Radiation/immunotherapy combo shows promise for recurrent/metastatic head and neck cancers
27 February 2020

A new phase II trial finds that a combination of radiation therapy and immunotherapy led to encouraging survival outcomes and acceptable toxicity for patients with locally advanced head and neck squamous cell carcinoma (HNSCC). The combination of radiation and pembrolizumab may offer a new treatment option for patients who are ineligible for cisplatin chemotherapy, part of standard treatment for the disease. Findings will be presented at the 2020 Multidisciplinary Head and Neck Cancers Symposium, taking place February 27-29 in Scottsdale, Arizona.

The single-arm trial included 29 patients with locally advanced HNSCC. All patients would have ideally received cisplatin with their radiation but were ineligible for platinum chemotherapy. Patients were treated with three cycles of pembrolizumab and concurrent radiation therapy over six weeks, followed by three additional cycles of the immunotherapy drug.

With a median follow-up of 21 months, the rates of one-year progression-free and overall survival were 76% [95% CI 56-88] and 86% [67-95], respectively. Estimated two-year PFS was 71% [49-84] and estimated two-year OS was 75% [51-88]. For patients with p16+ oropharynx cancer, the one-year PFS and OS rates were 88% and 94%, respectively; for the other patients, the rates were 58% and 75%, respectively.

Most toxicities were mild (grade 1-2) with the exception of grade 3-4 lymphopenia, which affected 59% of patients. "This toxicity profile is better than what patients generally experience with cisplatin and radiation," explained Dr. Weiss. "It was more consistent with what we see from radiation therapy alone, with the exception of a high rate of lymphopenia that warrants additional study."

"That is a common dilemma in the exam room because cisplatin, while effective, tends to be particularly toxic for patients and can lead to permanent side effects for some," explained lead author Jared Weiss, MD, an associate professor of medicine at the University of North Carolina Lineberger Comprehensive Cancer Center. "I will have patients I want to treat with platinum chemotherapy, but I also want to align treatment with their values. Is the patient willing to accept a risk of deafness or exacerbated ringing in their ears? These are not acceptable consequences for most people."

The single-arm trial was designed specifically for patients who normally would receive platinum chemotherapy together with radiation but may not be able to tolerate its side effects, most often due to preexisting hearing problems that place patients at risk of permanent hearing loss. Preexisting kidney damage and nerve damage also tend to be aggravated by cisplatin and place patients at risk for permanent side effects.
While engaging PD-1/PD-L1 blockade following chemoradiotherapy has improved survival in lung cancer, this trial is one of the first to show its potential efficacy for head and neck cancers. "There are convincing arguments that radiation sensitizes patients to immunotherapy and can enhance its effects. And the opposite direction also seems to be true—radiation therapy needs a functional immune system to work, and our hope was that pembrolizumab might be a radiation sensitizer for these patients," said Dr. Weiss.

Additionally, unlike chemoradiation therapy, the combination of radiation and pembrolizumab pairs two active modalities that can be curative by themselves. "If you look back to the historic studies, radiation alone often cures patients with this disease. Some of the first patients treated with pembrolizumab for recurrent/metastatic cancer are still alive many years out, with no evidence of disease," said Dr. Weiss. "And so, our concept was that, in addition to whatever synergy the immunotherapy might provide with radiation, we also conceived of it in a more straightforward way as a 'second shot on goal' toward cure."

Dr. Weiss cautioned that findings need confirmation in a randomized trial before the combination is recommended to patients.

Dr. Weiss will present "Progression-free survival, overall survival and immunophenotyping outcomes for patients with stage III-IV head and neck cancer and cisplatin contraindication treated with definitive radiotherapy plus pembrolizumab" February 28th during the symposium's Oral Abstract Session. The study was funded by Merck.

Provided by American Society for Radiation Oncology


This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.