

# Indian Dermatology Online Journal

[www.idoj.in](http://www.idoj.in)



Available as online and print editions



Publication of IADVL

## Recommendations for COVID Vaccination for Dermatological Patients on Immunosuppressive/Immunomodulatory Therapy (IADVL Academy)

### Abstract

Significant proportion of patients with dermatological disorders are on immunosuppressive or immunomodulatory therapy predisposing them to risk of acquisition of COVID-19 infection. However, the efficacy of COVID-19 vaccination among these patients is a matter of concern due to lack of adequate evidence for their protective effect owing to the drug induced immunosuppressed state. Hence, we from the IADVL academy have framed the recommendations to be followed for COVID-19 vaccination among dermatological patients on immunosuppressive therapy based on available related literature.

**Keywords:** COVID-19, dermatology, guidelines, immunosuppressant, recommendations, vaccination

### Introduction

The ongoing COVID-19 pandemic warrants an urgent need for effective counter measures for immediate control of the disease transmission. Vaccination apart from establishing acquired immunity at an individual level can pave the way to reach herd immunity.<sup>[1,2]</sup>

Majority of patients with autoimmune inflammatory dermatological conditions are either on short- or long-term treatment with immunosuppressants or immunomodulators that include systemic steroids, immunosuppressive agents, biologics, and small molecule inhibitors. The use of immunosuppressive therapies in these patients is often associated with an increased risk of infections and their associated complications.

While vaccinations are known to provide adequate protection from certain infectious diseases, the immunization rates among this subset of patients have always been suboptimal. This could largely be attributed to uncertainty about the efficacy or safety of the vaccines that have not been adequately studied in patients on immunosuppressive therapies.<sup>[3]</sup> However, the degree of immune response in these patients would largely depend upon specific drug used, regimen, type of vaccine, and other patient-related factors.

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow\_reprints@wolterskluwer.com

Currently with the ongoing COVID-19 pandemic, the new kids in the block for these patients are the COVID vaccines as these patients may be susceptible to serious COVID-19 disease. Hence, it is important that they get sufficient protection by a COVID-19 vaccine. However, these patients may also be at risk of a less robust vaccine response owing to their truncated immune response. As with most other vaccines, the immunogenicity of these COVID-19 vaccines, their safety, and efficacy have not been studied in the immunosuppressed population.

Hence, these recommendations are framed based on the literature and evidence available for other vaccines and recommendations for other non dermatological immune-mediated conditions.

### COVID-19 Vaccines

The various types of COVID-19 vaccines under research and development are listed in Table 1. They are nonreplicating viral vector vaccines, inactivated whole-virus vaccines, messenger RNA vaccines (mRNA), self-amplifying messenger RNA vaccines (saRNA), DNA vaccines, and protein subunit vaccines.<sup>[4-6]</sup>

As on June 8, 2021, 287 candidate vaccines for COVID-19 are being researched, out

**How to cite this article:** Munisamy M, Singh BS, Pandhi D. Recommendations for COVID vaccination for dermatological patients on immunosuppressive/immunomodulatory therapy (IADVL Academy). Indian Dermatol Online J 2021;12:S4-11.

**Received:** 26-Jun-2021. **Revised:** 18-Aug-2021.

**Accepted:** 20-Aug-2021. **Published:** 25-Nov-2021.

**Malathi Munisamy,  
Bhabani  
S. T. P. Singh<sup>1</sup>,  
Deepika Pandhi<sup>2</sup>**

*Department of Dermatology and STD, Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Puducherry, <sup>1</sup>Department of Dermatology, IMS and SUM Hospital, Bhubaneswar, Odisha, <sup>2</sup>Department of Dermatology and STD, University College of Medical Sciences and GTB Hospital, Delhi, India*

### Address for correspondence:

*Dr. Deepika Pandhi,  
Chairperson, IADVL  
Academy, Director Professor,  
Department of Dermatology  
and STD, Dilshad Garden,  
Delhi - 110 095, India.  
E-mail: pandhi.deepika@gmail.  
com*

