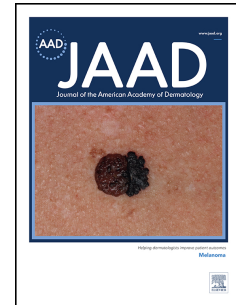


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COVID-19 vaccine safety and efficacy in patients with Immune-Mediated Inflammatory Disease: Review of available evidence

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Title: COVID-19 vaccine safety and efficacy in patients with Immune-Mediated Inflammatory Disease: Review of available evidence

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38 Abstract

39 Dermatologists diagnose and treat many immune-mediated inflammatory diseases (IMID).
40 Understanding the inherent immune dysregulation of these diseases as well as the additional
41 disruption that comes as a result of IMID treatments has been important during the COVID-19
42 pandemic. With vaccines becoming widely available, dermatologists need to be familiar with
43 the risks and benefits of vaccination in these patients, particularly those taking biologics, in
44 order to have informed discussions with their patients. In this review, we present the current
45 evidence related to COVID-19 vaccine safety and efficacy in patients with IMID and review
46 existing recommendations for vaccination against SARS-CoV-2. Given the current evidence,
47 there is minimal concern that these patients are at any greater risk of harm from COVID-19
48 vaccination compared to healthy controls. For most, the benefit of avoiding severe COVID-19
49 through vaccination will outweigh the theoretical risk of these vaccines. An outstanding
50 question is whether patients on biologics will generate a sufficient immune response to the
51 vaccine, which may be dependent on the specific biologic therapy and indication being treated.
52 This underscores the importance of following patients with IMID after vaccination to determine
53 vaccine safety, efficacy, and duration in this population.

54 Capsule summary

- 55 • Patients with Immune-Mediated Inflammatory Disease (IMID) may experience disease
56 flares or have diminished immune responses after COVID-19 vaccination, particularly
57 those receiving B cell-depleting therapies.
- 58 • More research is necessary to determine how biologic therapies impact vaccine
59 responses in patients with IMID and to develop strategies to optimize responses in this
60 population.

Introduction

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

There are two main concerns regarding vaccination against COVID-19 in patients with IMID: the potential that biologics will reduce efficacy of the immune response and concern that vaccination may cause a flare of the underlying inflammatory disease.^{1,2} Three vaccines have already received emergency use authorization (EUA) in the US, and more remain in development. While none have yet been tested in patients with IMID, including those on concurrent biologic therapy, as part of randomized clinical trials, 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 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, three have received EUA in the US- two mRNA vaccines and one adenovirus-based vaccine.^{4,5,6} More vaccines utilizing a variety of platforms remain in development.^{7,8,9}

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. 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 time period before the mRNA is quickly degraded. The spike proteins can then be recognized and presented by the cells via MHC 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 creation of memory T and B cells and production of neutralizing antibodies against spike protein.⁸ These

vaccines have demonstrated high levels of efficacy and can be produced rapidly, but they are challenging to transport and distribute due to the inherent instability of mRNA and require two doses to achieve maximum protection.¹⁰

Viral vector vaccines

The third vaccine having received EUA in the US is the Janssen adenovirus-based vaccine, Ad26.COVS.2. This vaccine uses a recombinant virus that is unable to replicate but still capable of entering human cells. Once within the host cell, the SARS-CoV-2 spike protein antigen is expressed, resulting in 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.COVS.2) but has not yet been granted EUA by the FDA.

