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VACCINE GUIDELINES FOR IMMUNOCOMPROMISED AND OTHER SPECIAL POPULATIONS

I. GENERAL PRINCIPLES

COVID-19 immunization is recommended for immunocompromised patients, including those receiving immune active therapy, with the understanding that there are limited data in these patients. The currently available COVID vaccines are not live virus vaccines and cannot transmit the SARS-CoV-2 virus. Antibody testing is not currently recommended to assess for immunity to COVID-19 following vaccination.

The current vaccine recommendations will be updated regularly based on availability of new data. There are important gaps in knowledge on vaccine immunogenicity in specific patient populations, including those with cancer and receiving certain immunomodulatory therapies. The durability of vaccine protection is being investigated in the general population and may be attenuated in immunocompromised patients.

Reasons for delay of vaccines are similar to those that impede delivery to the general public (e.g., recent exposure to COVID-19, history of anaphylaxis to vaccine, etc.), and there are also patient specific factors.

COVID-19 vaccines and other vaccines may now be administered without regard to timing. This includes simultaneous administration of COVID-19 vaccines and other vaccines on the same day. If multiple vaccines are administered at a single visit, administer each injection in a different injection site.

For patients on clinical trials, discussion with trial leads should be considered in advance to prevent protocol violations or exclusions.

II. SUMMARY TABLES

Table 1. Patients with Malignancy

Patients with malignancy Cancer / Treatment type	COVID-19 Vaccine Recommendations
Hematopoietic Cell Transplantation (HCT)/Cellular Therapy	

Autologous transplantation OR Cellular therapy (e.g., CAR-T)	Delay 30 days prior and 30 days post autologous stem cell transplant and HCT/cellular therapy [a,b]
Allogeneic transplantation	Delay vaccine 30 days prior and 90 days post allogenic stem cell transplant
Hematologic malignancies	
Receiving intensive cytotoxic chemotherapy (e.g., cytarabine/anthracycline based induction regimens for acute myeloid leukemia [AML])	Vaccine when offered
Marrow failure from disease and/or therapy expected to have limited or no Recovery	Vaccine when offered
Long-term maintenance therapy (e.g., targeted agents for chronic lymphocytic leukemia or myeloproliferative neoplasms [MPN])	Vaccine when offered
Thrombocytopenia with platelet count <30K	Patient to receive platelets the morning of each dose of vaccine and apply manual pressure to injection site for 10 minutes following vaccination
Solid tumor malignancies	
Receiving cytotoxic chemotherapy	Vaccine when offered [c, d]
Targeted therapy	Vaccine when offered [c]
Checkpoint inhibitors and other immunotherapy	Vaccine when available [e]
Radiation	Vaccine when offered [c]

a) Graft-versus-host disease (GVHD) and immunosuppressive regimens to treat GVHD are expected to blunt immune vaccine responses. Vaccine delays until therapy is reduced and/or based on immunophenotyping of T-cell and B-cell immunity can be considered.

b) Patients on maintenance therapies (eg, rituximab, Bruton tyrosine kinase inhibitors, Janus kinase inhibitors) may have attenuated response to vaccination.

c) Granulocytopenia a surrogate marker for recovery of adequate immunocompetence to respond to vaccines and sufficient platelet recovery to avoid bleeding complications from intramuscular administration. Due to short periods of neutropenia among solid tumor malignancies this is not used for timing of vaccination.

d) In patients receiving chemotherapy, optimal timing of vaccination in relation to cycles of chemotherapy is unknown. Given the variability of specific regimens and intervals between cycles, it is not possible to state whether immunization will be more effective if administered at the time of chemotherapy administration versus mid-cycle when the white blood cell (WBC) count might be at its nadir. In the absence of data, we recommend vaccination when available.

e) Theoretical risk of exacerbated immune-related adverse events in patients receiving immune checkpoint inhibitors; there are no data on timing of vaccine administration, so this may be considered on the same day as immunotherapy for convenience and to reduce added visits to the office whenever possible.

