REVIEW

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COVID-19 vaccine safety and efficacy in patients with immune-mediated inflammatory disease: Review of available evidence

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Dermatologists diagnose and treat many immune-mediated inflammatory diseases (IMID). Understanding the inherent immune dysregulation of these diseases as well as the additional disruption that comes as a result of IMID treatments has been important during the COVID-19 pandemic. With vaccines becoming widely available, dermatologists need to be familiar with the risks and benefits of vaccination in these patients, particularly those taking biologics, in order to have informed discussions with their patients. In this review, we present the current evidence related to COVID-19 vaccine safety and efficacy in patients with IMID and review existing recommendations for vaccination against SARS-CoV-2.

Given the current evidence, there is minimal concern that these patients are at any greater risk of harm from COVID-19 vaccination compared to healthy controls. For most, the benefit of avoiding severe COVID-19 through vaccination will outweigh the theoretical risk of these vaccines. A question that is still outstanding is whether patients on biologics will generate a sufficient immune response to the vaccine, which may be dependent on the specific biologic therapy and indication being treated. This underscores the importance of following patients with IMID after vaccination to determine the safety, efficacy, and duration of the vaccine in this population. (J Am Acad Dermatol 2021;85:1274-84.)

Key words: atopic dermatitis; autoimmune disease; autoimmunity; biologics; COVID-19; dermatomyositis; hidradenitis suppurativa; IMID; MCTD; myositis; pemphigoid; pemphigus; psoriasis; sarcoid; SARS-CoV-2; sclerosis; Systemic Lupus Erythematosus; vaccines; vasculitis.

INTRODUCTION

Biologics have revolutionized therapy for immune-mediated inflammatory diseases (IMIDs), including many dermatologic diseases. Although these drugs generally have a more favorable side effect profile than conventional immunosuppressive medications, these therapies cause some degree of immune disruption, depending on their mechanism. The implications of this have been important in helping patients navigate their treatment options during the COVID-19 pandemic.

There are 2 main concerns regarding vaccination against COVID-19 in patients with IMID: the potential that biologics will reduce the efficacy of the immune response and the concern that vaccination may cause an underlying inflammatory disease to flare.[1,2] Three vaccines have already received emergency use authorization (EUA) in the United States, and more remain under development. Although none have been tested in randomized clinical trials in patients with IMID on biologic therapy, several case series and observational studies of vaccine responses in patients with IMID have been published recently. These reports can help in predicting how these conditions and drugs may impact response to current and future COVID-19 vaccines and aid in counseling patients and developing clinical guidelines.

We present the current evidence for vaccination in patients with IMID and review existing recommendations for COVID-19 vaccination to assist dermatologists in having informed discussions with their patients. Evidence was collected using a search

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of the published PubMed-listed English-language literature.

CURRENT AND EMERGING COVID-19 VACCINES

The development of vaccines against SARS-CoV-2 represents a major achievement, with the vaccine development timeline accelerated from years to months.[3] Of those vaccines having completed phase III trials, 3 have received EUA in the United States: 2 mRNA vaccines and 1 adenovirus-based vaccine.[4-6] More vaccines using a variety of platforms remain under development.[7-9]

mRNA vaccines

SARS-CoV-2 is the first pathogen for which mRNA vaccine technology has been used widely. Both available COVID-19 vaccines of this type contain mRNA encoding the SARS-CoV-2 spike protein, the viral receptor-binding domain that recognizes and binds to the host receptor angiotensin-converting enzyme 2. The mRNA vaccines are unique in that they use the body's existing immune pathways to produce an immune response similar to a natural viral infection. Upon vaccine delivery, the mRNA is taken up by host cells and used by ribosomes to produce spike protein. This happens for a finite period of time before the mRNA is quickly degraded. The spike proteins can then be recognized and presented by the cells via major histocompatibility complex class I molecules, just as would occur with other endogenously produced antigens in a natural viral infection. This elicits a robust CD8$^+$ and CD4$^+$ T-cell–mediated response that ultimately leads to the creation of memory T cells and B cells and the production of neutralizing antibodies against the spike protein.[8] These vaccines have demonstrated high levels of efficacy and can be produced rapidly, but they are challenging to transport and distribute because of the inherent instability of mRNA, and they require 2 doses to achieve maximum protection.[10]