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 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 (ssRNA) activate endosomal toll-like receptors (TLR) including TLR3 and TLR7.¹¹ Both ssRNA and double stranded RNA (dsRNA) 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 (dsDNA) 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 (anti-PF-4).¹⁴ Thrombosis has occurred 1-2 weeks after vaccination, mostly in women, and primarily in the cerebral venous sinus. Administration of Ad26.COVS.2 was paused in the US while these cases were investigated, but the pause was lifted after FDA and CDC advisory committees determined that the known benefits of protection from COVID-19 outweigh the risks.¹⁵

While 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 (Table 1, Table 2). These data suggests that patients receiving biologics for 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 COVaRiPAD (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 COVaRiPAD measures the magnitude and quality of the acute humoral response compared to a healthy control group.¹⁶

The question of vaccine efficacy in patients with IMID has also been addressed by a number of smaller case series (Table 2). In a study by Geisen et al comparing vaccine response and side effects 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 patients and controls, though lower in those with inflammatory disease.¹⁷

By contrast, another study measured responses to BNT162b2 in a larger population (n= 84 patients with IMID, 182 controls) over time and found that patients with IMIDs develop antibody responses more slowly than controls, and 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 DMARD treatment, suggesting that the difference in response may be related to the underlying disease process, rather than the form of treatment.¹⁸

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 healthy patients in the vaccine trials, with 69% reporting at least one systemic side effect (most commonly fatigue). One patient reported confirmed COVID infection, one reported peripheral neuropathy, and none reported allergic reactions requiring epinephrine.¹⁹ Notably, most participants were female (96%) and white (89%). Data were collected only after the first dose, and since more severe side effects tend to occur after a second dose, the generalizability of these findings is potentially limited. There is 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 the above study by Geisen et al., 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.¹⁷

New-onset or flares of immune mediated disease with a temporal association to mRNA vaccination, primarily in patients with a known history of autoimmune and inflammatory disease, have been reported in a case series.²⁰

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 (BCDT) including rituximab, belimumab, and ocrelizumab. Deepak et al., Spiera et al., and Boyarsky et al. each measured vaccine responses in patients on several immunosuppressive therapies and found most significant reduction in antibody response in patients receiving BCDT, like rituximab, compared to other biologics and DMARDs.^{16,22,23} Spiera et al. also note that patients with even weakly reconstituted B cells had more robust vaccine responses, suggesting importance of timing vaccines with an interval between rituximab dosing and immunization. Deepak et al. conclude that BCDT have the most prominent effect on anti-spike protein IgG and neutralization titers in the 6 months after dosing, while 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.^{23,24} One of these case series, Salviani et al., highlighted two cases of patients receiving rituximab for ANCA-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.²³ In another case series focusing specifically on rituximab-treated patients, only 2 of 5 patients developed anti-spike 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.²⁴ These findings are consistent with the impact of BCDT on the responses to other, non-COVID-19 vaccines.^{25,26}

TNF-inhibitors

Results from initial case series and larger studies suggest that TNFi have a less substantial impact on immune response than BCDT, but patients on these therapies may mount less robust immune responses than those in seen healthy controls.^{27,28} In contrast, patients receiving TNFi in the larger cohort from COVaRiPAD were found to have similar antibody titers, but a reduction in neutralization activity, as compared to healthy controls.¹⁶

IL-17-inhibitors

Relatively fewer case reports are available regarding vaccination in patients receiving anti-IL-17 therapies, but those available suggest that these patients produce a detectable antibody response.²²

IL-12/23-inhibitors

Available data from cohorts including patients receiving IL-12/23-inhibitors do not suggest that this class meaningfully inhibits immune response to COVID-19 vaccines. Results from Deepak et al. found that IL-12/23-inhibitor use has a minimal impact on antibody titers compared to control and to other classes of biologics.¹⁶

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.^{27,29}

Limitations

These studies are all limited due to small sample size, which makes additional analysis to examine changes in response by disease process and specific therapy class challenging. While 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 receiving 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 3). While 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 (i.e. prior to two weeks after the final vaccine dose). Also, 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 what the optimal test is 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 presence of anti-spike protein IgG is indeed negatively correlated with developing 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.³⁰ 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.³¹ It will be important to understand

279 how the presence of different variants may impact how we assess for IMID patients' response
280 to vaccination.

281
282 We also have yet to determine if patients receiving immunomodulating therapies will require
283 alternative regimens to achieve a sufficient response, whether that be an additional vaccine
284 dose, a booster, or some combination of available vaccines. A third dose has been studied as a
285 way to bolster immune response to COVID vaccine in transplant recipients and seems like a
286 promising solution in this population.³² This could also be considered for patients with IMID and
287 warrants further investigation.