Table 2. Patients with Autoimmune Disease or Other Immunosuppressive Conditions

Patients with autoimmune disease	COVID -19 vaccination recommendations
Rheumatologic diseases	
Autoimmune, inflammatory and musculoskeletal rheumatic disease	Vaccine when offered See Appendix for recommendations around specific biologics and immunomodulators
Inflammatory bowel disease (IBD)	
Ulcerative colitis	Vaccine when offered
Crohn's disease	Vaccine when offered

Multiple sclerosis	
Patients receiving disease modifying therapies (DMTs) or S1P receptor modulators	Vaccine when offered See Appendix for examples of specific therapies
Patients receiving B-cell and T-cell inhibitors -alemtuzumab (Lemtrada) -cladribine (Mavenclad) -ofatumumab (Kesimpta) -ocrelizumab (Ocrevua) -rituximab (Rituxan)	If therapy has been initiated, delay vaccine by 3 months If therapy has not yet been initiated, complete vaccine series 4 weeks prior to initiation When possible, resume therapy 4 weeks or more following the second vaccine injection
HIV infection	
	Vaccine when offered
Primary immunodeficiencies	
	Vaccine when offered

Table 3. COVID-19 Vaccination Recommendations for Patients with Solid Organ Transplant, or Pre-Transplant

Patients with Solid Organ Transplant, or Pre-transplant	COVID -19 vaccination recommendations
Pre-transplant	When possible, administer COVID-19 vaccine in the pretransplant setting with the final dose at least 1-2 weeks prior to transplant. It is not necessary to postpone transplant while awaiting COVID-19 vaccination.
Post-transplant	Delay COVID-19 vaccine for 1 month after solid organ transplant regardless of induction therapy. In certain situations, it may be appropriate to wait for a longer period, such as when T- or B-cell ablative therapy (antithymocyte globulin or rituximab) was used at time of transplant. This can be decided on a case-by-case basis. For multi-dose vaccines, if the patient undergoes transplantation between the first and second doses, provide the second dose at 1 month post-transplant. Additional doses are not recommended.
Active treatment for acute rejection	Delay COVID-19 vaccination for a 1-month period from initiation of escalation of immunosuppression

Table 4. Non-immunocompromised Specific Populations

Other special populations or considerations	COVID -19 vaccination recommendations
Women's Health	
Pregnant patients in all trimesters	Vaccine when offered

Lactating patients	Vaccine when offered
Patients planned for breast imaging (Mammogram, MRI, etc.)	Vaccine when offered Consider scheduling breast radiology exams prior to the first dose of a COVID-19 vaccine, or 4-6 weeks following the second dose of vaccine (for multi-dose vaccines), due to axillary adenopathy that may occur post-vaccine.

Patients requiring vaccination with non-COVID vaccines COVID-19 vaccines and other vaccines may now be administered without regard to timing. This includes simultaneous administration of COVID-19 vaccines and other vaccines on the same day. If multiple vaccines are administered at a single visit, administer each injection in a different injection site. **Patients with prior history of COVID-19 infection** Vaccination should be deferred until the person has recovered from the acute illness and criteria have been met for them to discontinue isolation.
Patients who previously received passive antibody therapy (Convalescent plasma or Monoclonal antibody therapy) for COVID-19 disease Delay COVID-19 vaccine until >90 days after passive antibody treatment
Patients with a history of allergic reactions

History of severe allergic reaction after first dose of COVID-19 vaccine Any of the following occurring within 4 hours of receiving a vaccine or medication is concerning for an allergic reaction: - Hives or rash - Swelling of a body part - Wheezing or shortness of breath - Repeating vomiting or diarrhea - Low blood pressure - Treatment with epinephrine, hospitalization, intubation	Patients who received one dose of COVID-19 vaccine and had a severe allergic reaction should not receive a second dose until reaction was reviewed by Allergy specialist. Additional testing may be recommended.
Allergic reaction (any severity) to vaccines/medications containing polyethylene glycol (PEG) or polysorbate, without proven tolerance since index reaction	Vaccine when offered, including mRNA vaccine or viral vector vaccine, with 30 min post-vaccine observation period recommended Allergy consult not needed but reasonable if preferred
Allergic reaction (any severity) to food, animals, stinging insect venom, pollen,	Vaccine when offered, with 30 minute post-vaccine observation period recommended

