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Effect of COVID-19 (SARS-CoV-2) Vaccination on Patients with Atopic Dermatitis Treated with Dupilumab: A Multicenter, Observational Study

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Background: Atopic dermatitis (AD) patients usually wonder if their condition will worsen after vaccination or if they should continue with the treatment they are receiving. Considering that many patients treated with dupilumab had previously experienced severe AD symptoms and flares, the concerns are more understandable.
Objective: This study aimed to investigate the safety of the coronavirus disease 2019 (COVID-19) vaccination in patients with AD treated with dupilumab.
Methods: We enrolled 133 patients (101 dupilumab-treated and 32 systemic oral agents-treated as control group) with AD from six hospitals. Patients were asked about worsening pruritus and AD (5-point Likert scale) after vaccination. AD variables (eczema area and severity index [EASI], investigator's global assessment [IGA], itch numerical rating scale [NRS], sleep NRS, and patient-oriented eczema measure [POEM]) were compared pre- and post-vaccination. Adverse reactions to the COVID-19 vaccination were observed.
Results: The incidence of adverse reactions to COVID-19 vaccines and worsening AD symptoms in dupilumab-treated patients were not significantly different compared with that in the control group. The itch NRS score increased significantly after vaccination ($p<0.001$). However, there were no statistically significant differences between the pre-and post-EASI, IGA, and POEM scores. Eight patients (7.9%) had worse EASI scores and required rescue therapy; however, most were easily managed with low-dose steroids or topical agents. None of the patients discontinued dupilumab treatment.
Conclusion: No serious adverse reactions were observed in patients with AD after COVID-19 vaccination. Exacerbation of pruritus and AD symptoms was observed but was mostly mild and transient.

Keywords: Atopic dermatitis, COVID-19 vaccines, Dupilumab

INTRODUCTION

Vaccination is an important component of the current global effort to overcome the coronavirus disease 2019 (COVID-19) pandemic. Dermatologists are not free from questions related to vaccinations; patients with atopic dermatitis (AD) are aware of a predisposition to develop allergies, and wonder if their condition will worsen after vaccination, or if they should continue with the treatment they are receiving.

Dupilumab is a monoclonal antibody that targets the alpha subunit of the interleukin (IL)-13 receptor which has shown significant efficacy in patients with moderate-to-severe AD[1]. The current understanding and recommendations for COVID-19 show no indication that AD is a risk factor to alter

the vaccination schedule, and its potential to cause AD flare-up is unclear[2,3], while dupilumab is also not expected to cause vaccine attenuation[4]. However, considering that many patients treated with dupilumab have experienced moderate to severe AD symptoms and may have experienced flares, concerns regarding vaccination are understandable. Therefore, the aim of this study was to investigate whether the COVID-19 vaccines were safe for AD patients being treated with dupilumab, and whether vaccination caused a flare of AD symptoms in a real-world setting.

MATERIALS AND METHODS

Study design and population

This multicenter, observational study was conducted between July and October 2021 at six hospitals. Patients with AD aged ≥18 years who had been treating with dupilumab for at least 1 month and those who were vaccinated against COVID-19 within 2 weeks prior to the study were considered eligible. AD patients treated with systemic oral agents including cyclosporine or methotrexate of the same criteria were included as a control group. Patients taking concomitant topical steroids and oral antihistamines were included. Physicians evaluated the patients to determine the AD variables, and both demographic and clinical information was retrieved from the medical records. Patients who had insufficient medical records were excluded. The institutional review board of each participating site reviewed and approved the retrospective study protocol and waiver of informed consent (IRB number of the Chosun University Hospital: 2021-10-003).

Patient demographics included age, sex, underlying diseases, allergic disease history, and cutaneous allergic history. The checked records included an investigation of the type and dose of the vaccine, systemic and cutaneous adverse events, pruritus, any change in AD symptoms change (assessed on a 5-point Likert scale: much worse, worse, no change, better, much better), the type of aggravated AD symptoms (erythema, edema/papule, excoriation, dryness, lichenification), and its duration. If rescue therapy was performed due to worsening AD symptoms, treatment and progress were also collected.

