Yale New Haven Health
Department of Pharmacy

Clinical Guidance for Patients Receiving Immmunosuppressive Medications

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Purpose:

The purpose of this document is to provide guidance to clinicians on COVID-19 vaccination for their patients who receive immunosuppressive therapy. Given the lack of available data on the immune response to COVID-19 vaccination in patients receiving immunosuppressive therapy, clinical guidance is based on the mechanism of immunosuppression and extrapolating the likely effect on the immune response to a novel antigen in the COVID-19 vaccine from prior vaccine response studies in immunosuppressed patients and expert opinion.

Timing of COVID-19 vaccination and modifications to immunosuppressive regimens are disease- and patient-specific which necessitates individualized share decision-making in this process. The clinical guidance provided does not replace clinical judgment given the fluidity of the COVID-19 pandemic. Updates to this clinical guidance will be provided as clinical evidence becomes available. Note that the availability of COVID-19 vaccines for immunosuppressed patients is dependent on each State's vaccination criteria which can vary.

Finally, in order to facilitate patient-specific clinical recommendations, the guidance below may differ than current specialty-specific Society/College as it is based on expert opinion interpretation of the available medical literature.

General Principles:

1) Although current COVID-19 vaccines are safe to administer to immunosuppressed patients, clinicians should advise the patient that the expected post-vaccination immune response may be reduced compared to the population at large.

   Accordingly, it is critical that patients continue the usual COVID-19 mitigation practices of wearing a mask, maintaining social distancing, and frequent hand hygiene.

2) If disease activity allows, delay initiation of immunosuppressive regimens which may have the greatest impact of decreasing the post-vaccination immune response (e.g., anti CD20, anti CD52 therapies) until the patient has completed their COVID-19 vaccination series.

3) If disease activity allows, decrease the dosage of immunosuppressive medications to the lowest effective dose and/or decrease the number of immunosuppressive medications in order to maximize the post-vaccination immune response. Advise the patient that such changes in immunosuppression may potentially increase disease activity.

4) Advise household contacts of immunosuppressed patients to undergo COVID-19 vaccination to provide additional protection via a "Cocooning" effect when the vaccine is available for such individuals.

5) Advise patients that COVID-19 antibody testing pre and post vaccination is not recommended unless as part of a clinical investigation to determine vaccine efficacy. Current commercial COVID-19 antibody testing is not FDA approved for such an evaluation given the lack of a standard for the COVID-19 antibody level which correlates with known protection against COVID-19.

COVID-19 Vaccination

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Rheumatology

Medication Class	Medication	Likely Effect on COVID-19 Vaccine Response	COVID-19 Vaccination Recommendation	Mitigating Effect of Immunosuppression on COVID-19 Vaccination
Anti CD20	rituximab	Significant reduction in vaccine efficacy likely	Caution	If already on therapy, vaccinate 3 to 6 months after last dose and hold the next dose until 4 weeks after completing the vaccine series.
Corticosteroids	prednisone	Possible reduction in vaccine efficacy	Proceed with vaccination	Reduce prednisone to lowest possible dose with goal of < 20mg prednisone/day.
				Avoid intrarticular steroids for at least 2 weeks after vaccine.
MTX		Probable reduction in vaccine efficacy	Proceed with vaccination	Hold MTX for 2 weeks after vaccination if permitted by disease activity. Holding MTX after the first dose of COVID-19 vaccine should be prioritized if unable to hold MTX for both doses.
TNF α antagonists	adalimumab	Probable reduction in vaccine efficacy	Proceed with vaccination	If possible, time vaccination immediately prior to next scheduled dose (drug nadir) and delay dose until 2 weeks post vaccination.
	etanercept			
	infliximab			
	golimumab			
	certolizumab			
CTLA-4	abatacept	Probable reduction in vaccine efficacy	Proceed with vaccination	If possible, time vaccination immediately prior to next scheduled dose (drug nadir) and delay dose until 2 weeks post vaccination.
IL-1 blocker	anakinra	Probable reduction in vaccine efficacy	Proceed with vaccination	
JAK inhibitors	tofacitinib	Probable reduction in vaccine efficacy	Proceed with vaccination	Hold JAK inhibitor for 1 week after vaccination if permitted by disease activity. Holding the JAK inhibitor after the first dose of COVID-19 vaccine should be prioritized if unable to hold the JAK inhibitor for both doses.
	upadacitinib			
	baricitinib			
Anti- BlyS	benlimumab	Probable reduction in vaccine efficacy	Proceed with vaccination	If possible, time vaccination immediately prior to next scheduled dose (drug nadir) and delay dose until 2 weeks post vaccination.
IL-6 blocker	tocilizumab	Unlikely to reduce vaccine efficacy	Proceed with vaccination	
	sarilumab	Unlikely to reduce vaccine efficacy	Proceed with vaccination	
IL 17 blocker	secukinumab	Unlikely to reduce vaccine efficacy	Proceed with vaccination	
	ixekizumab			
IL 23 blocker	guselkumab	Unlikely to reduce vaccine efficacy	Proceed with vaccination	