latex, or vaccines/medications that do not contain polyethylene glycol (PEG) or polysorbate, including large or delayed injection site reactions. Allergic reaction (any severity) to non-COVID-19 vaccines/medications that contain PEG or polysorbate, but have tolerated PEG or polysorbate since the initial reaction History of mastocytosis, mast cell activation, idiopathic anaphylaxis Non-allergic reactions to medications/vaccines	Allergy consult not needed.
Family history of allergic reaction (any severity) to vaccines, injectable therapy, oral medications, or other allergies	Vaccine when offered
Patients with a history of neurological complications of vaccination	
Guillain-Barré syndrome (GBS) Bell's palsy	Vaccine when offered [a]

a) Per the CDC, persons who have previously had Guillain-Barre syndrome (GBS) may receive a COVID-19 vaccine. To date, no cases of GBS have been reported following vaccination among participants in the COVID-19 vaccine clinical trials. Patients are encouraged to speak with their medical team if they have concerns.

III. OVERVIEW

Therapy-Specific Guidelines

There is no direct evidence that immunomodulatory agents render the vaccine ineffective. Given potentially unique circumstances related to each individual patient, including COVID-19 risk factors, potential morbidity/mortality from the illness, and the nature of indications for the immunomodulatory

agents, administration may be appropriate inside of optimal waiting periods. Physicians should discuss the risks and benefits with their patients and involve them in the shared decision-making process.

Patients with Malignancy

Persons with active cancer are at increased risk of complications from COVID-19, and efforts to limit spread in high-risk patients is imperative. There are no vaccine data for cancer patients receiving active therapy available at this time. Available vaccines do not contain live virus and do not pose an immediate safety risk for immunosuppressed patients. However, immunosuppressed patients will likely have blunted immune responses when compared to the general population. The National Comprehensive Cancer Network (NCCN) COVID-19 Vaccination Advisory Committee feels strongly that COVID-19 vaccines should be given to all cancer patients, as well as household contacts and caregivers, when they are eligible to receive the vaccine. Recognizing the limited clinical data available in cancer patients, individuals should be vaccinated with the highest priority group for which they qualify. Finally, data from vaccine trials have demonstrated that vaccines decrease the incidence of COVID-19 disease and complications, but it is unclear if these vaccines prevent infection and subsequent transmission. Therefore, even if vaccinated, patients and close contacts should continue to wear masks, maintain social distancing guidelines, and follow other recommendations for COVID-19 prevention.

Patients with Inflammatory Bowel Disease (IBD)

Patients with IBD should receive COVID-19 vaccination. The best time to administer vaccination in patients with IBD is at the earliest opportunity to do so. SARS-CoV-2 vaccines including messenger RNA vaccines, replication incompetent vector vaccines, inactivated vaccines and recombinant vaccines are safe to administer to patients with IBD. Vaccination should not be deferred because a patient with IBD is receiving immune-modifying therapies. Patients should be counselled that vaccine efficacy may be decreased when receiving systemic corticosteroids.

Patients with other Autoimmune Diseases

The rheumatology community lacks important knowledge on how to best maximize vaccine-related benefits. Patients with rheumatic and musculoskeletal disease (RMD) exhibit high variability with respect to their underlying health condition, disease severity, treatments, degree of multimorbidity, and relationship with their specialist provider. These considerations must be considered when individualizing care. There is no reason to expect vaccine harms will trump expected COVID-19 vaccine benefits in RMD patients. The risk of deferring vaccination and thus failing to mitigate COVID-19 risk should be weighed against a possible blunted response to the vaccine if given under suboptimal circumstances. As a practical matter, this tension must be resolved in the context of imperfect prediction as to whether those circumstances may be transient, and a paucity of scientific evidence. Both individual and societal considerations related to a limited vaccine supply should be considered in issuing vaccine guidance and making policy decisions.