The AD variables pre- and post-vaccination were compared by physicians. The eczema area and severity index (EASI), 5-point investigator's global assessment (IGA), itch numeric rating scale (NRS), sleep NRS, and patient-oriented eczema measure (POEM) were included. The primary endpoint was the change in EASI score, and the changes in IGA, itch NRS, sleep NRS and POEM were considered as the secondary endpoint.

Statistical analysis

Pearson's chi-square test and Fisher's exact test were performed to determine significant differences in demographic data, adverse events, and change in pruritus and AD symptoms between dupilumab-treated and control group patients. Independent sample t-test was used for the difference in mean age between both groups. The Wilcoxon signed-rank test was performed to determine if there were statistically significant differences in AD variables, including EASI, IGA, itch NRS, sleep NRS, and POEM between pre- and post-vaccination. Statistical analysis was performed using SPSS 22.0 (IBM Corp., Armonk, NY, USA), and a p-value <0.05 was considered statistically significant.

RESULTS

Patient characteristics

A total of 133 patients (n=101 for dupilumab-treated and n=32 for control group) were included. In the dupilumab-treated group, the mean age of the patients was 31.9 years (range, 18~54 years). Males (n=67, 66.3%) outnumbered females (n=34, 33.7%), and the underlying diseases included hypertension (n=3, 3.0%), hyperlipidemia (n=3, 3.0%), psychiatric disorders (n=2, 2.0%), and cataracts (n=2, 2.0%). Other histories of cutaneous diseases included urticarial eruption (n=5, 5.0%), and one patient had a history of drug rash caused by erythromycin. None of the patients had a history of anaphylactic reaction. The most common history of allergic disease was allergic rhinitis (n=50, 49.5%), followed by allergic conjunctivitis (n=19, 18.8%), and asthma (n=12, 11.9%). The most commonly administered vaccine was Pfizer-BioNTech (BNT162b2) (n=71, 70.3%), followed by Moderna (mRNA-1273) (n=22, 21.8%) and Janssen (Ad26.COV2.S) (n=7, 6.9%). The first dose was administered to 77 patients (n=77, 76.2%) In the control group, 31 patients were treated with cyclosporine (100~200 mg/day) and 1 patient was treated with methotrexate (15 mg/week). The mean age of the patients was 29.3 years (range, 18~57 years) and there was no statistically significant difference with the dupilumab-treated group in sex, underlying disease, allergic disease history, vaccine type and dose (Table 1).

Adverse events

In the dupilumab-treated group, the most common complaint of systemic reactions after vaccination was myalgia (n=47, 46.5%), followed by fatigue/malaise (n=18, 17.5%), and fever/chills (n=15, 14.9%). The most common cutaneous reactions were injection site swelling and urticarial eruption in six patients (n=6, 5.9%). In the control group, the most complaint of systemic reaction and cutaneous reaction after vaccination were myalgia (n=15, 46.9%) and injection site erythema (n=2, 6.3%), respectively. There was no statistically significant difference between both groups in adverse events (Table 2). None of the patients experienced an anaphylactic reaction.

Change of pruritus and AD symptoms reported by patients

In the dupilumab-treated group, pruritus and AD symptoms worsened after vaccination in 23.8% and 25.7% of patients, respectively. Assessment of the 26 patients who answered that AD symptoms worsened, showed that erythema accounted for 88.5%, papule/edema 69.2%, dryness and excoriation 50.0%, and lichenification 38.5% (Table 3). Regarding the course of worsening symptoms, 61.5% of patients improved without treatment and 19.2% improved after treatment, including oral low-dose steroid (4~8 mg methylprednisolone/day), antihistamines, and topical corticosteroids. The rest of them did not improve immediately, but it was well controlled over time. The mean duration of aggravated AD symptoms was 6.1 days. None of the patients discontinued dupilumab treatment. In the control group, pruritus and AD symptoms worsened in 25.0% of patients. Assessment of the 8 patients who answered that AD symptoms worsened, showed that erythema accounted for 87.5%, followed by papule/edema and excoriation 75.0%. There was no statistically significant difference between both groups in pruritus and AD symptoms change by patients (Table 3).

