COVID-19 AND VACCINES: FREQUENTLY ASKED QUESTIONS

What are mechanisms of action for the currently used SARS-CoV-2 vaccines?

The SARS-CoV-2 vaccines being used utilize novel mechanisms of action to elicit an immune response in patients. Conventional methods include administration of attenuated inactivated (killed) virus or recombinant viral protein vaccines to develop immunity. The vaccines either include SARS-CoV-2 protein or portions of the genetic material (mRNA), which can encode specific SARS-CoV-2 protein. These vaccines have no ability to replicate the SARS components themselves, and depend on the individual's immune response to develop antibodies in response to the vaccine components.

How are the SARS-CoV-2 vaccines administered and what challenges exist for vaccination?

The vaccines being administered currently require two (2) separate doses separated by three (3) to four (4) weeks. Receiving the vaccine is voluntary once it is available to anyone.

What SARS-CoV-2 vaccines are approved for use in immunocompromised patients?

Despite several vaccine candidates being in phase 2/3 clinical trials, no current clinical trial of a COVID-19 vaccine has enrolled immunocompromised patients. Thus, the benefit and safety of a SARS-CoV-2 vaccine has not been established in the different immunocompromised patient populations.

Why might some hematology patients not respond to vaccines?

In order to generate optimal protective immunity following vaccination, intact host immunity is needed. Therefore, hosts lacking functional immune cells may be unable to generate a fully protective immune response to a SARS-CoV-2 vaccine approved for use in the general population. Such individuals could have attenuated or absent response to SARS-CoV-2 vaccines. This could be secondary to the underlying disease, or more importantly, the treatment for it.

What is known about the safety and efficacy of protein-based or killed (inactivated virus) vaccines in immunocompromised patients?

Vaccine safety encompasses acute and long-term side effects associated with a vaccine. Based on experience with other recombinant protein-

based and inactivated (killed) virus-based vaccines, no major side effects or unique side effects have been reported in immunocompromised patients. Common acute side effects associated with candidate SARS-CoV-2 vaccines reported to date include low-grade fever, muscle aches, headache, nausea, fatigue and soreness/redness at the injection site. These acute side effects were more pronounced after the booster dose (2nd vaccine dose) in some of the trials. Long-term side effects have not been defined for SARS-CoV-2 vaccines and will be available once phase 3 trials have completed long term follow up in healthy volunteers.

The benefit of protein-based or inactivated (killed) SARS-CoV-2 vaccines in immunocompromised patients has yet to be studied. Vaccine responses are influenced by the underlying disease and the type and timing of recent therapy.

The impact of lab testing parameters like blood counts, etc. on responses to SARS-CoV-2 vaccines is unknown.

Although there are no data for mRNA/DNA and using other viruses to deliver vaccines, what are the theoretical considerations in immunocompromised patients?

Given patients with certain malignancies like chronic lymphocytic leukemia, lymphoma or myelodysplasia and patients after allogeneic hematopoietic cell transplantation may be prone to other immune-mediated complications, there is some concern that generating anti-SARS-CoV-2 antibodies in these patients could lead to immune enhancement and a systemic inflammatory response. So far there has not been any evidence of this.

Are any trials of SARS-CoV-2 vaccines being done in immunocompromised populations?

Currently, no SARS-CoV-2 vaccine trial is enrolling patients receiving immunosuppressive therapy. Most trials require patients to be off immunosuppression for a certain period of time to be eligible. This may not be feasible in patients who are receiving therapy for solid organ transplant, graft versus host disease or hematologic malignancy. It is unclear how the different SARS-CoV-2 vaccine candidates will specifically affect different forms of immune abnormalities. Given the diversity of various immunocompromised patient populations, it is possible that candidate SARS-CoV-2 vaccines may differ in their efficacy and safety for these patients.

If immunocompromised patients were not included in the vaccine trials and are less likely to respond to a SARS-CoV-2 vaccine, should

they still receive it? What is the timing in relation to chemotherapy, transplant, antibody therapy, splenectomy etc. Should higher vaccine doses or multiple vaccine types be used?

The risks and benefits for immunocompromised patients receiving a SARS-CoV-2 vaccine should be weighed. There does not appear to be an obvious risk to the vaccine but in some patients, who are receiving active chemotherapy, immunotherapy or may have their underlying diagnosis not well-controlled, the vaccine may not produce an immune response and thus, may not be of sufficient benefit. If someone is on ongoing therapy and treatment cannot be interrupted for several weeks, then it may be recommended to proceed with the vaccine.

Importantly, vaccination does not change required precautionary behaviors such as masking, social distancing, and frequent hand hygiene. All healthcare workers and household contacts should receive a SARS-CoV-2 vaccine when available to help protect immunocompromised patients, similar to the recommendations for influenza.

Whether or not an immunocompromised patient is known to have been previously infected with SARS-CoV-2 should not affect the decision of whether to vaccinate. Although some immunity is anticipated from experiencing a COVID-19 clinical infection, this immunity may be insufficient or wane, especially in immunocompromised hosts. However, increased side effects could be seen with vaccination, similar to what is observed with the second dose in a two-dose vaccine series.

Until more is known, different SARS-CoV-2 vaccines should not be given to the same patient. Although measuring titers may eventually be helpful to assess response, more information is needed. Giving more inoculations or higher doses of an approved SARS-CoV-2 vaccine is not recommended at this time.

How is vaccine administration being prioritized by Mayo Clinic?

Mayo Clinic following the national vaccination roll out plan that phases as follows:

- **Phase 1a**: Health care personnel and long-term care residents.
- **Phase 1b**: Patients age 75 or older, plus "frontline essential workers" (firefighters, police, transit employees, postal workers, grocery workers, teachers, day care).
- **Phase 1c**: People age 65 or older, plus anyone age 16-64 with a high-risk condition and "other essential workers" (rest of transportation industry, food servers, lawyers, etc.).
- **Phase 2**: Congregate settings and adults with some increased risk.
- **Phase 3**: Young adults and children, all workers.

- **Phase** 4: Remaining adults not in the workforce or at high risk.

If an individual gets access to the vaccine through other healthcare sources, they should receive it there.