Patients with Solid Organ Transplant or Pre-transplant

The safety of COVID-19 vaccines is still under investigation in solid organ transplant recipients. There were no transplant recipients in the clinical trials, however, some transplanted individuals have already received vaccination with COVID-19 vaccines. Based on their mechanism of action, expert opinion is that these vaccines are unlikely to trigger rejection episodes or have novel or more severe side effects in transplant recipients. Solid organ transplant recipients may have generally lower antibody responses than those without transplants. Likewise, waning titers to other routine vaccines are well documented after transplantation. Lastly, patients vaccinated pre-transplant, may have reduced protection posttransplant. Based on previous vaccination guidelines for solid organ transplant recipients, it is recommended that all transplant candidates and their household members receive vaccination when it becomes available to them. Ideally, transplant candidates should be targeted for vaccination while they are awaiting transplant.

Pregnant and lactating patients

COVID-19 vaccines currently available have not been tested in pregnant or lactating patients. Therefore, there are no safety data specific to use in pregnancy or lactation. The currently available vaccines are not live virus vaccines and cannot transmit the SARS-CoV-2 virus to the patient or fetus. The American College of Obstetrics and Gynecology (ACOG) and Society of Maternal Fetal Medicine (SMFM) recommend that COVID-19 vaccines be administered to pregnant or lactating individuals who meet criteria for vaccination based on ACIP-recommended priority groups. Limited data are currently available from animal developmental and reproductive toxicity studies. No safety concerns were demonstrated in rats that received Moderna mRNA vaccine, the Pfizer-BioNTech mRNA vaccine, or the Johnson & Johnson-Janssen vaccine before or during pregnancy. A conversation between the patient and their clinical team may assist with decisions regarding the use of vaccines, but it should not be required prior to vaccination, as this may cause unnecessary barriers to access. There is no recommendation for routine pregnancy testing before receipt of a COVID-19 vaccine. Those who are trying to become pregnant do not need to avoid pregnancy after COVID-19 vaccination.

Patients recently vaccinated with non-COVID vaccines

COVID-19 vaccines and other vaccines may now be administered without regard to timing. This includes simultaneous administration of COVID-19 vaccines and other vaccines on the same day. If multiple vaccines are administered at a single visit, administer each injection in a different injection site.

Patients with prior history of COVID-19 infection

Vaccination should be offered to persons regardless of history of prior symptomatic or asymptomatic COVID-19 infection. Viral testing to assess for acute infection or serologic testing to assess for prior infection for the purposes of vaccine decision-making is not recommended.

Evidence suggests that the risk of SARS-CoV-2 reinfection is low in the months after initial infection but may increase with time due to waning immunity. Thus, while vaccine supply remains limited, persons with recent documented COVID-19 infection may choose to temporarily delay vaccination.

Patients who previously received passive antibody therapy for COVID-19 disease

Currently, there are no data on the safety and efficacy of COVID-19 vaccines in persons who received monoclonal antibodies or convalescent plasma as part of COVID-19 treatment. Based on the estimated half-life of such therapies as well evidence suggesting that reinfection is uncommon in the 90 days after initial infection, vaccination should be deferred for at least 90 days, as a precautionary measure until additional information becomes available, to avoid potential interference of the antibody therapy with vaccine-induced immune responses. This recommendation applies to persons who receive passive antibody therapy before receiving any vaccine doses as well as those who receive passive antibody therapy after the first dose but before the second dose, in which case the second dose should be deferred for at least 90 days following receipt of the antibody therapy.

Patients with a history of neurological complications of vaccination

Guillain Barré syndrome (a neurological disorder in which the body's immune system damages nerve cells, causing muscle weakness and sometimes paralysis) has occurred in some people who have received the Janssen/ Johnson & Johnson's COVID-19 Vaccine. In most of these people, symptoms began within 42 days following receipt of the Janssen COVID-19 Vaccine. The chance of having this occur is very low. You should seek medical attention right away if you develop weakness in legs and arms after receiving the Janssen COVID-19 Vaccine. Patients with a history of GBS should consider speaking with their medical team if they have questions or concerns about vaccination in this setting.

