OVERVIEW
Immunocompromised patients are at greater risk of infection and poor outcomes due to COVID-19. This category of patients includes recipients of:
- Solid organ and hematopoietic stem cell transplantation
- Active chemotherapy
- Corticosteroids
- Immunomodulatory and biologic therapies
- Acquired and heritable immune deficiencies

DISCUSSION
Vaccines have now been developed that stimulate robust humoral and cell-mediated response against the SARS-CoV-2 virus. Randomized, placebo-controlled trials suggest high-levels of vaccine effectiveness and acceptable tolerability and safety among non-immunocompromised study participants.

Although immunocompromised patients are high-priority for COVID-19 prevention, it is also well-recognized that immunocompromised patients may have lower rates of response to vaccination, depending on the type of vaccination and the net state of immunosuppression of a given patient. Immunogenicity correlates with the timing, intensity and type of suppression of cellular or humoral immunity. On the other hand, vaccine trials and real-world experience with vaccination in immunocompromised hosts suggest that although the response is predictably poorer, even partial immunity may confer potentially life-saving preventive advantage in immunocompromised patients.

Because immunocompromised patients were not included in COVID-19 vaccination clinical trials, clinical decisions about patient selection, risk versus benefit and timing of the SARS-CoV-2 vaccines must be based on the following:
- Evidence in these populations with other non-live vaccines, such as inactivated influenza
- Current community COVID-19 rates and relative risk of infection
- Efficacy, safety and availability of the SARS-CoV-2 vaccine

To develop these guidelines, we reviewed the current body of literature on vaccination in immunocompromised hosts, including guidelines from the Infectious Diseases Society of America, American Society of Transplantation, American Society for Hematology, American Society for Transplantation and Cellular Therapy, American College of Rheumatology, and the European Conference on Infections in Leukemia. We also conducted a survey of experts in fields of transplantation and infectious diseases. These guidelines have been approved by Intermountain Infectious Diseases, Oncology, Rheumatology, Bone Marrow Transplant and Solid Organ Transplant clinical leadership (see page 3).

RECOMMENDATIONS
COVID-19 vaccination is recommended for all immunocompromised patients without contraindications such as allergy. Currently there is no recommendation favoring one product (mRNA versus adenovirus vectored) over another. The following considerations for timing of vaccination are recommended:

Solid organ transplant recipients:
- **AST guidelines suggest vaccination as early as 1 month post transplant** unless T-cell depletion was used in induction.
- Defer vaccination for 3 months after T-cell depleting therapy.
RECOMMENDATIONS (CONTINUED)

- For patients who are transplanted after the first dose of mRNA vaccination but prior to receiving the second dose, **AST guidelines recommend deferring the second dose for at least one month after transplant.** The EUA does not currently permit restarting the vaccination series after transplant.
- **Vaccinate** all other solid organ transplant recipients at first availability.
- Although vaccine effectiveness is decreased in patients receiving non-specific anti-proliferative therapies (mycophenylate or azathioprine), **there is insufficient evidence to recommend routinely holding these therapies around the time of vaccination.**

**Autologous or allogeneic hematopoietic stem cell transplant:**

- **Defer** vaccination for three months from transplant or cellular therapy.
- **Offer** vaccination to all other HSCT recipients at first availability.
  - Patients with active graft versus host, on multiple immunosuppressive therapies or who have hypogammaglobulinemia or a CD4 count of <200 are less likely to have a response and should be addressed on case-by-case basis. For most patients, the protective advantage of even partial immunity justifies vaccination despite likelihood of poor response.
- **Offer** vaccination to pre-HSCT candidates who are not receiving cytotoxic chemotherapy and for whom transplant is not anticipated for 30 days.
  - For patients who are transplanted after the first dose of mRNA vaccination but prior to receiving the second dose, **the second shot in the series should be delayed until after engraftment.** The EUA does not currently permit restarting the vaccination series after transplant.

