathological mechanism of psoriasis [51, 52]. Even though these cases of de novo medical professionals are still advised to pay close attention to side effects and take appropriate measures in the treatment of the clinical condition on a case-by-case basis.

5.2 COVID-19 Vaccinations Which Exacerbates Psoriasis

5.2.1 Pfizer-BioNTech mRNA Vaccine

A number of studies have reported on exacerbations or flare-ups of psoriasis that may be linked to vaccination with the Pfizer-BioNTech mRNA vaccine: Durmaz et al. described three different cases where psoriasis was exacerbated after the first, second and third doses of the Pfizer-BioNTech vaccine [53]. A case study also reported exacerbation of existing psoriasis in a 40-year-old man after vaccination with the first dose of the same vaccine [54]. Two cases of underlying dermatitis were reported to be exacerbated upon receipt of the third dose of Pfizer-BioNTech vaccine [55]. In a recent study, Michkowska et al. reported a case of a 65-year-old male with a history of hepatocellular carcinoma previously treated with nivolumab and poorly controlled psoriasis that was exacerbated one week after he received the first dose of the Pfizer-BioNTech vaccine [56]. Another case study reported on a man who developed psoriatic lesions on the lower legs 5 days after a second dose of this vaccine [52]. Finally, one study reported on a 51-year-old man whose existing psoriatic lesions enlarged after receipt of his first dose of the Pfizer-BioNTech vaccine [57]. The same report described the case of a second man with a complaint of skin rash that started on his buttocks 1 month after the second dose of inactivated CoronaVac vaccine [57].

Table 18.1 Cases of psoriasis after COVID-19 vaccination

Case	Vaccine type	Vaccination dose	Psoriasis type before/after vaccination	Description of lesions	Result	Ref
66-year-old female	Oxford/AstraZeneca	1st dose	_/Generalized pustular psoriasis	1. Erythematous pustular rashes to the trunk and proximal part of th limbs	Development of psoriasis	[45]
65-year-old male		2nd dose	_/Psoriasis	1. Erythematous papules and plaques on the trunk and extremities	Development of psoriasis	[46]
56-year-old female	Covishield	1st and 2nd dose	Psoriasis/Psoriasis	_	Exacerbation of psoriasis	[46]
23-year-old female	Pfizer/BioNTech	1st dose	_/Guttate psoriasis	1. Erythematous papules and plaques on the dorsum of her hand, then on the elbows, arms, legs and trunk	Development of psoriasis	[47]
79-year-old female	Pfizer/BioNTech	1st and 2nd dose	_/Guttate psoriasis	1. Disseminated erythematous papules and scaly plaques on the arms and thighs	Developoing of psoriasis	[48]
76-year-old female	Pfizer/BioNTech	2nd dose	_/Nail psoriasis	1. Red spots and dilated capillaries in proximal nailfold 2. subungual parakeratosis and entrapment of neutrophils	Development of psoriasis	[49]
46-year-old male	Pfizer/BioNTech	2nd dose	Plaque psoriasis/Plaque psoriasis	Silver scaling and inflamed psoriatic plaques on legs, extremities and trunk	Exacerbation of psoriasis	[52]
64-year-old male	Pfizer/BioNTech	3rd dose	Psoriasis vulgaris/Psoriasis vulgaris	1. Erythematous, silver-coloured scaly plaques on the bilateral dorsum of the hand, elbow, leg extensor surfaces and intergluteal area	Exacerbation of psoriasis	[53]
64-year-old male	Pfizer/BioNTech	2nd dose	Palmoplantar psoriasis/ Palmoplantar psoriasis	1.Silvery-scaly plaques in the hypothenar region of palms 2. Hyperkeratotic plaques and fissures in the plantar area	Exacerbation of psoriasis	[53]

(continued)

Table 18.1 (continued)