### Access this article online

**Website:** www.idoj.in

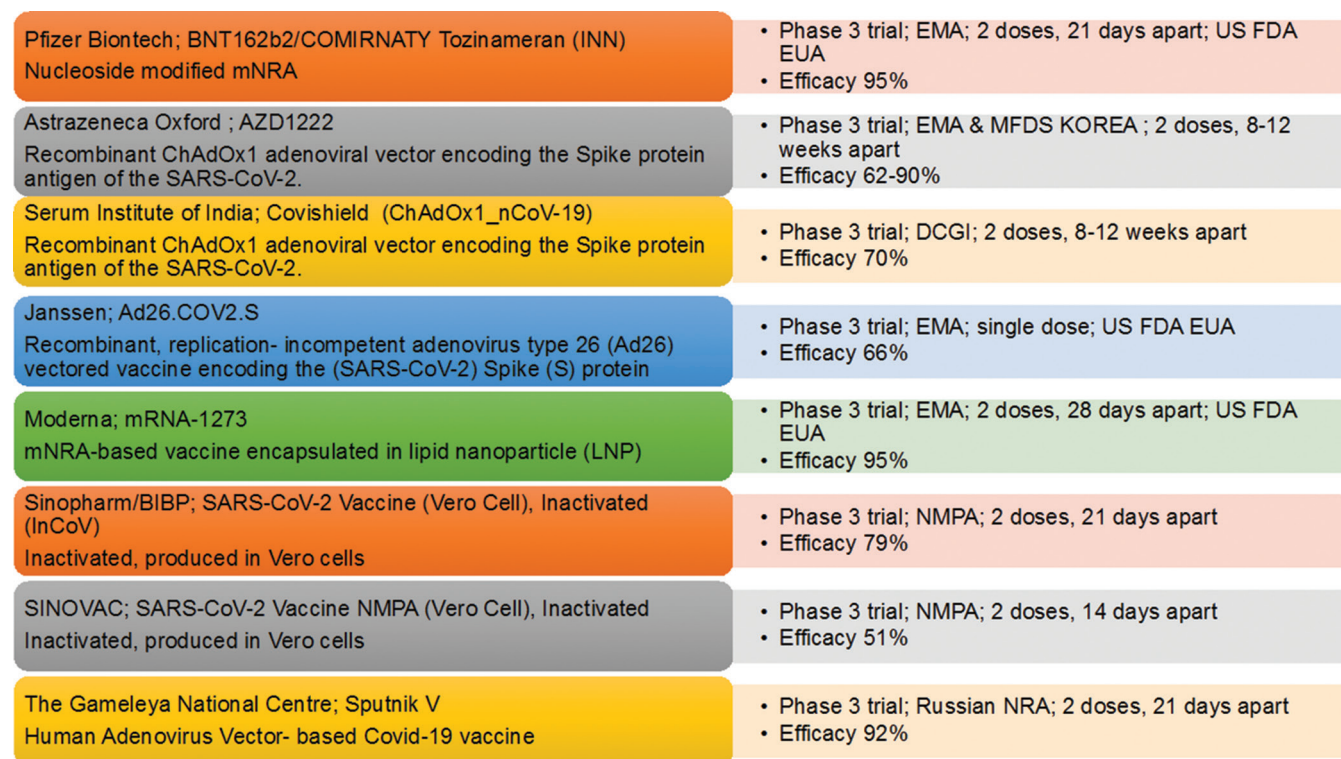
**DOI:** 10.4103/idoj.idoj\_412\_21

### Quick Response Code:



**Table 1: Various types of COVID-19 vaccines under research and development**

Types of vaccine	Mechanism	Example
Nonreplicating viral vector vaccines	Adenoviruses are rendered nonreplicating and are used as vectors to carry the spike protein antigen gene into human cells	ChAdOx1 nCoV-19 by Oxford/AstraZeneca (Covishield®); SputnikV® (Gam-COVID-Vac) by Gamaleya Research Institute; Ad26.COV2 S by Janssen. <sup>[4-6]</sup>
Inactivated whole-virus vaccines	SARS-CoV-2 virion variants cultured in Vero cell lines are inactivated by beta-propiolactone and then adsorbed onto aluminum hydroxide (adjuvant).	Covaxin® by Bharat Biotech; CoronaVac® by Sinovac. <sup>[4-6]</sup>
Messenger RNA vaccines (mRNA)	Lipid nanoparticle delivery of mRNA including an open reading frame of spike protein with a 3' polyadenylated tail.	mRNA-1273 by Moderna/NIAID®; BNT162b2 and BNT162b1 by BioNTech®/Fosun Pharma/Pfizer. <sup>[4-6]</sup>
Self-amplifying messenger RNA vaccines (saRNA)	Plasmids of Trinidad donkey Venezuelan equine encephalitis virus (VEEV) strains vaccines are used to synthesize the vaccine. While preserving the self-amplifying coding region of VEEV, the structural coding regions are replaced with prefusion spike protein of SARS-CoV-2 and delivered using nanoparticles	ARCT-021 by Arcturus/Duke-NUS; LNP-nCoVsaRNA by Imperial College London. <sup>[4-6]</sup>
DNA vaccines	SARS-CoV-2 spike glycoprotein sequence with an N-terminal IgE leader is designed as the DNA vaccine to enhance expression in target cells.	EINO-4800 by Inovio Pharmaceuticals; nCov Vaccine by Cadila Healthcare Limited; GX-19 by Genexine Consortium. <sup>[4-6]</sup>
Protein subunit vaccines	Recombinant full-length wild-type spike glycoprotein expressed in insect cell lines or Chinese hamster ovary cell lines which is resistant to proteolytic cleavage and has high affinity to ACE2 receptors is delivered via nanoparticles along with adjuvant	SARS-CoV-2 rS/Matrix-M1 by Novavax; Recombinant new coronavirus vaccine (CHO cell) by Institute of 2 Microbiology, Chinese Academy of Sciences. <sup>[4-6]</sup>



**Figure 1: COVID-19 vaccines approved by WHO. EUA—Emergency use authorization; National regulatory Agency—EMA—European Medicines Agency; DCGI—Drugs Controller General of India; NMPA—National Medical Products Administration (China); MFDS—Ministry of Food and Drug Safety (Korea)**

of which 102 are in the clinical phase and 185 are in the preclinical phase.<sup>[7]</sup> Most of the vaccines in the clinical phase are in phase 1 and 2 trials (saRNA, DNA, and protein subunit) while the inactivated whole-virus vaccines, nonreplicating vector vaccines, and mRNA vaccines have completed phase 3 trial and are being used worldwide for adult patients.

