The Use of Biologics During the COVID-19 Pandemic



Madison E. Jones, BA^a, Alison H. Kucharik, BS^b, Sarah P. Pourali, BS^c, Jeffrey R. Rajkumar, BS^d, Yasmin Gutierrez, BS^e, Rebecca M. Yim, BA^a, April W. Armstrong, MD, MPH^a,*

KEYWORDS

• COVID-19 • Biologics • Psoriasis • Atopic dermatitis • Hidradenitis suppurativa • TNF-Inhibitor

• IL inhibitor • Dupilumab

KEY POINTS

- For biologics used in psoriasis, such as tumor necrosis factor inhibitors, interleukin (IL)-12/23 inhibitors, IL-17 inhibitors, and IL-23 inhibitors, current data suggest that they do not seem to increase the risk of coronavirus disease 2019 (COVID-19) infection or worsened COVID-19 outcomes. It is generally recommended that patients with psoriasis not actively infected with severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) initiate or continue their biologics to treat moderate to severe psoriasis.
- Adalimumab is the only biologic currently US Food and Drug Administration (FDA) approved to treat hidradenitis suppurativa. In patients on adalimumab to treat hidradenitis suppurativa, current data suggest that adalimumab does not seem to increase the risk of COVID-19 infection or worsened COVID-19 outcomes. It is generally recommended that patients with hidradenitis suppurativa not actively infected with SARS-CoV-2 initiate or continue adalimumab to treat moderate to severe hidradenitis suppurativa.
- Dupilumab is the only biologic currently FDA approved to treat moderate to severe atopic dermatitis. In patients on dupilumab to treat atopic dermatitis, current data suggest that dupilumab does not seem to increase the risk of COVID-19 infection or worsened COVID-19 outcomes. It is generally recommended that patients with atopic dermatitis not actively infected with SARS-CoV-2 initiate or continue dupilumab to treat moderate to severe atopic dermatitis.

INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic has prompted questions regarding the use of biologics in patients with inflammatory skin conditions. Infection with COVID-19 incites

an initial antiviral response, followed by a systemic inflammatory response.¹ The multiphasic immune response involves numerous cytokines, few of which serve as biologic therapy targets. Note that the cytokines involved in the antiviral and systemic hyperinflammatory responses differ. Viral

E-mail address: armstrongpublication@gmail.com

Dermatol Clin 39 (2021) 545–553 https://doi.org/10.1016/j.det.2021.05.010 0733-8635/21/© 2021 Elsevier Inc. All rights reserved.

All hard copies of the journal edition may be mailed to the USC Dermatology Research Office: 1441 Eastlake Ave, Norris Topping Tower Suite 3427, Los Angeles, CA 90033.

^a University of Southern California Keck School of Medicine, Los Angeles, CA, USA; ^b Florida Atlantic University Charles E Schmidt College of Science, 777 Glades Road BC-71, Boca Raton, FL 33431, USA; ^c Vanderbilt University School of Medicine, 1161 21st Ave S # D3300, Nashville, TN 37232, USA; ^d University of Illinois College of Medicine at Chicago, 1853 W Polk St, Chicago, IL 60612, USA; ^e University of California Riverside School of Medicine, 92521 Botanic Gardens Dr, Riverside, CA 92507, USA

^{*} Corresponding author. University of Southern California, 1975 Zonal Avenue, KAM 510, MC 9034, Los Angeles, CA 90089.

clearance primarily involves interleukin (IL)-15, interferon alpha (IFN- α)/IFN- β , and IFN γ , whereas the systemic hyperinflammatory response primarily involves tumor necrosis factor (TNF), IL-6, IL-17A, granulocyte-macrophage colony-stimulating factor, and granulocyte colony-stimulating factor. Many biologics target the proinflammatory cytokines involved in the systemic hyperinflammatory phase, but they often do not target key antiviral cytokines, and thereby leave the antiviral response unaffected.² In addition, because biologics target specific mediators of the immune system, they do not cause broad immunosuppression. In certain circumstances, biologics may even exert beneficial effects by attenuating the hyperinflammatory state seen in severe COVID-19; several are being studied for their therapeutic effects in COVID-19.² This article discusses the latest guidance on biologic use during the COVID-19 pandemic for inflammatory skin conditions, including psoriasis, hidradenitis suppurativa, and atopic dermatitis (AD).

