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COMMENTARY

Novel Coronavirus Disease (COVID-19) and Biologic Therapy in Psoriasis: Infection Risk and Patient Counseling in Uncertain Times

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ABSTRACT

With the emergence of the novel coronavirus disease (COVID-19) viral pandemic, there is uncertainty whether biologic agents for psoriasis may place patients at a higher risk for infection or more severe disease course. This commentary offers patient counseling recommendations based on the current available evidence. While there are currently no specific data for psoriasis biologics and COVID-19, data are presented here from phase III clinical trials of psoriasis biologics on rates of upper respiratory infection, influenza, and serious infection. Overall these data reveal that on the whole, psoriasis biologics do not show major increases in infection risk compared to placebo during the course of these trials. However, as the COVID-19 virus is a novel pathogen that is associated with mortality in a subset of patients, a cautious approach is warranted. We discuss factors that may alter the benefit–risk ratio of biologic use during this time of COVID-19 outbreak. Ultimately, treatment decisions should be made on the basis of dialogue between patient and provider, considering each patient's individualized situation. Once this pandemic has passed, it is only a matter of time before a new viral disease reignites the same issues discussed here.

Keywords: Biologics; Coronavirus; COVID-19; Infection; Pandemic; Psoriasis; SARS-CoV-2

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Key Summary Points

With the emergence of the COVID-19 viral pandemic, there is uncertainty whether biologic agents for psoriasis may place patients at a higher risk for infection or worsened disease course.

While there are currently no specific data for psoriasis biologics and COVID-19, data are presented here from phase III clinical trials of psoriasis biologics on rates of upper respiratory infection, influenza, and serious infection.

Factors that should be considered when deciding whether to start or continue biologics include severity of underlying psoriasis or psoriatic arthritis; COVID-19 risk factors such as older age, cardiovascular disease, hypertension, lung disease, diabetes, or cancer; concomitant immunosuppressive medications or conditions; and risk of exposure to the COVID-19 virus based on geography, occupation, and living situation.

Ultimately, treatment decisions should be made on an individualized basis based on dialogue between patient and provider.

COMMENTARY

In late December 2019, the world was introduced to the novel coronavirus disease (COVID-19). As of March 2020, there were over 920,000 cases and 46,000 deaths worldwide, with these numbers expected to rise sharply. Upon review of 55,924 patients with COVID-19 [1], the clinical presentation generally involved fever in 87.9%, dry cough in 67.7%, fatigue in 38.1%, sputum production in 33.4%, shortness of breath in 18.6%, and sore throat in 13.9%. Gastrointestinal symptoms have also been reported with diarrhea in 3.7% of patients and nausea or vomiting in 5% of patients. Patients with COVID-19 generally develop signs and symptoms on average 5–6 days after infection (range 1–14 days) [1]. The goal of this article is to review the known clinical trial data on infection risk with biologic therapy for psoriasis and offer patient counseling recommendations based on the current available evidence.

There are currently 11 biologic therapies approved for psoriasis. These medications are engineered to target individual mediators of inflammation including tumor necrosis factor-alpha (TNFα), interleukin-17 (IL-17), and IL-23. Although the safety profiles of these biologic agents are generally preferable to those of traditional immunosuppressive therapies, there is concern that treatment with these agents may reduce resistance to infection. This concern is heightened during novel disease outbreaks and the resulting increased media coverage. As a result, patients are increasingly turning to healthcare providers for guidance regarding the use of biologic agents during disease outbreaks.

Given the novel nature and rapidly evolving knowledge of COVID-19, there are currently no specific data for how biologic therapy affects patients' risk of acquiring this coronavirus infection or COVID-19 outcomes. However, more general data on infection risk are available for psoriasis biologic agents from phase III clinical trial data. Infections typically reported in these studies include upper respiratory infections, influenza, sinusitis, urinary tract infection, opportunistic infections, and serious infections. Serious infections are defined as infections involving various organ systems that may lead to hospitalization or death including pneumonia, septic arthritis, erysipelas, cellulitis, diverticulitis, pyelonephritis, and prosthetic or post-surgical infection. Table 1 summarizes the rates of upper respiratory infections, rates of influenza, and risks of serious infections for all 11 currently approved biologic agents for psoriasis, as observed in phase III clinical trials. Overall these data reveal that on the whole, psoriasis biologics do not show substantial increases in infection risk compared to placebo, which is also consistent with long-term registry data [2]. The safety signal appears especially clean for etanercept, ustekinumab, tildrakizumab, guselkumab, and risankizumab,