These vaccines trigger both cellular and humoral immune responses of the immune system. The eight COVID-19 vaccines approved by World Health Organization (WHO) are summarized in Figure 1.<sup>[8]</sup> Three vaccines are approved for use in India which include Covaxin®, Covishield®, and Sputnik V®, the details of which are summarized in Table 2.<sup>[4,9-12]</sup> Out

**Table 2: COVID-19 vaccines approved for use in India**

Vaccine	Type of vaccine	Dosage schedule	Efficacy	Adverse effects	Contraindications	Special population representation
Covaxin® (Bharath Biotech, Hyderabad, India) Phase 3 clinical trial	Whole virion inactivated SARS-CoV-2 antigen with alum and TLR7/8 agonist	2 doses 4 weeks apart	81%	Injection site reactions, fever, malaise, headache, rashes, nausea, vomiting	History of allergy Bleeding disorder or on anticoagulants Immunocompromised individuals Pregnancy and lactation	Study done in India Immunosuppressed patients not included
Covishield® (Serum Institute of India, Pune, India) Phase 3 clinical trial	Recombinant Chimpanzee adenovirus ChAdOx1 as vector with spike protein	2 doses 3 months apart	70%	Injection site reactions, fever, fatigue, headache, rashes, nausea, myalgia, flu-like symptoms, decreased appetite, abdominal pain, lymphadenopathy, rashes; rarely thrombosis after 7-10 days of vaccination especially in younger individuals	Hypersensitivity to the active substance or to any of the excipients -L-Histidine, L-Histidine hydrochloride monohydrate, Magnesium chloride hexahydrate, Polysorbate 80, Ethanol, Sucrose, Sodium chloride, Disodium edetate dihydrate (EDTA). Patients who have experienced venous and/or arterial thrombosis in combination with thrombocytopenia following any COVID-19 vaccine. Severe allergic reaction after a previous dose of this vaccine.	5.6% Asians represented Immunosuppressed patients not included
Sputnik V® (Gam-COVID-Vac) Gamaleya Institute, Moscow Russia (Imported by Dr. Reddy's Laboratory) Phase 3 clinical trial	Heterologous human recombinant adenovirus 26 (Ad26) and adenovirus 5 (Ad5) as vectors with spike protein.	2 doses 3 weeks apart with different vectors at each dose	92%	Flu-like illness, injection site reactions, headache, and asthenia	Caution in individuals with thrombocytopenia, coagulation disorder, anticoagulation therapy	1.5% Asians represented Immunosuppressed patients not included

of these three vaccines, the final recommendation by WHO is available only for Covishield® while Covaxin® and Sputnik V® are still under assessment as on June 3, 2021.<sup>[8]</sup>

### Normal immune response to COVID-19 vaccines

Vaccines induce adaptive immune response, wherein T-helper lymphocytes are the key players regulating both T- and B-cell responses. The cytotoxic T-lymphocytes induce an immunological memory response which is responsible for long-term protection. B cells stimulated by T helper lymphocytes produce neutralizing antibodies specific to virus while stimulated cytotoxic T lymphocytes recognize and kill viral-infected cells. Immunological memory response results in a stronger and faster protective immune response whenever rechallenged by the same antigen. The primary immune response during the first encounter with the antigen takes on an average 10–14 days to establish while immunological memory shortens the response time further to less than 7 days during reexposure

to the same agent (booster dose or natural infection), thereby conferring long-lasting immunity which is known as the secondary immune response.<sup>[13,14]</sup> In general, larger time interval between doses improves vaccine efficacy.

Seroconversion following SARS-CoV-2 infection has been reported to occur after 7 days in 50% of cases and by 14<sup>th</sup> day in almost all cases. IgM response peaks by 7–10 days and IgG response by 3 weeks. COVID-19 vaccination also follows similar antigenic response as with a natural infection.<sup>[15]</sup> It is of utmost importance to know that vaccines are not 100% effective in preventing infection in vaccinated individuals; nevertheless, vaccines are effective in reducing the severity of the disease. A very small proportion of fully vaccinated people can still get severe disease. COVID-19 vaccines are no exception to this and vaccine breakthrough infections can occur. Centers for Disease Control and Prevention (CDC) has recommended surveillance for “Vaccine breakthrough infection” defined as detection of SARS-CoV-2 RNA or



antigen in a respiratory specimen collected over 14 days after completing the vaccination of an FDA-authorized COVID-19 vaccine.<sup>[16]</sup>

### Vaccine response to COVID-19 vaccines in patients with immune-mediated inflammatory diseases using immunosuppressive medications

Generally, individuals with altered immunocompetence are at risk of severe systemic disease with live vaccines owing either to their disease status or drug-induced immunosuppression. This could be attributed to uninhibited growth of the attenuated live virus. Hence, these vaccines are deferred unless the patient is in remission or off immunosuppressive drugs. Live vaccines are administered only after improvement of immune function.

