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568. Comparison of Humoral Immune Response to the SARS-CoV-2 BNT162b2 Vaccine Between Solid Organ Transplant Recipients and Healthy Controls

Ahmad Yanis, MD[1]; Zaid Haddadin, MD[2]; Andrew Speaker, PhD[1]; Danya Waqfi, MD[1]; Rana Talj, MD[1]; Danielle A. Rankin, MPH, CIC[2]; Lauren Ezzell, n/a[1]; Marcia Blair, MS[1]; Joan Eason, LPN[1]; Rebekkah Varjabedian, BS[2]; Lora Thomas, MD[1]; James Chappell, MD, PhD[1]; Natasha B. Halasa, MD, MPH[1]; Natasha B. Halasa, MD, MPH[1]; [1]Vanderbilt University Medical Center, Nashvill, Tennessee; [2]Vanderbilt University Medical Center; Division of Pediatric Infectious Diseases, Nashville, Tennessee

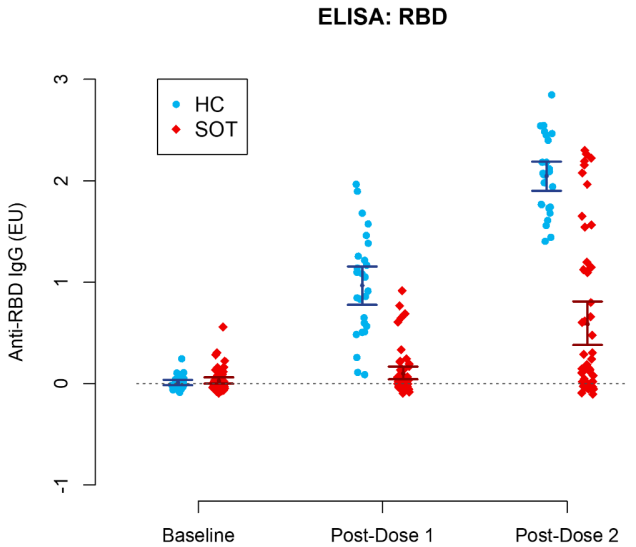
Session: P-25. COVID-19 Vaccines

Background. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is associated with increased morbidity and mortality in immunocompromised individuals, including solid organ transplant recipients (SOTR). Despite being excluded from phase 1-3 SARS-CoV-2 vaccine clinical trials, SOTR were identified as high-risk populations and prioritized for vaccination in public health guidelines. We aimed to evaluate the antibody response to two doses of the BNT162b2 (Pfizer-BioNTech) vaccine in SOTR as compared to healthy controls (HC).

Methods. SOTR and HC scheduled to receive two doses of BNT162b2 vaccine and able to complete required follow-up visits were enrolled. Blood specimens were collected from participants before receiving the first and second doses and 21-42 days after the second dose. Enzyme-linked immunosorbent assay (ELISA) was used to detect immunoglobulin G (IgG) to the SARS-CoV-2 spike receptor-binding domain (RBD). Generalized estimating equations with a working independence correlation structure were used to compare anti-RBD IgG levels between SOTR and HC at each study visit and within each group over time. All models were adjusted for age, sex, and pre-vaccination seroreactivity in the ELISA.

Results. A total of 54 SOTR and 26 HC were enrolled, with mean (SD) ages of 72 (3.6) and 62 (6.7) years, 61% and 35% were male, and 91% and 88% were white, respectively. The most common organ transplant types were kidney (41%) and liver (37%). All SOTR were receiving calcineurin inhibitors. The median time post-transplantation was 7 years. SOTR had markedly lower mean anti-RBD IgG levels when compared to HC with adjusted mean differences of -0.76 (95%CI: [-1.04, -0.47]; $p < 0.001$) ELISA units (EU) and -1.35 (95%CI [-1.68, -1.01]; $p < 0.001$) EU after the first and second doses, respectively (Figure 1). Both groups had a significant increase in anti-SARS-CoV-2 IgG levels after the second dose. However, the magnitude was lower in SOTR, 0.49 (95%CI [0.31, 0.69]; $p < 0.001$) EU than in HCs, 1.08 (95% CI [0.91, 1.24]; $p < 0.001$) EU.

