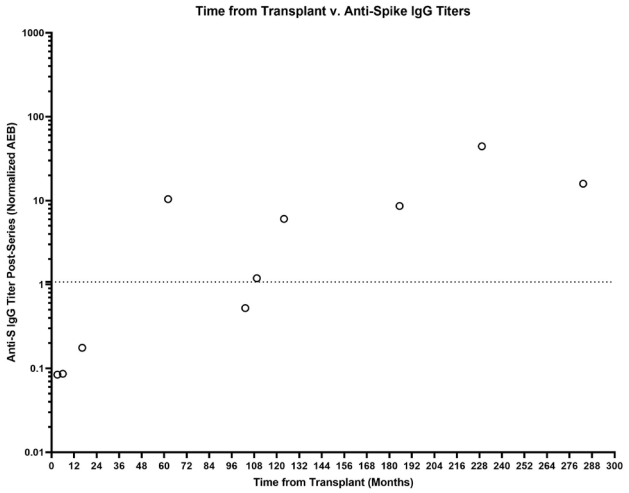
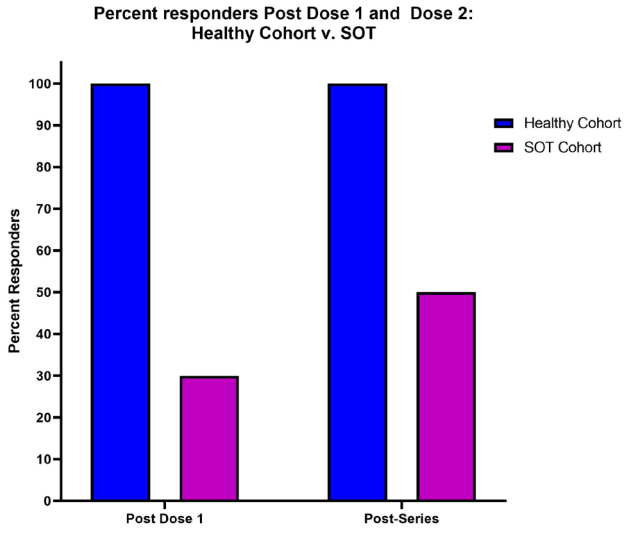
Figure 3: Time from Transplant v. anti-S IgG Titer



SOT recipients further out from transplant tend to have a higher anti-S IgG response. The dotted line denotes an internally validated cutoff, with anti-S IgG titers greater than 1.07 indicating a positive response.

Conclusion. SOT recipients had a significantly decreased humoral response to mRNA COVID-19 vaccines compared to the healthy cohort, with those further out from transplant more likely to respond. Further research is needed to evaluate T-cell responses and clinical efficacy to maximize the SARS-CoV-2 vaccine response among SOT recipients.



Disclosures. **Ann E. Woolley, MD, MPH**, **COVAX** (Consultant) **David Walt, PhD**, **Quanterix Corporation** (Board Member, Shareholder)

25. Immunogenicity and Reactogenicity of COVID-19 mRNA Vaccines in Allogeneic Stem Cell Transplant Recipients

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Session: O-05. Clinical Quandries in Viral Infections in ICH

Background. Allogeneic stem cell transplant (SCT) recipients are at an increased risk of poor outcomes from COVID-19. While the mRNA-1273 (Moderna) and BNT162b2 (Pfizer) COVID-19 mRNA vaccines are highly immunogenic in the general population, the immune response in SCT recipients is poorly understood. We characterized the immunogenicity and reactogenicity of COVID-19 mRNA vaccines in a cohort of SCT patients.

Methods. We performed a prospective cohort study of 16 allogeneic SCT patients and 23 healthy controls. Blood samples for both cohorts were collected prior to first vaccination (baseline), at the time of second vaccination, and approximately 28 days post-second vaccination. Anti-Spike (S), anti-S1, anti-receptor binding domain (RBD), and anti-Nucleocapsid (N) IgG levels were measured quantitatively from plasma using a multiplexed single molecule array (Simoa) immunoassay. Reactogenicity was captured for the SCT cohort via a self-reported post-vaccination diary for 7 days after each dose.