But there has been no contraindication to inactivated vaccines or subunit vaccines. However, they have been reported to be associated with lower efficacy. The general recommendation in cases where inactivated vaccine has been given during the period of altered immunocompetency is to repeat the inactivated vaccine once immune function has improved or to consider booster doses. In case of subunit vaccines, increased doses of the vaccine have been recommended during periods of immunosuppression to improve vaccine efficacy.<sup>[3,17-19]</sup>

There are no FDA-approved mRNA and DNA vaccines for human use until faced with the COVID-19 pandemic when human trials on these vaccine platforms are undertaken. Hence, their response in immunosuppressed individuals is not known.<sup>[19]</sup>

There has been an accelerated process of vaccine development owing to the emergency pandemic situation. Hence, special populations like the elderly, children, pregnant and lactating women, patients with comorbidities, and immunosuppressed patients are not adequately represented in the initial phases of the COVID-19 vaccine trials. Though the current vaccine trials include some of these special populations like the elderly, children, and patients with comorbidities; patients on immunosuppressive agents are excluded in almost all the trials.<sup>[19]</sup> Reassuringly, as none of the COVID-19 vaccines developed so far are live attenuated vaccines, they do not pose the risk of vaccine-induced infection, a major concern in immunosuppressed patients.

However, the blunted immune response in these patients may result in reduced vaccine efficacy predisposing them to an increased susceptibility to COVID-19 infection and its associated complications.<sup>[17-19]</sup> This situation could further be worsened by the false sense of protection in patients after receiving vaccination. However, the vaccine response largely depends on the degree of immunosuppression which in turn depends on the type of immunosuppressant, dose, duration, and general condition of patient. Patients on higher dose of steroids for a long duration and those on biologic therapy are considered to have severe immunosuppression while those

on low dose of steroids (<20 mg) for short term (<2 weeks) and on low dose methotrexate  $\leq 0.4$  mg/kg/week) and azathioprine  $\leq 3$  mg/kg/day are considered to have mild immunosuppression.<sup>[18,19]</sup> A recent study on immune response to Pfizer mRNA vaccine in renal transplant patients reported reduced immune response with antibody responses in only 17.8% of cases and specific T-cell response in 57.8% of cases after the second dose.<sup>[20]</sup>

Hence, future studies should address the immunogenicity of these COVID-19 vaccines in patients on immunosuppressive therapy, which would help in deciding the vaccine dose, frequency, and timing with regards to the specific immunosuppressive agent. These data would also help in making decisions on withholding or interrupting immunosuppressive therapy for COVID-19 vaccination.

The possibility of occurrence of vaccine-associated enhanced respiratory disease needs to be considered in these patients on immunosuppressive therapy if protective antibody titers post vaccination is inadequate and skewed to a T helper type 2 phenotype. In this scenario, vaccination could increase the severity of subsequent infection with the same virus.<sup>[6]</sup>

Another concern has been raised with the use of COVID-19 vaccine in this group of patients with immune-mediated inflammatory diseases not related to immunosuppressive agents but to the disease *per se*. It is the fear of mRNA vaccines causing a flare-up of these diseases or precipitating these diseases in predisposed individuals owing to the mechanism of molecular mimicry that needs to be answered in future studies.<sup>[21]</sup>

### Recommendations for COVID-19 vaccines for dermatological patients on immunosuppressive therapy

The recommendations for COVID-19 vaccines for dermatological patients on immunosuppressive therapy have been drafted based on the general recommendations for vaccination in immunosuppressed patients, recommendations for COVID-19 vaccination for patients on immunosuppressive agents for nondermatological conditions, and recommendations by expert groups for dermatological conditions and are summarized in Table 3.<sup>[6,22-28]</sup>

The Australasian Medical Dermatology Group recommends vaccination for all patients on immunomodulatory drugs and/or biologic agents using standard vaccination protocols available with no specific preference for type of vaccines. If immunomodulatory therapy is planned, they recommend expedited COVID-19 vaccination prior to initiation of therapy to maximize vaccine response. For those already on treatment, they recommend vaccination to be administered at least 7 days either side of biologic or immunomodulator dosing at a different anatomical location.<sup>[26]</sup>

The European Association of Dermatology and Venereology recommends COVID-19 vaccination to be

**Table 3: Recommendations for COVID 19 vaccination for dermatological patients on immunosuppressive agents**

Immunosuppressive agent	Effect on immune response	Recommendations
Corticosteroids	Impaired humoral response at dose >10 mg and reduced humoral response >20 mg	Continue therapy Taper steroid therapy to <10 mg prednisolone daily if possible
Methotrexate	Reduced humoral response	Withhold methotrexate for 2 weeks post vaccination
Azathioprine	No significant impairment of humoral response	Continue therapy
Cyclosporine	No significant impairment of humoral response	Continue therapy
Cyclophosphamide	No significant impairment of humoral response	If oral-continue therapy If intravenous-1 week after each vaccine dose
Mycophenolatemofetil	No significant impairment of humoral response at doses <2 g	Continue therapy
Rituximab	Reduced humoral response	Avoid vaccinating ideally for 6 months post rituximab. The next cycle of rituximab should be started 4 weeks after the second vaccine dose.
TNF alpha inhibitors	No significant impairment of humoral response	Continue therapy
IL-12/23 inhibitors	No significant impairment of humoral response	Continue therapy
IL-17 inhibitors	No significant impairment of humoral response	Continue therapy
Omalizumab	No significant impairment of humoral response	Continue therapy
Dupilumab	No significant impairment of humoral response	Continue therapy
Jak kinase inhibitors	Reduced humoral response	Withhold 1-week post vaccination
IvIg	No significant impairment of humoral response if vaccination prior to IvIg. Reduced humoral response if vaccination is given after IvIg	Continue therapy

