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Dermatology patients on biologics and certain other systemic therapies should receive a "booster" messenger RNA COVID-19 vaccine dose: A critical appraisal of recent Food and Drug Administration and Advisory Committee on Immunization Practices recommendations

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On August 12, 2021, the US Food and Drug Administration expanded the emergency use authorization of both messenger RNA (mRNA) COVID-19 vaccines "to allow for the use of an additional dose in certain immunocompromised individuals."[1] This announcement may leave dermatologists wondering whether certain patients should receive the third dose of the mRNA COVID-19 vaccine. Herein, we have summarized the data supporting the Food and Drug Administration/Advisory Committee on Immunization Practices (ACIP) expansion of vaccine authorization and subsequently applied these data to dermatology practice.[1]

Abbreviations used:

ACIP: Advisory Committee on Immunization Practices
mRNA: messenger RNA

Who is "immunocompromised?"

Patient groups that may be primarily managed by a dermatologist that are categorized as "immunocompromised" by the Centers for Disease Control and Prevention have been listed here.[1] Under the mRNA COVID-19 vaccines' expanded authorization, immunocompromised individuals who are immunocompromised to a degree that is similar to the solid organ transplant recipients include patients receiving the following[2]:

1. Active treatment for solid malignancy
2. Prednisone at the dosage of ≥20 mg or equivalent daily (chronic use)
3. Transplant-related immunosuppressive drugs
4. Tumor necrosis factor blockers
5. Biologic agents that are immunosuppressive or immunomodulatory
6. Methotrexate (not specifically mentioned in ACIP definition; however, evidence of impaired

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Table I. Author recommendations regarding administration of an additional dose of the messenger RNA COVID-19 vaccine to certain dermatology patient populations

Patient population	Evidence-based risk	Recommendation
Receiving systemic glucocorticoids	Patients receiving >20 mg prednisone or equivalent daily are at risk of inadequate response to the standard 2-dose mRNA COVID-19 vaccine series	(1) Patients receiving systemic glucocorticoids should receive an additional dose of the mRNA COVID-19 vaccine (2) Conscious efforts should be made to taper patients on prednisone below 20 mg daily
Receiving oral immunosuppressants, including methotrexate, mycophenolate mofetil, cyclosporine, and JAKis	Patients receiving oral immunosuppressants are at risk of inadequate response to the standard 2-dose mRNA COVID-19 vaccine series	(1) Patients receiving oral immunosuppressants should receive an additional dose of the mRNA COVID-19 vaccine (2) Patients who have not yet been vaccinated who are receiving these medications or who are considering initiation of these medications should be preferentially offered a less immunosuppressing biologic, if indicated clinically
Receiving B-cell depletion (ie, anti-CD20 monoclonal antibodies)	Patients receiving B-cell depletion are more likely than not to mount an inadequate response to the standard 2-dose mRNA COVID-19 vaccine series	(1) Patients undergoing B-cell depletion should receive an additional dose of the mRNA COVID-19 vaccine. The ideal timing of this additional dose is discussed in the referenced article[5] (2) Patients with conditions that can be adequately treated with therapeutics other than B-cell depletion (eg, bullous pemphigoid) should be preferentially offered a less immunosuppressing biologic, if indicated clinically
Receiving TNF blockers and IL-17 inhibitors	Patients receiving TNF blockers and IL-17 inhibitors may mount lower absolute titers to the standard 2-dose mRNA COVID-19 vaccine series; however, there is insufficient evidence to suggest that these patients are at increased risk of mounting an inadequate immune response to the 2-dose series	(1) As an aggregate, patients receiving TNF blocker and IL-17 inhibitor monotherapy do not appear to need the third dose of the mRNA COVID-19 vaccine based on existing data; however, the third dose may be indicated for patients with comorbidities that predispose the patient to severe COVID-19 infection. Shared decision making with all patients on these medications is recommended. (2) There are no specific data regarding the ideal timing of vaccination; however, like other nonlive vaccinations, the mRNA COVID-19 vaccine can likely be administered without interruption in biologic therapy