Viral vector vaccines

The third vaccine having received EUA in the United States is the Janssen adenovirus-based vaccine, Ad26.COV2.S. This vaccine uses a recombinant virus that is unable to replicate but is still capable of entering human cells. Once within the host cell, the SARS-CoV-2 spike protein antigen is expressed, resulting in the host generation of a T-cell–mediated immune response. The AstraZeneca adenovirus-based vaccine (ChAdOx1 nCoV-19) is currently being administered widely in Europe (in addition to Pfizer BNT162b2, Moderna mRNA-1273, and Ad26.COV2.S) but has not yet been granted EUA by the US Food and Drug Administration.

SAFETY OF COVID-19 VACCINES IN PATIENTS WITH IMID

In addition to presenting antigen as the target of the immune response, vaccines must also contain an adjuvant that activates the innate immune system and provides the necessary second signal for T-cell activation and the generation of a robust immune response. For mRNA vaccines, the mRNA both encodes the antigen and acts as an adjuvant. Upon entry into a cell, single-stranded RNA activates endosomal toll-like receptors (TLR), including TLR3 and TLR7.[11] Both single-stranded RNA and double-stranded RNA activate the inflammasome in the cytosol. These trigger an inflammatory response and the generation of type I interferons, which are known to flare autoimmune disease. However, vaccine developers have implemented modifications to reduce interferon activation and reduce this risk, including the addition of stabilizing adjuvants and removal of interferon-stimulating double-stranded mRNA from final preparations.[12,13]

Adenoviral vector vaccines also function as adjuvants. The double-stranded DNA inside the viral vector both encodes the spike protein antigen and induces the production of type I interferons via activation through TLR9.[11] In addition to the concerns about potentially flaring inflammatory disease via the production of type I interferons, some inflammatory diseases are associated with an increased risk of thrombosis. Adenoviral vaccines carry a rare but increased risk of thrombosis with thrombocytopenia, potentially due to the production of autoantibodies to platelet factor 4.[14] Thrombosis has occurred 1-2 weeks after vaccination, mostly in women and primarily in the cerebral venous sinus. The administration of Ad26.COV2.S was paused in the United States while these cases were being investigated, but the pause was lifted after advisory

CAPSULE SUMMARY

- Patients with immune-mediated inflammatory disease (IMID) may experience disease flares or have diminished immune responses after COVID-19 vaccination, particularly those receiving B-cell–depleting therapies.

- More research is necessary to determine how biologic therapies impact vaccine responses in patients with IMID and to develop strategies to optimize responses in this population.

committees from the Food and Drug Administration and Centers for Disease Control determined that the known benefits of protection from COVID-19 outweigh the risks.[15]

Although the prospective randomized studies for the currently available mRNA and adenovirus COVID-19 vaccines excluded patients on immunomodulatory medications, several groups have published case series of patients with IMID who have been vaccinated (Tables I and II).[16-28] These data suggest that patients receiving biologics for the treatment of inflammatory and autoimmune disease can safely receive, and are able to mount a detectable immune response to, the COVID-19 vaccines, with a few notable exceptions.

The COVID-19 Vaccine Responses in Patients with Autoimmune Disease study is a longitudinal observational study of the immune response to SARS-CoV-2 vaccines in patients with autoimmune and inflammatory disease. The initial phase of the COVID-19 Vaccine Responses in Patients with Autoimmune Disease study measures the magnitude and quality of the acute humoral response compared to a healthy control group.[20]

The question of vaccine efficacy in patients with IMID has also been addressed by a number of smaller case series (Table II). In a study by Geisen et al,[21] vaccine response and side effects were compared in 42 healthy controls and 26 patients with chronic inflammatory disease (of whom 20 were taking a biologic drug). Antibody titers and neutralization activity were detectable in all the patients and controls, although lower in those with inflammatory disease.

