COVID-19 Vaccine FAQ Sheet
(updated 3/18/2021)

The AST has received queries from transplant professionals and the community regarding the COVID-19 vaccine. The following FAQ was developed to relay information on the current state of knowledge. This document is subject to change and will be updated frequently as new information or data becomes available.

What kinds of vaccines are available or under development to prevent COVID-19?
There are currently several vaccine candidates in use or under development. In the United States, the Government is supporting six separate vaccine candidates. Several other vaccines are also undergoing development outside of the United States government sponsorship and further information can be found here:

- **NYTimes Coronavirus Vaccine Tracker:** https://www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.html
- **Washington Post Vaccine Tracker:** https://www.washingtonpost.com/graphics/2020/health/covid-vaccine-update-coronavirus/

The types of vaccines are as follows (March 1, 2021) [1]:

Table 1: Vaccines Under Development or Available Through EUA

Vaccine Type	Compound Name [Sponsor]	Clinical Trial Phase	Notes
mRNA	mRNA-1273 [Moderna]	Phase 3	Emergency use in U.S., E.U., other countries Approved in Canada
	BNT162b2 (Comirnaty) [Pfizer]	Phase 2/3	Emergency use in U.S., E.U., other countries Also approved in Canada and other countries
Replication-defective adenoviral vector	AZD1222 (Covishield) [AstraZeneca]	Phase 2/3	Emergency use in U.K., India, other countries (not U.S.)
	JNJ-78326735/Ad26.COV2.S [Janssen/Johnson&Johnson]	Phase 3	Emergency use in the U.S.
	rAd26 and rAd5 (Sputnik V) [Gameleya Research Institute]	Phase 3	Emergency use in Mexico, Russia, other countries (not U.S.)
Recombinant-subunit-adjuvanted protein	NVX-CoV2373 [Novavax]	Phase 3	
	Recombinant SARS-CoV-2 Protein Antigen + AS03 Adjuvant [Sanofi Pasteur/GSK]	Phase 2	
Inactivated coronavirus	CoVaxin [Bharat Biotech]	Phase 3	Emergency Use in India
	BBIBP-CorV (CoronaVac) [Sinopharm]	Phase 3	Approved China, Bahrain, UAE; Emergency use other countries (not U.S.)

Both of the mRNA SARS-CoV-2 vaccines (Moderna, Pfizer) have been authorized by Emergency Use Authorization (EUA) by the U.S. Food and Drug Administration (FDA), require 2 doses and cold storage.[2] The Janssen/Johnson & Johnson vaccine uses a replication-deficient Adenovirus 26 for the vaccine vector and has been authorized by EUA by the FDA as a 1 dose vaccine.

When will these vaccines become available to transplant recipients?
The Pfizer and Moderna mRNA vaccines and Janssen/Johnson & Johnson Adenovirus-vector vaccine are approved for Emergency Use Authorization (EUA) in the U.S. (Current: March 17, 2021).

The CDC Advisory Committee on Immunization Practices (ACIP) has proposed a phased distribution for the vaccine.[3, 4] Individual states and local health departments have implemented phased distribution with a range of allocation strategies. Vaccine prioritization is driven by a balance of competing factors, including individual risk and community benefit. The ACIP has provided guidance from which each state in the U.S. has developed a prioritization plan. Please check with your local and state health departments to find out when transplant candidates and recipients will be eligible for vaccination in your own area.

Further updated information on vaccinations administered across the U.S. can be found here:

- **Bloomberg Vaccine Tracker:** https://www.bloomberg.com/graphics/covid-vaccine-tracker-global-distribution/

Information for patients on where to find vaccines nearby can be found here:
- **NPR Vaccine Distribution Information per State:** https://www.npr.org/sections/health-shots/2021/02/18/967448680/how-to-sign-up-for-a-covid-19-vaccine-in-your-state
- **Vaccine Finder:** https://vaccinefinder.org/

What is known about the safety of these vaccines?

Table 2. Vaccine safety

Local and Systemic Reactions Day 0-7	**v-safe/VAERS reports**				**FDA Briefing Documents**				
	All mRNA vaccines %	Pfizer-BioNtech %		Moderna %	Pfizer-BioNtech %		Moderna %		Janssen/ J&J %
		Dose 1	Dose 2	Dose 1	Dose 1 N=4,093	Dose 2 N=3,758	Dose 1 N=15,163	Dose 2 N=13,944	
Injection site pain	70.7	67.7	74.8	70.1	77.8	72.6	83.7	88.4	46.9
Fatigue	33.4	28.6	50.0	29.7	41.5	55.5	37.2	65.2	38.2
Headache	29.4	25.6	41.9	26.0	34.5	46.1	32.7	58.6	38.9
Myalgia	22.8	17.2	41.6	19.6	18.0	33.5	22.7	57.6	33.2
Chills	11.5	7.0	26.7	9.3	10.6	29.6	8.3	43.7	N/A
Fever	11.4	7.4	25.2	9.1	2.7	13.6	0..8	15.6	9.0
Swelling	11.0	6.8	26.7	13.4	6.1	6.8	6.2	12.2	5.2
Joint Pain	10.4	7.1	21.2	8.6	9.9	20.5	16.6	42.6	N/A
Nausea	8.9	7.0	13.9	7.7	N/A	N/A	8.3	18.9	14.2
Vomiting	N/A	N/A	N/A	N/A	0.9	1.4			N/A

* Data from reports through v-safe/VAERS as reported in ACIP meeting (Jan 27, 2021) with v-safe lock point Jan 14, 2021. Side effects reported on at least one health check-in completed on days 0-7 after receipt of vaccine. Pfizer-BioNtech with N=7,307, Moderna with N=1,786.	