Case	Vaccine type	Vaccination dose	Psoriasis type before/after vaccination	Description of lesions	Result	Ref
25-year-old female	Pfizer/BioNTech	1st dose	Pustular psoriasis/Pustular psoriasis	1.Non-follicular pustules and localized scaling on erythematous plaques in the anterior-posterior of the trunk, arms and proximal thighs	Exacerbation of psoriasis	[53]
40-year-old male	Pfizer/BioNTech	1st dose	Acute generalized pustular psoriasis/Acute generalized pustular psoriasis	Erythematous patches and plaques on abdomen, arms, legs and buttocks Psoriasiform dermatitis with intraepidermal neutrophilic pustules	Exacerbation of psoriasis	[54]
71-year-old male	Pfizer/BioNTech	2nd and 3rd dose	_/Vesicular and discoid eczema	Discoid plaques and multiple deep-seated vesicles on the palms and trunk Eczematous and weeping discoid plaques on the limbs and chest	Exacerbation of eczema	[55]
80-year-old female	Pfizer/BioNTech	3rd dose	Quiescent psoriasis/Guttate psoriasis	Scaly erythematous plaques and papules on lateral side of lower right limb	Exacerbation of psoriasis	[55]
65-year-old male	Pfizer/BioNTech	1st dose	Hepatocellular carcinoma/psoriasis	Erythematous scaly plaques on chest, abdomen, back and extremities	Exacerbation of psoriasis	[56]
51-year-old male	Pfizer/BioNTech	1st and 2nd dose	Plaque psoriasis/Plaque psoriasis	Confluent, erythematous, scaly, thick plaques on knees, upper extremities, buttocks, trunk, thighs and legs	Exacerbation of psoriasis	[57]
52-year-old male	CoronaVac	2nd dose	Plaque psoriasis/Plaque psoriasis	Erythematous and scaly plaques on extremities, neck and trunk	Exacerbation of psoriasis	[57]
34-year-old female	Oxford/AstraZeneca	1st dose	Psoriasis vulgaris/Psoriasis vulgaris	Papules and plaques on trunk and extremities	Exacerbation of psoriasis	[58]
12 patients	Pfizer/BioNTech Oxford/AstraZeneca	1st or 2nd dose	Plaque psoriasis or pustular psoriasis/Plaque psoriasis or pustular psoriasis	_	Exacerbation of psoriasis	[59]

89-year-old male	Moderna	2nd dose	_/psoriasis	1. lesions on the scalp, torso, arms, legs 2. 60% body surface area	Developing of psoriasis	[60]
6 patients	Moderna (5 cases) Pfizer/BioNTech (1 case)	1st and 2nd dose (1 case) 2nd dose (5 cases)	_	_	Exacerbation of psoriasis	[60]
14 patients	Pfizer/BioNTech Oxford/AstraZeneca Moderna	1st or 2nd dose	13 cases plaque psoriasis and 1 case guttate psoriasis/plaque psoriasis	Generalized papulosquamous rash	Exacerbation of psoriasis	[61]
11 patients	Pfizer/BioNTech Oxford/AstraZeneca Moderna	Mainly 2nd dose	10 cases plaque and 1 case guttate psoriasis/plaque or guttate psoriasis	_	Exacerbation of psoriasis	[62]
51 patients	Moderna Oxford/AstraZeneca	_	Psoriasis/psoriatic arthritis or guttate psoriasis	Erythematous scaly patches Increase in PASI index	Exacerbation of psoriasis/changing type of psoriasis	[63]
72-year-old male	CoronaVac	1st dose	Plaque psoriasis/generalized pustular psoriasis	Ddesquamation, diffuse erythema and coalescing pustules all over the body	Changing type of psoriasis	[64]
57-year-old male	Pfizer/BioNTech	_	Plaque psoriasis/palmo plantar psoriasis	_	Changing type of psoriasis	[65]
63-year-old female	Pfizer/BioNTech	_	Plaque psoriasis/Pustular plantar psoriasis	_	Changing type of psoriasis	[65]
83-year-old female	Pfizer/BioNTech	2nd dose	Palmoplantar psoriasis/ Psoriatic arthritis	Stiffness, swelling and desquamation of palmar skin of hands Edema on the back of left hand and wrist joint.	Changing type of psoriasis	[66]
58 patients	Moderna Janssen Pfizer/BioNTech Oxford/AstraZeneca	1st or 2nd dose	_	Erythematous plaques, silvery scale Epidermal acanthosis, confluent parakeratosis with trapped neutrophils and focal spongiform pustules Reduced thickness of the granular layer in the trunk, extremities, head, neck and face	Exacerbation of psoriasis	[82]