By contrast, another study measured responses to BNT162b2 in a larger population (n = 84 patients with IMID and 182 controls) over time. They found that patients with IMIDs develop antibody responses more slowly than controls and that a greater proportion of the IMID group did not respond at all to the vaccine compared to the control group. These differences were found even when comparing patients with IMID who were not receiving any kind of biologic or disease-modifying antirheumatic drug treatment, suggesting that the difference in response may be related to the underlying disease process rather than the form of treatment.[22]

Association with disease flares or other adverse effects

An observational cohort of 325 patients with rheumatic and musculoskeletal disease who received either BNT162b2 or mRNA-1273 were recruited using social media and asked to complete a questionnaire about local and systemic side effects they experienced during the first week following their first vaccine dose. Side effects were similar in severity and frequency to those of healthy patients in the vaccine trials, with 69% reporting at least 1 systemic side effect (most commonly fatigue). One patient reported confirmed COVID infection, 1 reported peripheral neuropathy, and none reported allergic reactions requiring epinepherine.[16] Notably, most participants were female (96%) and White (89%). Data were collected only after the first dose, and because more severe side effects tend to occur after a second dose, the generalizability of these findings is potentially limited. There was also potential for participation bias, as those with side effects may have been more likely to participate in the survey than those without side effects.

In a study by Geisen et al,[21] investigators also measured arthritis activity prior to vaccination and after each vaccine dose; it was not found to be increased in these patients. Systemic side effects also tended to be milder among those patients treated for inflammatory disease than in healthy controls.

THE IMPACT OF BIOLOGIC THERAPY ON RESPONSE TO COVID 19 VACCINES
B-cell−depleting therapies

The most significant reduction in immune response to the available COVID-19 vaccines has been in patients receiving B-cell−depleting therapies (BCDTs), including rituximab, belimumab, and ocrelizumab. Deepak et al,[20] Spiera et al,[24] and Boyarsky et al[23] each measured vaccine responses in patients on several immunosuppressive therapies and found the most significant reduction in antibody response in patients receiving BCDT, like rituximab, compared to other biologics and disease-modifying antiheumatic drugs.

Spiera et al[24] also note that patients with even weakly reconstituted B cells had more robust vaccine responses, suggesting the importance of timing vaccines with an interval between rituximab dosing and immunization. Deepak et al[20] concluded that BCDT has the most prominent effect on antispike protein immunoglobulin G and neutralization titers

Table I. COVID-19 vaccine safety outcomes in patients with immune-mediated inflammatory disease

Study	Vaccine given	Population	Therapies used at the time of vaccination	Response to COVID-19 vaccine
Connolly et al[16]	BNT162b2 or mRNA-1273	325 IMID patients surveyed about side effects in first week after initial dose of vaccine	DMARDs (44%) Biologics (19%) Combination therapy (37%)	• Local and systemic reactions were transient, mild, and similar to those reported in vaccine trials • 89% reported local symptoms (most commonly pain) • 69% reported systemic symptoms (most commonly fatigue) • No allergic reactions requiring epinephrine • One case of PCR-confirmed COVID 19 infection • One case of peripheral neuropathy
Watad et al[17]	ChAdOx1 nCoV-19, BNT162b2, or mRNA-1273	Collection of cases (n = 27, 17 flares, and 10 new-onset IMID) in patients with IMID in 28 days following COVID vaccination	Mixed group including biologics, steroids, and DMARDs Biologics included: infliximab, certolizumab, adalimumab, tocilizumab, apremilast, vedolizumab	• Findings of new-onset disease rare and likely close to the background incidence of these conditions • Flares were temporally associated with vaccination, but no way to determine causation • Most (81%) of cases treated with glucocorticoids; no cases of severe, resistant, or progressive disease
Damiani et al[18]	All BNT162b2	4 patients with psoriasis	Biologics included: secukinumab, risankizumab, ixekiuzmab	• All patients developed detectable anti-SARS-CoV-2 receptor-binding domain antibodies • No patients modified or discontinued their biologic in preparation for vaccination • Patients experienced pain at the injection site but no psoriatic flares or other cutaneous manifestations
Boekel et al[19]	ChAdOx1 nCoV-19, BNT162b2, or mRNA-1273	505 patients with IMID; 203 healthy controls	No treatment (31%) Methotrexate (33%) Glucocorticoids (15%) Biologics (29%) - predominately TNFi and BCDT	• No significant difference in frequency of adverse events between patients with IMID and controls (51% of patients vs 52% of controls experienced mild AEs; 21% patients vs 19% controls reported moderate AEs)