Results. Demographics and SCT recipients' characteristics are shown in Table 1. In the SCT cohort, we observed a significantly lower anti-S ($p< 0.0001$), S1 ($p< 0.0001$), and RBD ($p< 0.0001$) IgG responses as compared to healthy controls, both at the time of dose 2 and 28 days post-vaccine series (Fig 1). Overall, 62.5% of SCT recipients were responders after vaccine series completion, as compared to 100% of healthy controls (Fig 2). While no patients had a reported history of COVID-19 diagnosis, 2 patients in the SCT cohort had elevated anti-S IgG levels and 1 showed elevated anti-N at baseline.

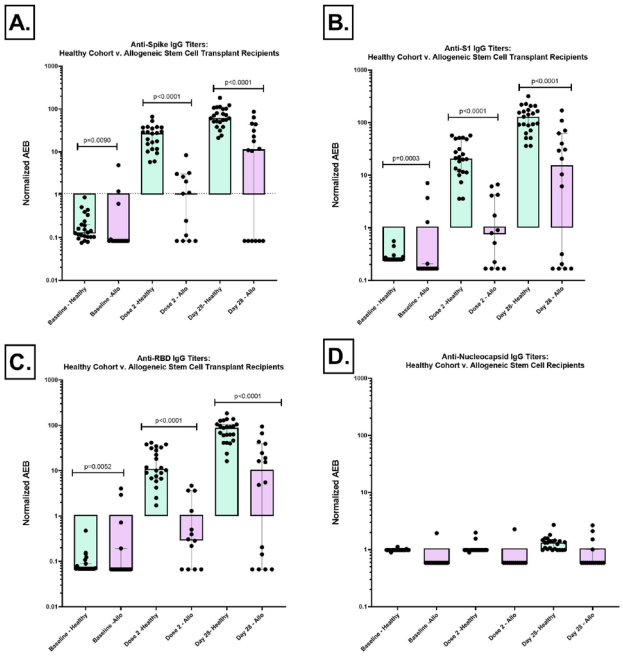
10/16 participants in the SCT cohort completed at least one post-vaccination diary. Local and systemic reactions were reported by 67% and 22% of participants, respectively, after dose 1, and 63% and 50% after dose 2 (Figure 3). All reported events were mild.

Table 1: Demographics

	Healthy Cohort (n=23)	Allogeneic Stem Cell Transplant (n=16)
Median Age (Range)	24 (22-56)	67 (41-79)
Female Sex - no. (%)	13 (56.5)	7 (43.8)
Race - no. (%)		
White	11 (47.8)	16 (100)
Black	1 (4.3)	0
Asian	4 (17.4)	0
Native American/Alaskan Native	1 (4.3)	0
Ethnicity - no. (%)		
Hispanic/LatinX	5 (21.7)	0
Vaccine Type - no. (%)		
Moderna	14 (60.1)	4 (25.0)
Pfizer	9 (39.1)	12 (75.0)
Median Time from Transplant, Days (Range)	NA	251 (97-2323)
Diagnosis - no. (%)		
MDS	NA	5 (31.3)
AML	NA	6 (37.5)
ALL	NA	2 (12.5)
HLH	NA	1 (6.3)
Aplastic Anemia	NA	1 (6.3)
BPDCN	NA	1 (6.3)

MDS: myelodysplastic syndromes, AML: acute myeloid leukemia, ALL: Acute lymphocytic leukemia, HLH: Hemophagocytic lymphohistiocytosis, BPDCN: Blastic plasmacytoid dendritic cell neoplasm

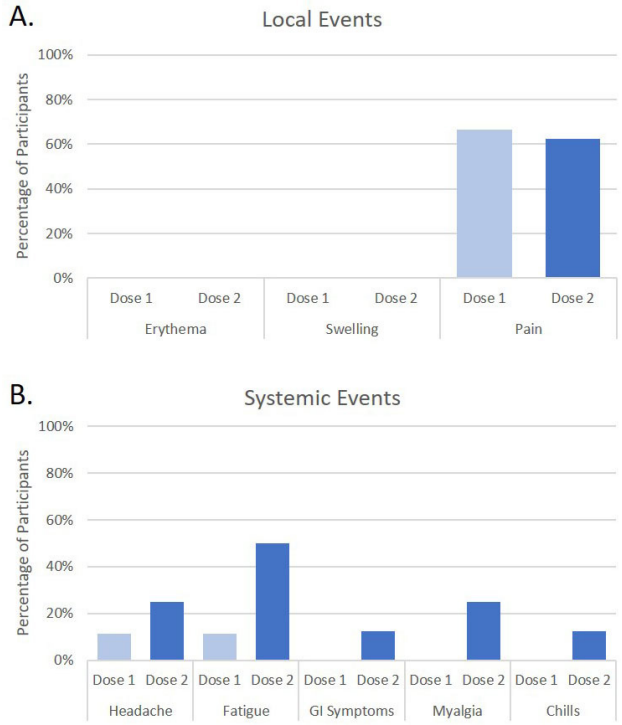
Figure 1: Plasma IgG Titers



Anti-Spike (A), anti-S1 (B), anti-RBD (C), and anti-nucleocapsid (D) IgG titers were measured at baseline, time of second dose, and approximately 28 days after second