5.2.2 Oxford/AstraZeneca Vaccine

There have also been reports of exacerbated psoriasis conditions linked to vaccination with the AstraZeneca vaccine. For example, Fang et al. reported a case of a 34-year-old woman with a history of psoriasis who was being treated successfully with biologic and immunosuppressant drugs [58]. One week after being injected with the first dose of the AstraZeneca vaccine, an erythematous scaly plaque was seen around the injection site and psoriasis plaques developed on her trunk and extremities. Another case presented by Nagrani et al. described a 56-year-old woman with a history of psoriasis who showed a flare-up of psoriatic lesions after receiving her first dose of the Covishield version of the AstraZeneca vaccine [46].

5.2.3 Studies Carried Out at Single Centres

In a retrospective study, Koumaki et al. identified 12 patients at a single centre who showed an exacerbation in their psoriasis condition after receiving either the Pfizer-BioNTech or AstraZeneca vaccine [59]. Likewise, Wei et al. carried out a retrospective analysis at a single centre in New York to investigate cases of new-onset or exacerbation of existing psoriasis after COVID-19 vaccination [60]. They identified 7 patients who showed new onset or psoriasis flare-ups of pre-existing psoriasis after receiving either the Modena or Pfizer-BioNTech mRNA vaccines. Sotiriou et al. reported 14 cases of psoriasis flares from a single centre after patients were vaccinated with either of the Pfizer, Moderna or AstraZeneca vaccines [61]. Similarly, Megna et al. reported on 11 cases of psoriasis exacerbation over a 6-month period in early 2021 following vaccination with Pfizer-BioNTech, Moderna or Oxford-AstraZeneca vaccines [62].

In a larger study, Huang et al. recruited 32 volunteers with psoriasis who had never been immunized and 51 psoriasis patients who had been vaccinated who had been vaccinated with either the Moderna or AstraZeneca vaccine [63]. They observed 15 cases of exacerbations that occurred within 9 days of vaccination compared to two cases in the non-vaccinated control group. Taken together these results suggest that there is some risk of flare-ups or exacerbations of pre-existing psoriasis conditions following the administration of many of the COVID-19 vaccines.

5.3 COVID-19 Vaccination Changing Type of Psoriasis

Onsun et al. reported on a case involving a 72-year-old male patient with a history of plaque psoriasis using a topical treatment for his condition [64]. Four days after receiving the first dose of the CoronaVac vaccine, he manifested a number of alterations in his condition including desquamation, diffuse erythema and coalescing pustules. Another study showed that two cases of mild plaque-type psoriasis appeared to develop into the pustular palmoplantar psoriasis form one month after

administration of the Pfizer-BioNTech vaccine [65]. Finally, Quattrini et al. reported the case of an 83-year-old female with a history of palmoplantar psoriasis. Two days after being administered her second dose of the Pfizer-BioNTech vaccine, she presented to the hospital with symptoms of stiffness, swelling and desquamation of palmar skin of both hands along with oedema on the back of the left hand and wrist [66].

6 Conclusions and Future Perspectives

The current vaccines currently approved by the WHO consist of four different types [67] which can be classified as:

1. mRNA (spike protein)
   (a) Comirnaty (Pfizer/BioNTech)
   (b) Spikevax (Moderna)
2. Viral vector (spike protein)
   (a) Vaxzevria (Oxford/AstraZeneca)
   (b) Covishield (Oxford/AstraZeneca)
   (c) Jcovden (Janssen),
   (d) Convidecia (CanSino)
3. Inactivated virus
   (a) Covilo (Sinopharm)
   (b) CoronaVac (Sinovac)
   (c) Covaxin (Bharat Biotech)
4. Recombinant spike protein
   (a) COVOVAX (Novavax)
   (b) Nuvaxovid (Novavax)