Table 1 Rates of upper respiratory infection, influenza, and serious infection in the phase III clinical trials of US FDA-approved biologics for psoriasis

Medication, year of FDA approval, mechanism of action	Rates of URI (vs. placebo)	Rates of influenza (vs. placebo)	Rates of serious infections (vs. placebo)
Adalimumab, 2002, TNFα inhibitor	REVEAL [7]	REVEAL	REVEAL
	7.2% (40 mg) vs. 3.5% (placebo) at week 16	NR	0.6% (40 mg) vs. 1% (placebo) at week 16
	CHAMPION [8]	CHAMPION	CHAMPION
	28% (40 mg) vs. 20.8% (placebo) at week 16 for nasopharyngitis	0% (40 mg) vs. 1.9% (placebo) at week 16 for viral infection	0% (40 mg) vs. 0% (placebo) at week 16
Etanercept, 2004 TNFα inhibitor	Tyring et. al. [9]	Tyring et. al. [9]	Tyring et. al. [9]
	20.2/100 PY (50 mg) vs. 24.3/100 PY (placebo) through week 96	NR	1.2/100 PY (50 mg) vs. 1.5/100 PY (placebo) through week 96
	Papp et al. [10]	Papp et al. [10]	Papp et al. [10]
	13% (50 mg) vs. 13% (25 mg) vs. 13% (placebo) at week 12	4% (50 mg) vs. 5% (25 mg) vs. 2% (placebo) at week 12 for "flu syndrome"	NR (< 5% reported in study)
	Leonardi et. al. [11]	Leonardi et. al. [11]	Leonardi et. al. [11]
	5% (50 mg BIW) vs. 9% (25 mg BIW) vs. 10% (25 mg QWK) vs. 11% (placebo) at week 12	NR (< 5% reported in study)	NR (< 5% reported in study)
Infliximab, 2006, TNFα inhibitor	EXPRESS 1 [12]	EXPRESS 1	EXPRESS 1
	15% (5 mg/kg) vs. 16% (placebo) at week 24	NR	NR
	EXPRESS 2 [13]	EXPRESS 2	EXPRESS 2
	16% (3 mg/kg) vs. 13.4% (5 mg/kg) vs. 14% (placebo) at week 14	NR	NR

Table 1 continued

Medication, year of FDA approval, mechanism of action	Rates of URI (vs. placebo)	Rates of influenza (vs. placebo)	Rates of serious infections (vs. placebo)
Certolizumab, 2018, PEGylated TNFα inhibitor	CIMPASI 1 [14]	CIMPASI 1	CIMPASI 1
	9.1% (400 mg) vs. 7.4% (200 mg) vs. 5.9% (placebo) at week 16	NR	0% (400 mg) vs. 0% (200 mg) vs. 0% (placebo) at week 16
	CIMPASI 2 [14]	CIMPASI 2	CIMPASI 2
	5.7% (400 mg) vs. 4.4% (200 mg) vs. 4.1% (placebo) at week 16	NR	1.1% (400 mg) vs. 0% (200 mg) vs. 0% (placebo) at week 16
	CIMPACT [28]	CIMPACT	CIMPACT
	3.6% (200 mg) vs. 10.5% (placebo) at week 12	NR	0% vs. 0% at week 12
Ustekinumab, 2009, anti-IL-12/23	PHOENIX 1 [15]	PHOENIX 1	PHOENIX 1
	7.1% (45 mg) vs. 6.3% (90 mg) vs. 6.3% (placebo) at week 12	NR	0% (45 mg) vs. 0.8% (90 mg) vs. 0.4% (placebo) at week 12
	PHOENIX 2 [16]	PHOENIX 2	PHOENIX 2
	4.4% (45 mg) vs. 2.9% (90 mg) vs. 3.4% (placebo) at week 12	NR	0% (45 mg) vs. 0.2% (90 mg) vs. 0.5% (placebo) at week 12