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Gastroenterology

Medication Class	Medication	Likely Effect on COVID-19 Vaccine Response	COVID-19 Vaccination Recommendation	Mitigating Effect of Immunosuppression on COVID-19 Vaccination
Corticosteroids	prednisone	Possible reduction in vaccine efficacy	Proceed with vaccination	Reduce prednisone to lowest possible dose with goal of < 20mg prednisone/day.
MTX		Probable reduction in vaccine efficacy	Proceed with vaccination	Hold MTX for 2 weeks after vaccination if permitted by disease activity. Holding MTX after the first dose of COVID-19 vaccine should be prioritized if unable to hold MTX for both doses.
Anti-metabolites	azathioprine 6MP	Probable reduction in vaccine efficacy	Proceed with vaccination	Reduce medication to lowest effective dose if disease activity permits.
Calcineurin inhibitors	tacrolimus	Probable reduction in vaccine efficacy	Proceed with vaccination	Reduce medication to lowest effective dose if disease activity permits.
	cyclosporine			
TNF α antagonists	adalimumab	Probable reduction in vaccine efficacy	Proceed with vaccination	If possible, time vaccination immediately prior to next scheduled dose (drug nadir) and delay dose until 2 weeks post vaccination.
	infliximab			
	golimumab			
	certolizumab			
JAK inhibitors	tofacitinib	Probable reduction in vaccine efficacy	Proceed with vaccination	Hold JAK inhibitor for 1 week after vaccination if permitted by disease activity. Holding the JAK inhibitor after the first dose of COVID-19 vaccine should be prioritized if unable to hold the JAK inhibitor for both doses.
IL 12/23 blocker	ustekinumab	Unlikely to reduce vaccine efficacy	Proceed with vaccination	
anti-integrin Ab	vedolizumab	Unlikely to reduce vaccine efficacy	Proceed with vaccination	

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Pulmonology

Medication Class	Medication	Likely Effect on COVID-19 Vaccine Response	COVID-19 Vaccination Recommendation	Mitigating Effect of Immunosuppression on COVID-19 Vaccination
Anti CD20	rituximab	Significant reduction in vaccine efficacy likely	Caution	If already on therapy, vaccinate 3 to 6 months after last dose and hold the next dose until 4 weeks after completing the vaccine series.
Corticosteroids	prednisone	Possible reduction in vaccine efficacy	Proceed with vaccination	Reduce prednisone to lowest possible dose with goal of < 20mg prednisone/day.
MTX		Probable reduction in vaccine efficacy	Proceed with vaccination	Hold MTX for 2 weeks after vaccination if permitted by disease activity. Holding MTX after the first dose of COVID-19 vaccine should be prioritized if unable to hold MTX for both doses.
mycophenolate		Probable reduction in vaccine efficacy	Proceed with vaccination	Reduce medication to lowest effective dose if disease activity permits.
azathioprine		Probable reduction in vaccine efficacy	Proceed with vaccination	Reduce medication to lowest effective dose if disease activity permits.
tacrolimus		Probable reduction in vaccine efficacy	Proceed with vaccination	Reduce medication to lowest effective dose if disease activity permits.
cyclophosphamide		Probable reduction in vaccine efficacy	Proceed with vaccination	
TNF α antagonists	infliximab	Probable reduction in vaccine efficacy	Proceed with vaccination	If possible, time vaccination immediately prior to next scheduled dose (drug nadir) and delay dose until 2 weeks post vaccination.
nintedanib		Unlikely to reduce vaccine efficacy	Proceed with vaccination	
pirfenidone		Unlikely to reduce vaccine efficacy	Proceed with vaccination	
IL 5 blocker	benralizumab	Unlikely to reduce vaccine efficacy	Proceed with vaccination	
	mepolizumab			
	reslizumab			

