Acta Dermatovenerol APA

Acta Dermatovenerologica
Alpina, Pannonica et Adriatica

2021;30:67-69
doi: 10.15570/actaapa.2021.16

Vaccines for COVID-19 in patients with atopic dermatitis: three things every dermatologist should know

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Abstract

Almost 13 months have passed since the World Health Organization (WHO) declared the coronavirus disease 19 (COVID-19) pandemic, caused by the SARS-CoV-2, on March 11th, 2020. During this period, we have realized that the most effective weapon we have to prevent SARS-CoV-2 infection, or to make it less aggressive, is vaccines. Currently, according to the WHO document "Draft landscape of COVID-19 candidate vaccines," there are 275 vaccines in development against the virus, although at the moment there are four preparations in distribution in the United States and in Europe. The characteristics of these vaccines are quite different from each other and may even be unfamiliar in the medical field. In particular, among dermatologists, knowledge of vaccines is of fundamental importance, especially in atopic dermatitis. Atopic patients are aware of having a predisposition to develop allergies, and so they are asking dermatologists about the safety of the vaccines currently available against the SARS-CoV-2. This article provides an up-to-date overview of this topic by reviewing current literature and sharing our personal experience.

Keywords: coronavirus, SARS-CoV-2, dermatology, atopic dermatitis, immunization

Received: 2 March 2021 | **Returned for modification:** 19 April 2021 | **Accepted:** 5 May 2021

Introduction

The most effective weapon we have to prevent SARS-CoV-2 infection, or to make it less aggressive, is vaccines. Currently, according to the document "Draft landscape of COVID-19 candidate vaccines," there are 275 vaccines in development against the virus, although there are currently three preparations authorized by both the Food and Drug Administration (FDA) and the European Medicines Agency (EMA) for emergency use, produced by Pfizer-BioNTech®, Moderna®, and Janssen®, respectively, and one preparation currently authorized only by the EMA, which is the vaccine produced by AstraZeneca® (1).

There is a strong emerging need to understand the crucial role of the vaccine for all clinicians, including dermatologists, who should focus attention on the need to vaccinate patients with atopic dermatitis (AD), considering vaccine timing with respect to therapies in progress in atopic patients. Atopic patients are aware that they have a predisposition to develop allergies, and so they are asking dermatologists whether safety information is available for the vaccines currently available against SARS-CoV-2 (2–3). This article briefly reviews three things that dermatologists should know about COVID-19 vaccines to be better prepared for managing AD patients.

What are the characteristics of the vaccines available against SARS-CoV-2?

The first two vaccines developed against COVID-19 currently authorized by the FDA and EMA are BNT162 (Comirnaty®) and mRNA-1273, produced by Pfizer/BioNTech® and Moderna®, respectively (Table 1). They consist of a lipid nanoparticle–formulated, nucleoside-modified RNA (modRNA) encoding the SARS-CoV-2 full-length spike, capable of eliciting high SARS-CoV-2 neutralizing antibody titers and robust antigen-specific CD8+ and Th1-type CD4+ T-cell responses (4–5).

The advantage of mRNA vaccines is that they are easily producible and have a low cost, but they require storage at low temperatures. In particular, the Pfizer vaccine requires storage at a temperature between –60 °C and –90 °C, whereas the Moderna vaccine requires a storage temperature between –25 °C and –15 °C. The storage temperature of the Moderna vaccine is therefore the temperature of a standard freezer, which is much more available than the ultra-cold deep freezers needed for storage of the Pfizer vaccine (6). According to data published by the two companies, the two vaccines seem to have an efficacy of about 95% (7, 8).

The other two vaccines approved by both the FDA and the EMA, and by the FDA only, respectively, are Ad26.CoV2.S and AZD1222,

Table 1 | **Features of the four vaccines against SARS-CoV-2 (1).**

COVID-19 vaccine developer/ manufacturer	Vaccine platform	Type of candidate vaccine	Number of doses	Timing of doses	Route of administration
Moderna / NIAID	RNA	LNP-encapsulated mRNA	2	28 days apart	Intramuscular
BioNTech / Fosun Pharma / Pfizer	RNA	3 LNP-mRNAs	2	21 days apart	Intramuscular
Janssen Pharmaceutical Companies	Non-replicating viral vector	Adenovirus type 26 vector	1	Single dose	Intramuscular
University of Oxford / AstraZeneca	Non-replicating viral vector	ChAdOx1-S or AZD1222	2	4–12 weeks apart	Intramuscular

LNP = lipid nanoparticle.

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produced by Janssen Pharmaceutical Companies and the Universitiy of Oxford/AstraZeneca respectively (Table 1). These are "viral vector vaccines," and they work by providing cells with genetic instructions to make antigens. These vaccines are made from adenovirus vectors that have been genetically engineered so they cannot reproduce in the human body. They are also engineered to contain DNA sequences for the S protein. Once inside the vaccine recipient's cells, the DNA is transcribed into mRNA, which is then translated into a viral S protein just like the mRNA vaccines. Once this protein is produced, an immune response involving both innate and adaptive immunity is triggered, which can confer a certain level of protection from SARS-CoV-2 infection. Unlike mRNA vaccines, these two vaccines produced by Janssen and AstraZeneca do not need to be stored at extremely low temperatures but can be stored for at least 6 months in a refrigerator, at a temperature between 2 and 8 °C (9, 10).