Table 1 continued

Medication, year of FDA approval, mechanism of action	Rates of URI (vs. placebo)	Rates of influenza (vs. placebo)	Rates of serious infections (vs. placebo)
Secukinumab, 2015, anti-IL-17A	ERASURE [17]	ERASURE	ERASURE
	3.7% (300 mg) vs. 4.1% (150 mg) 0% (placebo) at week 12	2% (300 mg) vs. 1.2% (150 mg) vs. 1.2% (placebo) at week 12	1% (300 mg) vs. 0.7% (150 mg) vs. 1.5% (placebo) at week 52
	FIXTURE [17]		FIXTURE
	2.1% (300 mg) vs. 3.1% (150 mg) vs. 0.9% (placebo) at week 12		1.1% (300 mg) vs. 0.6% (150 mg) vs. 0.3% (placebo) at week 52
	FEATURE [18]		
	5.1% (300 mg) vs. 5.1% (150 mg) vs. 8.5% (placebo) at week 12 for nasopharyngitis		
	JUNCTURE [19]		
	Sinusitis: 5% (300 mg) vs. 1.6% (150 mg) vs. 0% (placebo); Nasopharyngitis: 31.7% (300 mg) vs. 23% (150 mg) vs. 16.4% (placebo) at week 12		
Brodalumab, 2017, anti-IL-17	AMAGINE 1 [20]	AMAGINE 1	AMAGINE 1
	8.2% (140 mg Q2W) vs. 8.1% (210 mg Q2W) vs. 6.4% (placebo)	NR	0.9% (140 mg Q2W) vs. 0.5% (210 mg Q2W) vs. 0% (placebo) at week 12
			4.5% (140 mg Q2W) vs. 1.2% (210 mg Q2W) at week 52
	AMAGINE 2 [21]	AMAGINE 2	AMAGINE 2
	NR	NR	NR
	AMAGINE 3 [21]	AMAGINE 3	AMAGINE 3
	NR	NR	NR

Table 1 continued

Medication, year of FDA approval, mechanism of action	Rates of URI (vs. placebo)	Rates of influenza (vs. placebo)	Rates of serious infections (vs. placebo)
Ixekizumab, 2017, anti-IL-17A	UNCOVER 1, 2, 3 (pooled) [22]	UNCOVER 1, 2, 3 (pooled)	UNCOVER 1, 2, 3 (pooled)
	3.9% (Q4W) vs. 4.4% (Q2W) vs. 3.5% (placebo) at week 12	NR	0.7% (Q4W) vs. 0.4% (Q2W) vs. 0.4% (placebo) at week 12
	10% (IXE all exposure) at week 60		1.4% (IXE all exposure) at week 60
Guselkumab, 2017, anti-IL-23	VOYAGE 1 [23]	VOYAGE 1	VOYAGE 1
	7.6% (100 mg) vs. 5.2% (placebo) at week 16	NR	0% (100 mg) vs. 0% (placebo) at week 16
	VOYAGE 2 [24]	VOYAGE 2	VOYAGE 2
	3.2% (100 mg) vs. 4.0% (placebo) at week 16	NR	0.2% (100 mg) vs. 0.4% (placebo) at week 16
Tildrakizumab, 2018, anti-IL-23	RESURFACE 1 [25]	RESURFACE 1	RESURFACE 1
	3% (100 mg) vs. 5% (200 mg) vs. 6% (placebo) at week 12	NR	< 1% (100 mg) vs. < 1% (200 mg) vs. 0% (placebo) at week 12
	RESURFACE 2 [25]	RESURFACE 2	RESURFACE 2
	0% (100 mg) vs. 0% (200 mg) vs. 0% (placebo) at week 12	NR	0% (100 mg) vs. < 1% (200 mg) vs. 1% (placebo) at week 12

Table 1 continued

Medication, year of FDA approval, mechanism of action	Rates of URI (vs. placebo)	Rates of influenza (vs. placebo)	Rates of serious infections (vs. placebo)
Risankizumab, 2019, anti-IL-23	ULTIMMA-1 [26]	ULTIMMA-1	ULTIMMA-1
	Part A: 5.59% (150 mg) vs. 1.96% (placebo) at week 16	Part A: 6.58% (150 mg) vs. 5.88% (placebo) at week 16 viral upper respiratory infection	Part A: 0.3% (150 mg) vs. 0% (placebo) at week 16
	Part B: 10.10% (150 mg) vs. 8.25% (placebo) at weeks 16–52	Part B: 13.47% (150 mg) vs. 15.46% (placebo) at weeks 16–52 for viral upper respiratory infection	Part B: 0.7% (150 mg) vs. 1% (placebo) at weeks 16–52
	ULTIMMA-2 [26]	ULTIMMA-2	ULTIMMA-2
	Part A: 3.74% (150 mg) vs. 2.04% (placebo) at week 16	Part A: 2.04% (150 mg) 1.02% (placebo) at week 16 for influenza	Part A: 1% (150 mg) vs. 0% (placebo) at week 16
	Part B: 8.25% (150 mg) vs. 9.57% (placebo) at weeks 16–52	Part B: 1.37% (150 mg) vs. 2.13% (placebo) at weeks 16–52 for influenza	Part B: 0.7% (150 mg) vs. 0% (placebo) at weeks 16–52
	IMMHANCE [27]	IMMHANCE	IMMHANCE
	Part A1: 1.47% (150 mg) vs. 5% (placebo) at week 16	Part A1: 0.74% (150 mg) vs. 1% (placebo) at week 16	0% (150 mg) vs. 0% (placebo) at week 16 for viral infection, bronchitis, and bacterial meningitis

NR not reported, *NS* not significant, *PY* patient year

although it is important to note that the data from these trials were derived from a relatively short period and do not fully reflect real-world settings.