Table I. Cont'd

Study	Vaccine given	Population	Therapies used at the time of vaccination	Response to COVID-19 vaccine
				• 44% of patients and 40% of controls reported systemic AEs, most commonly fatigue and headache • Patients with IMID more frequently reported joint pain than controls (10% vs 1%) • Only 5% of patients reported worsening of their IMID up to 2 months post vaccination

AEs, Adverse events; BCDT, B-cell–depleting therapy; DMARDs, disease-modifying antirheumatic drugs; IMID, immune-mediated inflammatory disease; PCR, polymerase chain reaction; TNFi, tumor necrosis factor inhibitor.

in the 6 months after dosing, whereas other case series have observed that patients receiving regular rituximab have failed to mount any detectable antibody response, even with a 6-month interval between rituximab dosing and vaccination.[29,30]

One of these case series, Salviani et al[29] highlighted 2 cases of patients receiving rituximab for antineutrophil cytoplasmic antibody-associated vasculitis. Although both patients received their last dose of rituximab approximately 7 months prior to vaccination, neither had recovered B-cell counts at time of vaccination and subsequently did not produce a detectable immune response. In another case series focusing specifically on rituximab-treated patients, only 2 of 5 patients developed antispike protein antibodies, both of whom had detectable $CD19^+$ B cells. Interestingly, all 5 patients showed SARS-CoV-2 specific T-cell reactivity as measured by interferon-γ response to SARS-CoV-2 peptides.[30] These findings are consistent with the impact of BCDT on the responses to other, non-COVID-19 vaccines.[31,32]

TNF inhibitors

Results from initial case series and larger studies suggest that tumor necrosis factor inhibitor has a less substantial impact on immune response than BCDT, but patients on these therapies may mount less robust immune responses than those seen in healthy controls.[25,26] In contrast, patients receiving tumor necrosis factor inhibitor in the larger cohort from the COVID-19 Vaccine Responses in Patients with Autoimmune Disease study were found to have similar antibody titers but a reduction in neutralization activity, when compared to healthy controls.[20]

Interleukin 17 inhibitors

Relatively fewer case reports are available regarding vaccination in patients receiving anti-interleukin (IL) 17 therapies, but those available suggest that these patients produce a detectable antibody response.[24]

IL-12/23 inhibitors

Available data from cohorts including patients receiving IL-12/23 inhibitors do not suggest that this class inhibits immune response to COVID-19 vaccines in any meaningful way. Results from Deepak et al[20] found that IL-12/23 inhibitor use has a minimal impact on antibody titers compared to control and to other classes of biologics.[20]

Table II. COVID-19 vaccine efficacy in patients with immune-mediated inflammatory disease

	Vaccine given	Population	Therapies used at the time of vaccination	Response to COVID-19 vaccine

