

1413 IMMUNOGENICITY OF SARS-COV-2 MRNA VACCINES IN INDIVIDUALS WITH THYMIC EPITHELIAL TUMORS

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Background Thymic epithelial tumors (TETs) are associated with defects of the immune system which can increase the risk of infections and compromise the efficacy of vaccines.¹⁻² Limited data are available on the effectiveness of SARS-CoV-2 vaccines in patients with TETs.³⁻⁵ To further characterize the immunogenicity of SARS-CoV-2 mRNA vaccines in patients with TETs, we measured antibody and T-cell-specific immune responses and compared these results with a fully vaccinated population of individuals employed in a healthcare setting.

Methods Twenty-two individuals with TETs enrolled in an NIH IRB-approved clinical trial (NCT02146170) and a control cohort of 57 healthcare personnel presenting for vaccination were included in this study. All participants had received two doses of a SARS-CoV-2 mRNA vaccine (BNT162b2 or mRNA-1273) and 8 individuals with TET had received a booster dose. Individuals with paraneoplastic autoimmunity and patients receiving anticancer therapy or immunosuppressive medicines were included. A known history of prior COVID-19 infection was an exclusion factor. Plasma samples were analyzed for SARS-CoV-2 anti-spike (S) antibody (ab), anti-nucleocapsid (N) ab, and neutralizing abs using the Roche anti-SARS-CoV-2-S/anti-SARS-CoV-2-N immunoassays, and the Imanis IMMUNO-COV SARS-CoV-2 Neutralizing Antibody Test, respectively. Peripheral blood mononuclear cells collected after booster vaccination were analyzed for T-cell-specific immune responses. Continuous variables were analyzed using Wilcoxon rank sum tests and Spearman correlations, and Fisher's exact test was used for comparison of categorical features.

Results Baseline characteristics are presented in table 1. Anti-N abs were absent in all individuals tested (TET = 12, Controls = 57), confirming absence of prior SARS-CoV-2 infection. Ab responses to vaccination are presented in table 2. There was no statistical difference in log(anti-S) ab titers between the TET and control groups (p=0.40). Neutralizing abs were detected in all evaluable participants with thymic carcinoma (6/6) versus 70% with thymoma (7/10). Clinical correlates of response in the TET cohort included vaccine type (BNT162b2 or mRNA-1273; p=0.0052), paraneoplastic autoimmunity (p=0.0085), and immunosuppressant use (p=0.031). CD3 and CD19 counts had strong, positive correlations with log(anti-S) ab titers ($\rho = 0.70$ and $\rho = 0.81$, respectively). Six of 8 participants with TETs had an increase in anti-S ab titers in response to booster vaccination. T-cell responses to vaccination are under analysis and will be reported.

Conclusions A majority of patients with TETs have a demonstrable response to COVID-19 mRNA vaccines, which is influenced by clinical and biological factors including vaccine type, paraneoplastic autoimmunity, immunosuppressant use, and lymphocyte subsets (CD3 and CD19).

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Ethics Approval All patients with TETs included in this study provided written informed consent for participation in a clinical trial that was approved by the National Institutes of Health Institutional Review Board (NIH IRB) (ClinicalTrials ID: NCT02146170; NCI Clinical Trial ID: 14-C-0105). Use of samples from individuals in the control group was deemed exempt by the NIH IRB.

Abstract 1413 Table 1 Participant characteristics

	TET cohort (n = 22)	Controls (n = 57)
Age, median (range)	56 (37-70)	57 (20-70)
Sex, n (%)		
Male	12 (55)	29 (51)
Female	10 (45)	28 (49)
Vaccine, n (%)		
BNT162b2	11 (50)	48 (84)
mRNA-1273	11 (50)	9 (16)
Immunohistology, n (%)		
Thymoma	11 (50)	10 (18)
Thymic carcinoma	11 (50)	0 (0)
Anticancer treatment, n (%)		
Chemotherapy	1 (5)	2 (4)
Surgery	2 (9)	0 (0)
Paraneoplastic autoimmunity, n (%)	11 (50)	2 (4)
Immunosuppressant use, n (%)		
Steroid	2 (9)	0 (0)
Other	9 (41)	0 (0)
Both	1 (5)	1 (2)
Small intestine resection, n (%)	1 (5)	2 (4)
Time from vaccination to analysis, median (range)	102	177

Abstract 1413 Table 2 Antibody response to COVID-19 mRNA vaccination

	Seropositivity (n, %)	Anti-S ab Titer (Median, IQR)	Neutralizing Ab Titer (Median, IQR)
Controls (n = 57)	57 (100)	10000	> 100000
All TETs (n = 22)	21 (95)	6.15	30000
Thymic carcinoma (n = 11)	10 (91)	7.25	17000
Thymoma (n = 11)	11 (100)	6.00	30000

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