Figure 1.



Anti-SARS-CoV-2 RBD IgG levels in solid organ transplant recipients and healthy controls before receiving the BNT162b2 vaccine (baseline), post-vaccine dose 1, and post-vaccine dose 2.

Conclusion. Our study showed SOTR mounted weaker humoral immune responses than HC to SARS-CoV-2 vaccines. Given a lower response, SOTR should continue to practice social distancing and masking until data on vaccine efficacy are available in this vulnerable population.

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569. Characterization of COVID-19 Vaccine Breakthrough Infections in Metropolitan Detroit

Nicholas sturla, MD[1]; Rita Kassab, DO[1]; Rafa Khansa, DO[1]; Thomas Chevalier, RN, BSN, CIC[2]; David Allard, MD[1]; Robert Tibbetts, Ph.D. D(ABMM), F(CCM)[2]; Linoj Samuel, PhD[2]; Geehan Suleyman, MD[1]; [1]Henry Ford Hospital, Detroit, MI; [2]Henry Ford Health System, Detroit, MI

Session: P-25. COVID-19 Vaccines

Background. Although COVID-19 vaccines are very effective, vaccine breakthrough infections have been reported, albeit rarely. When they do occur, people generally have milder COVID-19 illness compared to unvaccinated people. A total of 10,262 (0.01%) SARS-CoV-2 vaccine breakthrough infections had been reported as of April 30, 2021. The objective of this study was to evaluate the effectiveness of COVID-19 vaccines and characterize breakthrough infections in our patient population.

Methods. This was a retrospective review of all consecutive COVID-19 vaccine breakthrough infections at Henry Ford Health System (HFHS) in metropolitan Detroit, Michigan, from December 17, 2020 to June 7, 2021. Centers for Disease Control (CDC)'s breakthrough infection definition (detection of SARS-CoV-2 RNA or antigen in a respiratory sample ≥14 days after completion all recommended doses of COVID-19 vaccine) was used to identify cases. Vaccination status was extracted from the electronic medical records using Epic™ SlicerDicer.

Results. A total of 228,674 patients, including healthcare workers (HCW), were fully vaccinated in our healthcare system. We evaluate 299 patients for breakthrough infection but only 179 (0.08%) patients met the definition; 108 (60%) were female with median age of 59, 60 (33%) were HCW, and 11 (6%) were immunocompromised. The majority (92%) were asymptomatic (62 or 35%) or had mild/moderate illness (102 or 57%); 14 (8%) had severe or critical illness. The status of one patient was unknown. Of those who were symptomatic, 24 (13%) required hospitalization, and 3 (2%) required intensive unit care. One patient admitted for heart failure exacerbation died unexpectedly prior to being discharged. Nine had previous COVID-19 within 4 months but only one was symptomatic; this likely represented residual shedding in the asymptomatic patients.

Conclusion. COVID-19 vaccine was very effective among our patients and breakthrough infections were rare. Moreover, the vaccine reduced disease severity and mortality. Efforts should aim to increase vaccine uptake.

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570. Prioritized Access to COVID-19 Vaccines Among Vulnerable Communities Increases Vaccination Rates

Leonor Fernandez, MD[1]; Ashley O'Donoghue, PhD[1]; Peter Shorett, MBA[2]; Jonathan Blair, MBA[2]; Lawrence Markson, MD[1]; Tenzin Dechen, MS[1]; Jennifer Stevens, MD[1]; Sharon Wright, MD[2]; [1]Beth Israel Deaconess Medical Center, Boston, MA; [2]Beth Israel Lahey Health, Boston, MA

Session: P-25. COVID-19 Vaccines

Background. Based on national recommendations,[1] Beth Israel Lahey Health (BILH) in Eastern Massachusetts (MA) prioritized vulnerable communities in our distribution of COVID-19 vaccines. We hypothesized that creating prioritized access to appointments for patients in these communities would increase the likelihood vaccination.