Deepak et al[20]	BNT162b2 or mRNA-1273	133 adults with IMID; 53 immunocompetent controls	Prednisone (12.8%)
			MTX (21.8%)
			Hydroxychloroquine (22.6%)
			TNFi (28.6%)
			BCDT (7.5%)
			NSAIDs (20.3%)
				• 3-fold reduction in antibody titers and 2.7-fold decrease in neutralization in patients with IMID vs immunocompetent controls 1-2 weeks after first dose
				• Seropositivity rates: 98% in immunocompetent controls; 92% in IMID participants not on prednisone; 65% in IMID participants on prednisone
				• Reduction in antibody and neutralization titers by therapy:
				    Glucocorticoids: 10-fold reduction; antimetabolites: 2-3x reduction; and BCDT: 36x reduction
				    IL-12/23 inhibitors, vedolizumab, TNFi, antimalarials: minimal impact on titers

Geisen et al[21]	BNT162b2 or mRNA-1273	42 healthy controls; 26 patients with IMID	Biologics +/- concomitant DMARDs or steroid including: TNFi, IL-6i, IL-17i, anti-integrin, IL-12/23i, BCDT	• Detectable antibody titers and neutralization activity in all participants 7 days after second vaccine dose • Total titers and neutralizing activity lower in patients than in controls • Side effects comparable in both groups, more mild side effects in inflammatory disease group • No severe adverse effects or flares of arthritis observed
Simon et al[22]	All BNT162b2	84 patients with IMID; 182 controls	Biologics (42.9%): TNFi, IL-6i, IL-23i, IL-17i Nonbiologic DMARDs (23.9%) No treatment (28.6%)	• Serology 10 or more days after first vaccine dose; 96% had both doses, none with previous COVID infection or baseline antibodies • Patients with IMID, including those without any current treatment, had delayed and reduced immune response relative to healthy controls (lower mean titers at day 28, but equivalent by day 70) • 0.5% of the controls failed to develop neutralizing antibody activity (vs 9.5% of patients with IMID) • Lower incidence of side effects in patients than in controls
Boyarsky et al[23]	BNT162b2 or mRNA-1273	123 vaccinated patients with IMID	No treatment (28%), nonbiologic DMARDs (19%), biologics (14%), combination therapy (37%) Biologics included: TNFi, IL-6i, IL-17i, IL-12/23i, BCDT, abatacept	• Only measured response to single dose of vaccine • Only biologic associated with failure to make detectable antibodies was rituximab • Mycophenolate associated with failure to mount detectable antibody response

Continued

Table II. Cont'd

	Vaccine given	Population	Therapies used at the time of vaccination	Response to COVID-19 vaccine
				• Nearly universal response in patients receiving TNFi (16 patients with antibodies, 1 nonresponder)
Spiera et al[24]	BNT162b2 or mRNA-1273	89 adult patients with IMID	Nonbiologic DMARDs and/or biologics: rituximab, belimumab, adalimumab, secukinumab, etanercept, tocilizumab	• 21 of 89 patients had no serological response to vaccine: 20 received rituximab, 1 received belimumab • No patients receiving rituximab in the preceding 6 months had a detectable response • All on adalimumab, secukinumab, and etanercept had detectable antibody response
Wong et al[25]	BNT162b2 or mRNA-1273	48 IBD patients; 43 controls (not on biologics)	41 (85%) of patients receiving biologics including: TNFi, vedolizumab, ustekinumab, guselkumab	• All IBD patients (n = 26) who completed two-dose vaccine schedules seroconverted (22 had titers sufficient to be considered for convalescent plasma donation) • Lower titers compared to controls in patients on TNFi and vedolizumab
Kennedy et al[26]	BNT162b2 or ChAdOx1 nCoV-19	1293 patients with IBD	All patients treated with either Infliximab or vedolizumab	• Diminished titers in patients treated with infliximab compared to vedolizumab • Responses lower in patients on concomitant DMARD • Responses higher among patients with history of COVID infection
Al-Janabi et al[27]	BNT162b2 or ChAdOx1 nCoV-19	120 patients with IMID: Primarily Psoriasis (107) and PsA (25)	Oral immunomodulators and/or biologics including: abatacept, TNFi, brodalumab, guselkumab, ixekizumab, risankizumab, secukinumab, tildrakizumab, ustekinumab	• Median time from vaccination was 34 days (2-12 weeks after first dose) • 15% had no antibody response to spike, 41% had no detectable IgG to spike protein; all participants with previous COVID did mount an antibody response (22 patients) • MTX reduced response relative to biologics (adjusted OR = 0.31 for any antibody response to spike)
Khan et al[28]	BNT162b2 or mRNA-1273	14,697 IBD patients; 7,321 received at least one vaccine dose	Therapies included: 5-aminosalicylic acid, thiopurines, TNFi, vedolizumab, ustekinumab, tofacitinib, methotrexate, and corticosteroid	• Full vaccination status associated with a 69% reduction in infection relative to an unvaccinated status (HR, 0.31; 95% CI, 0.17-0.56; $P < .001$) • No patients taking TNFi, ustekinumab, or methotrexate experienced SARS-CoV-2 infection >7 days after the second vaccine dose