safe for administration to patients with psoriasis and autoimmune blistering diseases under treatment with biologics/immunomodulatory agents. However, they recommend vaccinating before planned immunosuppression if feasible as vaccination is most effective when the degree of immunosuppression is low. However, with regards to rituximab, vaccination within three months of rituximab therapy is not preferable as it may not be fully effective. There is no recommendation to lower the dose of immunosuppressive drugs before vaccination due to risk of disease flare. Precaution should be taken where patients have a history of anaphylaxis to drugs in general, especially to vaccinations and in patients with systemic mastocytosis or idiopathic anaphylaxis. All these patients are recommended to undergo a drug allergy diagnostic workup for allergy prior to vaccination. Documented, severe allergic reactions to ingredients of the respective COVID-19 vaccines, that is, polyethylene glycol, present both in the BioNTech/Pfizer (Comirnaty) and the Moderna (mRNA-1273) vaccines, is a definite contraindication to these two vaccines.<sup>[27]</sup>

The British Association of Dermatology recommends COVID-19 vaccination for all patients on immunosuppressants except pregnant women and children as a priority as they are extremely vulnerable population at a very high risk of severe illness from COVID-19. They do not recommend stopping or delaying immunosuppressive therapy for the sake of vaccination.<sup>[28]</sup>

The American Academy of Dermatology recommends nonviral or inactivated SARS-CoV-2 vaccine

subtypes for patients on systemic immunosuppressant or immunomodulatory therapy and nonviral SARS-CoV-2 vaccine subtype for those on biologic therapy without significant modification of ongoing treatments. They recommend for assessment of antibody titers after vaccination and consider booster doses based on titers.<sup>[6]</sup>

Until new evidence becomes available, the prevailing national policy should be adhered to with decisions on the type of vaccine, timing of vaccine, and immunosuppressant therapy be taken on a case-to-case basis and must be a shared decision making. The current National policy recommends COVID-19 vaccination in all patients above the age of 18 years irrespective of comorbidities. At present, vaccination is contraindicated only for pregnant women and children aged less than 18 years and those with a history of anaphylaxis or allergy to the vaccine constituents or the first dose of vaccine or immediate or delayed onset anaphylaxis or allergic reactions to vaccines or injectable therapies. Vaccination is temporarily contraindicated for those who have current COVID-19 infection or those who have recently recovered from infection (12 weeks) and those patients who are acutely unwell and hospitalized. Lactating mothers can be vaccinated.<sup>[29]</sup>

Hence, all patients on immunosuppressant therapy should be encouraged for vaccination, except during a disease flare when vaccination should be generally avoided. Since rituximab and methotrexate have been reported to suppress the production of neutralizing antibodies to neoantigens, the adjustment of the timing of therapy during vaccination with these two agents as well as JAK kinase inhibitors is

required, while the other immunosuppressive agents can be safely continued during vaccination.<sup>[6,19,22]</sup>

Vaccination of all eligible household contacts and other close contacts of these patients on immunosuppressives is very important as it can prevent the potential transmission of infection from their contacts by way of herd immunity. The COVID-appropriate behavior should be followed by the patients as well as their close contacts even after getting fully vaccinated. Vaccination of all dermatologists and their staff is equally important to minimize risk to the patients.

### Coadministration of COVID-19 vaccines with other vaccines

Past experiences of combining non-COVID-19 vaccines suggest that adverse event possibilities are generally similar with simultaneous administration of different vaccines as with their isolated administration.

CDC recommends COVID-19 vaccines and other non-COVID-19 vaccines may be coadministered either on the same day or within 14 days. It is not fully known whether other reactogenic vaccines like live or adjuvant vaccines potentiate the immunogenicity of the COVID-19 vaccines.<sup>[30]</sup> The Australasian Medical Dermatology Group recommends administration of other vaccines either at least 7 days prior to COVID-19 vaccination or at least 7 days after the completion of the two-dose COVID-19 vaccination. However, the urgency of the need for a non-COVID vaccine indication should be potentially high.<sup>[26]</sup>

Multiple vaccines can be administered on the same site preferably deltoid muscle in adults separated by one inch apart using different syringes. In case of vaccines known to cause local reactions like tetanus toxoid, different limbs should be chosen as the site of injection.<sup>[30]</sup>

Vaccines used in dermatology include measles–mumps–rubella (MMR) vaccine, BCG vaccine, leprosy vaccine, and human papillomavirus (HPV) vaccine. MMR and BCG vaccines are used intralesionally at a much lower dose for treatment of warts while leprosy vaccines

and HPV vaccine are administered in their full dose. Since none of the COVID-19 vaccines used are live vaccines, these non-COVID vaccines can safely be used along with the COVID-19 vaccines, as per the recommendation of the CDC.