Table 1. Demographic data of the patients

Variable	Dupilumab-treated group (n=101)	Control group (n=32)*	*p*-value
Age (yr)	31.9 (18~54)	29.3 (18~57)	0.181†
Sex			0.559‡
Male	67 (66.3)	23 (71.9)	
Female	34 (33.7)	9 (28.1)	
Underlying disease			
Hypertension	3 (3.0)	0 (0)	>0.999§
Diabetes mellitus	1 (1.0)	1 (3.1)	0.425§
Hyperlipidemia	3 (3.0)	0 (0)	>0.999§
Psychiatric disorder	2 (2.0)	0 (0)	>0.999§
Cataract	2 (2.0)	0 (0)	>0.999§
Allergic disease history			
Allergic rhinitis	50 (49.5)	19 (59.4)	0.418‡
Allergic conjunctivitis	19 (18.8)	4 (12.5)	0.593§
Asthma	12 (11.9)	6 (18.8)	0.322‡
Vaccine type			0.292‡
Pfizer-BioNTech (BNT162b2)	71 (70.3)	26 (81.3)	
Moderna (mRNA-1273)	22 (21.8)	3 (9.4)	
Janssen (Ad26.COV2.S)	7 (6.9)	2 (6.3)	
Astrazeneca (ChadOx1 nCoV-19)	1 (1.0)	1 (3.1)	
Dose			0.064‡
First dose	77 (76.2)	19 (59.4)	
Second dose	24 (23.8)	13 (40.6)	

Values are presented as mean (range) or number (%). *Included atopic dermatitis patients treated with cyclosporine (n=31) and methotrexate (n=1). †Independent sample t-test. ‡Pearson's chi-square test. §Fisher's exact test.

Table 2. Adverse events after COVID-19 vaccination

Variable	Dupilumab-treated group (n=101)	Control group (n=32)*	*p*-value
Systemic reactions			
Fever/chill	15 (14.9)	5 (15.6)	0.915†
Fatigue/malaise	18 (17.8)	6 (18.8)	0.905†
Headache	12 (11.9)	4 (12.5)	>0.999‡
Myalgia	47 (46.5)	15 (46.9)	0.849†
Arthralgia	6 (5.9)	0 (0)	0.335‡
Nausea	4 (4.0)	3 (9.4)	0.358‡
Cutaneous reactions			
Injection site swelling	6 (5.9)	1 (3.1)	>0.999‡
Urticarial eruption	6 (5.9)	0 (0)	0.335‡
Eczematous eruption	2 (2.0)	0 (0)	>0.999‡
Injection site erythema	1 (0.9)	2 (6.3)	0.144‡

Values are presented as number (%). *Included atopic dermatitis patients treated with cyclosporine (n=31) and methotrexate (n=1). †Pearson's chi-square test. ‡Fisher's exact test.

Change of AD variables

When comparing mean scores before and after vaccination, the primary endpoint (EASI score) improved from 6.42 to 6.07, but the difference was not statistically significant in the dupilumab-treated group. The secondary endpoint including IGA, sleep NRS and POEM changed after vaccination, but the differences were not statistically significant. The itch NRS score increased significantly after vaccination ($p<0.001$) (Table 4). Eleven patients had an itch NRS score of 3 points or more, of whom seven patients were female, showing a higher proportion than the entire study population. Of the patients with NRS≥3, except for one who received the Janssen vaccine, the remaining 10 patients were all vaccinated with the Pfizer vaccine. Eight patients (7.9%) had a worsened EASI score and required rescue therapy, which was considered an AD flare. In the control group, the primary endpoint (EASI score) improved from 13.8 to 13.0. The secondary endpoint including itch NRS score, and POEM score improved from 4.6 to 4.4, and 13.5 to 12.1, respectively. IGA and sleep NRS were slightly increased, from 2.31 to 2.41 and 2.81 to 3.03, respectively. However, all the differences were not statistically significant.

