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SARS-CoV-2 mRNA vaccines sensitize tumors to immune checkpoint blockade

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Background

mRNA cancer vaccines sensitize tumors to immune checkpoint inhibitors (ICIs) in part by stimulating a surge in inflammatory cytokines. We hypothesized that mRNA vaccines targeting non-tumor antigens, such as those targeting SARS-CoV-2 spike protein, would also sensitize tumors to ICIs.

Methods

We extracted clinical data from institutional databases for patients with non-small cell lung cancer (NSCLC) with biopsies between January 2017 and September 2022, melanoma treated with ICIs between January 2019 and December 2022, and any tumor histology with biopsy samples evaluating PD-L1 from January 2020 to October 2023. We evaluated differences with Kaplan-Meier curves, propensity score matching and cox proportional hazards regression. We then utilized mouse models and samples from healthy human subjects for mechanistic studies. All experiments were approved by the MD Anderson institutional review board and IACUC.

Results

Administration of a SARS-CoV-2 mRNA vaccine within 100 days of initiating ICI was associated with increased overall survival among patients with NSCLC (median OS 20.6 months vs. 37.3 months, three-year OS 30.6% vs 55.8%, adj HR 0.51, 95% CI 0.37-0.71, $p < 0.0001$) and metastatic melanoma (median OS 26.67 months vs unmet, 36-month OS 44.1% vs 67.5%, adj HR 0.34, 95% CI 0.17-0.69, p=0.0029). Survival benefits were maintained with propensity score matching and among patients with immunologically “cold” tumors (TPS<1%). In preclinical models, SARS-CoV-2 mRNA vaccination stimulated a surge in Type I interferon that prompted antigen presenting cells to prime CD8 T cells targeting multiple tumor antigens and tumor cells to upregulate PD-L1 expression. Combination therapy enhanced responses to ICIs in multiple tumor models. SARS-CoV-2 mRNA vaccination was associated with similar increases in Type I interferon and APC activation in human subjects, and increased PD-L1 expression on tumor biopsies from a diverse cohort of cancer patients.

Conclusions

SARS-CoV-2 mRNA vaccines sensitize tumors to ICIs in preclinical models and are associated with substantial improvements to overall survival among patients with NSCLC and melanoma treated with ICIs.

Legal entity responsible for the study

The authors.

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Disclosure

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