COVID-19 Vaccination and Dermatologic Patients on Immunotherapy & Biologic Therapies
A Position Paper from the Philippine Dermatological Society

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KEY POINTS

- Immunocompromised patients have a higher risk of developing severe and life-threatening COVID-19 infections compared to the general population.
- The three Philippine FDA-approved COVID-19 vaccines, which are all non-live vaccines, may benefit dermatologic patients with immunosuppressed states or who are taking immunomodulating medications, upon appropriate advice and counseling.
- COVID-19 vaccination should not replace transmission prevention measures, such as proper mask wearing, frequent disinfection, and physical distancing.

I. INTRODUCTION

SARS-CoV-2, the virus causing COVID-19, has infected more than 100 million people and has caused more than two million deaths worldwide since it was first detected in 2019.[1] Patients with diabetes mellitus, chronic obstructive pulmonary disease, cardiovascular disease, hypertension, malignancies, and other immunocompromised states could develop severe and life-threatening infections.[2]

Numerous dermatologic conditions result from immune dysfunction or necessitate chronic and prolonged treatment with agents that may cause drug-induced immunosuppression. Patients with psoriasis, eczemas, connective tissue diseases, and blistering disorders are often maintained on drugs such as topical and systemic corticosteroids, methotrexate, rituximab, azathioprine, mycophenolate mofetil & mycophenolic acid, cyclosporine, intravenous immunoglobulin (IVIG), and other biologic agents. This subset of potentially vulnerable patients requires specialized care and advice.

With the introduction of COVID-19 vaccines worldwide and the ongoing pandemic, we still do not have enough evidence to definitively guide us in the recommendation, administration, and management of complications arising from vaccine rollouts in these patients. As of this writing, the Philippine Food and Drug Administration (FDA) has issued emergency use authorization (EUA) for three vaccines, namely Pfizer-BioNTech COVID-19 Vaccine

(BNT162b2), AstraZeneca/Oxford ChAdOx1-S[recombinant], and Sinovac Biotech CoronaVac.[3]

In this position paper, we aim to provide guidance for dermatologists and other healthcare workers involved in the care of these patients based on the best available data we have at the time. Should we have more relevant data in the coming months, we will update this statement.

II. IMMUNOSUPPRESSIVE AGENTS, IMMUNOMODULATORS & DERMATOLOGIC CONDITIONS REQUIRING THESE AGENTS

Immunosuppressants used in dermatology are categorized according to the risk for COVID-19, depending on the immunity of the individual.

Table 1. Risk stratification for COVID-19 with commonly used immunomodulators in dermatology.[4]

Low risk	Sulfasalazine, Apremilast, Hydroxychloroquine
Intermediate risk	Methotrexate, Azathioprine
High risk	Cyclophosphamide, Cyclosporine, Leflunomide, Mycophenolate Mofetil, Prednisolone, Biologics

Dermatologic conditions that require immunosuppressives include atopic dermatitis, psoriasis, autoimmune blistering diseases, and connective tissue diseases. These patients have a higher risk of developing infections due to their underlying immunologic condition, the immunosuppressive drugs that they are on, and the comorbidities that they may have.

III. SARS-CoV-2 VACCINES

There are different types of vaccines according to its components and how it stimulates the immune response. These include live attenuated vaccines, inactivated vaccines, subunit vaccines, and nucleic acid vaccines.[5]

1. **Live attenuated**
   a. Uses weakened (or attenuated) virus or bacteria.
   b. Due to the similarity to a natural infection that they help prevent, they create a strong and long-lasting immune response. After the first or second dose of most live vaccines, it can give a lifetime of protection.
   c. Examples: MMR combined vaccine, rotavirus, smallpox & chickenpox vaccines
2. **Inactivated**
   a. Uses the killed version of the microbe that causes a disease.
   b. These do not provide immunity that is as strong as live vaccines. One may need several doses over a period of time (booster shots) in order to get ongoing immunity against diseases.
   c. Examples: Flu shot, hepatitis, polio & rabies vaccines
3. **Subunit**
   a. Subunit, recombinant, polysaccharide, and conjugate vaccines use specific pieces of the microbe, such as its protein, sugar, or capsid.
   b. Because these vaccines use only specific pieces of the microbe, they give a very strong immune response that is targeted to key parts of the microbe.