PSORIASIS

Among inflammatory skin conditions, moderate to severe plaque psoriasis currently has the most biologics US Food and Drug Administration (FDA) approved for its treatment. The latest guidance for each biologic class FDA approved to treat psoriasis is discussed here, including TNF- α inhibitors, IL-12/23 inhibitors, IL-17 inhibitors, and IL-23 inhibitors in the context of the COVID-19 pandemic.

Tumor Necrosis Factor Alpha Inhibitors (Adalimumab, Certolizumab, Etanercept, and Infliximab)

The TNF- α inhibitors currently FDA approved to treat psoriasis and psoriatic arthritis (PsA) include adalimumab, certolizumab, etanercept, and infliximab. These biologics work by inhibiting TNF- α , a proinflammatory cytokine, effectively reducing the downstream surge in inflammation seen in psoriasis.³

Several studies have investigated the effect of TNF-inhibitors on COVID-19 susceptibility. In order to assess this effect, a meta-analysis used data from previous clinical trials to extrapolate the potential risk of a medication based on its respiratory tract infection (RTI) rate compared with placebo.⁴ The data included reported findings from phase 3 pivotal trials for adalimumab, infliximab, etanercept, and certolizumab.⁴ The meta-analysis found that there was no significant risk of RTI in TNF inhibitors compared with placebo (odds ratio [OR], 1.06; 95% confidence interval [CI], 0.81–1.40; P = .55).⁴

Observational studies have gathered real-world data to assess the effect of TNF inhibitors on COVID-19. A prospective case series in New York assessed 86 patients with known immunemediated inflammatory disease (IMID) who were receiving biologics or other immunomodulatory therapies when they contracted COVID-19.5 The level of patient care required to treat COVID-19 was then characterized by capturing whether the patients were hospitalized or received only outpatient care. Importantly, this study found that the incidence rate for COVID-19 hospitalization among patients with IMID was consistent with the general population.⁵ Furthermore, TNF inhibitors were not associated with increased odds of COVID-19 hospitalization (OR, 0.15; 95% CI, 0.02–1.12).⁵ Similarly, a retrospective cohort study based in Detroit, Michigan, assessed 213 patients with IMID who were receiving treatment with immunosuppressive therapies during the COVID-19 pandemic.⁶ The IMID cohort receiving immunosuppressive treatment had similar odds of COVID-19 infection, hospitalization, need for invasive ventilation, and mortality compared with the general population.⁶ Furthermore, biologics predicted a decreased rate of hospitalization (OR, 0.26; 95% CI, 0.066-0.95), which was driven by anti-TNF monotherapy (OR, 0.16; 95% CI, 0.032-0.72).6

Together, the current clinical trial and real-world data suggest that being on TNF inhibitors does not seem to increase patients' risk of contracting severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), and, when infected, patients do not seem to experience worsened COVID-19 outcomes compared with the general population. Additional recommendations by US and international organizations for biologics used in psoriasis are provided later and are outlined in **Table 1**. The American Academy of Dermatology (AAD) also provides non-disease-specific guidance for the use of systemic medications in dermatology.⁷

interleukin -12/23 Inhibitors (Ustekinumab)

There is currently only 1 FDA-approved biologic for psoriasis and PsA that inhibits IL-12/23, which is ustekinumab. Ustekinumab works by binding to the p40 protein subunit used by both IL-23 and IL-12.³ Ustekinumab disrupts IL-23–mediated and IL-12–mediated signaling of T-helper (Th) 17 and Th1 pathways, thereby reducing the feed-forward inflammatory mechanism in psoriasis.³

To help inform the impact of IL-12/23 inhibitors on COVID-19 susceptibility, a meta-analysis using phase 3 clinical trial data evaluated the risk of RTIs in patients with autoimmune disease on IL-12/23 and IL-23 inhibitors compared with those on

Table 1

Summary of recommendations on psoriasis management by international and US organizations during the coronavirus disease 2019 pandemic, as of April 1, 2021^a