Table 3. Change in pruritus and AD symptoms reported by patients

Variable	Dupilumab-treated group (n=101)	Control group (n=32)*	*p*-value
Change of pruritus			0.618§
Much better	0 (0)	0 (0)	
Better	0 (0)	0 (0)	
No change	77 (76.2)	24 (75.0)	
Worse	23 (22.8)	7 (21.9)	
Much worse	1 (1.0)	1 (3.1)	
Change of AD symptoms			>0.999§
Much better	0 (0)	0 (0)	
Better	3 (3.0)	1 (3.1)	
No change	72 (71.3)	23 (71.9)	
Worse	25 (24.8)	8 (25.0)	
Much worse	1 (1.0)	0 (0)	
Aggravated AD symptoms†			
Erythema	23 (88.5)	7 (87.5)	0.314‡
Papule/edema	18 (69.2)	5 (62.5)	0.722‡
Dryness	13 (50.0)	2 (25.0)	0.257§
Excoriation	13 (50.0)	6 (75.0)	0.213‡
Lichenification	10 (38.5)	3 (37.5)	>0.999§

Values are presented as number (%). AD: atopic dermatitis. *Included atopic dermatitis patients treated with cyclosporine (n=31) and methotrexate (n=1). †Based on the results of allowing multiple answers in patients who reported that their AD symptoms worsened (much worse or worse). ‡Pearson's chi-square test. §Fisher's exact test.

Table 4. Change in each AD variables in the dupilumab-treated group

Variable	Pre-vaccination	Post-vaccination	*p*-value
EASI	6.42±6.06	6.07±4.95	0.321
IGA	1.76±0.88	1.71±0.86	0.275
Itch NRS	2.57±2.08	3.08±2.25	<0.001
Sleep NRS	1.87±2.77	2.02±2.74	0.522
POEM	7.53±6.43	7.56±5.86	0.861

Values are presented as mean±standard deviation. AD: atopic dermatitis, EASI: eczema area and severity index, IGA: investigator's global assessment, NRS: numeric rating scale, POEM: patient-oriented eczema measure.

DISCUSSION

The major concerns of dermatology patients receiving COVID-19 vaccines are adverse events, including cutaneous reactions, and the worsening of underlying skin diseases. Safety

issues associated with COVID-19 vaccines have been extensively reported; these issues depend on the type of vaccine, and include systemic and local reactions. In a clinical trial of the Pfizer vaccine[5] in patients aged 16 to 55 years of age, the systemic reaction (first/second dose) was 4%/16% for fever, 47%/59% for fatigue, 42%/52% for headache, and 21%/37% for myalgia. Meanwhile, in a clinical trial of the Moderna vaccine[6], the systemic reactions were 0.5%/16% for fever, 37%/66% for fatigue, 33%/59% for headache, and 22%/58% for myalgia. Compared to the above results, the systemic reactions in this study showed similar or lower rates of fever, fatigue, headache, and myalgia (15%, 18%, 12%, and 47%, respectively) in the dupilumab-treated patients. The most common cutaneous adverse events of COVID vaccination are local injection site reactions, including erythema, swelling, tenderness, and pain[7]. Erythema and swelling at the injection site have been reported in up to 9% and 12% of participants, respectively, in clinical studies of Pfizer[5], Moderna[6], and Janssen[8] vaccines. In this study, erythema and swelling were observed in 0.6% and 6% of dupilumab-treated patients, respectively. Serious adverse reactions were not observed. The above results show that patients with AD treated with dupilumab do not significantly differ from healthy individuals in terms of COVID-19 vaccine safety. Furthermore, there was no significant difference in AD patients treated with dupilumab compared to the group of patients treated with systemic oral agents in this study. A retrospective cohort analysis in 55 healthcare organizations has demonstrated that COVID-19 vaccinated AD patients, even those receiving immunomodulatory treatment, did not have significant differences in adverse events compared to controls[9]. Urticarial-like eruption was observed in 6 patients (5.9%) of this study. It is important to differentiate whether urticarial eruption occurs immediately within 4-hour after vaccination because it may be an immunoglobulin E-medicated (type 1) allergic reaction[10]. This is most likely due to the vaccine ingredient, and if it occurred in the first dose, it could be a potential contraindication of the second dose of the same vaccine[11]. However, none of the patients in this study experienced immediate reaction, angioedema, or anaphylaxis. Furthermore, there is a view that allergic cutaneous symptoms such as urticarial eruption may not be an allergy to the vaccine, but may instead be an immune response to nonsteroidal anti-inflammatory agents taken due to fever or pain after vaccination[11]. Delayed local hypersensitivity reactions with erythema, induration, and pain may occur approximately one week after vaccination[12], but this was not observed in this study.

