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Checkpoint inhibitor shrinks advanced squamous cell skin cancer

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Clinical trials show that an immune checkpoint inhibitor shrinks the tumors of nearly half of patients with an incurable, advanced form of a common skin cancer, an international team led by a researcher at The University of Texas MD Anderson Cancer Center reports in the *New England Journal of Medicine*.

"These results mark a potential paradigm shift in the treatment of patients with advanced cutaneous squamous cell carcinoma, who to date have had very limited results with chemotherapy and targeted therapies," said lead author Michael Migden, M.D., associate professor of Dermatology and of Head and Neck Surgery.

Migden is principal investigator of the international, multicenter phase II registrational clinical trial of cemiplimab, an immune checkpoint inhibitor that works by blocking PD1, a surface receptor on T cells that shuts down immune response to cancer.

Cutaneous squamous cell carcinoma is the second most common skin cancer, with an estimated 1 million new cases diagnosed annually. More than 95 percent of patients are cured by surgery and radiation at the disease's early stages. But for the fraction who progress, there are no systemic therapies approved as a standard of care, the researchers note.

At a median follow-up of 7.9 months, 28 of 59 patients with metastatic disease (47.5 percent) had an objective response to cemiplimab, defined as at least 30 percent tumor shrinkage observed via imaging. Four were

complete responses, 24 had partial responses, and 82 percent of responders remain on the drug.

"Patients continue to do well, so median progression-free survival and overall survival have not been reached yet," said Migden, a Mohs surgeon and dermatologic oncologist at MD Anderson. The durable disease control rate of responders plus those with stable disease for at least 105 days was 61 percent. Migden notes that response rates to chemotherapy regimens or targeted therapy against the epidermal growth factor receptor (EGFR) now used against advanced cutaneous squamous cell carcinoma range from 15-25 percent, with many debilitating side effects.

Immunotherapies pose risks of inflammatory side effects that have to be monitored, but otherwise have fewer day-to-day complications than chemotherapy and EGFR inhibitors, Migden said.

Common side effects in the cemiplimab phase II trial were diarrhea, fatigue, nausea, constipation, and rash. Four patients (6.8 percent) had to discontinue treatment. Three patients died of adverse events during the trial, but the deaths were not considered related to treatment.

Median age of patients in the phase II trial was 71, with 33 (55.9 percent) having received prior systemic therapy and 50 (84.7 percent) having received radiotherapy.

In the phase I trial of patients with metastatic or locally advanced but inoperable disease, 13 of 26 (50 percent) had a partial response. At 11 months median follow-up, seven patients remained in response. Two patients (7.7 percent) had to discontinue treatment due to adverse events. Median age was 73.

The U.S. Food and Drug Administration has granted an application for

breakthrough therapy status for the drug, providing a faster potential route for FDA approval. Regeneron Pharmaceuticals, Inc., and Sanofi are co-developing cemiplimab.

Cutaneous squamous cell carcinoma develops from genetic damage caused by exposure to UV light. These tumors have a high mutation burden, providing a target-rich environment for immune system attack and this cancer also is strongly associated with immune suppression. Those factors made it a strong candidate for PD1 inhibition, which unleashes the immune system to attack cancer.

The clinical trials are funded by Regeneron and Sanofi.

Cutaneous squamous cell carcinoma is not included in national cancer registries, so the incidence of the disease and its mortality rates are unknown. Estimates or annual diagnoses range from 700,000 to 1 million. One study estimated that between 3,900 and 8,700 people died from this cancer in 2012.

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