Status of Infection	International Recommendation: IPC and the EADV Psoriasis Task Force/SPIN	US Recommendation: NPF
No active COVID-19 infection, on systemic therapy (ie, biologics or oral medications)	Continue taking systemic therapy (EADV)	Continue taking systemic therapy
High-risk group, on immunomodulatory agents	Consult a health care provider regarding these risk factors ^b (EADV)	Consult a health care provider regarding these risk factors ^c
No active COVID-19 infection, being considered to initiate immunomodulatory agents	No statement at the time of writing	Consult a health care provider
COVID-19 infection, on systemic therapy (ie, biologics or oral medications)	Discontinue or postpone taking immunosuppressant treatment (IPC, EADV)	Consult a health care provider
Recovered from COVID-19	No statement at the time of writing	Consult a health care provider
Professional Organization	Resource	
IPC	https://www.psoriasiscouncil.org/blog/Statement-on- COVID-19-and-Psoriasis.htm	
EADV Psoriasis Task Force/SPIN	https://www.eadv.org/cms-admin/showfile/7_ PSORIASIS-SPIN%20TF%20Recommandations_ Covid-Corner.pdf	
NPF	https://www.psoriasis.org/advance/coronavirus	

Abbreviations: EADV, European Association of Dermatology and Venereology; IPC, International Psoriasis Council; NPF, National Psoriasis Foundation.

^a The American Academy of Dermatology (AAD) also issued recommendations for biologics, but they are not specific to a particular disease state. They are recommendations for all patients with dermatologic diseases on immunosuppressive agents during the COVID-19 pandemic.

^b For EADV, high-risk is defined as advanced age (60 or older), have underlying health conditions (ie, obesity, diabetes, hypertension, cardiovascular disease, chronic lung disease, asthma), and those who live in an area of high incidence of COVID-19 or those who have close contacts of confirmed persons with COVID-19.

^c For NPF, high risk is defined as advanced age (65 years or older) and having comorbidities such as chronic lung, heart, or kidney disease and metabolic disorders such as diabetes and obesity.

placebo.⁸ The analysis distinguished between upper RTIs (URTIs) and viral URTIs; viral URTI served as the model for coronavirus infection comparison. IL-12/23 and IL-23 antagonists were found to increase risk of URTIs (Mantel-Haenszel risk difference [MHRD], 0.019; 95% CI, 0.005–0.033; P = .007), but not viral URTIs (MHRD, 0.001; 95% CI, -0.002-0.003; P = .60).⁸ When examined alone, ustekinumab did not increase the risk of viral URTIs (MHRD, 0.001; 95% CI, -0.002-0.004; P = .42).⁸

Real-world data also suggest that IL-12/23 inhibitors may be used safely during the COVID-19 pandemic.⁵ In the New York-based case series examining patients with IMID, ustekinumab was not associated with increased rates of COVID-19 hospitalization (OR, 0.86; 95% CI, 0.65–1.15).⁵

Together, the current clinical trial and real-world data suggest that being on IL-12/23 inhibitors does not seem to increase patients' risk of contracting SARS-CoV-2, and, when infected, patients do not seem to experience worsened COVID-19 outcomes compared with the general population. Additional recommendations are provided later and outlined in Table 1.

Interleukin -17 Inhibitors (Secukinumab, Ixekizumab, and Brodalumab)

The IL-17 inhibitors currently FDA approved to treat psoriasis and PsA include secukinumab and

ixekizumab. Brodalumab is FDA approved for psoriasis, and it is also approved in other countries for PsA. By inhibiting IL-17, these medications mitigate the downstream inflammatory response in psoriasis.³ Although IL-17 is not a key contributor to viral clearance, it is important to understand the impact of IL-17 inhibition in the context of COVID-19.⁹

A meta-analysis using pivotal clinical trial data for secukinumab, ixekizumab, and brodalumab assessed the risk of RTIs in patients on IL-17 inhibitors compared with placebo.⁹ The study found an increased risk of RTIs in patients receiving IL-17 inhibitors compared with placebo (OR, 1.56; 95% CI, 1.04–2.33).⁹ However, this study noted that evaluating the risk of RTI in clinical trials is difficult because the diagnosis of RTI is made clinically, without objective testing.⁹ Therefore, the cause of RTI symptoms is unknown and could be viral, bacterial, or allergic. This study suggested that further evaluation is needed to understand the impact of IL-17 on RTIs in the setting of the COVID-19 pandemic.⁹

