Pembrolizumab shows promise for some advanced, hard-to-treat rare cancers

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A study conducted by researchers at The University of Texas MD Anderson Cancer Center demonstrated acceptable toxicity and anti-tumor activity in patients with four types of advanced, hard-to-treat rare

cancers. Study findings were published in the March 17 online issue of the *Journal for ImmunoTherapy of Cancer*.

The open-label, Phase II study followed 127 patients who had advanced rare cancers: squamous cell carcinoma of the skin (cSCC), carcinoma of unknown primary (CUP), adrenocortical carcinoma (ACC), and paraganglioma-pheochromocytoma. Patients received 200 milligrams of the immunotherapy treatment pembrolizumab administered every three weeks between August 2016 and July 2018. All patients had tumors that had progressed on standard therapies.

"Our findings that pembrolizumab has a favorable toxicity profile and anti-tumor activity in patients with these rare cancers supports further evaluation in these populations," said Aung Naing, M.D., associate professor of Investigational Cancer Therapeutics. "Finding solutions for treatment is vital given that patients with advanced rare cancers have poor prognosis and few treatment options."

Rare cancers are defined by the American Cancer Society as those with an incidence of fewer than six cases per 100,000 people per year. CUP is a type of cancer in which the primary cancer site is not always known, but has spread to other areas within the body, while ACC occurs when malignant cells form in the outer layer of the adrenal glands. Paraganglioma-pheochromocytoma are tumors formed in nerve-like cells near the adrenal glands (pheochromocytomas) and near blood vessels or nerves in the head, neck, chest, abdomen, and pelvis. cSCC is the second most common type of skin cancer and is treatable in early stages, but harder to treat if in advanced stages.

The primary objective of the study was to find the proportion of patients who were alive and progression-free (non-progression rate) at 27 weeks on treatment with pembrolizumab. The median non-progression rate at that time was 28% for 127 patients with advanced rare cancers.

Complete response, partial response or stable disease after four months was observed in 38% of the patients. Non-progression rates for each cancer group were: 36% for cSCC, 33% for CUP, 31% for ACC, and 43% for paraganglioma-pheochromocytoma. Treatment-related adverse events occurred in 52% of patients, with the most common side effects being fatigue and rash, with six deaths reported that were unrelated to treatment.

"Studies such as this one are key since rare cancers collectively accounted for 13% of all new cancer diagnoses and 25% of all cancer-related deaths in adults in 2017," said Naing. "The five-year survival rate is 15% to 20% lower than for more common cancers. The poor outcomes associated with rare cancers have been attributed to difficulty or delay in diagnosis, limited access to centers with expertise such as MD Anderson, and limited therapeutic options."

Naing added that, despite the significant burden and aggressive nature of these diseases, research that could lead to development and approval of new therapies are few. However, MD Anderson has the patient volume and research resources that uniquely positions its researchers to conduct this work.

"Findings from our study support further investigation to confirm the clinical activity of pembrolizumab in advanced rare cancers, and to identify immune signatures predictive of response to treatment,"said Naing.

More information: Aung Naing et al, A first-in-human phase 1 dose escalation study of spartalizumab (PDR001), an anti–PD-1 antibody, in patients with advanced solid tumors, *Journal for ImmunoTherapy of Cancer* (2020). DOI: 10.1136/jitc-2020-000530