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Neurology

Medication Class	Medication	Likely Effect on COVID-19 Vaccine Response	COVID-19 Vaccination Recommendation	Mitigating Effect of Immunosuppression on COVID-19 Vaccination
Anti CD20	ocrelizumab rituximab	Significant reduction in vaccine efficacy likely	Caution	If already on therapy, vaccinate 3 to 6 months after last dose and hold the next dose until 4 weeks after completing the vaccine series.
Anti CD52	alemtuzumab	Significant reduction in vaccine efficacy likely	Caution	If possible, vaccinate at least 6 months after last dose.
purine analog	cladribine	Significant reduction in vaccine efficacy likely	Caution	If already on therapy, vaccinate 3 to 6 months after last dose and hold the next dose until 4 weeks after completing the vaccine series.
Corticosteroids	prednisone	Possible reduction in vaccine efficacy	Proceed with vaccination	Reduce prednisone to lowest possible dose with goal of < 20mg prednisone/day.
S1P inhibitor	fingolimod ozanimod	Probable reduction in vaccine efficacy	Proceed with vaccination	
Anti-VLA4	natalizumab	Unlikely to reduce vaccine efficacy	Proceed with vaccination	
Unknown mechanism	dimethyl fumarate monomethyl fumarate	Unlikely to reduce vaccine efficacy	Proceed with vaccination	

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Solid Organ Transplant

Transplant Type	Immunosuppressive Regimen		Likely Effect on COVID-19 Vaccine Response	COVID-19 Vaccination Recommendation
Renal, Liver, Heart	Basiliximab induction ≤ 3 months from transplant		Significant reduction in vaccine efficacy likely	Consider delaying vaccination until after 2-3 months post-transplant.
Renal, Liver, Heart	Thymoglobulin induction ≤ 3 months from transplant		Significant reduction in vaccine efficacy likely	Consider delaying vaccination until after 3 months post-transplant.
Renal	Alemtuzumab induction ≤ 6 months from transplant		Significant reduction in vaccine efficacy likely	Consider delaying vaccination until after 6 months post-transplant.
Renal, Liver, Heart	ACR treatment with thymoglobulin ≤ 3 months prior		Significant reduction in vaccine efficacy likely	Consider delaying vaccination until after 3 months post-treatment of rejection.
Renal, Liver, Heart	AMR treatment with rituximab ≤ 6 months prior		Significant reduction in vaccine efficacy likely	Consider delaying vaccination until after 6 months post-rituximab treatment.
Renal, Liver, Heart	ACR treatment with methyprednisolone		Possible reduction in vaccine efficacy	Consider delay vaccination until patient resumes stable dosed immunosuppression.
Renal, Liver, Heart	Stable chronic immunosuppression without any of the above conditions	prednisone + mycophenolate + tac/siro/CSA	Probable reduction in vaccine efficacy	Proceed with vaccination
Renal, Liver, Heart		prednisone + azathioprine + tac/siro/CSA		
Renal	Stable chronic immunosuppression without any of the above conditions	belatacept + mycophenolate	Probable reduction in vaccine efficacy	
Liver	Stable chronic immunosuppression without any of the above conditions	prednisone + tacrolimus	Probable reduction in vaccine efficacy	

References:

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