Real-world data suggest that patients on IL-17 inhibitors do not experience worsened COVID-19 disease severity compared with the general population.⁵ For example, the New York-based case series found that patients with IMID taking IL-17 inhibitors do not have increased odds of COVID-19 hospitalization compared with the general population (OR, 0.48; 95% CI, 0.03–1.23).⁵

Together, the current clinical trial and real-world data suggest that being on IL-17 inhibitors does not seem to increase patients' risk of contracting SARS-CoV-2, and, when infected, patients do not seem to experience worsened COVID-19 outcomes compared with the general population. Additional recommendations are provided later and outlined in Table 1.

Interleukin-23 Inhibitors (Guselkumab, Tildrakizumab, and Risankizumab)

The IL-23 inhibitors currently FDA approved to treat psoriasis include guselkumab, tildrakizumab, and risankizumab. Guselkumab is also FDA approved for PsA. IL-23 plays a central role in maintaining Th17 cells. Although IL-23 is not a key contributor to antiviral response, because of its effect on mucosal immunity, it is important to understand IL-23 inhibition in the context of COVID-19 infection.⁸

As previously mentioned, a meta-analysis of pivotal clinical trial data investigated the impact of IL-12/23 and IL-23 antagonists on COVID-19 susceptibility. This meta-analysis found that IL-12/23 and IL-23 antagonists increased the risk of

URTIs, but they did not increase the risk of viral URTIs.⁸ When evaluated alone, IL-23 antagonists did not increase the risk of viral URTIs (OR, 1.15; 95% CI, 0.88–1.49).⁸

Real-world data corroborate the safe usage of IL-23 inhibitors during the pandemic. In the New York prospective case series of patients with IMID, IL-23 blockers were not associated with increased hospitalization compared with the general population (OR, 0.75; 95% CI, 0.50–1.12).⁵

Together, the current clinical trial and real-world data suggest that being on IL-23 inhibitors does not seem to increase patients' risk of contracting SARS-CoV-2, and, when infected, patients do not seem to experience worsened COVID-19 outcomes compared with the general population. Additional recommendations are provided later and outlined in Table 1.

Additional Real-world Data of Psoriasis Biologics in Coronavirus Disease 2019

Several studies investigating the impact of psoriasis biologics on COVID-19 do not delineate results by the different biologic classes, and instead group the results of biologics together as a whole. In 1 study, 2 Italian provinces collected data from telemedicine visits in 246 patients with psoriasis on biologic or small-molecule therapy.¹⁰ Only 1 patient tested positive for COVID-19, and this patient remained asymptomatic.¹⁰ The study concluded that psoriasis (whether treated by biologic or small-molecule therapy or not) does not confer a higher risk of COVID-19 infection.¹⁰ A separate study in Verona, Italy, compared the risk of hospitalization or death caused by COVID-19 in 980 patients with psoriasis on biologics versus the general population of Verona.¹¹ Patients with psoriasis on biologics did not have increased rates of hospitalization and death compared with the general population.¹¹ A global registry-based study investigated the impact of biologics on COVID-19 outcomes in patients with psoriasis.¹² Out of 374 patients with psoriasis with confirmed or suspected COVID-19, 71% were receiving a biologic, 18% were receiving a nonbiologic, and 10% were not receiving any systemic treatment of psoriasis.¹² The study found that hospitalization was more frequent in patients using nonbiological therapy than in those using biologics (OR, 2.84; 95% CI, 1.31–6.18).¹²

Summary of Recommendations for the Use of Psoriasis Biologics in Coronavirus Disease 2019

In order to provide evidence-based guidelines on psoriasis management during the pandemic, the National Psoriasis Foundation (NPF) in the United States established a COVID-19 Task Force. This task force issued guidelines that are a so-called living resource and are amended when necessary by the rapidly evolving science of COVID-19.13 This article provides a summary of these guidelines (see Table 1). The NPF guidelines state that existing data generally suggest that psoriatic therapies do not meaningfully alter the risk of acquiring COVID-19 infection or having worse COVID-19 outcomes. For patients with psoriasis who are not infected with COVID-19, the NPF recommends continuing biologic therapies. In addition, patients and physicians are encouraged to undergo shared decision making to guide discussions about biologic use during the pandemic. If patients with psoriasis become infected with COVID-19, the NPF recommends that they monitor their symptoms and discuss treatment management with their physicians. If the decision is made to hold biologics during infection, the resumption of biologics should be decided on a case-by-case basis. In general, most patients can resume their psoriasis biologics after complete resolution of COVID-19 symptoms.¹³