Many cases of underlying dermatologic diseases flared after COVID vaccination have been reported. In a registry-based study analyzing the 414 cutaneous manifestations of mRNA COVID-19 vaccines (Pfizer and Moderna), the flares of underlying dermatology conditions included herpes simplex virus (HSV) (4 cases), AD (2 cases), and psoriasis (2 cases)[11]. In a nationwide Spanish cross-sectional study, among 405 cutaneous manifestations, flare/reactivation of skin diseases were found to include cases of varicella zoster virus (41 cases), HSV (15 cases), and psoriasis (6 cases)[13]. There have also been reports of generalized eczematous reactions after Pfizer COVID-19 vaccination in patients with a personal or family history of atopy[14,15]. According to a study evaluating post-COVID-19 vaccination flares in 407 dupilumab-treated AD patients[16], 11 patients (2.7%) reported exacerbation of EASI score or required rescue therapy. In all patients, the condition was controlled with topical corticosteroids or calcineurin inhibitors, and none of the patients discontinued dupilumab. In this study, the 8 patients with AD flares who had worsened EASI scores and received rescue therapy accounted for 7.9% of the patients. Similar to previous studies, all patients with AD flares were mostly controlled with low-dose steroids (4~8 mg methylprednisolone/day) or topical corticosteroids, and none of the patients discontinued vaccination or dupilumab. Additionally, in this study, the absence of a statistically significant difference in EASI and IGA before and after vaccination suggests that COVID-19 vaccination may not be discouraged in patients with AD treated with dupilumab.

Indeed, an essential feature of AD is that it is a disease with a chronic or relapsing course[17]. Various triggers may be involved, but whether vaccines have an effect has been debated. Although previous studies have shown that live attenuated vaccines affect AD relapse or complications, such as eczema herpeticum[18,19], COVID-19 vaccines are non-live vaccines. Although it is known that egg-related allergic reactions are high in patients with AD[20], COVID-19 vaccines are not egg-based and therefore do not carry this risk. In addition, the currently used COVID-19 vaccine is relatively safe and stable because it is based on a non-replicating recombinant viral vector that cannot replicate inside the host cell[21,22]. However, the self-replicating viral vector based COVID-19 vaccines are in clinical trials[22], future vaccines may have different effects.

Consequently, relapsing patterns or exacerbations of AD after vaccination are most likely coincidental rather than vaccine-related. However, in this study, the results showed that 26 patients (25.8%) reported that their AD symptoms had worsened, representing a higher proportion than those diagnosed by their physicians as AD flares. This result may reflect the patient's concerns and sensitive psychological state that their skin disease can worsen after vaccination. From this point of view, informed discussion and reassurance of dermatologists with their AD patients may play an important role in the control of AD symptoms after vaccination. As such, it may be necessary to recognize that pruritus control may be required considering dupilumab-treated patients showed increase in itch NRS ($p<0.001$) after vaccination, and 24 patients (23.8%) reported that pruritus worsened.