The unprecedented speed of the vaccine development has been built upon prior research conducted in previous coronaviruses as well as vaccine approaches for other novel viruses. Rigorous standards for safety were set forth by the FDA in June 2020, and all vaccine candidates must meet safety and effectiveness standards.

Although there are no licensed mRNA vaccines in the United States, they have been studied for decades for cancer and other infectious diseases. The safety profile of the mRNA SARS-CoV-2 vaccines administered to over 70,000 participants has not revealed any significant concerns at a median of 2 months follow up. At the time of this update, over 77 million doses have also been administered under the Emergency Use Authorization without additional concerns. The mRNA SARS-CoV-2 vaccines, similar to other common vaccines, are noted to cause fevers, muscle aches, and headaches; most are mild to moderate in severity, but some may be severe enough to briefly limit activities and typically resolve within 1-2 days. At this time, given the available data and that with other vaccines, the vast majority of serious side effects, if any, are noted in the first few days after vaccination, we do not expect that there will be significant side effects reported beyond the early post vaccination period.

The potential for anaphylaxis to either mRNA vaccine may range from 2.5-4.7/million doses[5]; this is currently being closely monitored in the US and other countries. Persons with a known (diagnosed) allergy to polyethylene glycol (PEG), another mRNA vaccine component, or polysorbate, have a contraindication to vaccination. Individuals with any immediate allergic reaction to other vaccines or injectable therapies should be counseled about the unknown risk of severe allergic reaction and should be monitored for 30 minutes after vaccine. Likewise, patients with allergy to oral medication, history of food, pet, insect, venom, environmental or latex allergies or family history of allergy should obtain the vaccine but also be monitored for 30 minutes after vaccine.[6] At this time, it is recommended that all vaccine recipients should be monitored on site immediately following vaccination.

The safety of mRNA vaccines is still under investigation in solid organ transplant recipients. There were no transplant recipients in the phase 3 trials for Moderna or Pfizer, however, some transplanted individuals have already received vaccination as part of the EUA. 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, but more data will be needed in.

Preliminary data of 187 SOT recipients who received their first SARS-CoV-2 vaccine doses has recently provided early insight into safety and efficacy of the mRNA vaccine in this population. Equal numbers of recipients received the Pfizer and Moderna vaccines and had low rates of local (61% pain, 7% redness, 16% swelling at injection

site) and systemic (4% fever, 9% chills, fatigue 38%, headache 32% and myalgias 15%) reactions. No episodes of graft rejection were reported in these patients.[7]

The safety of Adenovirus-vector vaccines is still under investigation in solid organ transplant recipients as transplant recipients were not included in the phase 3 trials of the Janssen/Johnson & Johnson vaccine. Unlike live virus vaccines, Adenovirus-vector vaccines have been genetically engineered to not replicate, and therefore cannot cause Adenovirus infection in the recipient. Based on the mechanism of action, expert opinion is that this vaccine is unlikely to trigger rejection episodes or have novel or more severe side effects in transplant recipients, but more data are needed.

The safety of other candidate vaccines will be updated as they get closer to emergency use authorization by updating this document.

How effective are these vaccines in transplant recipients?

The Pfizer and Moderna mRNA vaccines have data in immunocompetent people showing 94.1-95% efficacy in preventing infection COVID-19; vaccine efficacy appears similar in patients older than 65 years of age compared to younger patients. Data also suggest that when breakthrough infection occurs, disease is generally mild, showing the vaccines are also effective in preventing severe disease. Data regarding the durability of vaccine titers are still being gathered although it currently appears that antibody titers persist for at least 4 months.[8]

The Janssen vaccine trials in immunocompetent people shows a 66% efficacy to prevent COVID-19 infection. Data from US patients demonstrated a 72% overall efficacy against symptomatic COVID-19 infection and 86% efficacy in preventing severe forms of COVID-19.

Any of the currently authorized vaccines can be used when indicated, we currently do not state a product preference. Efficacy rates may be lower than the general population for any of the available vaccines and relative efficacy of different products is not known in the transplant setting. The effectiveness of COVID-19 vaccines will need to be further studied in the solid organ transplant recipient. 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 post-transplant, particularly if therapies that reduce B-cell function (e.g. rituximab) are utilized. The impact of specific therapies, such as belatacept also warrant specific study.

When should a transplant recipient or candidate receive these vaccines?