The International Psoriasis Council (IPC) provides similar guidelines as the NPF (see **Table 1**).¹⁴ However, for patients who have active COVID-19 infection, the IPC recommends discontinuing biologics.¹⁴

HIDRADENITIS SUPPURATIVA

The only biologic currently FDA approved to treat hidradenitis suppurativa (HS) is adalimumab. When the TNF- α inhibitor, adalimumab, is used to treat HS, it is administered every week, compared with the frequency of once every 2 weeks for psoriasis indication in adults.

Based on data from phase 3 pivotal trials in HS, the rates of respiratory infection in patients with HS on adalimumab were similar to those of patients on placebo.^{15,16}

Observational studies have also investigated the impact of adalimumab on patients with HS during the COVID-19 pandemic. In northern Italy, a retrospective study of 96 patients with HS on systemic therapy was conducted; 48% of these patients were on adalimumab.¹⁷ There were no cases of hospitalization or deaths from COVID-19 in patients with HS.¹⁷ This finding was particularly significant, given that patients with HS are generally burdened by metabolic and cardiovascular comorbidities. Similarly, a retrospective study in southern Italy observed 93 patients with HS on systemic therapy; 80% of these patients were on adalimumab.¹⁸ There were no formally reported

COVID-19 cases; only 1 patient reported COVID-19 symptoms, which spontaneously resolved.¹⁸ In addition to these completed observational studies, an ongoing global registry has been developed to monitor and report outcomes of COVID-19 in patients with HS.¹⁹

Using the most recent COVID-19 data, the North America-based Hidradenitis Suppurativa Foundation (HSF) assembled recommendations to guide HS clinical management during the pandemic.²⁰ A summary of these important guidelines is provided in Table 2. The guidelines state that existing data suggest that biologics are not associated with an increased risk of COVID-19 in patients with HS. Therefore, if patients with HS are well controlled on biologics, they should continue their current regimens. Discontinuing biologics is not recommended because this could lead to skin symptom flare, which could lead patients with HS to seek care at a health care facility and have potential exposure. If patients with HS develop symptoms of COVID-19, the HSF recommends that patients consult their health care providers, who may recommend delaying a dose of the biologic. For patients with HS recovered from COVID-19, there is currently no recommendation statement issued by the HSF.²⁰

International guidelines developed by European Academy of Dermatology and Venereology (EADV) and European Hidradenitis Suppurativa Foundation (EHSF) are similar to the North America-based HSF guidelines (see **Table 2**).²¹ For patients infected with COVID-19, the international guidelines recommend discontinuing biologics.²¹

ATOPIC DERMATITIS

For the treatment of AD, dupilumab is the only biologic currently FDA approved. Dupilumab is an IL- 4α receptor antagonist that inhibits IL-4 and IL-13 signaling. IL-4 is critical in mediating type 2 Th2 cell polarization and humoral immunity.²²

A clinical trial meta-analysis investigated infection rates with dupilumab in pivotal phase 3 trials for AD.²² This study examined rates of overall infection, URTI, and nasopharyngitis. Across these 3 infection categories, the rate of infection was not increased in dupilumab-treated patients compared with placebo.²²

Several case reports have examined the effect of dupilumab on the clinical course and outcomes of patients with AD with COVID-19. In 2 of these cases, the patients who tested COVID-19 positive became symptomatic and were continued on dupilumab.²³ One patient experienced a mild course of the disease and recovered without complications.²³ The other patient developed

Table 2

Summary of recommendations on hidradenitis suppurativa management by international and North American organizations during the coronavirus disease 2019 pandemic, as of April 1, 2021^a

