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Community of Practice: COVID Updates

Here's how Natera is helping you in the world of COVID-19

3rd edition, May 2021

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In the third installment of our bimonthly newsletter, Natera considers the questions arising in the midst of our transition into the new normal.

At this point, vaccine impact on transplant patients and ways to embrace telehealth are hot topics to consider when preparing for this new life.

This issue discusses various points of view, novel research and approaches to provide guidance on these top-of-mind areas.

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EDITORIAL

COVID-19 Vaccines in the Transplant Population

As a completely new pathogen, the SARS-CoV-2 virus entered the scene and began quickly spreading globally in late 2019 and early 2020. It has been a challenging virus to study, and its impact has been particularly devastating on people with comorbidities and preexisting conditions. Three vaccines currently have emergency use authorization (EUA) in the United States. There is little data about how kidney transplant recipients will react to the vaccine, whether enough antibodies will form, and whether the vaccine would compromise the allograft.

The American Society of Transplantation (AST) published a vaccine FAQ sheet[1], with guidelines and information about giving the COVID-19 vaccine to transplant patients. The studies leading to the EUA reported efficacy data for healthy populations, but the most vulnerable populations were not studied in depth. No transplant recipients took part in the phase 3 studies for the Moderna, Pfizer or Johnson & Johnson vaccines.

What is known about COVID-19 vaccines and the transplant population

As a new platform using mRNA, side effects are a potential issue for the Moderna and Pfizer vaccines. The J&J vaccine relies on a previously used platform. Here is some preliminary data from transplant patients who received their first doses of either the Moderna or Pfizer vaccines.

Reactions to first doses by transplant patients:

The AST FAQ shared data from transplant patients who received the first dose of Moderna or Pfizer vaccines under the EUA, based on research conducted at Johns Hopkins University.[2] The FAQ noted that "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…" They shared preliminary data[3] from 187 SOT (solid organ transplant) recipients receiving their first Pfizer or Moderna vaccine.

- **About half (52%)** of those studied were kidney transplant recipients.
- **Researchers reported** giving the Pfizer and Moderna vaccines to SOT patients in equal numbers, with no reported graft rejection.
- **Patients had** low levels of local side effects including 61% experiencing pain, 7% experiencing redness, and 16% with injection-site swelling.
- **Systemic side effects** include fever in 4%, chills in 9%, fatigue in 38%, headaches in 32%, and myalgias in 15%.

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The AST shared preliminary data for another Johns Hopkins study[4], which included 436 organ transplant patients.

- 48% were kidney transplant recipients.
- This study showed that after the first mRNA vaccine dose, 17% overall produced antibodies to the spike protein a median of 20 days after the first dose, including 14% of kidney transplant recipients.
- Of those producing antibodies, 41% were kidney transplant recipients.
- They do not have data following the second dose.

	ANTIBODY, NO. (%)	
TYPES OF ORGAN TRANSPLANT[h]	**DETECTABLE (N=76)**	**UNDETECTABLE (N=360)**
Kidney	31 (41)	188 (53)
Liver	28 (37)	50 (14)
Heart	9 (12)	57 (16)
Lung	4 (5)	45 (13)
Pancreas	1 (1)	4 (1)
Other (multiorgan)	2 (3)	12 (3)

The AST recommends that based on prior vaccination guidelines for solid organ recipients:

- **All transplant candidates** and household members should receive a COVID-19 vaccination when available.
- **Transplant candidates** should be vaccinated while awaiting transplant, preferably at least 2 weeks before the procedure, or at least 1 month after transplantation.
- **Patients receiving** T- or B-cell ablative therapy (anti-thymocyte globulin or rituximab) at transplant time may want to wait 3 months.

REFERENCES

1. American Society of Transplantation, COVID-19 Vaccine FAQ Sheet, updated 3/18/21. https://www.myast.org/sites/default/files/2021%2003%2018%20COVID19%20VACCINE%20FAQS_update.pdf
2. Boyarsky, Brian J. MD1; Ou, Michael T. BS1; Greenberg, Ross S. BA1; Teles, Aura T. BS1; Werbel, William A. MD2; Avery, Robin K. MD2; Massie, Allan B. PhD1; Segev, Dorry L. MD, PhD1; Garonzik-Wang, Jacqueline M. MD, PhD1 Safety of the First Dose of SARS-CoV-2 Vaccination in Solid Organ Transplant Recipients, Transplantation: February 4, 2021 - Volume Online First - Issue - doi: 10.1097/TP.0000000000003654S. https://journals.lww.com/transplantjournal/Citation/9000/Safety_of_the_First_Dose_of_SARS_CoV_2_Vaccination.95390.aspx
3. Johns Hopkins news release, 2/9/21. Covid-19 Story Tip: Study Indicates COVID-19 Vaccines Are Safe for Organ Transplant Patients. https://www.hopkinsmedicine.org/news/newsroom/news-releases/covid-19-story-tip-study-indicates-covid-19-vaccines-are-safe-for-organ-transplant-patients
4. Boyarsky BJ, Werbel WA, Avery RK, et al. Immunogenicity of a Single Dose of SARS-CoV-2 Messenger RNA Vaccine in Solid Organ Transplant Recipients. JAMA. Published online March 15, 2021. doi:10.1001/jama.2021.4385

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EDITORIAL

Natera study of kidney transplant beneficiaries; immune resonses to the COVID-19 vaccine

While the data from Johns Hopkins is helpful, there is still a data gap in transplantation to understand vaccine response in kidney recipients. The Hopkins study showed that immunosuppressed SOT patients appear not to mount a normal immune response. “From what we know about the anti-rejection drugs these patients are taking, we expect to see a blunted response to the vaccine,” said Phil Gauthier, MD, transplant nephrologist and Natera’s Medical Director of Organ Health. “We may see less durability.” The Natera study hopes to find answers to these three unanswered questions:

- **What is the time course** of the induction of immune response to the vaccine by kidney transplant recipients?
- **What are the longevity and durability** of any immune response to the vaccine from kidney transplant recipients?
- **What does the Prospera transplant assessment test** show from vaccination through six months-post COVID-19 vaccination?