Another major concern for AD patients who will be vaccinated against COVID-19 is the reduced efficacy of the immune response. No studies have yet demonstrated changes in the immune response to COVID-19 vaccines in patients with AD. According to the available results of studies with other vaccines, an open label study of 336 AD and non-AD patients showed similar seroprotection rates for either influenza B, H1N1, or H3N2 when inoculated by intradermal inection[23]. In addition, the study demonstrated that the immune response was reduced by intradermal injection rather than intramuscular injection in AD patients colonized with *Staphylococcus aureus*[23]. However, since the COVID-19 vaccines are administered by intramuscular injection, there is no such risk factor. A randomized, double-blinded study with dupilumab or placebo in AD patients showed similar positive immune responses to non-live vaccines, including tetanus and meningococcal polysaccharides[4]. Because dupilumab acts on the type 2 cytokines IL-4 and IL-13, it is different from the main cytokine profile of the COVID-19 vaccine immune response of CD4+ or CD8+ T cells[24]. As a result, neither the atopic status or dupilumab treatment appears to have a significant effect on COVID-19 vaccine-induced immunity, but further studies are needed to demonstrate this.

As for the time-lag between COVID-19 vaccination and dupilumab injection, the authors believed that the time-lag would not be important, based on the results of this study and the above literature reviews. However, if patients are concerned about it, dermatologists may recommend that the best time-lag between COVID-19 vaccination with dupilumab injection could be one week because dupilumab is administrated every two weeks, so that half time point may minimize the impact of the COVID-19 vaccine[25].

This study had some limitations. Most of the patients' data were collected after the first dose; therefore, there is a possibility that adverse events or worsening of AD symptoms may not be fully reflected in this study. In addition, the generalizability of AD patients may be limited because most subjects were patients whose AD symptoms were well controlled with dupilumab and all participating hospitals were university or general hospitals.

In conclusion, this study was significant in that AD patients treated with dupilumab did not show significant differences in adverse event or AD symptoms change after COVID-19 vaccination compared to AD patients treated with systemic oral agents or the general population in a real-world setting. Some patients experienced exacerbation of pruritus and AD symptoms, but most were mild and transient. As ongoing vaccination against different strains is likely to be recommended under the impact of the COVID-19 pandemic, the authors believe that the results of this study will help to understand and explain to patients with AD who are about to be vaccinated or who have undergone vaccination.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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DATA SHARING STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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REFERENCES