Status of Infection	International Recommendation: EADV Acne, Rosacea, HS Task Force, and the EHSF	North American Recommendation: HSF
Without symptoms of COVID- 19, on biologic therapy	Take extra precaution with TNF-alpha inhibitors	Continue current biologic regimen
No active COVID-19 infection, not on immunomodulatory agents, but being considered to initiate immunomodulatory agents	No statement at the time of writing	No statement at the time of writing
With symptoms suspicious of COVID-19, on systemic therapies (ie, biologics or oral medications)	Consult a health care provider and/or postpone or discontinue systemic therapy	Consult a health care provider, may recommend delaying a dose of the immunomodulator ^b
Active COVID-19 infection, on systemic therapies (ie, biologics or oral medications)	Discontinue taking immunomodulatory agent and consult a doctor	Consult a health care provider
Recovered from COVID-19	No statement at the time of writing	No statement at the time of writing
Professional Organization:		Resource
EADV Acne, Rosacea, HS Task Force, and the EHSF		https://eadv.org/cms-admin/ showfile/_HS%20TF% 20Recommandations_ COVID%20Corner.pdf
HSF		https://www.hs-foundation. org/hidradenitis- suppurativa-treatment-and- covid-19-coronavirus/

^a The AAD also issued recommendations for biologics, but they are not specific to a particular disease state. They are recommendations for all patients with dermatologic diseases on immunosuppressive agents during the COVID-19 pandemic. ^b For HSF, the recommendation for this cohort also includes persons with known COVID-19 exposure.

interstitial pneumonia, but recovered after 10 days; this patient's spouse (who was not on dupilumab) also contracted COVID-19 and developed interstitial pneumonia, but passed away.²³ A third case report features a high-risk patient (aged >65 years) who tested positive for 9 consecutive weeks, but remained asymptomatic. This patient was continued on dupilumab during the period he tested positive.²⁴

Researchers have theorized about the potential benefits of using dupilumab in patients with COVID-19. In patients who died of COVID-19, excess Th2 cytokines have been observed.²⁵ The increase in IL-4 level, and thus Th2 level, during COVID-19 illness could worsen the hyperinflammatory response.²⁵ Therefore, IL-4 inhibition might be beneficial. In addition, IL-6 plays a large role in the cytokine storm, which causes lung damage in patients with COVID-19.²⁶ IL-6 shifts the Th1/Th2

balance toward the Th2 direction.²⁶ Differentiation of Th2 by IL-6 depends on production of IL-4, whose activity is reduced by dupilumab.²⁶ However, this theoretic advantage is not yet supported by robust clinical data. Thus, physicians treating patients with AD should remain informed about developing data.

Although no explicit guidelines are currently offered by the National Eczema Association (NEA) in the United States, a record of expert panel discussion is available on their Web site. The AAD issued recommendations regarding systemic immuno-modulatory therapies for skin conditions; however, these recommendations are not specific to AD.⁷

The International Eczema Association (IEC) has issued guidelines specific for AD management during the COVID-19 pandemic (**Table 3**).²⁷ For patients with no infection, or who are asymptomatic or mildly symptomatic, the IEC recommends continuing biologic treatment. For patients with Table 3

Summary of recommendations on atopic dermatitis management by international organizations during the coronavirus disease 2019 pandemic, as of April 1, 2021^a

Status of Infection		International Recommendation: IEC
No active COVID-19 infection or asymptomatic/mildly symptomatic of COVID-19, on systemic therapy (ie, on biologics or oral medications)		Continue systemic immunosuppressant treatment
No active COVID-19 infection, not on immunomodulatory agents, but being considered to initiate immunomodulatory agents		No statement at the time of writing
Active COVID-19 infection or symptomatic of COVID-19, on systemic therapy (ie, on biologics or oral medications)		Discontinue or dose-reduced systemic therapy
Recovered from COVID-19		No statement at the time of writing
Professional Organization:	Resource:	
IEC	https://iecc.memberclicks.net/iec-statement-on-covid-19	

^a The AAD also issued recommendations for biologics, but they are not specific to a particular disease state. They are recommendations for all patients with dermatologic diseases on immunosuppressive agents during the COVID-19 pandemic.

active COVID-19 infection, the IEC recommends discontinuing or reducing the dose of biologics; however, patients with comorbid asthma should continue systemic therapy because asthma is a risk factor for severe COVID-19 infection.²⁷

SUMMARY

Across inflammatory skin conditions, current data suggest that biologics used for psoriasis, HS, and AD do not seem to increase the risk of COVID-19 infection or lead to worsened COVID-19 outcomes, likely because the existing biologics for these dermatologic conditions target cytokines involved in the systemic hyperinflammatory response but often do not substantially affect cytokines involved in viral clearance.² Of note, some biologics may even be beneficial by mitigating the hyperinflammatory state seen in patients with severe COVID-19.^{2,25,26} Data on this topic are currently evolving, and the guidelines continue to be updated accordingly. Clinicians should remain vigilant for the evolution of scientific evidence and closely follow their patients with dermatologic diseases on biologics.