BCDT, B-cell−depleting therapy; *DMARDs*, disease-modifying antirheumatic drugs; *HR*, hazard ratio; *IBD*, inflammatory bowel disease; *IgG*, immunoglobulin G; *IL-6i*, interleukin 6 inhibitor; *IL-12i*, interleukin 12 inhibitor; *IL-17i*, interleukin 17 inhibitor; *IL-23i*, interleukin 23 inhibitor; *IMID*, immune-mediated inflammatory disease; *MTX*, methotrexate; *NSAIDs*, nonsteroidal anti-inflammatory drugs; *OR*, odds ratio; *PsA*, psoriatic arthritis; *TNFi*, tumor necrosis factor inhibitor.

Table III. Current society recommendations regarding COVID-19 vaccination

Society	Recommendations
National Psoriasis Foundation[33]	• All patients with psoriasis should accept a vaccine as soon as it becomes available to them • Psoriasis and/or psoriatic arthritis are not contraindications to vaccination
International Psoriasis Council[34]	• No specific guidance regarding vaccination • Stated that registry data should be collected to inform whether SARS-CoV-2 vaccines either positively or negatively affect psoriasis outcome
International Pemphigus and Pemphigoid Foundation[35]	• Patients with autoimmune bullous diseases should be vaccinated when a vaccine is available to them, as these patients are also at high risk for complications of COVID-19 • In most cases, immunosuppressive treatment should not be interrupted to receive a vaccine as this could result in relapse or flare of disease • In patients treated with rituximab, vaccination should be completed 2 weeks prior to the start of rituximab treatment whenever possible, otherwise it is best to wait 4-6 months after the last rituximab infusion
National Eczema Association[36]	• Atopic dermatitis is not a contraindication to vaccination • Any patients with history of anaphylaxis or reaction to a vaccine ingredient should consult with their allergist prior to vaccination
Hidradenitis Suppurativa Foundation[37]	• People with HS are not at increased risk for severe COVID-19 due to HS or any subsequent treatment and should be able to safely receive the vaccine when it is available to them • Patients should not stop any biologics in order to receive a vaccine and should speak to their physician regarding any concerns
American College of Rheumatology[38,39]	• Patients with autoimmune and inflammatory rheumatologic disease should be prioritized for vaccination • For patients with rheumatologic conditions, the theoretical risk of disease flares due to COVID-19 vaccination is outweighed by the definite risk of severe COVID-19 infection • For those with well-controlled disease: recommend to hold methotrexate and JAK inhibitors for one week after each vaccine dose, to hold subcutaneous abatacept 1 week prior to and after the first COVID-19 vaccine dose only, and that patients taking cyclophosphamide should time their infusion to be 1 week after each vaccine dose if possible • In patients treated with rituximab: vaccine series should be initiated 4 weeks prior to the next scheduled cycle, and the next dose be delayed for 2-4 weeks after the second vaccine dose, if the patient's disease activity allows • No recommendation for dose or timing modifications for patients taking oral steroids, hydroxychloroquine, IVIG, apremilast, sulfasalazine, leflunamide, oral cyclophosphamide, azathioprine, TNFi, IL-17 inhibitors, IL-12/23 or IL-23 inhibitors, belimumab, or oral calcineurin inhibitors

HS, Hidradenitis suppurativa; *IL*, interleukin; *IVIG*, intravenous immunoglobulin; *JAK*, janus kinase; *TNFi*, tumor necrosis factor inhibitor.