In addition, there are adapted bivalent versions of authorized COVID-19 vaccines from Pfizer/BioNTech and Moderna Biotech using the mRNA spike protein strategy for broader protection against the variants [68]:

1. Pfizer/BioNTech
   (a) Comirnaty bivalent – Original + Omicron BA.1 spike protein (Authorized: September 1, 2022)
   (b) Comirnaty bivalent – Original + Omicron BA.4-5 (Authorized: September 9, 2022)
2. Moderna Biotech
   (a) Spikevax bivalent Original/Omicron BA.1 (Authorized: September 1, 2022)
   (b) Spikevax bivalent Original/Omicron BA.4-5 (Under evaluation: from September 26, 2022)

Like all medications, vaccines can cause side effects such as psoriasis [50, 69]. Since the COVID-19 vaccines work in different ways, this is likely to occur via some overlapping and some distinct mechanisms. However, this review revealed that most of the above types of COVID-19 vaccines were associated with psoriatic side effects. Also, given that psoriasis cases were reported in response to SARS-CoV-2 infections before the COVID-19 vaccines were rolled out [15–18], a likely common mechanism is through perturbations in immune and/or inflammatory pathways, including potential autoimmune responses [19–23]. This suggests that individuals with pre-existing psoriasis or other autoimmune-related conditions should be advised and then monitored for worsening of their conditions after a COVID-19 infection or vaccination. In cases where a de novo eruption or exacerbation does occur, treatment with some biologics, immunosuppressive agents and anti-inflammatory drugs can be helpful [21, 70, 71]. However, some of these could also lead to a worsening of the condition, which suggests that techniques for monitoring potential autoimmune and pro-inflammatory effects should be applied.

Four psoriasis-associated autoantigens have been identified as cathelicidin LL-37, melanocyte A disintegrin-like and metalloprotease domain containing thrombospondin type 1 motif-like 5 (ADAMTSL5), phospholipase A2 group IVD (PLA2G4D) and keratin 17, and autoreactive T cells against these have been found in some psoriasis patients [72]. Another study reported on the discovery of autoantibodies against LL-37 and ADAMTSL5 associated with both psoriasis and psoriatic arthritis, suggesting a potential role of these autoantibodies in disease pathogenesis [73]. We suggest the use of screening panels for monitoring the levels of these and other autoantibodies, using platforms such as those developed by the German companies CellTrend [74] and EUROIMMUN [75]. Other technologies such as multiplex immunoassay [76] and cytokine arrays [77] could be used to detect inflammation-related changes for disease detection and monitoring. For more rapid analyses in a doctor's office or clinic, lab-on-a-chip devices incorporating rapid and sensitive tests for some of these biomarkers could be employed for point-of-care-testing [78–80].

At this stage, no specific emphasis can be given on the cause of psoriasis onset or exacerbation based on the type of COVID-19 vaccine. The matter is further complicated by the fact that some cases were apparently caused in people who did not have a history of psoriasis, and some existing psoriasis cases had received biological or immunosuppressant drug therapies, while others were in remission. In addition, where cases emerged or were exacerbated, these varied in their degree of severity or chronicity. Also, the low severity of the disease in some cases was so low that receiving an emollient was sufficient for the symptom relief. Furthermore, 0.1–0.5% of the European population have reported any adverse responses associated with a COVID-19 vaccination [81].

Considering that cutaneous reactions to COVID-19 vaccination are rare and, when they do occur, they are mostly minor and self-limiting, there is a general consensus that the benefits of vaccination outweigh the potential risks of experiencing such side effects [63, 82–86]. This is especially true since bivalent vaccines are now available which are capable of neutralizing the highly infectious omicron variant,

maximizing the benefit-to-risk ratio. Nevertheless, healthcare workers administering the vaccines must be made aware of these potential risks and advise the recipients accordingly. To add an extra layer of safety, careful monitoring for potentially deleterious autoimmune and hyperinflammatory responses can be employed. These can include screening for the presence of autoantibodies and inflammation-related molecules for both risk assessment and for monitoring patient responses to either COVID-19 infection, COVID-19 vaccination or biologic and anti-inflammatory treatments.

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