Cases of Bell's palsy were reported in participants in the Moderna and Pfizer mRNA COVID-19 vaccine clinical trials as well as the Johnson & Johnson-Janssen vaccine trials. However, the Food and Drug Administration (FDA) does not consider these to be above the rate expected in the general population. They have not concluded these cases were caused by vaccination. Therefore, persons who have previously had Bell's Palsy may receive a COVID-19 vaccine.

APPENDIX. Medication-specific recommendations

Medications	COVID-19 Vaccine Recommendations
Corticosteroids	
Topical therapy Intraarticular injection Intramuscular injection Epidural injection	Vaccine when offered
Systemic (IV / PO) therapy	Vaccine when offered High-dose pulse intravenous steroids are expected to blunt immune vaccine responses. Vaccine delays until therapy is reduced and/or completed can be considered on a case-by-case basis. Please see Tables 1 and 3 for recommendations specific to malignancy and solid organ transplant populations
Biologic agents	
TNF-alpha inhibitors Examples: -adalimumab (Humira) -certolizumab (Cimzia) -etanercept (Enbrel) -golimumab (Simponi) -infliximab (Remicade)	Vaccine when offered

Interleukin inhibitors Examples: -anakinra (Kineret) -canakinumab (Ilaris) -ixekizumab (Taltz) -secukinumab (Cosentyx)	Vaccine when offered

-sarilumab (Kevzara) -tocilizumab (Actemra) -ustekinumab (Stelara)	
Abatacept (Orencia)	Abatacept SQ : hold for one week before and after dose #1 Abatacept IV: delay vaccine for 1 month after abatacept infusion and do not resume therapy until 1 week after vaccine dose #1
Cyclophosphamide (Cytoxan)	Patients should discuss with their clinician(s) regarding timing. A two week interval between vaccine dosing and cyclophosphamide dosing is ideal, when possible

Other B-cell and T-cell inhibitors Examples: -alemtuzumab (Campath, Lemtrada) -belimumab (Benlysta) -ofatumumab (Kesimpta) -ocrelizumab (Ocrevus) -rituximab (Rituxan, Truxima)	Vaccine when offered Please see Table 2 and Table 3 for recommendations specific to multiple sclerosis and solid organ transplant populations
Integrin inhibitors Examples: -vedolizumab (Entyvio)	Vaccine when offered

Other monoclonal antibodies Examples: -bevacizumab (Avastin) -ranibizumab (Lucentis) -trastuzumab (Herceptin)	Vaccine when offered
Other immunomodulators	
Methotrexate Thiopurines Examples: -azathioprine -mercaptopurine Purine and Pyrimidine synthesis inhibitors Examples:	Vaccine when offered

-Mycofenolate (CellCept, Myfortic) -Leflunomide (Arava) -Teriflunomide (Aubagio) Calcineurin inhibitors (CNI) Examples: -cyclosporin (Neoral, Gengraf) -pimecrolimus (Elidel) -tacrolimus (Prograf) Janus kinase (JAK) inhibitors Examples: -baricitinib (Olumiant) -tofacitinib (Xeljanz/Jakvinus) -upadacitinib (Rinvoq) S1P receptor modulators Examples: -fingolimod (Gilenya) -ozanimod (Zeposia) -siponimod (Mayzent) Disease modifying therapies (DMTs) Examples: -dimethyl fumarate (Tecfidera) -diroximel fumarate (Vumerity) -glatiramer acetate (Copaxone, Glatopa) -interferon beta-1 (Avonex, Betaseron, Extavia, Rebif) -peginterferon beta-1a (Plegridy) -monomethyl fumarate (Bafiertam) -natalizumab (Tysabri) -teriflunomide (Aubagio) Intravenous immunoglobulin IVIG)	