**Active cytotoxic chemotherapy**

- **Perform** vaccination prior to initiating chemotherapy where possible.
- For hematological malignancy: **Defer** vaccination until count recovery between cycles; for patients with marrow failure not anticipated to recover, vaccinate when available.
- For solid tumor malignancy: **Vaccinate** while on chemotherapy without delay due to less profound and shorter lasting immunosuppression in this group.
- Patients on checkpoint inhibitors can develop robust inflammatory responses. However, current evidence does not suggest a safety concern in these patients. **Consider** COVID-19 vaccination for these patients, but close monitoring is recommended.

**B cell-targeted (CD19, CD20) therapy and chimeric antigen receptor T cell therapy (CAR-T)**

- **Defer** vaccination for 6 months after last treatment.
- For patients on chronic maintenance anti-B cell monoclonal therapy, the American College of Rheumatology recommends **timing the vaccine series to be completed at least 2 weeks prior to the next dose of rituximab.**

**TNF inhibitors, other immunomodulators, biologics and systemic corticosteroid use**

Patients receiving these therapies are less likely to mount an adequate vaccine response.

- Where possible, **vaccinate** prior to initiation of immunosuppressive therapy.
- For patients on temporary courses of immunosuppressive treatment whose immunosuppression is anticipated to be reduced in the near future (6-12 weeks), **consider** deferring vaccination to optimize immunogenicity. This includes including patients on short-term or tapering corticosteroid doses of more than 20 mg prednisone-equivalent per-day, or induction immunomodulatory therapy for new or exacerbations of autoimmune diseases.
- For patients on chronic, maintenance immunosuppression, **offer** vaccination at first availability, acknowledging that partial immunity is preferable to none. Where possible, **consider** modifying dosing schedule of immunosuppressive therapy or timing of the vaccine to optimize immune function at the time of administration.
Acquired or heritable humoral deficiency
Patients receiving immunoglobulin supplementation are not precluded from vaccination but do have lower rates of response.

OTHER NOTES

- **Genetically-inactivated vaccines.** Adenovirus-vectored SARS-CoV-2 vaccines (Johnson & Johnson and others used globally) are genetically inactivated (replication genes have been deleted) vaccines. Like other inactivated vaccines, the adenovirus in these vaccines is not capable of replicating. As with the other current FDA-authorized vaccines, there is very little clinical trial data about safety or effectiveness in immunocompromised hosts. However, the adenovirus vaccines are NOT contraindicated in patients with mild or moderate immunosuppression, such as in patients on biologic agents for rheumatological conditions. Severely immunocompromised patients (recent recipients of solid organ or bone marrow transplant or active hematological malignancy) should discuss with their provider before vaccination.

- **Informed consent.** Providers should be familiar with reported side effects and discuss risk versus potential benefits and alternatives to vaccination with patients.

- **Post-vaccine antibody response.** Not all immunoassays check for Spike IgG; the Abbot assay available through Intermountain Central Laboratory does not. The ARUP Euroimmun assay does, however (Test number 3002723, COVID-19 IgG by ELISA). Sensitivity has not been well established for evaluating post-vaccine seroconversion.

- **Continued precaution.** Because patients in these groups may have an incomplete protective vaccine response, and because others who are vaccinated may still be able to shed virus asymptptomatically, immunocompromised patients and their close contacts must continue to follow other precautions, including limiting social interactions, social distancing, mask adherence and hand hygiene. Vaccination is a supplement to these practices that may offer an additional layer of protection should other measures fail.

- **Vaccination after acute COVID-19.** Patients should defer vaccination until they are outside the isolation window and symptoms improved. Patients who have received COVID-19 specific neutralizing monoclonal antibody therapy or convalescent plasma should defer vaccination for 90 days to avoid the theoretical risk that these products will interfere with immunogenicity.

REFERENCES


REFERENCES (CONTINUED)


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