### Antibody/serology testing after COVID-19 vaccination

The two most important structural protein of SARS-CoV-2 virus are the S (spike) and the N (nucleocapsid) protein. The receptor-binding domain (RBD) of the virus through which it enters the human cells is located on the S1 subunit of the spike protein. This is the principal target of neutralizing antibodies. In case of natural infection, there is a heterologous antibody response to the S and N protein. Patients with antibody to N protein only but not to the S protein do not exhibit neutralizing potential.<sup>[31]</sup>

The immunogenicity of the vaccines has been tested by assessing the antibodies specific to RBD of S protein (Sputnik V), S binding antibodies (Covishield), and S1 protein RBD and nucleocapsid protein (Covaxin). The interpretation of results of antibody testing in a vaccinated individual based on scientific evidence is provided in Table 4.<sup>[31]</sup>

Thus, it is evident that serologic tests need to be interpreted carefully taking into consideration history of vaccination and/or prior infection which might have been asymptomatic and hence undiagnosed. None of the currently authorized FDA-approved serologic tests have been authorized to be used to assess immune response in vaccinated individuals. The protective effect of T cell-mediated immunity with natural infection as well as with vaccination has also not been well established.<sup>[31]</sup> Hence, CDC or WHO or ICMR does not recommend antibody testing to assess for immunity produced by COVID-19 vaccination or to assess the need for vaccination in an unvaccinated person. Hence, the same may be considered for patients on immunosuppressive agents until further evidence is available. However, there are ongoing long-term follow-up studies to assess the immune responses following vaccination and natural infection, threshold for vaccine failure and reinfection, potential need for booster doses, the impact of vaccination on new viral variants, and immune response in immunosuppressed individuals.<sup>[31]</sup>

### Special scenarios

#### COVID-19 vaccination for people living with HIV and on HAART

Few COVID-19 vaccine trials have included a small proportion of people living with HIV (PLHIV). Despite the availability of limited data, WHO recommends COVID-19 vaccines (Pfizer/BioNtech, Oxford/AstraZeneca, Johnson and Johnson) for all PLHIV with or without HAART. As they are not live vaccines and vaccine components had no interactions with HAART, HAART needs to be continued. However, there are concerns regarding reports of adenovirus vector-based

**Table 4: Interpretation of antibody testing after vaccination\***

Antibody to S protein	Antibody to N protein or other antigens of SARS CoV2	Inference
Present	Absent	Vaccine-induced antibody is present and the person was never infected with SARS-CoV-2
Present or Absent	Present	Resolving or resolved SARS-CoV-2 infection that could have occurred before or after vaccination.

\*Covaxin® being a whole-virus inactivated vaccine can produce both anti-spike glycoprotein as well as anti-nucleocapsid protein antibody

**Table 5: Common cutaneous adverse effects seen with COVID 19 vaccines**

Covaxin®	Pfizer/BioNTech	Moderna	Oxford/AstraZeneca	Covishield®	Sputnik V®
Pain and swelling itching at the injection site, generalized rash <sup>[35]</sup>	Pain, swelling, redness at injection site, anaphylaxis <sup>[34]</sup> urticaria, angioedema, and morbilliform rashes, delayed injection site reactions. <sup>[38]</sup>	Pain, swelling, redness at the site of vaccine. <sup>[34]</sup> Maculopapular rash, urticaria, Type 1 hypersensitivity reaction, Delayed injection site reaction (Covid arm) <sup>[37]</sup>	Anaphylaxis, Local site reaction. <sup>[36]</sup>		Allergic skin reaction: Itching: Itching of the upper limbs, petechial rash extremity abscess Eczema. <sup>[12]</sup>

vaccines potential to increased susceptibility to HIV infection among men who received adenovirus vector-based vaccine probably due to altered CD4 cell susceptibility in earlier trials. But no such reports exist for COVID-19 vaccines and their altered immune response that needs to be explored.<sup>[32]</sup>

#### *COVID-19 vaccination for people with history of allergy to first dose*

CDC does not recommend second dose of vaccine for those who developed anaphylaxis or severe allergic reactions (requiring epinephrine or hospitalization) or non severe immediate allergic reactions (within 4 hours) to the first dose of COVID-19 mRNA vaccine. But other allergic reactions are not contraindications for second dose.<sup>[33]</sup> The same has been recommended for Covishield® and Covaxin® in India.

#### *Dermatological adverse effects with COVID-19 vaccines*

The COVID-19 vaccines are relatively safe and are associated with mostly local cutaneous side effects that are self-limiting, not requiring any pharmacological intervention.<sup>[34-38]</sup> The adverse effects associated with these vaccines are not more common or severe in persons on immunosuppressive or immunomodulator drugs compared to healthy persons as none of the approved vaccines for use are live vaccines. The common cutaneous adverse effects seen with the COVID-19 vaccines are listed in Table 5. Rarely seen dermatological side effects with mRNA vaccines are erythromelalgia, herpes zoster, erythema multiforme, facial edema, and Bell's palsy, reactions to dermatological fillers, chilblains, vasculitis, and pityriasis rosea.<sup>[34]</sup>

### **Conclusion**

In dermatological patients on immunosuppressive therapy, the risk of acquiring COVID-19 infection and subsequent severe disease posed by deferring vaccination should be weighed against the concerns of lack of safety and efficacy data of these vaccines. Similarly, the risk of worsening of primary dermatological condition by stopping or reducing the immunosuppressive therapy should be weighed against the risk of acquiring COVID-19 infection.

