Six-month Antibody Kinetics and Durability After 3 Doses of SARS-CoV-2 Vaccine in Solid Organ Transplant Recipients: A Case Series

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Solid organ transplant recipients (SOTRs) are less likely to develop antibodies and have lower median antibody levels after severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccination versus the general population.[1-3] Some SOTRs with low or negative antibody levels after 2 mRNA vaccines can develop higher levels after a third dose (D3), but long-term antibody durability is unknown.[4] Currently, the Centers for Disease Control and Prevention allows for a fourth vaccine dose 6 mo after an "additional primary vaccine," but there is a paucity of information to inform this policy.[5] We describe 6-mo SARS-CoV-2 antibody kinetics and durability in 32 SOTRs who received D3 (April 1, 2021–June 26, 2021) and were followed through December 9, 2021.

Participants were enrolled in our national observational study of SARS-CoV-2 vaccination outcomes in SOTRs.[1,3] Semiquantitative antispike serological testing using the Roche Elecsys anti–SARS-CoV-2 S or EUROIMMUN anti-S1 assays was performed. Cutoff values for a "positive" response were ≥0.8 U/mL and >1.1 arbitrary units for the Roche and EUROIMMUN immunoassays, respectively. This study was approved by the Johns Hopkins Institutional Review Board.

The median age was 54 (interquartile range, 45–71) y, and the median time since transplant was 7.6 (3.6–13.0) y. Twenty-two (69%) were female, and 31 (97%) were White. There were 27 kidney recipients, 4 kidney-pancreas recipients, and 1 kidney-liver recipient. Twenty-nine of 32 (91%) were on mycophenolate; 29 of 32 (91%) were on a calcineurin inhibitor. Seventeen of 32 (53%) received BNT162b2 primary series, and 15 of 32 (47%) received mRNA-1273 primary series. For D3, 18 of 32 (56%) received Ad.26.COV2.S, 10 of 32 (31%) BNT162b2, and 4 of 32 (13%) mRNA-1273. Nine of 32 (28%) were seropositive, and 23 of 32 (72%) seronegative pre-D3 (Table 1). Serological antibody testing was performed a median of 30 (28–38.3) d after D3 and repeated a median of 168.5 (154.5–183.5) d after D3.

Over 6 mo of follow-up after D3, among 30 of 32 tested on the same platform, antibody levels increased in 16 of 30 (53%), remained stable in 6 of 30 (20%) (3 negative and 3 above the assay limit), and decreased in 8 of 30 (27%). One month post-D3, 23 of 32 (72%) were seropositive, and 9 of 32 (28%) were seronegative. Three months post-D3, 25 of 28 (89%) were seropositive, and 3 of 28 (11%) remained seronegative (4 missed their 3-mo antibody check). Six months post-D3, 28 of 32(88%) were seropositive and 4 of 32 (12%) were seronegative. All 4 nonresponders received the BNT-162b2 primary series; 1 received Ad.26.CoV2.S, and the others received BNT-162b2 for D3. This

Received 3 December 2021. Revision received 29 December 2021.

Accepted 31 December 2021.

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This work was generously supported by the Ben-Dov and Trokhan Patterson families; The American Society for Transplant Surgeons Fryer Resident Scientist Award (J.M.); grants T32DK007713 (J.L.A.), F32DK124941 (D.L.S.), K01DK101677 (A.B.M.), and K23DK115908 (J.M.G.-W.) from the National Institute of Diabetes and Digestive and Kidney Diseases; and grant K24AI144954 (D.L.S.) and grants U01AI138897 and K23AI157893 (W.A.W.) from the National Institute of Allergy and Infectious Diseases.

D.L.S. has received consulting and speaking honoraria from Sanofi, Novartis, CLS Behring, Jazz Pharmaceuticals, Veloxis, Mallinckrodt, Thermo Fisher Scientific, Regeneron, and Astra Zeneca. R.K.A. has study/grant support from Aicuris, Astellas, Chimerix, Merck, Oxford Immunotec, Qiagen, Regeneron, Takeda/Shire, and Vir/GSK and is an Associate Reviewer for Transplantation. M.L.L. is the Social Media Editor for Transplantation. The other authors declare no conflicts of interest.

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A.T.A., J.L.A., J.D.K., L.T., J.M., T.P.Y.C., R.K.A., A.A.R.T., M.L.L., D.S.W., A.B.M., J.M.G.-W., D.L.S., and W.A.W. provided substantial contributions to the conception or design of the work or the acquisition, analysis, or interpretation of data for the work. A.T.A., J.L.A., J.D.K., L.T., J.M., T.P.Y.C., R.K.A., A.A.R.T., M.L.L., D.S.W., A.B.M., J.M.G.-W., D.L.S., and W.A.W. participated in drafting the work or revising it critically for important intellectual content. A.T.A., J.L.A., D.L.S., and W.A.W. gave final approval of the version to be published. A.T.A., J.L.A., J.D.K., L.T., J.M., T.P.Y.C., R.K.A., A.A.R.T., M.L.L., D.S.W., A.B.M., J.M.G.-W., D.L.S., and W.A.W. agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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ISSN: 0041-1337/20/1065-e281

DOI: 10.1097/TP.0000000000004069

TABLE 1.