Is it reasonable to believe that these vaccines can cause reactivation of eczema in subjects with atopic dermatitis?

AD is an immune-mediated inflammatory disease of the skin with a chronic relapsing course that affects 20% of children and 10% of adults (11, 12). It is often accompanied by increased serum IgE levels and a personal and family history of "atopic diathesis," which includes type 1 allergies, allergic rhinitis, and asthma. The pathogenesis of the disease is extremely complex, with a multifactorial etiology involving genetic, immunologic, and environmental factors that result in disruption of the skin barrier and the skin immune system (12).

Vaccines currently available against SARS-CoV-2 are only targeted toward the adult population (the Pfizer vaccine is available for those 16 years and older). The population of phase III studies conducted on COVID-19 vaccines does not include children, although children play an active role in the COVID-19 pandemic—not so much as victims of the virus, but as vectors of viral transmission (6–10, 13).

When and if a vaccine is available for children, however, parents of atopic patients should be reassured that 1) it is not expected that common childhood vaccines promote atopic disease, and any future development of atopic symptoms is most likely not related to vaccination but is coincidental, and 2) vaccines that have been associated with a relapse of AD or complications (not without discussion), such as eczema vaccinatum, belong to the category of live attenuated vaccines, a category different from the vaccines currently available (14–15).

In addition, unlike seasonal influenza vaccines, the vaccines currently available against SARS-CoV-2 are not egg-based, and so there is no risk of allergic reactions in atopic adults and children in whom the prevalence of egg sensitization and allergy is higher (16).

Regarding the hypothesis that atopic subjects have a different immunization risk to SARS-CoV-2 vaccine than non-atopic subjects, no data are available in the literature. The only available data are related to the seasonal influenza vaccine. A study by Leung et al. showed that seroprotection rates for influenza B, H1N1, and H3N2 were not different i) between participants with and without AD receiving intradermal vaccination and ii) between participants with AD receiving intradermal and intramuscular vaccination, respectively (17). In addition, after intradermal but not after intramuscular vaccination, participants with AD colonized with *Staphylococcus aureus* exhibited a reduced immune response to influenza vaccination compared with noncolonized participants. Because the majority of patients with AD are colonized with *S. aureus*, the authors have argued that intramuscular influenza vaccination should be given preference in these patients (17–18). This is reassuring because SARS-CoV-2 vaccines are administered intramuscularly.

In conclusion, there are no data to support a warranted fear of vaccines against SARS-CoV-2 in atopic patients.

Will atopic patients taking immunosuppressive drugs or dupilumab be able to receive the vaccine?

Unfortunately, data on the efficacy or safety of vaccines against COVID-19 in patients affected by chronic inflammatory diseases on immunosuppressive therapy are not available because these patients are naturally excluded from clinical trials. The only data in this type of population that can be extrapolated from the literature refer to other types of vaccines, such as the seasonal influenza vaccine (19).

Corticosteroids and many disease-modifying anti-rheumatic drugs (DMARDs) may contribute to reduced vaccine immunogenicity (19). For example, treatment with prednisone ≥ 10 mg/day equivalent doses have been shown to decrease humoral responses to influenza vaccines in patients with systemic lupus erythematosus (20). Likewise, methotrexate (MTX) reduced humoral responses to influenza and pneumococcal vaccines (21–23). To optimize the immunogenicity of inactivated vaccines in patients naive to immunosuppressive drug, Papp et al. suggested that immunization be performed, if possible, at least 2 weeks before the start of immunosuppressive therapy (19).

Because they do not belong to these categories of vaccines, the currently available vaccines for SARS-CoV-2 should not have this type of effect and are expected to be safe for patients on immunotherapeutics (20). It will be necessary to use a case-by-case approach to assess the risk-benefit ratio of a possible preventive discontinuation of immunosuppressive therapy before performing vaccination.

Dupilumab is a fully human monoclonal antibody that binds to the alpha subunit of the interleukin-4a (IL-4Ra) receptor, which inhibits both IL-4 and IL-13 signaling (24). Dupilumab has been shown to improve signs and symptoms of moderate-to-severe AD, asthma, eosinophilic esophagitis, and chronic sinusitis with nasal polyposis, and it is approved in the European Union, the United States, Japan, and other countries for the treatment of adults with moderate to severe AD in whom topical therapies are not recommended or do not adequately control the disease (25).

In this case as well, the only available data are related to other vaccines. In particular, Blauvelt et al. have conducted a phase 2, randomized, double-blinded, multicenter, placebo-controlled, parallel-group study, with the aim of evaluating the effects of tetanus toxoid with reduced diphtheria toxoid and acellular pertussis vaccine (Tdap) and quadrivalent meningococcal polysaccharide vaccine (MPSV4) in adult patients receiving dupilumab. They concluded that non-live vaccines such as Tdap and MPSV4 can be indicated as safe and are not immunogenic in adult patients with moderate to severe AD treated with dupilumab (26).

Because SARS-CoV-2 vaccines are mRNA or viral vector vaccines, there should be no additional risk in patients treated with dupilumab.

Conclusions

Further study will be required to define the safety and efficacy of SARS-CoV-2 vaccines in vulnerable populations. However, with the current state of knowledge and following an extensive review of the literature presented, there are no contraindications to vaccinating people with AD, either on immunosuppressive therapy or on dupilumab therapy.

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