vaccination. IgG levels were measured quantitatively using multiplexed single molecule array (Simoa) immunoassays, and are reported as Normalized Average Enzymes per Bead (AEB). Allogeneic stem cell transplant recipients (mauve) showed significantly lower anti-S, S1, and RBD IgG responses as compared to healthy controls (mint). Low titers of anti-N IgG demonstrates no history of COVID-19 natural infection during the course of the study.

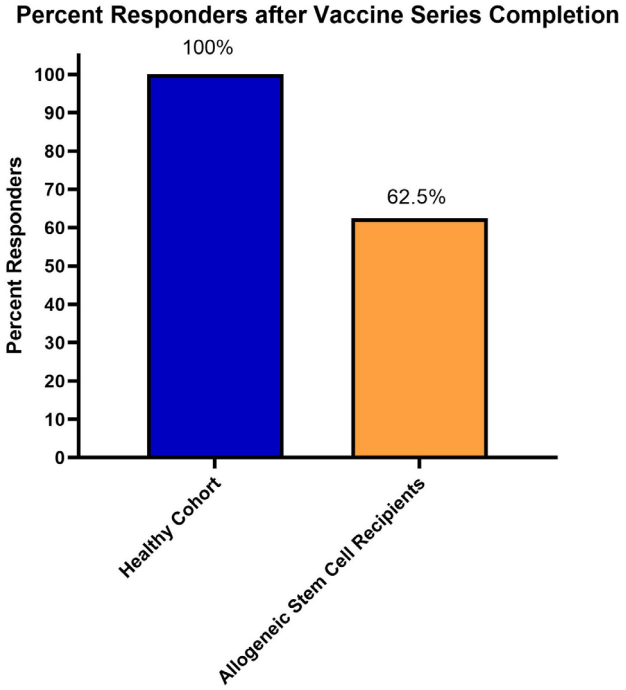
Figure 3. Solicited Local and Systemic Adverse Events



10 allogeneic stem cell transplant recipients completed at least one diary for 7 days after vaccination. Reactions after dose 1 are shown in light blue, and reactions after dose 2 are shown in dark blue. Local reactions (A) were reported by 67% (6/9) of participants after dose 1, and 63% (5/8) after dose 2. Systemic reactions (B) were reported by 22% (2/9) of participants after dose 1, and 50% (4/8) after dose 2. All reported events were mild (Grade 1).

Conclusion. Among SCT recipients, mRNA COVID-19 vaccines were well-tolerated but less immunogenic than in healthy controls. Further study is warranted to better understand heterogeneous characteristics that may affect the immune response in order to optimize COVID-19 vaccination strategies for SCT recipients.

Figure 2: Response Rate to COVID-19 Vaccination



An internally validated threshold for responders was established using pre-pandemic sera from healthy adults. A positive antibody response was was defined as individuals with anti-Spike IgG levels above the 1.07 Normalized AEB threshold.

Disclosures. **Amy Joyce, NP**, **Kadmon** (Advisor or Review Panel member) **Lewis A. Novack, MS**, **Lumicell Inc.** (Scientific Research Study Investigator, Research Grant or Support)**Precision Healing, Inc.** (Scientific Research Study Investigator, Research Grant or Support) **David Walt, PhD**, **Quanterix Corporation** (Board Member, Shareholder) **Robert Soiffer, MD**, **alexion** (Consultant)**gilead** (Advisor or Review Panel member)**jazz** (Advisor or Review Panel member)**juno/bms** (Advisor or Review Panel member)**kiadis** (Board Member)**precision bioscience** (Consultant)**Rheos** (Consultant)**takeda** (Consultant) **Nicolas C. Issa, MD**, **AiCuris** (Scientific Research Study Investigator)**Astellas** (Scientific Research Study Investigator)**GSK** (Scientific Research Study Investigator)**Merck** (Scientific Research Study Investigator)