IL-23 inhibitors

In small case series, patients receiving these therapies have produced detectable immune responses with no reported cases of reduced antibody response thus far.[25,27]

Limitations

These studies are all limited due to small sample size, which makes additional analysis examining changes in response by disease process and specific therapy class challenging. Although antibody titers and neutralizing antibodies are relatively straightforward to measure, the most important outcome is COVID-19 infection, particularly severe infection.

This highlights the need to follow patients with IMIDs after they receive mRNA vaccines to confirm that they are indeed protective and to fully elucidate any impact they may have on disease flares or new IMID pathogenesis.

DISCUSSION

Several professional societies have offered guidance for COVID-19 vaccination for patients on immunomodulatory treatment (Table III).[33-39] Although recommendations differ by group, none suggest any contraindications to vaccinations in patients with IMID. Additionally, the growing body of evidence from studies of vaccination in these

patients suggests that these new vaccines are comparable in safety and efficacy to existing vaccines and that side effects are similar to those seen in the healthy population.

Based on the available data, the chief concern for patients with IMID appears to be the efficacy of the immune response these patients will be able to generate, depending on the specific biologic therapy and indication being treated. It is important to note that several early studies are small, some lack a healthy control group, and some report antibody titers captured prior to the time point at which maximum immunity would be expected (ie, prior to 2 weeks after the final vaccine dose). In addition, vaccine-induced immunity likely has both a cell-mediated and a humoral response, and the studies presented measure only humoral responses, which may not correlate directly with protection from infection. Given findings that antibody titers may be slower to reach their peak value in patients with IMID, it is important to remind these patients that they should take seriously the guidance to wait at least 2 weeks after their final vaccine dose to consider themselves fully vaccinated. Current data are not sufficient to offer guidance on masking.

Although the currently available evidence provides perspective in guiding IMID patients through initial vaccination efforts, it also leaves many unanswered questions. For example, at this point it is not clear which is the optimal test for assessing for adequate vaccine response in this population, whether that be total antibody titers, neutralization assays, or some other study. Data in healthy populations suggest that the presence of antispike protein immunoglobulin G is indeed negatively correlated with the development of COVID-19 infection, but our limited knowledge about the mechanism of vaccine-induced immunity limits how broadly we can generalize these data to patients with IMID.[40] The emergence of new variants adds another variable to this consideration, as patients with equal titers of antibodies may not necessarily be equivalent when tested by neutralization assay with different variants.[41] It will be important to understand how the presence of different variants may impact how we assess for the response of patients with IMID to vaccination.

We also have yet to determine whether patients receiving immunomodulating therapies will require alternative regimens to achieve a sufficient response, whether that is an additional vaccine dose, a booster, or some combination of available vaccines. A third dose has been studied as a way to bolster immune response to COVID vaccine in transplant recipients and seems like a promising solution in this population.[42] This could also be considered for patients with IMID and warrants further investigation.

CONCLUSIONS

With COVID-19 vaccines becoming widely available, dermatologists need to be prepared to discuss the risks and benefits of vaccination with their patients with IMID. Available data from initial studies of COVID-19 vaccination in these patients suggest that neither IMID nor concurrent biologic use is a contraindication to vaccination. However, patients receiving biologics, and particularly those on BCDT, may produce diminished immune responses. It is not yet clear what the clinical significance of this altered immune response may actually be. It is essential that we continue to follow patients with IMID after vaccination to determine the safety, efficacy, and duration of the vaccine in this population.

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