Vaccine demonstrates potential in delaying relapse of KRAS-mutated pancreatic and colorectal cancers

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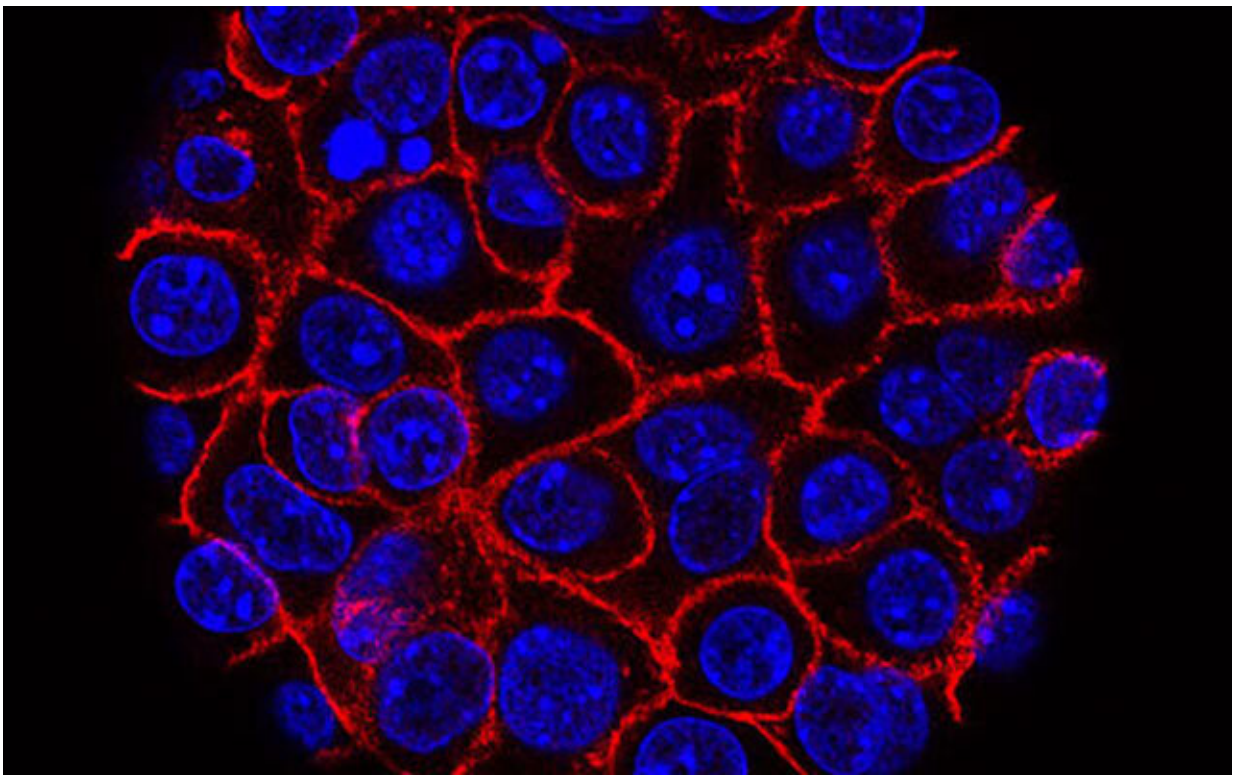

Pancreatic cancer cells (blue) growing as a sphere encased in membranes (red). Credit: National Cancer Institute

A vaccine has shown potential to prevent relapse of KRAS-mutated pancreatic and colorectal cancers for patients who had previously

undergone surgery, according to a Phase I trial led by researchers at The University of Texas MD Anderson Cancer Center. Results are published in *Nature Medicine*.

In the trial, patients with pancreatic and colorectal cancer who were considered at high risk of relapse received a maximum of 10 doses of the ELI-002 vaccine targeted toward KRAS G12D and G12R mutations. T cell responses were seen in 84% of all patients and in 100% of those in the two highest-dose cohorts, including those who received the recommended Phase II dose of 10 mg.

T cell responses were predictive of reductions in tumor biomarkers and ctDNA clearance, and they correlated with an 86% reduction in risk of relapse or death. For patients above the median T cell response level, median recurrence-free survival had not yet been reached, compared to 4.01 months in the group with a T cell response level below the median. This was a statistically significant improvement.

"Patients who have undergone surgery for pancreatic cancer are still at risk for relapse of the disease, even after they finish chemotherapy. This is especially true for patients who are positive for circulating tumor DNA (ctDNA), which puts them at a higher risk for relapse," said principal investigator Shubham Pant, M.D., associate professor of Gastrointestinal Medical Oncology. "When these patients do relapse, the disease is not curable, so this is certainly an area of unmet need."

The multicenter AMPLIFY-201 trial is evaluating ELI-002, a lymph node-targeted cancer vaccine designed to lower the likelihood of these relapses by "training" T cells to recognize KRAS mutations, allowing them to identify and eliminate KRAS-mutant cells. ELI-002 also is an off-the-shelf vaccine, meaning it does not have to be specially formulated to each individual. KRAS-mutated cancers make up about a quarter of all solid tumors, including 90% of pancreatic cancer patients,

who most commonly have the G12D mutation.

No patients experienced dose-limiting toxicities, cytokine release syndrome or any treatment-emergent adverse events of any kind above Grade 3. The most common adverse events of any grade were fatigue (24%), injection site reaction (16%) and myalgia (12%).

Twenty-five patients participated in the trial, with a median age of 61. Of these, 84% were white, 8% were Asian and two patients were of an unreported ethnicity. Patients were 60% female. All 25 had previously had surgery or another procedure designed to be curative, and seven had previously received radiation therapy.

"It's early, but we saw some promising results that this vaccine may help many of these patients avoid relapse, which could increase survival," Pant said. "It also showed a favorable safety profile, which is exciting."

Results from this trial have led to a Phase II trial that will begin later this year, with a new formulation of ELI-002 targeting additional KRAS mutations. Preliminary data from this trial was presented in 2023 at the American Society of Clinical Oncology (ASCO) Annual Meeting and at the American Association for Cancer Research (AACR) Special Conference on Pancreatic Cancer.

More information: Lymph Node Targeted Amphiphile Vaccine Induces mKRAS-specific T Cells in Minimal Residual Disease-Positive Pancreatic and Colorectal Cancer: The AMPLIFY-201 Trial, *Nature Medicine* (2024). doi: 10.1038/s41591-023-02760-3 , www.nature.com/articles/s41591-023-02760-3

Provided by University of Texas M. D. Anderson Cancer Center

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