Hence, patients on immunosuppressive therapy should be recommended COVID-19 vaccination if they do not have any absolute contraindications for the vaccine until further data are available. Antibody testing post vaccination is not currently recommended. Considering the constraints in vaccine resources, booster doses should not be considered

in these patients, anticipating reduced efficacy until adequate evidence is available. Recommending vaccination along with COVID-appropriate behavior even after vaccination and vaccination of household contacts would reduce the risk of acquiring COVID-19 infection in this vulnerable group of patients.

### **Acknowledgements**

We acknowledge all members of the IADVL Academy including ex-officio members for their critical inputs in the preparation of this manuscript.

### **References**

- Frederiksen LSF, Zhang Y, Foged C, Thakur A. The long road toward COVID-19 herd immunity: Vaccine platform technologies and mass immunization strategies. *Front Immunol* 2020;11:1817.
- Randolph HE, Barreiro LB. Herd immunity: Understanding COVID-19. *Immunity* 2020;52:737-41.
- Papp KA, Haraoui B, Kumar D, Marshall JK, Bissonnette R, Bitton A, *et al.* Vaccination guidelines for patients with immune-mediated disorders taking immunosuppressive therapies: Executive summary. *J Rheumatol* 2019;46:751-4.
- Worldwide COVID-19 vaccine candidates. Available from <https://vaccine.icmr.org.in/covid-19-vaccine>. [Last accessed on 2021 May 22].
- Izda V, Jeffries MA, Sawalha AH. COVID-19: A review of therapeutic strategies and vaccine candidates. *ClinImmunol* 2021;222:108634.
- Gresham LM, Marzario B, Dutz J, Kirchhof MG. An evidence-based guide to SARS-CoV-2 vaccination of patients on immunotherapies in dermatology. *J Am Acad Dermatol* 2021;84:1652-66.
- COVID-19 vaccine tracker and landscape. Available from <https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines>. [Last assessed on 21 Jun 08].
- Status of COVID-19 Vaccines within WHO EUL/PQ evaluation process. Available from: [https://extranet.who.int/pqweb/sites/default/files/documents/Status\\_COVID\\_VAX\\_19August2021.pdf](https://extranet.who.int/pqweb/sites/default/files/documents/Status_COVID_VAX_19August2021.pdf). [Last assessed on 2021 Jun 08].
- Phase 3 Clinical Trial of COVAXIN, developed by ICMR and Bharat Biotech, shows 81% efficacy. Available from: [https://www.icmr.gov.in/pdf/press\\_realease\\_files/Press\\_Release\\_ICMR\\_03\\_March\\_2021.pdf](https://www.icmr.gov.in/pdf/press_realease_files/Press_Release_ICMR_03_March_2021.pdf). [Last accessed on 2021 May 22].
- Ella R, Vadrevu KM, Jogdand H, Prasad S, Reddy S, Sarangi V, *et al.* Safety and immunogenicity of an inactivated SARS-CoV-2 vaccine, BBV152: Adouble-blind, randomised, phase 1 trial. *Lancet Infect Dis* 2021;21:637-46.
- Ramasamy MN, Minassian AM, Ewer KJ, Flaxman AL, Folegatti PM, Owens DR, *et al.* Safety and immunogenicity of ChAdOx1 nCoV-19 vaccine administered in a prime-boost



