

Keytruda Immunotherapy Before and After Surgery Improves Outcomes in Head and Neck Cancer

This is the first study in more than 20 years to show improvement over standard care for patients with locally advanced head and neck cancer.

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Patients with locally advanced head and neck cancer who received the immune checkpoint inhibitor pembrolizumab [Keytruda] before, during and after standard-of-care surgery had longer event-free survival without the cancer coming back and higher rates of substantial tumor shrinkage prior to surgery, according to the first interim analysis of a randomized, open-label phase 3 clinical trial led by investigators from [Dana-Farber Brigham Cancer Center](#) and Washington University School of Medicine in St. Louis.

This trial, called KEYNOTE-689, is the first study in more than 20 years to show improvements in outcomes over standard of care for this patient group. Current standard of care for resectable head and neck cancer involves surgery, radiation and chemotherapy, though only 40% to 50% of patients survive five years.

“This is a practice-changing study,” said [Robert Haddad, MD](#), chief of the [Division of Head and Neck Oncology](#) and the McGraw Chair in Head and Neck Oncology at Dana-Farber, and Professor of Medicine at Harvard Medical School. Haddad is the Dana-Farber Brigham Cancer Center principal investigator and member of the KEYNOTE-689 steering committee.

“Not only has this regimen improved event-free survival, but we also observed that fewer patients required chemotherapy as part of standard of care after receiving immunotherapy before surgery.”

The results [were] presented by the study global chair, [Ravindra Uppaluri, MD, PhD](#), director of Head and Neck Surgical Oncology at Dana-Farber and Brigham and Women’s Hospital, and Brigham and Women’s Hospital Endowed Chair in Otolaryngology, at the [American Association of Cancer Research \(AACR\) Annual Meeting](#).

Douglas Adkins, MD, professor of medicine and director of the Section of Head and Neck and Thyroid Medical Oncology at WashU Medicine who worked closely with the Dana-Farber Brigham

Cancer Center team in a previous phase 2 trial, is the co-senior author.

The KEYNOTE-689 trial randomized 714 patients with newly diagnosed stage III or stage IVA head and neck squamous cell cancer to receive either pembrolizumab before (called neoadjuvant), during and after (called adjuvant) standard of care or standard of care alone. The investigators also measured the presence of the target of pembrolizumab, PD-L1, in tumors to determine if higher scores of PD-L1 in tumors would affect response to treatment.

They found that patients who received pembrolizumab had longer event-free survival regardless of their PD-L1 scores. Median event-free survival across all patients was 51.8 months with pembrolizumab and 30.4 without after a median of 38.3 months of follow-up. The team also observed significantly higher rates of major pathologic response, a substantial immune mediated tumor destruction seen in surgical resections, across all patients taking pembrolizumab.

The treatment was found to be safe with no new observed side effects. Further, patients taking pembrolizumab received surgery in a timely manner and were not delayed by immunotherapy-related side effects prior to surgery.

“The ability for surgery to occur without delay was a very important observation,” Haddad said.

Based on these results, the U.S. Food and Drug Administration is reviewing potential approval of this regimen for this patient population.

“It is very exciting to see this first positive trial of upfront immunotherapy moving forward with the potential to become the new standard of care for patients with head and neck cancer worldwide,”

said Uppaluri, who expects further analysis of the study data after a longer follow-up later this year.

This new regimen would represent a substantial change in workflow for head and neck cancer care.

Currently, patients see a surgeon for a definitive diagnosis via biopsy and, if positive, move straight into surgery. The addition of immunotherapy prior to surgery requires a robust multidisciplinary approach.

“The value of multidisciplinary care in head and neck cancer becomes even more important with this approach of providing immunotherapy prior to surgery,” Haddad said. “The mindset of many surgical oncologists in the U.S. and the world will need to evolve to incorporate this paradigm shift.”

“Our multidisciplinary teams are now focused on determining if this progress can be improved upon with different agents or with combinations of neoadjuvant and adjuvant therapies in head and neck cancer,” Uppaluri said. “This study really has opened up the potential for neoadjuvant treatment to make a difference for our patients with head and neck cancers.”

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