Methods. The BILH health system sent vaccine invitations first to patients of two clinics in vulnerable neighborhoods in Boston (Wave 1), followed by other patients from vulnerable communities (Wave 2) up to 1 day later, and then by all other patients (Wave 3) after up to 1 more day later. To identify whether early access/prioritization increased the likelihood of receipt of vaccine at any site or a vaccine at a BILH clinic, we compared patients in Wave 1 in a single community with high cumulative incidence of COVID-19 (Dorchester) to patients in Wave 2 during a period of limited vaccine access, 1/27/21-2/24/21. Each wave was modeled using logistic regression, adjusted for language and race. By taking the difference between these two differences, we are left with the impact of early vaccination invitation in Wave 1 for a subset of our most vulnerable patients (termed difference-in-differences; Stata SE 16.0).

Results. In our study of Waves 1 and 2, we offered vaccinations to 24,410 patients. Of those, 6,712 (27.5%) scheduled the vaccine at BILH (Table 1). Patients in Wave 1 were much more likely to be vaccinated at BILH than patients in Wave 2. Patients offered the vaccine in Wave 1 and living in Dorchester were 1.7 percentage points more likely to be vaccinated at all (p=0.445) and 9.4 percentage points more likely to be vaccinated at BILH than another site in MA (p-value = 0.001), relative to patients living outside of Dorchester and offered the vaccine in Wave 2 (Table 2).

Table 1: Descriptive Statistics of Sample Population by Wave

	Overall		Wave 1		Wave 2	
	n	%	n	%	n	%
Total	24,410	100.0%	6,149	100.0%	18,261	100.0%
Race						
White	12,271	50.3%	3,444	56.0%	8,827	48.3%
Black	5,551	22.7%	1,373	22.3%	4,178	22.9%
Asian	935	3.8%	166	2.7%	769	4.2%
Other	3,772	15.5%	769	12.5%	3,003	16.4%
Unknown	1,881	7.7%	397	6.5%	1,484	8.1%
Ethnicity						
Hispanic	3,264	13.4%	686	11.2%	2,578	14.1%
Non-Hispanic	18,845	77.2%	4,961	80.7%	13,884	76.0%
Unknown	2,301	9.4%	502	8.2%	1,799	9.9%
Language						
English	16,897	69.2%	4,575	74.4%	12,322	67.5%
Spanish	1,892	7.8%	533	8.7%	1,359	7.4%
Chinese	252	1.0%	< 10	-	244	1.3%
Russian	89	0.4%	< 10	-	74	0.4%
Other	2,230	9.1%	985	16.0%	1,245	6.8%
Unknown	3,050	12.5%	33	0.5%	3,017	16.5%
City						
Dorchester	2,462	10.1%	706	11.5%	1,756	9.6%
Other	21,948	89.9%	5,443	88.5%	16,505	90.4%
Vaccination Site						
BILH Site	6,712	27.5%	2,792	45.4%	3,920	21.5%
Other MA Site	8,613	35.3%	1,309	21.3%	7,304	40.0%
Not Vaccinated	9,085	37.2%	2,048	33.3%	7,037	38.5%

Table 2: Results by Wave and town of residents

The coefficient of interest is on Wave1*Dorchester, 0.094. This indicates that residents of Dorchester who were offered the vaccine in Wave 1 were 9.4 percentage points more likely to receive the vaccine at BILH, given that they were vaccinated, relative to patients living outside of Dorchester and offered the vaccine in Wave 2.

	Point estimate (95% CI)	
	Pr(Vaccinated at BILH | Vaccinated)	Pr(Vaccinated At All)
Wave1*Dorchester	0.094* (0.039 to 0.149)	0.017 (-0.028 to 0.062)
Dorchester	0.093* (0.065 to 0.124)	0.02 (-0.004 to 0.043)
Wave 1	0.311* (0.293 to 0.329)	0.041* (0.026 to 0.055)

* denotes p-value < 0.001.