Determining answers to these questions allows clinicians to understand the vaccine’s effects and effectiveness on kidney transplant patients’ immunity, and the degree to which the allograft is impacted by the vaccination, if at all.

Study details

Three sites, Columbia University Medical Center, Yale New Haven Health, and University of Pennsylvania Health System, will each enroll 100 patients. The study will monitor patients immediately prior to their first vaccine, during the vaccination process for one or two doses (two for Moderna and Pfizer, and one for J&J), and six months out. Investigators will collect data on how quickly the patients form antibodies and to what magnitude.

Enrollment should be completed within six to nine months. The study will track which patients receive doses from which manufacturer, but the study will not control for that. “If possible, we could do a sub-analysis or cohort analysis if we get enough enrolled from all three manufacturers,” said Phil Gauthier, MD, transplant nephrologist and Natera’s medical director.

This will be a prospective non-controlled study. Investigators will compare the data with the greater population receiving the vaccines, using observational data potentially from the manufacturers’ reports. Data from vaccinated patients can also be compared to observational data from transplant patients who did not receive the vaccine.

As part of the study, Prospera will be used to monitor the allograft. Since vaccines rely on activation of the immune system, there is a question of whether the vaccine will put the allograft at risk. Prospera will show whether the transplanted kidney/s remain stable during the immunization process and antibody development. “If there is an early warning signal that they are at risk, we can better manage those patients moving forward,” said Gauthier.

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Changing the norms for how telehealth is provided

The pandemic brought huge usage changes to telehealth. Prior to the COVID-19 pandemic, around 15,000 Medicare beneficiaries took part in telehealth visits every week. The Centers for Medicare and Medicaid (CMS) rules previously stipulated that only certain populations were eligible for these visits to be reimbursed. The pandemic changed all that. By the end of April 2020, almost 1.3 million Medicare beneficiaries[1] received telehealth visits each week, and CMS agreed to cover 144 additional services at least through the public health emergency. Of the country's 63 million Medicare beneficiaries, about 24.5 million participated in telehealth between mid-March and mid-October 2020.

While telehealth clearly exploded during the pandemic, the extent it will continue to be reimbursed is uncertain, after the pandemic ends. "Telehealth has been held back by reimbursement issues," said Gauthier. Some of the allowances and reimbursement changes will be permanent, and others will be evaluated. Congressional approval will be needed for some changes.[2]

Especially during the pandemic's early days, transplant patients were understandably nervous to go to their doctor's offices or get routine blood draws completed. In response, Natera developed and funded the **ProReach Program**, so treating nephrologists could order a mobile phlebotomist to collect blood samples from patients at their homes. This way, patients could avoid potential exposure at a medical or laboratory site.

This also allowed patients to be monitored remotely. "We want to make sure their treating physicians are not missing any rejection signs," which can be reassuring to both the doctor and patient, said Gauthier. Natera offers a complimentary mobile phlebotomy service, while insurance typically covers lab processing. "We realized how important this was during the pandemic, so we provided the service because it was the right thing to do."

Nephrologists like Wayne Kotzker, MD found that ProReach was helpful to his patients, as the phlebotomist could draw all serum samples at once. "The patient is only stuck once, which is a benefit for patients who are going for frequent labs to be able to get the Prospera test and their complete transplant profile at the same time. That includes their drug levels, serum creatinine and even some of the other routine tests we get on the transplant patient on a regular basis," said Kotzker, a general clinical nephrologist at Florida Kidney Physicians.

> "Having the Prospera test and its reliability makes me more confident that when I am taking care of the patient, I am caring for them and making better decisions"
>
> **WAYNE KOTZKER, MD**

With the ProReach program, Natera's mobile phlebotomist can draw blood for 15 tests plus Prospera. That includes BK Virus, Hemoglobin A1c, CBC, Lipid Panel Magnesium, Comprehensive Metabolic Panel, Phosphate, COVID Antibody, Sirolimus Levels, Cyclosporin Levels, Tacrolimus Levels, Cytomegalovirus, Uric Acid, Epstein-Barr Virus, Urinalysis, Everolimus Levels, and Prospera. Doctors like Kotzker find it simple to place the Prospera order in the provider portal while requesting a mobile draw for the patient. The phlebotomist schedules the visit based on the patient's availability, and then coordinates shipping to Natera and its partner lab. Results are shared on Prospera's standard delivery channels and the routine lab channels.

While it took some effort to get ProReach set up during the pandemic, "we learned that patients and physicians placed a high value on remote services, and the ProReach program worked well," said Gauthier. "We always wondered if we could individualize the follow-ups, and we learned from ProReach that we can."

Natera plans to extend this service post-pandemic as it has been a value-added service to patients and physicians.

REFERENCES

1. CMS newsroom, press release, 12/1/20. Trump Administration Finalizes Permanent Expansion of Medicare Telehealth Services and Improved Payment for Time Doctors Spend with Patients. https://www.cms.gov/newsroom/press-releases/trump-administration-finalizes-permanent-expansion-medicare-telehealth-services-and-improved-payment
2. American Telemedicine Association newsroom, 12/2/20. The American Telemedicine Association Responds to CMS Physician Fee Schedule Final Rule That Permanently Expands Medicare Telehealth Services https://www.americantelemed.org/press-releases/the-american-telemedicine-association-responds-to-cms-physician-fee-schedule-final-rule-that-permanently-expands-medicare-telehealth-services/

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