c. Examples: HPV, hepatitis B, shingles, pneumococcal & meningococcal vaccines

4. **Nucleic acid**
   a. Makes proteins in order to trigger an immune response.
   b. Benefits include shorter manufacturing times and, because they do not contain a live virus, no risk of causing disease in the person getting vaccinated.
   c. Example: COVID-19 vaccines

Table 2. SARS-CoV-2 vaccines available or currently in development as of this writing.[6]

Manufacturer	Type	Dosage	Storage	Efficacy against severe COVID-19	Overall efficacy	Philippine approval
Pfizer-BioNTech (US)	mRNA	X2	-80 to -60 °C (6 months)	88.9% after 1st dose	52% after 1st dose 94.6% after 2nd dose	EUA*
AstraZeneca/Oxford (UK)	Viral vector (genetically modified virus)	X2	2-8 °C (6 months)	100% 21 days after 1st dose	64.1% after 1st dose 70.14% after 2nd dose	EUA*
Sinovac (China)	Inactivated virus	X2	2-8 °C (Lifespan: unknown)	Brazil: 50.38% (mild) and 78% (mild to severe) Indonesia: 65% Turkey: 91.25% (Dec 2020)		EUA**
Moderna (US)	mRNA	X2	-25 to -15 °C (7months)	100% after 2nd dose	92.1% after 1st dose 94.1% after 2nd dose	-
Novavax, Inc. (US)	Protein subunit	X2	2-8 °C (6 months)	-	89.3% after 2 doses (UK); 60% (South Africa)	-
Johnson & Johnson (US)	Viral vector	1 Dose	2-8 °C (3 months)	85% after 28 days 100% after 49 days	57-72% (at 28 days)	-
Sinopharm 1/2 (China)	Inactivated virus	X2	2-8 °C (Lifespan: unknown)	-	79-86% (unpublished)	-
Gamaleya National Research Center for Epidemiology and Microbiology (Russia)	Viral vector	X2	-18 °C (Liquid form); 2-8 °C (freeze dried) for up to 6 months	100% after 1st dose	87.6% after 1st dose 91.1% after 2nd dose	-
CureVac/ GlaxoSmithKline (Germany)	mRNA	X2	2-8 °C (3 months)	Unknown (Phase 3 Trial ongoing)		-

*EUA: Emergency Use Authorization by the Philippine FDA.
**18-59 years old healthy population, and not recommended for healthcare workers with direct exposure to COVID-19 patients.

IV. POSITION OF THE GROUP REGARDING VACCINATION WHILE ON AN IMMUNOMODULATING OR IMMUNOSUPPRESSIVE THERAPY (INCLUDING BIOLOGICS)

A. On the type of vaccine to be administered

LIVE attenuated vaccines SHOULD NOT be given concomitantly with immunosuppressive and biologic therapy. The administration of NON-LIVE vaccines may be done to such patients.

According to the National Psoriasis Foundation COVID-19 Task Force, systemic medications (and biologics) for psoriasis and psoriatic arthritis are NOT CONTRAINDICATED with the mRNA-based COVID-19 vaccines. The Task Force also recommends that those who receive the mRNA-based COVID-19 vaccines continue their biologic and oral therapies for psoriasis and psoriatic arthritis as scheduled.[7]

The vaccines approved by the Philippine FDA do not contain live or replicating subunits of SARS-CoV-2, and may therefore be used. However, as there are currently scarce data on the safety of these vaccines in special populations, patients must be properly counseled regarding the unknown safety profile in immunocompromised groups, as well as the potential for reduced immune responses.

