Research Letter

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Antibody Response to 2-Dose SARS-CoV-2 mRNA Vaccine Series in Solid Organ Transplant Recipients

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In contrast to immunocompetent participants in vaccine trials,[1,2] a low proportion (17%) of solid organ transplant recipients mounted a positive antibody response to the first dose of SARS-CoV-2 messenger RNA (mRNA) vaccines, with those receiving anti–metabolite maintenance immunosuppression less likely to respond.[3] In this study, we assessed antibody response after the second

dose.

Methods

Transplant recipients without prior polymerase chain reaction–confirmed COVID-19 were recruited from across the US to participate in this prospective cohort through a digital campaign. Those who completed the 2-dose SARS-CoV-2 mRNA vaccine series between December 16, 2020, and March 13, 2021, were included and followed up through April 13, 2021. As described previously,[3] semiquantitative antispike serologic testing was undertaken with the Roche Elecsys anti–SARS-CoV-2 S enzyme immunoassay, positive cutoff of at least 0.8 U/mL, which tests for the receptor-binding domain of the SARS-CoV-2 spike protein, or the EUROIMMUN enzyme immunoassay, positive cutoff of at least 1.1 arbitrary units, which tests for the S1 domain of SARS-CoV-2 spike protein, both key measures of humoral immune response.[4,5] This study was approved by the Johns Hopkins institutional review board; participants provided informed consent electronically.

The proportion of patients who developed a positive antibody response was assessed with an exact binomial confidence interval. The Fisher exact test was used to compare categorical variables, such as antimetabolite immunosuppression, and the Kruskal-Wallis test for continuous variables. All tests were 2-sided with $\alpha = .05$. Analyses were performed using Stata 16.1/Windows.

Results

We studied 658 transplant recipients who received 2 doses of SARS-CoV-2 mRNA vaccine (**Table**); the first-dose results of 396 of these recipients were previously reported.[3] At a median (IQR) of 21 (18-25) days after dose 1, antibody was detectable in 98 participants (15%) (95% CI, 12%-18%). At a median (IQR) of 29 (28-31) days after dose 2, antibody was detectable in 357 participants (54%) (95% CI, 50%-58%).

Overall, of the 658 participants, 98 (15%) had measurable antibody response after dose 1 and dose 2; 301 (46%) had no antibody response after dose 1 or dose 2; and 259 (39%) had no antibody response after dose 1 but subsequent antibody response after dose 2 (**Figure**).

Among all 658 participants, median (IQR) antibody levels after dose 2 were 2.14 U/mL (<0.4-245.8) (Roche) and 1.23 arbitrary units (0.13-6.38) (EUROIMMUN). Among the 357 with detectable antibody after dose 2, median (IQR) antibody levels were 142.1 U/mL (9.44->250) (Roche) and 6.48 arbitrary units (3.75-8.72) (EUROIMMUN) overall; 34.7 U/mL (5.38->250) (Roche) and 5.05 arbitrary units (2.33-7.02) (EUROIMMUN) in the 259 with no antibody response after dose 1; and >250 U/mL (>250->250) (Roche) and 9.23 arbitrary units (8.62-9.73) (EUROIMMUN) in the 98 with antibody response after dose 1.

Among the 473 receiving antimetabolites, 38 participants (8%) had antibody response after dose 1 and dose 2; 268 (57%) had no antibody response after dose 1 or dose 2; and 167 (35%) had no antibody response after dose 1 but subsequent antibody after dose 2. Among the 185 participants not receiving antimetabolites, 60 (32%) had antibody response after dose 1 and dose 2; 33 (18%) had no antibody response after dose 1 or dose 2; and 92 (50%) had no antibody response after dose 1 but subsequent antibody after dose 2.

Discussion

In this study of the humoral response to 2 doses of mRNA SARS-CoV-2 vaccine among solid organ transplant recipients, the majority had detectable antibody responses after the second dose, although participants without a response after dose 1 had generally low antibody levels. Poor humoral response was persistently associated with use of antimetabolite immunosuppression.

Although no threshold has been established for protective immunity, antibody levels were well below that which has been observed in immunocompetent vaccinees.[6]

Limitations of this study include a sample that may lack external validity, lack of an immunocompetent control group, lack of assessment of postvaccination SARS-CoV-2, and lack of exploration of memory B-cell or T-cell responses.

Although this study demonstrates an improvement in antispike antibody responses in transplant recipients after dose 2 compared with dose 1, these data suggest that a substantial proportion of transplant recipients likely remain at risk for COVID-19 after 2 doses of mRNA vaccine. Future studies should address interventions to improve vaccine responses in this population, including additional booster doses or immunosuppression modulation.

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