Investigational personalized vaccine provides clinical benefit for some patients with resected head and neck cancers

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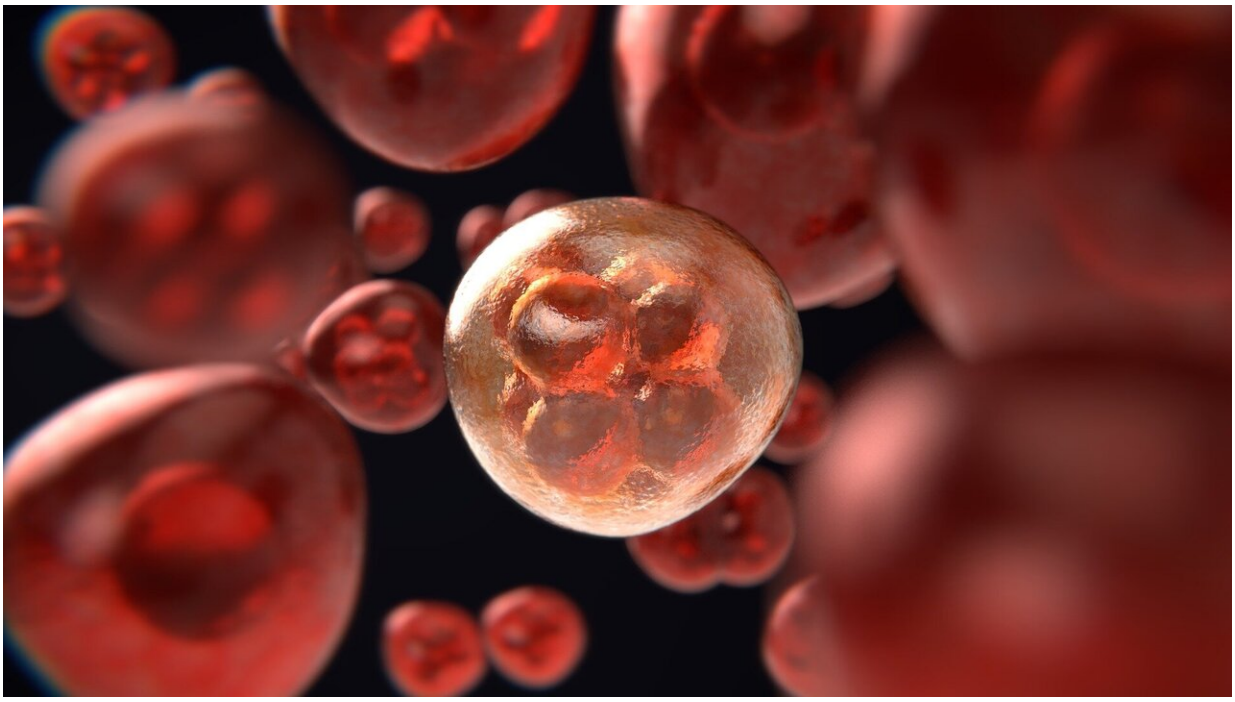

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TG4050, a personalized neoantigen vaccine, induced tumor-specific

immune responses and led to low rates of disease relapse in patients with surgically resected HPV-negative head and neck squamous cell cancer (HNSCC), according to results reported at the American Association for Cancer Research (AACR) Annual Meeting 2024, held April 5–10.

Patients with locoregional HNSCC have a high risk of disease relapse after surgery, and currently available treatments, including immune checkpoint inhibitors, offer limited efficacy against relapsed disease, according to Olivier Lantz, MD, Ph.D., a clinical immunologist and researcher at Institut Curie in Paris.

He and colleagues tested the hypothesis that a personalized therapeutic vaccine could delay relapse of surgically resected HNSCC.

"A therapeutic vaccine tailored to each patient's unique tumor may lead to strong immune responses, which could eliminate any minimal residual disease that may eventually lead to disease relapse," Lantz explained, adding that vaccines could also make the tumor more responsive to other forms of immunotherapy.

TG4050 is an individualized vaccine that uses a nonpathogenic form of poxvirus to deliver 30 personalized neoantigens (proteins unique to each patient's tumor) that induce activation and expansion of antitumor T cells. The researchers used artificial intelligence and machine learning tools to analyze the genome of each patient's tumor and identify relevant mutations and immunogenic neoantigens to develop individualized vaccines.

The safety and efficacy of TG4050 are being evaluated in a phase I clinical trial, which includes 33 patients with stage 3 or 4 HPV-negative HNSCC who have undergone surgery and standard of care adjuvant

radiation and chemotherapy. Patients were randomly assigned to one of two arms: the 17 patients in the treatment arm (Arm A) are assigned to receive TG4050 immediately after standard of care treatments, while the 16 patients in the observational arm (Arm B) are assigned to receive TG4050 upon disease relapse.

None of the evaluable patients in Arm A experienced disease relapse after a median follow-up of 16.2 months. Three patients in Arm B experienced disease relapse—one after 6.2 months, another after 8.8 months, and a third after 18.5 months.

Of the 17 evaluable vaccinated patients (16 in Arm A and one in Arm B) whose immune responses were evaluated, 16 showed evidence of activated neoantigen-specific T cells. The majority of neoantigen-specific T cells were not present prior to vaccination, indicating that they were induced by TG4050. The number of neoantigen-specific T cells increased rapidly upon vaccination and remained stable up to 7 months after vaccination.

Further characterization demonstrated that the neoantigen-specific T cells had an effector memory phenotype, suggesting they may have antitumor activity, and evidence of expansion of tumor-infiltrating lymphocytes was found in five patients.

In addition, Lantz reported that adverse events associated with TG4050 were mild to moderate, and the most common TG4050-related adverse event was a reaction at the injection site.

"Our findings indicate that TG4050 is safe and promotes an immune response against several neoantigens in most patients," Lantz summarized.

"We are really excited by these preliminary data, as well as by the body

of evidence that is being built by the community in favor of neoantigen-based vaccines," he added. "Studies like ours are demonstrating the potential of individualized neoantigen-based therapeutic vaccines to be a part of tomorrow's standard of care."

Limitations of the study included the small sample size, short follow-up, and incomplete immune response data for some patients.

Provided by American Association for Cancer Research

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