The immunogenicity and efficacy of COVID-19 vaccines are unknown in transplant recipients. However, 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. Ideally, transplant candidates should be targeted for vaccination while they are awaiting transplant. In general, vaccines are recommended for completion at least 2 weeks prior to transplantation or starting at 1 month after transplantation.[9] If given prior to transplant, ideally both doses should be completed before transplant to allow full protection however, transplant deferral to complete the vaccine series should not be routinely done and needs to be

decided on a case-by-case basis. In certain situations, it may be appropriate to wait until 3 months after transplantation to vaccinate, such as when T- or B-cell ablative therapy (anti-thymocyte globulin or rituximab) was used at time of transplant. If someone is transplanted after receipt of only 1 dose of vaccine, the optimal timing of the second dose is not defined. Expert opinion suggests waiting for at least 4 weeks to administer the second dose of vaccine, in order to allow time to decrease immunosuppression prior to second dose administration.

Can a transplant recipient still receive the vaccine even if they have had COVID-19?

The current guidance is that everyone receives the vaccine, irrespective of past COVID-19 infection or prior evidence of humoral immunity. There are case reports of immunosuppressed patients developing COVID-19 reinfection,[10] suggesting lack of appropriate immune response or waning immunity after the first infection. If a transplant recipient has had COVID-19, he/she should wait until all symptoms are resolved and the period of isolation has ended. The CDC currently recommends that vaccination should be postponed for 90 days following a more remote COVID-19 infection or following receipt of convalescent plasma or monoclonal antibody. The ideal period for vaccination after infection is still being investigated, however.

If a patient develops COVID-19 infection *after* the first dose of mRNA vaccination, but before the second dose, if possible, the second dose should be given once symptoms have resolved and the patient is outside the infectious window.

The impact of delaying the second dose on vaccine efficacy and durability has not been studied and should be avoided where possible. However, if a delay occurs because of incident COVID-19 infection, vaccine unavailability, or interval transplantation, delay should be kept as short as possible. Infectious diseases consultation is advisable in these situations.

Can patients stop wearing a mask after vaccination?

No. After vaccination, patients should be counseled to continue to practice COVID-19 safety measures including wearing masks around others, hand hygiene, and physical distancing in public places. It is likely that the efficacy and immunogenicity of vaccine in transplant recipients will be lower than shown in the vaccine clinical trials. In addition, although vaccination substantially reduces the risk of symptomatic illness, it may not eliminate the risk of asymptomatic transmission of SARS-CoV-2.

Although the CDC has stated that fully vaccinated people may gather indoors with other fully vaccinated people without wearing masks, this approach is not recommended for transplant recipients. We recommend continued adherence to masking and physical distancing when with non-household members until more is known about the immune response and clinical effectiveness of the vaccine in the transplant population.

Can the COVID-19 vaccines be given at the same time as other vaccines?

There are no data on safety or efficacy of the mRNA COVID-19 vaccines when administered with other vaccines. Therefore, the Advisory Committee on Immunization Practices recommends that the COVID-19 vaccine series should be administered alone and with a minimum of 14 days before or after giving any other vaccines.

Should we check for antibody response after vaccination in solid organ transplant recipients?

Currently we do not recommend routinely checking antibody responses to vaccine. There are a range of assays with different targets, not all detect neutralizing antibodies, and most do not provide results with titers. As such, presence of antibodies may represent reaction to vaccine but not protection from infection. Further, there is not a well-established protective threshold to target. Assessment of responses should be done in the context of trials with experts who can interpret results and provide data on titers of neutralizing antibodies.

Preliminary data on 436 organ transplant patients showed that 17% produced antibody to the SARS-CoV-2 spike protein a median of 20 days after the first dose of mRNA COVID vaccine.[11] We do not have cellular immunity data or clinical correlation at this time. Nor do we have data reflecting responses following completion of the two dose vaccine series or response rates to other types of vaccines. Further data are pending and will be helpful to better understand the response rates of SOT recipients to mRNA vaccines.

Should we hold mycophenolate mofetil or other immunosuppressants around the time patients are vaccinated?

There was a signal of decreased antibody response in patients on antimetabolites in the preliminary data published in patients after receipt of only 1 of 2 doses of mRNA vaccine.[11] This is consistent with other vaccine response studies. These data are insufficient to support the reduction or cessation of any immunosuppression to improve vaccine efficacy. We are awaiting further information regarding antibody response, cellular immune response and clinical effectiveness of COVID vaccination in the transplant population. At this time, we do NOT recommend adjustment of immunosuppression prior to vaccination.

Are there other things that transplant recipients need to consider about the vaccine?

Weighing the risks and benefits of getting vaccinated is important. While data are currently lacking specific to the vaccine in transplant recipients, it is reasonable to anticipate that vaccination will offer benefit. Likewise, transplant recipients may have clinically worse outcomes from SARS-CoV-2 infection compared to non-transplant recipients due to comorbidities or immunosuppression.[12] Thus, the benefits of vaccination outweigh any theoretical risks especially in countries where SARS-CoV-2 transmission continues at a high level. The transplant community is encouraged to collect data with regards to vaccination in order to inform future recommendations.

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