CLINICS CARE POINTS

 For biologics used in psoriasis, including TNFinhibitors, IL-12/23 inhibitors, IL-17 inhibitors, and IL-23 inhibitors, current data suggest that they do not increase the risk of COVID-19 infection or worsened COVID-19 outcomes. It is generally recommended that psoriasis patients not actively infected with SARS-CoV-2 initiate or continue their biologics to treat moderate-to-severe psoriasis.

- Adalimumab is currently the only biologic FDA-approved to treat HS. In patients with on adalimumab to treat HS, adalimumab does not increase the risk of COVID-19 infection or worsened COVID-19 outcomes. It is generally recommended that HS patients not actively infected with SARS-CoV-2 initiate or continue adalimumab to treat moderateto-severe HS.
- Dupilumab is the currently the only biologic FDA-approved to treat moderate-to-severe AD. In patients on dupilumab to treat AD, current data suggest that dupilumab does not appear to increase the risk of COVID-19 infection or worsened COVID-19 outcomes. It is generally recommended that AD patients not actively infected with SARS-CoV-2 initiate or continue dupilumab to treat moderate-tosevere AD.

DISCLOSURE

Dr A.W. Armstrong has served as a research investigator and/or scientific advisor to AbbVie, BMS, Incyte, Leo, UCB, Janssen, Lilly, Novartis, Ortho Dermatologics, Sun, Dermavant, Dermira, Sanofi, Regeneron, Pfizer, and Modmed. Madison Jones, Alison Kucharik, Sarah Pourali, Jeffrey Rajkumar, Yasmin Gutierrez, and Rebecca Yim have nothing to disclose.

REFERENCES

- Damiani G, Pacifico A, Bragazzi NL, et al. Biologics increase the risk of SARS-CoV-2 infection and hospitalization, but not ICU admission and death: real-life data from a large cohort during RED-ZONE declaration. Dermatol Ther 2020;e13475.
- Schett G, Sticherling M, Neurath MF. COVID-19: risk for cytokine targeting in chronic inflammatory diseases? Nat Rev Immunol 2020;20(5):271–2.
- Armstrong AW, Read C. Pathophysiology, clinical presentation, and treatment of psoriasis: A review. JAMA 2020;323(19):1945–60.
- 4. Syed MN, Shah M, Shin DB, et al. Effect of antitumor necrosis factor therapy on the risk of respiratory tract infections and related symptoms in patients with psoriasis—A meta-estimate of pivotal phase 3 trials relevant to decision making during the COVID-19 pandemic. J Am Acad Dermatol 2020;84(1):161–3.
- Haberman R, Axelrad J, Chen A, et al. Covid-19 in immune-mediated inflammatory diseases—case series from New York. N Engl J Med 2020;383(1): 85–8.
- Veenstra J, Buechler CR, Robinson G, et al. Antecedent immunosuppressive therapy for immunemediated inflammatory diseases in the setting of a COVID-19 outbreak. J Am Acad Dermatol 2020; 83(6):1696–703.
- American Academy of Dermatology. Guidance on the use of immunosuppressive agents. 2020. Available at: https://www.aad.org/member/practice/ coronavirus/clinical-guidance/biologics. Accessed January 2021.
- Akiyama S, Yamada A, Micic D, et al. The risk of respiratory tract infections and interstitial lung disease with IL-12/23 and IL-23 antagonists in patients with autoimmune diseases: a systematic review and meta-analysis. J Am Acad Dermatol 2021;84(3): 676–90.
- Wan MT, Shin DB, Winthrop KL, et al. The risk of respiratory tract infections and symptoms in psoriasis patients treated with IL-17-pathway inhibiting biologics: A meta-estimate of pivotal trials relevant to decision-making during the COVID-19 pandemic. J Am Acad Dermatol 2020;83(2): 677–9.
- Vispi M, Corradin T, Peccianti C, et al. Psoriasis, biological drugs and Coronavirus Disease 2019: Real life experience of two Italian provinces. Dermatol Rep 2020;12(1).
- Gisondi P, Zaza G, Del Giglio M, et al. Risk of hospitalization and death from COVID-19 infection in patients with chronic plaque psoriasis receiving a biologic treatment and renal transplant recipients in maintenance immunosuppressive treatment. J Am Acad Dermatol 2020;83(1):285–7.