1. Lee DH, Ko HC, Na CH, Roh JY, Park KY, Park YL, et al. Real-world experience of long-term dupilumab treatment for atopic dermatitis in Korea. Ann Dermatol 2022;34:157-160.
2. Ring J, Worm M, Wollenberg A, Thyssen JP, Jakob T, Klimek L, et al. Risk of severe allergic reactions to COVID-19 vaccines among patients with allergic skin diseases - practical recommendations. A position statement of ETFAD with external experts. J Eur Acad Dermatol Venereol 2021;35:e362-e365.
3. Thyssen JP, Vestergaard C, Barbarot S, de Bruin-Weller MS, Bieber T, Taieb A, et al. European Task Force on Atopic Dermatitis: position on vaccination of adult patients with atopic dermatitis against COVID-19 (SARS-CoV-2) being treated with systemic medication and biologics. J Eur Acad Dermatol Venereol 2021;35:e308-e311.
4. Blauvelt A, Simpson EL, Tyring SK, Purcell LA, Shumel B, Petro CD, et al. Dupilumab does not affect correlates of vaccine-induced immunity: a randomized, placebo-controlled trial in adults with moderate-to-severe atopic dermatitis. J Am Acad Dermatol 2019;80:158-167.e1.
5. Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, et al. Safety and efficacy of the BNT162b2 mRNA COVID-19 vaccine. N Engl J Med 2020;383:2603-2615.
6. Baden LR, El Sahly HM, Essink B, Kotloff K, Frey S, Novak R, et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. N Engl J Med 2021;384:403-416.
7. Sun Q, Fathy R, McMahon DE, Freeman EE. COVID-19 vaccines and the skin: the landscape of cutaneous vaccine reactions worldwide. Dermatol Clin 2021;39:653-673.
8. Sadoff J, Gray G, Vandebosch A, Cárdenas V, Shukarev G, Grinsztejn B, et al. Safety and efficacy of single-dose Ad26.COV2.S vaccine against COVID-19. N Engl J Med 2021;384:2187-2201.
9. Pakhchanian H, Raiker R, Wolf M, Trotter SC. Examining the risk of breakthrough infection and COVID-19 vaccination safety in patients with atopic dermatitis. Br J Dermatol 2022;187:251-253.
10. Gambichler T, Boms S, Susok L, Dickel H, Finis C, Abu Rached N, et al. Cutaneous findings following COVID-19 vaccination: review of world literature and own experience. J Eur Acad Dermatol Venereol 2022;36:172-180.
11. McMahon DE, Amerson E, Rosenbach M, Lipoff JB, Moustafa D, Tyagi A, et al. Cutaneous reactions reported after Moderna and Pfizer COVID-19 vaccination: a registry-based study of 414 cases. J Am Acad Dermatol 2021;85:46-55.
12. Bellinato F, Maurelli M, Gisondi P, Girolomoni G. Cutaneous adverse reactions associated with SARS-CoV-2 vaccines. J Clin Med 2021;10:5344.
13. Català A, Muñoz-Santos C, Galván-Casas C, Roncero Riesco M, Revilla Nebreda D, Solá-Truyols A, et al. Cutaneous reactions after SARS-CoV-2 vaccination: a cross-sectional Spanish nationwide study of 405 cases. Br J Dermatol 2022;186:142-152.
14. Corbeddu M, Diociaiuti A, Vinci MR, Santoro A, Camisa V, Zaffina S, et al. Transient cutaneous manifestations after administration of Pfizer-BioNTech COVID-19 Vaccine: an Italian single-centre case series. J Eur Acad Dermatol Venereol 2021;35:e483-e485.
15. Leasure AC, Cowper SE, McNiff J, Cohen JM. Generalized eczematous reactions to the Pfizer-BioNTech COVID-19 vaccine. J Eur Acad Dermatol Venereol 2021;35:e716-e717.
16. Potestio L, Napolitano M, Bennardo L, Fabbrocini G, Patruno C. Atopic dermatitis exacerbation after COVID-19 vaccination in Dupilumab-treated patients. J Eur Acad Dermatol Venereol 2022;36:e409-e411.
17. Abuabara K, Margolis DJ, Langan SM. The long-term course of atopic dermatitis. Dermatol Clin 2017;35:291-297.
18. Reed JL, Scott DE, Bray M. Eczema vaccinatum. Clin Infect Dis 2012;54:832-840.
19. Simonetti O, Radi G, Molinelli E, Rizzetto G, Diotallevi F, Offidani A. Recommendations for dermatologists treating patients with atopic dermatitis during the Covid-19 pandemic: a look into the past for a conscious vaccination management. Hum Vaccin Immunother 2021;17:3268-3275.
20. Martorell A, Alonso E, Boné J, Echeverría L, López MC, Martín F, et al. Position document: IgE-mediated allergy to egg protein. Allergol Immunopathol (Madr) 2013;41:320-336.
21. Robert-Guroff M. Replicating and non-replicating viral vectors for vaccine development. Curr Opin Biotechnol 2007;18:546-556.
22. Chavda VP, Bezbaruah R, Athalye M, Parikh PK, Chhipa AS, Patel S, et al. Replicating viral vector-based vaccines for COVID-19: potential avenue in vaccination arena. Viruses 2022;14:759.
23. Leung DYM, Jepson B, Beck LA, Hanifin JM, Schneider LC, Paller

AS, et al. A clinical trial of intradermal and intramuscular seasonal influenza vaccination in patients with atopic dermatitis. J Allergy Clin Immunol 2017;139:1575-1582.e8.

24. Law JC, Koh WH, Budylowski P, Lin J, Yue F, Abe KT, et al. Systematic examination of antigen-specific recall T cell responses to SARS-CoV-2 versus influenza virus reveals a distinct inflammatory profile. J Immunol 2021;206:37-50.

25. Pfaar O, Klimek L, Hamelmann E, Kleine-Tebbe J, Taube C, Wagenmann M, et al. COVID-19 vaccination of patients with allergies and type-2 inflammation with concurrent antibody therapy (biologicals) - a position paper of the German Society of Allergology and Clinical Immunology (DGAKI) and the German Society for Applied Allergology (AeDA). Allergol Select 2021;5:140-147.