Point estimates displayed with 95% confidence intervals in parentheses. Column 1 has the dependent variable of vaccinated at BILH vs. vaccinated elsewhere (sample limited to patients who were vaccinated).

Column 2 has the dependent variable vaccinated anywhere vs. unvaccinated.

The coefficient of interest is on Wave1*Dorchester, 0.094. This indicates that residents of Dorchester who were offered the vaccine in Wave 1 were 9.4 percentage points more likely to receive the vaccine at BILH, given that they were vaccinated, relative to patients living outside of Dorchester and offered the vaccine in Wave 2.

Conclusion. Patients residing in an urban community given prioritized access to vaccination had a higher likelihood of vaccination at our health system, given that they were vaccinated, than patients in other urban communities without prioritized access. We provide an example of a successful effort to move towards equity in access to COVID-19- vaccines, in contrast to larger national trends.[2,3] Health systems can use a prioritization approach to improve vaccination equity.

Citations

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571. Safety and Immunogenicity of INO-4800, a COVID-19 DNA Vaccine as a Primary Series and Booster

Pablo Tebas, MD[1]; Joseph Agnes, PhD[2]; Mary Giffear, BS[2]; Kimberly A. Kraynyak, PhD[2]; Elliott Blackwood, MS[2]; Dinah Amante, BS[2]; Emma Reuschel, PhD[2]; Neiman Liu, MS[2]; Mansi Purwar, PhD[3]; Aaron Christensen-Quick, PhD[2]; Viviane M. Andrade, PhD[2]; Julie Carter, MHD[2]; Gabriella Garufi, PhD[2]; Malissa Diehl, PhD[2]; Albert Sylvester, MS[2]; Matthew P. Morrow, PhD[2]; Patrick P. Pezzoli, BS[2]; Abhijeet J. Kulkarni, MS[4]; Faraz I. Zaidi, MS[5]; Drew Frase, MS[5]; Kevin Liaw, PhD[5]; Ami Patel, PhD[3]; Karen R. Buttigieg, PhD[6]; John E. Ervin, MD[7]; Jan Pawlicki, PhD[2]; Elisabeth Gillespie, PhD[2]; Igor Maricic, MSc[2]; Katherine Schultheis, MSc[2]; Hedieh Badie, PhD[2]; Timothy A. Herring, MPH[8]; Keiko O. Simon, PhD[2]; Trevor R. F. Smith, PhD[2]; Stephanie Ramos, PhD[2]; Robert Spitz, MD[9]; Jessica Lee, MPH[2]; Michael Dallas, PhD[2]; Ami Shah Brown, PhD[2]; Jacqueline E. Shea, PhD[2]; J Joseph Kim, PhD[2]; David Weiner, PhD[3]; Kate Broderick, PhD[2]; Trevor McMullan, MSc[2]; Jean Boyer, PhD[2]; Laurent Humeau, PhD[2]; Mammen P. Mammen Jr., MD[2]; [1]Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania; [2]INOVIO Pharmaceuticals, Plymouth Meeting, Pennsylvania; [3]Wistar Institute, philadelphia, Pennsylvania; [4]Wistar, Philadelphia, Pennsylvania; [5]Wistar Institute Vaccine Center, Philadelphia, Pennsylvania; [6]National Infection Service, Public Health England, Salisbury, United Kingdom; [7]Alliance for Multispecialty Research - KCM, KANSAS CITY, Missouri; [8]Inovio Pharmaceuticals, Inc., Plymouth Meeting, Pennsylvania; [9]ICON GPHS, Hinckley, Ohio

Session: P-25. COVID-19 Vaccines

Background. DNA vaccines are safe, tolerable, elicit humoral and cellular responses, allow for repeated dosing over time, are thermostable at room temperature, and are easy to manufacture. We present a compilation of Phase 1 and Phase 2 data of Inovio's US COVID-19 DNA Vaccine (INO-4800) targeting the full-length Spike antigen of SARS-CoV-2. A South Korean Phase 2 study is ongoing.