- Mahil SK, Dand N, Mason KJ, et al. Factors associated with adverse COVID-19 outcomes in patients with psoriasis-insights from a global registry-based study. J Allergy Clin Immunol 2021;147(1): 60–71.
- Gelfand JM, Armstrong AW, Bell S, et al. National psoriasis foundation COVID-19 task force guidance for management of psoriatic disease during the pandemic: Version 1. J Am Acad Dermatol 2020; 83(6):1704–16.
- International Psoriasis Foundation. IPC Statement on the Coronavirus (COVID-19) Outbreak. 2020. Available at: https://www.psoriasiscouncil.org/blog/Statementon-COVID-19-and-Psoriasis.htm. Accessed January 16, 2021.
- Blaszczak A, Trinidad JCL, Cartron AM. Adalimumab for treatment of hidradenitis suppurativa during the COVID-19 pandemic: Safety considerations. J Am Acad Dermatol 2020;83(1):e31.
- Kimball AB, Okun MM, Williams DA, et al. Two phase 3 trials of adalimumab for hidradenitis suppurativa. N Engl J Med 2016;375(5):422–34.
- Giulia R, Alice R, Teresa FM, et al. Moderate to severe hidradenitis suppurativa under systemic therapy during the COVID-19 outbreak. Dermatol Ther 2020; 33(4):e13680.
- Marasca C, Ruggiero A, Megna M, et al. Biologics for patients affected by Hidradenitis suppurativa in the COVID-19 era: data from a referral centre of Southern Italy. J Dermatol Treat 2020;1–3 (justaccepted).
- University of California San Francisco. Global Hidradenitis Suppurativa COVID-19 Registry. Available at: https://hscovid.ucsf.edu/.
- Hidradenitis Suppurativa Foundation. Frequently Asked Questions about Hidradenitis Suppurativa (HS) and COVID-19. 2020. Available at: https://www.hsfoundation.org/hidradenitis-suppurativa-treatmentand-covid-19-coronavirus/. Accessed January 16, 2021.
- European Academy of Dermatology and Venereology. Systemic Therapy for Patients with Hidradenitis suppurativa/Acne inversa during the pandemic phase of SARS-CoV-2 (Coronavirus). 2020. Available at: https://eadv.org/cms-admin/showfile/_HS%20TF %20Recommandations_COVID%20Corner.pdf. Accessed January 16, 2021.
- 22. Kearns DG, Uppal S, Chat VS, et al. Assessing the risk of dupilumab use for atopic dermatitis during the COVID-19 pandemic. J Am Acad Dermatol 2020;83(3):e251–2.
- Ferrucci S, Romagnuolo M, Angileri L, et al. Safety of dupilumab in severe atopic dermatitis and infection of Covid-19: two case reports. J Eur Acad Dermatol Venereol 2020;34(7):e303–4.
- 24. Caroppo F, Biolo G, Belloni Fortina A. SARS-CoV-2 asymptomatic infection in a patient under treatment

with dupilumab. J Eur Acad Dermatol Venereol 2020; 34(8):e368.

- 25. Förster-Ruhrmann U, Szczepek AJ, Bachert C, et al. COVID-19 in a patient with severe chronic rhinosinusitis with nasal polyps during therapy with dupilumab. J Allergy Clin Immunol 2020;146(1): 218–20.
- 26. Patruno C, Stingeni L, Fabbrocini G, et al. Dupilumab and COVID-19: what should we expect? Dermatol Ther 2020;33(4):e13502.
- 27. International Eczema Foundation. IEC Statement on COVID-19. 2020. Available at: https://iecc. memberclicks.net/iec-statement-on-covid-19. Accessed January 16, 2021.