Biologic medications for psoriasis are meant to be taken continuously. There are risks to stopping biologic therapy since psoriasis flares and erythroderma may lead to poor quality of life and hospitalization. Also, stopping and restarting some biologic agents may result in reduced efficacy [3, 4]. On the other hand, given the absence of specific data on psoriasis biologics and COVID-19, which can potentially be fatal, a cautious approach is warranted. In particular, the presence of risk factors for COVID-19 mortality such as age > 60, cardiovascular disease, hypertension, lung disease, diabetes, or cancer may alter the benefit–risk ratio for biologic therapy, particularly in the short term whereby biologic reduction or discontinuation may not lead to immediate disease flare [5] (Table 2).

Table 2 Considerations for use of psoriasis biologic medications during the COVID-19 pandemic

Factors favoring biologic discontinuation or reduction in immunomodulatory regimen	Factors favoring biologic continuation
Any active infection, including COVID-19	Young age
COVID-19 risk factors including: age > 60, cardiovascular disease, hypertension, lung disease, diabetes, or cancer	No COVID-19 high risk co-morbidities
Concomitant immunosuppression (e.g., methotrexate, prednisone, cyclosporine)	Biologic monotherapy
Immunosuppressive condition (e.g., HIV)	Severe underlying psoriasis or psoriatic arthritis, with history of rapid flares or unstable subtypes (pustular, erythrodermic)
History of infections while on biologic	No concomitant immunosuppressive conditions
Mild-to-moderate underlying psoriasis	Low risk of exposure to COVID-19 virus
High risk of exposure to COVID-19 virus (e.g., endemic area, healthcare worker, nursing home resident, household member or co-worker with COVID-19 infection)	Long duration of COVID-19 pandemic
Short duration of COVID-19 pandemic	

Therefore, at the current time, the following guidance may be given to patients with psoriasis:

1. All patients should be reminded to practice good infection prevention measures such as frequent hand washing, social distancing, and the use of telehealth resources when available.
2. There is no evidence to recommend prophylactically stopping or postponing biologic therapy in all patients with psoriasis; however, patients should have individualized discussions with their medical providers taking into account the following factors:
    - COVID-19 risk factors such as older age, cardiovascular disease, hypertension, lung disease, diabetes, or cancer
    - Severity of underlying psoriasis or psoriatic arthritis
    - Concomitant immunosuppressive medications or conditions
    - Risk of exposure to COVID-19 based on occupation or living situation
3. If a reduction in immunosuppressive treatment is desired, options include:
    - Temporary discontinuation of the biologic
    - Reduction in biologic dose frequency
    - Transition to an alternative biologic
    - Reduction or discontinuation of concomitant immunosuppressants (e.g., methotrexate)
    - Increase in use of topical agents, home phototherapy, or other non-immunosuppressive medications
4. Patients who test positive for COVID-19 infection should be advised to hold their biologic dose until their infection clears. This requires resolution of fever without the use of fever-reducing medications, improvement in respiratory symptoms (e.g., cough, shortness of breath), and two negative COVID-19 test performed 24 h apart. However, if COVID-19 retesting is not available, then a conservative approach would be to avoid restarting biologic therapy until 30 days after resolution of fever and

respiratory symptoms. This estimate is based on a mean duration of COVID-19 viral shedding from illness onset of 20 days (range 8–37 days) in hospitalized patients [6].

5. The risks and benefits of initiating biologic therapy should be considered on an individual patient basis, according to the factors listed above.

It is important to remember that this is a novel, rapidly changing situation, and recommendations may change as more data become available. This article is based on previously conducted studies and does not contain any studies with human participants or animals performed by any of the authors. This worldwide pandemic of substantial human disease caused by a type of virus previously thought to be relatively benign highlights the perpetual challenge of emerging infectious diseases, the importance of long-term monitoring of patients on biologic therapy, and shared decision-making with patients on biologic therapy. Once this pandemic has passed, it is only a matter of time before a new viral disease reignites the same issues discussed here.

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