Methods. Participants in the open-label Phase 1 trial received 0.5 mg, 1.0 mg or 2.0 mg intradermally (ID) followed by electroporation (EP) at Days 0 and 28. An optional booster dose was administered >6 months post-dose 2. The Phase 2 further compared the 1.0 mg and 2.0 mg doses against placebo in a total of 401 participants randomized at a 3:3:1:1 ratio. ClinicalTrials.gov identifiers: NCT04336410 and NCT04642638

Results. The majority of adverse events (AEs) related to INO-4800 across both trials were mild in severity and did not increase in frequency with age and subsequent doses. In Phase 1, 78% (14/18) and 84% (16/19) of subjects generated neutralizing antibody responses with geometric mean titers (GMTs) of 17.4 (95%CI 8.3, 36.5) and 62.3 (95% CI 36.4, 106.7) in the 1.0 and 2.0 groups, respectively (Figure 1). By week 8, 74% (14/19) and 100% (19/19) subjects generated T cell responses by Th1- associated IFNγ ELISPOT assay . Following a booster dose, neutralizing GMTs rose to 82.2 (95% CI 38.2, 176.9) and 124.7 (95% CI 62.8, 247.7) in the 1.0 mg and 2.0 mg groups, respectively, demonstrating the ability of INO-4800 to boost (Figure 2). In Phase 2, neutralizing antibody responses demonstrated GMTs of 93.6 (95%CI 77.3, 113.4) in the 1.0 mg dose group and 150.6 (95%CI 123.8, 183.1) in the 2.0 mg dose group (Figure 3).

Pseudovirus Neutralization by Dose Group in Phase I

	1.0 mg INO-4800 + EP	2.0 mg INO-4800 + EP
Week 0 GMT Reciprocal Titer (95% CI)	n = 39 3.3 (1.8, 6.1)	n=39 3.3 (1.8, 6.0)
Week 6 GMT Reciprocal Titer (95% CI)	n = 37 17.4 (8.3, 36.5)	n=38 62.3 (36.4, 106.7)
Geometric Mean Fold Rise (GMFR) (95% CI)	n=37 4.9 (2.2, 10.8)	n=38 18.4 (8.5, 39.6)

Pseudovirus Neutralization by Dose Group (all subjects who received booster dose) in Phase 1

	1.0 mg INO-4800 + EP	2.0 mg INO-4800 + EP
Pre-booster GMT Reciprocal Titer (95% CI)	n = 23 7.4 (2.8, 20.0)	n = 31 14.3 (6.2, 33.1)
Post-booster GMT Reciprocal Titer (95% CI)	n = 26 82.2 (38.2, 176.9)	n = 32 124.7 (62.8, 247.7)
GMFR (95% CI)	n = 22 8.1 (3.5, 18.3)	n = 29 9.8 (5.0, 19.1)

Pseudovirus Neutralization by Dose Group in Phase 2

	1.0 mg INO-4800+ EP	Placebo for 1.0 mg group + EP	2.0 mg INO-4800+ EP	Placebo for 2.0 mg group + EP
Day 0 GMT Reciprocal Titer (SD)	n = 124 32.2 (0.38)	n = 46 30.3 (0.40)	n = 114 35.8 (0.45)	n = 43 36.3 (0.43)
Week 6 GMT Reciprocal Titer (SD)	n = 125 93.6 (0.47)	n = 45 32.5 (0.33)	n = 115 150.6 (0.46)	n = 43 35.3 (0.41)
GMFR (SD)	n = 124 2.9 (0.45)	n = 45 1.2 (0.32)	n = 113 4.3 (0.53)	n = 43 1.0 (0.34)

Conclusion. INO-4800 appears safe and tolerable as a primary series and as a booster with the induction of both humoral and cellular immune responses. In addition to eliciting neutralizing antibodies, INO-4800 also induced T cell immune responses as demonstrated by IFNγ ELISpot. Finally, as a homologous booster, INO-4800, when administered 6-10.5 months following the primary series, resulted in an increased immune response without increase in reactogenicity. The 2.0 mg dose was selected for Phase 3 evaluation.

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