Adding Immunotherapy to Neoadjuvant Chemoradiation May Improve Outcomes in Esophageal Cancer

Combination of radiation, chemotherapy and immunotherapy can shrink tumors and allow surgery, with much better survival rate than non-surgical treatment alone.

November 22, 2024 By American Association for Cancer Research

---

In patients with unresectable, locally advanced esophageal cancer, the triple combination of radiation, chemotherapy, and immunotherapy made tumors more amenable to surgery, which was associated with significantly improved outcomes, according to data from a phase II clinical trial published in Clinical Cancer Research, a journal of the American Association for Cancer Research.

“Curative resection unequivocally serves as the cornerstone for treating resectable esophageal squamous cell carcinoma (ESCC); however, because of lack of symptoms and early detection, fewer than half of patients have resectable disease at the time of diagnosis,” said Yin Li, MD, senior author of the study and director of section of esophageal and mediastinal oncology at the Chinese Academy of Medical Sciences and Peking Union Medical College. “The neoadjuvant treatment approach we tested has the potential to make initially unresectable tumors resectable, giving patients the opportunity to have a durable cancer-free state.”

Given the unfavorable long-term prognosis of patients who receive chemoradiation alone—only about 36% survive at least five years, according to Li—there is a desperate need for improved strategies.

Immune checkpoint inhibitors, both alone and in combination with chemotherapy, are standard –of care for those with advanced, recurrent, and metastatic ESCC. They’re also approved for adjuvant therapy after complete resection following neoadjuvant chemoradiation. But Li and his team wanted to investigate whether adding immune checkpoint inhibitors to chemoradiation can help downstage tumors and improve resectability.

To address this possibility, in a Phase II clinical trial, patients between the ages of 18-75 were enrolled at their institution to receive three steps of treatment: radiation in conjunction with nab-paclitaxel (Abraxane) and cisplatin chemotherapy in step 1, the immune checkpoint inhibitor tislelizumab (Tevimbra) plus chemotherapy in step 2, and, if possible, surgery in step 3.

Of the 30 patients enrolled, five discontinued treatment during chemoradiotherapy and one patient received surgery ahead of schedule without subsequent immunotherapy. Of the 24 patients who also received subsequent chemoimmunotherapy, four discontinued the treatment, and 19 received surgery. Overall, 20 patients underwent surgery and had complete resections.

Of these 20 patients, 19 had experienced major pathologic responses at the time of surgery, with 13 having complete pathologic responses. Most importantly, compared to the 10 patients who did not undergo surgery, the 20 who had surgery had significantly longer survival, both overall and without disease progression, with 82% and 72% reductions in risk of death and progression, respectively, at one year follow-up. More than half of those who underwent surgery were still free of disease at two years.

“Our trial clearly demonstrated the effectiveness of combining chemoradiotherapy, chemoimmunotherapy, and surgery compared to nonsurgical management alone,” according to Li. “We were confident in potential benefits of adding immunotherapy to chemoradiotherapy, but the remarkable pathologic complete response and the strong survival outcomes far exceeded our expectations.”

The clinical study also utilized circulating tumor DNA (ctDNA)-based liquid biopsies throughout the course of care, including monitoring for relapse, which, Li said, “allowed us to gain valuable insights into the molecular landscape and minimal residual disease trajectory of these patients.”

Limitations of the study include its small sample size, due in part to treatment discontinuations, and thus point to the need for phase III trials to validate these findings as well as explore the optimal sequencing of therapies.

This study was supported by Beijing Xisike Clinical Oncology Research Foundation and Special Program for Basic Resource Survey of the Chinese Ministry of Science and Technology.

This news release was published by the American Association for Cancer Research on November 15, 2024.