Continued

Table I. Cont'd

Patient population	Evidence-based risk	Recommendation
Receiving IL-12/23, IL-23, and IL-4/13 inhibitors	There are inadequate real-world data to assess the effect of IL-12/23, IL-23, and IL-4/13 inhibitors on mRNA COVID-19 vaccine response	(1) Based on the mechanism of action of these medications, it is unlikely that these medications predispose patients to an increased risk of mounting an inadequate response to the standard 2-dose mRNA COVID-19 vaccine series. Additional prospective data are needed to confirm the presumed immunogenicity of the mRNA COVID-19 vaccine in patients receiving these medications. At this time, shared decision making is recommended given the paucity of available data
Patients with metastatic melanoma, squamous cell carcinoma, or other internal malignancy undergoing active treatment	Patients undergoing treatment for metastatic melanoma, squamous cell carcinoma, and other malignancies are at risk of inadequate response to the standard 2-dose mRNA COVID-19 vaccine series	(1) Patients undergoing treatment for metastatic skin cancer should be encouraged to urgently contact their oncologist about whether they should receive an additional dose of the mRNA COVID-19 vaccine

IL, Interleukin; *JAKi*, Janus kinase inhibitor; *mRNA*, messenger RNA; *TNF*, tumor necrosis factor.

response to COVID-19 vaccine has been demonstrated in references discussed in the later sections, which were presented at the ACIP meeting)

This definition is according to the "CDC Yellow Book" and has not been specifically modified for application to the mRNA COVID-19 vaccine.

Are there studies supporting this definition?

Many dermatologists may question this broad definition based on consensus from the National Psoriasis Foundation COVID-19 Task Force that "Existing data generally suggest that treatments for psoriasis and/or psoriatic arthritis do not meaningfully alter the risk of acquiring SARS-CoV-2 infection or having worse COVID-19 outcomes."[2] Similarly, biologic therapies have been associated with a decreased risk of hospitalization in cohorts with psoriasis.[3]

Although publications support consensus statements regarding the safety of certain medications during the pandemic, ACIP's recommendations were made based on emerging data that individuals receiving certain medications are "less likely" to mount an adequate immune response to the mRNA COVID-19 vaccine 2-dose series.[1]

Specifically, studies have demonstrated reduced seroconversion in individuals with chronic inflammatory diseases such as psoriasis and psoriatic arthritis receiving glucocorticoids, mycophenolate mofetil, methotrexate, and anti-CD20 monoclonal antibodies, including rituximab.[1] One study evaluated vaccine response in 24 individuals with psoriasis, 9 of whom were receiving methotrexate and found that the rate of adequate response to the vaccine was 20% lower in individuals receiving methotrexate.[4] They also observed a slight decrease in vaccine response among individuals receiving Janus kinase inhibitors.[4] However, although lower titers have been observed in patients receiving anti—tumor necrosis factor and anti—interleukin 17 biologics than those in controls, no difference in the rate of seroconversion has been observed in these patients.[1]

When should "immunocompromised individuals" receive an additional dose of the mRNA COVID-19 vaccine?

ACIP has recommended that individuals categorized as "immunocompromised" receive the third dose >28 days after the completion of their 2-dose mRNA COVID-19 vaccine series.[1] Patients should receive the same vaccine that they initially received. Specific recommendations have not been made for patients who received the Johnson & Johnson vaccine. There is no recommendation to use serologies

to determine whether a patient should receive the third vaccine dose.

Are there data supporting the safety and efficacy of an additional dose of the mRNA COVID-19 vaccine?

Data supporting the safety and efficacy of the third vaccine dose were derived from 3 prospective studies.[1] Two studies evaluated the third dose in individuals receiving hemodialysis and 1 evaluated the third dose in transplant recipients. These studies demonstrated that "Among those who had no detectable antibody response to an initial mRNA vaccine series, 33% to 50% developed an antibody response to an additional dose."[1] No serious adverse events were identified in these studies.

How should dermatologists adjust their practice in response to the expanded authorization of the mRNA COVID-19 vaccine?

Our recommendations based on these data are summarized in Table I.[5]

Conflicts of interest

Dr Waldman has served as a subinvestigator on clinical trials sponsored by AbbVie, Eli Lilly, Janssen, Regeneron/Sanofi, and Galderma. He has also served as a subinvestigator on the CorEvitas Registry. He received no direct compensation for participation in these trials/registries. He has received direct compensation for participation on an advisory board for a drug aimed at the treatment of myasthenia gravis sponsored by Argenx. Dr Grant-Kels has no conflicts of interest to declare.

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