288 289 **Conclusion**

290 With COVID-19 vaccines becoming widely available, dermatologists need to be prepared to
291 discuss risks and benefits of vaccination with their patients with IMID. Available data from initial
292 studies of COVID-19 vaccination in these patients suggest that neither IMID nor concurrent
293 biologic use are contraindications to vaccination. However, patients receiving biologics, and
294 particularly those on BCDT, may produce diminished immune responses. It is not yet clear what
295 the clinical significance of this altered immune response may actually be. It is essential that we
296 continue to follow patients with IMID after vaccination to determine vaccine safety, efficacy,
297 and duration in this population.
298

299 Table 1: COVID-19 vaccine safety outcomes in patients with immune-mediated inflammatory disease (IMID)

	Vaccine given	Population	Therapies used at time of vaccination	Response to COVID-19 vaccine
Connolly et al.	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 ¹⁹
Watad et al.	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 ²⁰
Damiani et al.	All BNT162b2	4 patients with psoriasis	Biologics included: secukinumab, risankizumab, ixekizumab	-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 ³⁴
Boekel et al.	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, and 21% patients vs 19% controls reported moderate AEs) -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 ³⁵

301 Table 2: COVID-19 vaccine efficacy in patients with immune-mediated inflammatory disease (IMID)

	Vaccine given	Population	Therapies used at time of vaccination	Response to COVID-19 vaccine
Deepak et al. *pre-print	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; BCDT: 36x reduction; - IL-12/23 inhibitors, vedolizumab, TNFi, antimalarials: minimal impact on titers ¹⁶
Geisen et al.	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 ¹⁷
Simon et al.	All BNT162b2	84 patients with IMID; 182 controls	Biologics (42.9%): TNFi, IL-6i, IL-23i, IL-17i Non-biologic 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 ¹⁸
Boyarsky et al.	BNT162b2 or mRNA-1273	123 vaccinated patients with IMID	No treatment (28%), Non-biologic 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 -nearly universal response in patients receiving TNFi (16 patients with antibodies, 1 non-responder) ²¹
Spiera et al.	BNT162b2 or mRNA-1273	89 adult patients with IMID	Non-biologic DMARDs and/ or biologics: Rituximab, belimumab, adalimumab, secukinumab, etanercept, tocilizumab	-21/89 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 ²²
Wong et al.	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 ²⁷
Kennedy et al.	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 ²⁸
Al-Janabi et al.	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) ²⁹
Khan et al.	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 (hazard ratio [HR] 0.31, 95% confidence interval [CI] 0.17-0.56, p<0.001) -no patients taking TNFi, ustekinumab, or methotrexate experienced SARS-CoV-2 infection >7 days after the 2nd vaccine dose ³³

303 Table 3: Current society recommendations regarding COVID-19 vaccination

Society	Recommendations
National Psoriasis Foundation	- 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.³⁶
International Psoriasis Council	- 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.³⁷
International Pemphigus and Pemphigoid Foundation	- 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.³⁸
National Eczema Association	- 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.³⁹
Hidradenitis Suppurativa Foundation	- 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.⁴⁰
American College of Rheumatology	- 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 one 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 four 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.^{41,42}

Abbreviations and Acronyms

305	
306	BCDT – B cell depleting therapy
307	DMARD – Disease-modifying anti-rheumatic drug
308	dsDNA – double stranded DNA
309	dsRNA – double stranded RNA
310	EUA – Emergency Use Authorization
311	IL-6i – IL-6 inhibitor
312	IL-12i – IL-12 inhibitor
313	IL-17i – IL-17 inhibitor
314	IL-23i – IL-23 inhibitor
315	IMID – Immune Mediated Inflammatory Disease
316	MTX – methotrexate
317	ssRNA – single stranded RNA
318	TLR – Toll-like receptor
319	TNFi – Tumor Necrosis Factor inhibitor

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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.