- regimen in young and old adults (COV002): A single-blind, randomised, controlled, phase 2/3 trial. *Lancet* 2021;396:1979-93.
12. Logunov DY, Dolzhikova IV, Shcheblyakov DV, Tukhvatulin AI, Zubkova OV, Dzharullaeva AS, *et al.* Safety and efficacy of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine: An interim analysis of a randomised controlled phase 3 trial in Russia. *Lancet* 2021;397:671-81.
  13. Pollard AJ, Bijker EM. A guide to vaccinology: From basic principles to new developments. *Nat Rev Immunol* 2021;21:83-100.
  14. Siegrist CA. Vaccine Immunology. Available from [https://www.who.int/immunization/documents/Elsevier\\_Vaccine\\_immunology.pdf](https://www.who.int/immunization/documents/Elsevier_Vaccine_immunology.pdf). [Last accessed on 2021 Jun 08].
  15. Speiser DE, Bachmann MF. COVID-19: Mechanisms of vaccination and immunity. *Vaccines (Basel)* 2020;8:404.
  16. COVID-19 Vaccine Breakthrough Case Investigation and Reporting. Available from: <https://www.cdc.gov/vaccines/covid-19/health-departments/breakthrough-cases.html>. [Last accessed on 2021 Jun 08].
  17. General Best Practice Guidelines for Immunization: Best Practices Guidance of the Advisory Committee on Immunization Practices (ACIP). Available from: <https://www.cdc.gov/vaccines/hcpacip-recs/general-recs/immunocompetence.html#-01>. [Last accessed on 2021 May 22].
  18. Arvas A. Vaccination in patients with immunosuppression. *Turk Pediatri Ars.* 2014;49:181-5.
  19. Sonani B, Aslam F, Goyal A, Patel J, Bansal P. COVID-19 vaccination in immunocompromised patients. *Clin Rheumatol* 2021;40:797-8.
  20. Korth J, Jahn M, Dorsch O, Anastasiou OE, Sorge-Hädicke B, Eisenberger U, *et al.* Impaired humoral response in renal transplant recipients to SARS-CoV-2 vaccination with BNT162b2 (Pfizer-BioNTech). *Viruses* 2021;13:756.
  21. Talotta R. Do COVID-19 RNA-based vaccines put at risk of immune-mediated diseases? In reply to "potential antigenic cross-reactivity between SARS-CoV-2 and human tissue with a possible link to an increase in autoimmune diseases". *Clin Immunol* 2021;224:108665.
  22. Arnold J, Winthrop K, Emery P. COVID-19 vaccination and antirheumatic therapy. *Rheumatology (Oxford)* 2021;60:3496-502.
  23. Park JK, Lee EB, Shin K, Sung YK, Kim TH, Kwon SR, *et al.* COVID-19 vaccination in patients with autoimmune inflammatory rheumatic diseases: Clinical guidance of the Korean College of Rheumatology. *J Korean Med Sci* 2021;36:e95.
  24. Santosa A, Xu C, Arkachaisri T, Kong KO, Lateef A, Lee TH, *et al.* Recommendations for COVID-19 vaccination in people with rheumatic disease: Developed by the Singapore Chapter of Rheumatologists. *Int J Rheum Dis* 2021;24:746-57.
  25. Curtis JR, Johnson SR, Anthony DD, Arasaratnam RJ, Baden LR, Bass AR, *et al.* American College of Rheumatology Guidance for COVID-19 vaccination in patients with rheumatic and musculoskeletal diseases-Version 1. *Arthritis Rheumatol* 2021;73:1093-107.
  26. Wang C, Rademaker M, Tate B, Baker C, Foley P. SARS-CoV-2 (COVID-19) vaccination in dermatology patients on immunomodulatory and biologic agents: Recommendations from the Australasian Medical Dermatology Group. *Australas J Dermatol* 2021;62:151-6.
  27. Covid-19 Vaccination: Advice of the EADV Task Forces. Available from: <https://www.eadv.org/covid-19/task-force>. [Last accessed on 2021 Jun 08].
  28. COVID-19: Provisional guidance on vaccination. Available from: <https://www.bad.org.uk/shared/get-file.ashx?itemtype=document&id=6956>. [Last accessed on 2021 Jun 08].
  29. Information regarding COVID-19 vaccine. Available from: [https://www.mohfw.gov.in/covid\\_vaccination/vaccination/index.html](https://www.mohfw.gov.in/covid_vaccination/vaccination/index.html). [Last accessed on 2021 Jun 08].
  30. Interim Clinical Considerations for use of COVID-19 vaccines/CDC. Available from: <https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html#Coadministration>. [Last accessed on 2021 May 23].
  31. Interim Guidelines for COVID-19 antibody testing. Available from: <https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antibody-tests-guidelines.html>. [Last accessed on 2021 Jun 08].
  32. Coronavirus disease (COVID-19): COVID-19 vaccines and people living with HIV. Available from: [https://www.who.int/news-room/q-a-detail/coronavirus-disease-\(covid-19\)-covid-19-vaccines-and-people-living-with-hiv](https://www.who.int/news-room/q-a-detail/coronavirus-disease-(covid-19)-covid-19-vaccines-and-people-living-with-hiv). [Last accessed on 2021 Jun 18].
  33. Allergic reactions. Available from: <https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/allergic-reaction.html>. [Last accessed on 2021 Jun 18].
  34. Meo SA, Bukhari IA, Akram J, Meo AS, Klonoff DC. COVID-19 vaccines: Comparison of biological, pharmacological characteristics and adverse effects of Pfizer/BioNTech and Moderna Vaccines. *Eur Rev Med Pharmacol Sci* 2021;25:1663-9.
  35. Ella R, Reddy S, Jogdand H, Sarangi V, Ganneru B, Prasad S, *et al.* Safety and immunogenicity of an inactivated SARS-CoV-2 vaccine, BBV152: Interim results from a double-blind, randomised, multicentre, phase 2 trial, and 3-month follow-up of a double-blind, randomised phase 1 trial. *Lancet Infect Dis* 2021;21:950-61.
  36. Voysey M, Clemens SAC, Madhi SA, Weckx LY, Folegatti PM, Aley PK, *et al.* Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: An interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. *Lancet* 2021;397:99-111.
  37. Blumenthal KG, Freeman EE, Saff RR, Robinson LB, Wolfson AR, Foreman RK, *et al.* Delayed large local reactions to mRNA-1273 vaccine against SARS-CoV-2. *N Engl J Med* 2021;384:1273-7.
  38. 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.