B. Effect of immunomodulators/immunosuppressants on the efficacy of vaccines

The effect of these therapies on the efficacy of COVID-19 vaccines is unknown. The following show the effect of these systemic therapies on different vaccines:

- Methotrexate lowers the humoral response to seasonal flu and pneumococcal vaccines, thus temporary discontinuation for 2 weeks after immunization to improve immunogenicity is advised.[8,9]
- TNF-inhibitors and tofacitinib do not significantly affect the humoral response to flu vaccine, but reduce immune response to pneumococcal vaccine.[10-12]
- Ustekinumab[13], secukinumab[14,15] & ixekizumab[16] do not interfere with the immune response to both influenza or pneumococcal vaccines.
- No data for cyclosporine, anti-IL-23 biologics, aprelimast, or acitretin on the efficacy of any approved vaccine.[7]

The immunogenicity of non-live vaccines appear to be preserved during the use of biologic agents, whereas methotrexate may significantly impair humoral response to vaccines.

In high-risk situations wherein the potential risk of infection is considered to outweigh the risk related to the administration of live vaccines, vaccination could be considered according to an infectious disease specialist.[17]

C. On the timing of vaccination

Non-live vaccines are preferred to be given when the patient's dermatologic condition is stable, and may be given concomitantly with immunomodulatory or immunosuppressive therapies. If feasible, it is recommended to vaccinate before planned immunosuppression. Vaccines are most effective when the level of immunosuppression is low.

As recommended by the American College of Rheumatology (ACR), the timing considerations for immunomodulatory therapy and COVID-19 vaccination are as follows.

Table 3. ACR recommendations for timing of vaccination and immunotherapy.[18]

MEDICATION	TIMING	LEVEL OF TASK FORCE CONSENSUS
Hydroxychloroquine; IVIG; Prednisone <20mg/day	No modification to either immunomodulatory therapy or vaccination	Strong-moderate
Mycophenolate; Azathioprine; Cyclophosphamide (oral); TNFi; IL-17i; IL-12/23i; IL-23i; Prednisone > 20mg/day	No modification to either immunomodulatory therapy or vaccination	Moderate
Methotrexate	Hold MTX 1 week after each vaccine dose, for those with well-controlled disease; no modifications to vaccine timing	Moderate
Cyclophosphamide IV	Time administration so that it will occur approximately 1 week after each vaccine dose, when feasible	Moderate
Rituximab	Assuming that patient's COVID-19 risk is low or is able to be mitigated by preventive health measures (e.g., self-isolation), schedule vaccination so that the vaccine series is initiated approximately 4 weeks prior to next scheduled rituximab cycle; after vaccination, delay RTX 2-4 weeks after 2nd vaccine dose, if disease activity allows	Moderate

*TNFi: Tumor necrosis factor inhibitors; MTX: Methotrexate; RTX: Rituximab

D. On the risk of allergy

There is no evidence that autoimmune conditions are at any greater risk of vaccine allergy than the general population. The Center for Disease Control and Prevention (CDC) recommendations state that COVID-19 vaccination is NOT CONTRAINDICATED for patients who are receiving immunomodulatory and immunosuppressive agents for as long as they do not have any history of severe allergic reactions to any of the components of the COVID-19 vaccine, such as Polyethylene Glycol (PEG) and polysorbate. These patients should first be evaluated by an allergologist to determine the safety of the vaccine.[19-22]

E. Post-vaccination monitoring

The Philippine Society of Allergy, Asthma, and Immunology (PSAAI) recommends observing patients who have been vaccinated for at least 30 minutes after the procedure.[21] There is limited data regarding how safe and effective the vaccines are among autoimmune conditions in preventing transmission. It is still advised that all safety preventive measures be followed post-vaccination.

V. CONCLUSION

It is therefore recommended that all patients on an immunomodulatory or immunosuppressive agent for any dermatologic condition be vaccinated by any of the Philippine FDA-approved COVID-19 vaccines to prevent infection. Patients must be evaluated on an individualized approach, with the benefits and risks clearly stated and understood. It is also imperative that vaccinated patients are reminded that vaccination cannot and must not replace transmission prevention measures in all patients and their immediate contacts. Proper mask wearing, frequent disinfection, and physical distancing must still be practiced at all times.

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