Demographics, vaccine type, and antibody levels of SOTRs receiving 3 doses of SARS-CoV-2 vaccine

Age, sex	Organ type	Years since transplant	Initial series	Pre-D3	Dose 3 type	Month 1	Month 6
49 M	Kidney	1.6	BNT162b2	<0.4 R	BNT162b2	<0.4 R	**<0.8 R**
57 F	Kidney	1.4	BNT162b2	<0.4 R	BNT162b2	<0.4 R	**<0.8 R**
38 F	Kidney	23.2	BNT162b2	<0.4 R	BNT162b2	2 R	**<0.8 R**
42 F	Kidney	11.8	BNT162b2	<0.4 R	BNT162b2	<0.4 R	11.6 R
71 F	Kidney	16.7	BNT162b2	<0.4 R	BNT162b2	0.6 R	63.9 R
77 F	Kidney	22.3	BNT162b2	0.73 E	BNT162b2	3.94 E	724 R
48 F	Kidney, pancreas	3.2	BNT162b2	Negative[a]	BNT162b2	>2500 R	1554 R
44 M	Kidney	3.2	BNT162b2	0.55 E	BNT162b2	3.67 E	1.47 E
74 F	Kidney, liver	6.0	BNT162b2	0.12 E	BNT162b2	0.2 E	3.21 E
47 F	Kidney	7.7	BNT162b2	0.36 E	BNT162b2	7.02 E	6.93 E
68 F	Kidney	6.1	mRNA-1273	<0.4 R	mRNA-1273	<0.4 R	183 R
60 F	Kidney, pancreas	5.9	mRNA-1273	1.23 R	mRNA-1273	1274 R	338 R
66 M	Kidney	11.8	mRNA-1273	15.9 R	mRNA-1273	1082 R	989.5 R
57 F	Kidney	19.8	mRNA-1273	319.7 R	mRNA-1273	>2500 R	>2500 R
76 F	Kidney	9.5	BNT162b2	<0.4 R	Ad.26.COV2.S	<0.4 R	**<0.4 R**
50 M	Kidney	1.8	BNT162b2	<0.4 R	Ad.26.COV2.S	2.3 R	166 R
30 M	Kidney	5.8	BNT162b2	0.7 R	Ad.26.COV2.S	76.6 R	530 R
67 M	Kidney	13.0	BNT162b2	20.6 R	Ad.26.COV2.S	>2500 R	1009 R
59 F	Kidney	17.1	BNT162b2	189.5 R	Ad.26.COV2.S	>2500 R	>2500 R
59 F	Kidney	5.7	BNT162b2	0.33 AU[a]	Ad.26.COV2.S	4.35 E	7.09 E
67 M	Kidney	3.3	BNT162b2	0.3 E	Ad.26.COV2.S	8.37 E	10.31 E
54 F	Kidney, pancreas	10.4	mRNA-1273	<0.4 R	Ad.26.COV2.S	1893 R	>250 R
71 F	Kidney	1.1	mRNA-1273	<0.4 R	Ad.26.COV2.S	114.5 R	437.5 R
71 F	Kidney	10.8	mRNA-1273	29.72 R	Ad.26.COV2.S	791.2 R	545.8 R
75 F	Kidney	4.9	mRNA-1273	Negative[a]	Ad.26.COV2.S	317.2 R	578.8 R
57 F	Kidney	2.2	mRNA-1273	<0.4 R	Ad.26.COV2.S	1.1 R	582.2 R
41 F	Kidney	15.1	mRNA-1273	<0.4 R	Ad.26.COV2.S	40.5 R	853 R
83 M	Kidney	13.0	mRNA-1273	16.2 R	Ad.26.COV2.S	604.7 R	1088 R
72 F	Kidney	15.2	mRNA-1273	65.5 R	Ad.26.COV2.S	>2500 R	>2500 R
43 F	Kidney, pancreas	8.8	mRNA-1273	0.11 E	Ad.26.COV2.S	0.32 E	2.47 E
71 M	Kidney	4.6	mRNA-1273	1.2 E	Ad.26.COV2.S	5.5 E	8.7 E
61 M	Kidney	7.4	mRNA-1273	0.05 E	Ad.26.COV2.S	0.59 E	6.14 E

Values in bold indicate those that tested negative for antibodies 6 mo post D3.
[a]Self-reported.
AU, arbitrary unit; D3, third dose; E, EUROIMMUN assay anti-S1 (negative cutoff <1.1 AU); F, female; M, male; R, Roche assay anti-RBD (negative cutoff <0.8 U/mL); SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SOTR, solid organ transplant recipient.

difference in seroconversion after D3 was not statistically significant (Fisher exact = 0.3168) between D3 type. Zero participants sero-reverted or reported coronavirus disease 2019 (COVID-19) diagnosis before vaccination or during the study period. The small sample size, observational nature of this study, and lack of measuring antinucleocapsid antibodies to discern COVID-19 infection status are limitations to consider.

We observed high seroconversion rates 6 mo after D3, with marked heterogeneity in timing and strength of response depending upon baseline antibody level among this series of SOTRs with similar immunosuppression regimens (mycophenolate and calcineurin inhibitor). This emphasizes the importance of antibody testing in SOTRs to better understand individual risk after COVID-19 vaccination. The finding of delayed rise in antibody titers, particularly among those receiving Ad.26.COV2.S, demonstrates durable immunogenic potential of additional vaccine doses and the need for dedicated analysis of heterologous boosting strategies. Taken together, these preliminary findings affirm the call for evidence-based recommendations regarding timing of additional doses and vaccine selection in this vulnerable population.

ACKNOWLEDGMENTS

The authors thank the participants of the Johns Hopkins COVID-19 Transplant Vaccine Study, without whom this research could not be possible. They also thank the members of the study team, including Brian J. Boyarsky, MD, PhD; Mayan S. Teles, BS; Rivka Abedon; Alexa Jefferis, BS; Nicole Fortune Hernandez; Chunyi Xia; Kim Hall; Mary Sears; Alex Alex; and Jonathan Susilo. They also thank Andrew H. Karaba, MD, PhD, and Ms Yolanda Eby for project support and guidance.

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