26. Risk of Post–COVID-19 Dyspnea and Interstitial Lung Disease (ILD) in a Real-World Cohort of Patients Hospitalized with COVID-19 in the United States

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Session: O-06. COVID-19 Complications, Co-infections and Clinical Outcomes 1

Background. While COVID-19 carries substantial morbidity and mortality, the extent of long-term complications remains unclear. Reports suggest that acute lung damage associated with severe COVID-19 can result in chronic respiratory dysfunction. This study: (1) estimated the incidence of dyspnea and ILD after COVID-19 hospitalization, and (2) assessed risk factors for developing dyspnea and ILD in a real-world cohort of patients hospitalized with COVID-19 using US electronic health records (EHR).

Methods. Patients in the Optum de-identified COVID-19 EHR database who were hospitalized for COVID-19 (lab confirmed or diagnosis code) between February 20 and July 2020 and had at least 6 months of follow-up were eligible for analysis. Dyspnea and ILD were identified using diagnosis codes. The effects of baseline characteristics and hospitalization factors on the risk of incident dyspnea or ILD 3 to 6 months' post discharge were evaluated.

Results. Among eligible patients (n=26,339), 1705 (6.5%) had dyspnea and 220 (0.8%) had ILD 3 to 6 months after discharge. Among patients without prior dyspnea or ILD (n=22,613), 110 (0.5%) had incident ILD (**Table 1**) and 1036 (4.6%) had incident dyspnea (**Table 2**) 3 to 6 months after discharge. In multivariate analyses, median (IQR) length of stay (LOS; 5.0 [3.0, 9.0] days in patients who did not develop ILD vs 14.5 [6.0, 26.0] days in patients who developed ILD; RR: 1.12, 95% CI: 1.08, 1.15; P=4.34 x 10^{-10}) and age (RR: 1.02, 95% CI: 1.01, 1.03; P=4.63 x 10^{-3}) were significantly associated with ILD. Median (IQR) LOS (5.0 [3.0, 9.0] days in patients who did not develop dyspnea vs 7 [4.0, 14.0] days in patients who developed dyspnea; RR: 1.04, 95% CI: 1.02, 1.06; P=8.52 x 10^{-4}), number of high-risk comorbidities (RR: 1.18, 95% CI: 1.12, 1.24; P=3.85 x 10^{-9}), and obesity (RR: 1.52, 95% CI: 1.25, 1.86; P=2.59 x 10^{-4}) were significantly associated with dyspnea.

Table 1. Selected Baseline Risk Factors for Incident ILD

Risk Factors for Incident ILD						
		Missing	Overall	ILD (-)	ILD (+)	*P* Value
n			22,613	22,503	110	
Age, median (Q1, Q3), years		0	55.0 (40.0, 66.0)	54.0 (40.0, 66.0)	64.0 (56.0, 71.0)	<0.001
US region, n (%)	Midwest	728	7928 (36.2)	7882 (36.2)	46 (42.2)	0.307
	Northeast		7824 (35.8)	7783 (35.7)	41 (37.6)	
	South		4658 (21.3)	4641 (21.3)	17 (15.6)	
	West		1475 (6.7)	1470 (6.8)	5 (4.6)	
Race, n (%)	African American	5222	6207 (35.7)	6188 (35.8)	19 (20.9)	0.012
	Asian		726 (4.2)	721 (4.2)	5 (5.5)	
	Caucasian		10,458 (60.1)	10,391 (60.1)	67 (73.6)	
Ethnicity, n (%)	Hispanic	2299	4774 (23.5)	4754 (23.5)	20 (20.6)	0.582
	Not Hispanic		15,540 (76.5)	15,463 (76.5)	77 (79.4)	
Sex, n (%)	Female	0	11,230 (49.7)	11,180 (49.7)	50 (45.5)	0.43
	Male		11,383 (50.3)	11,323 (50.3)	60 (54.5)	
Overweight, n (%)	No	0	14,510 (64.2)	14,447 (64.2)	63 (57.3)	0.158
	Yes		8103 (35.8)	8056 (35.8)	47 (42.7)	
N high risk comorbidities, median (Q1, Q3)		0	1.0 (0.0, 2.0)	1.0 (0.0, 2.0)	2.0 (1.0, 3.0)	<0.001