Commentary: Closing the curtain on upfront surgery for esophageal squamous cell carcinoma

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The authors present an excellent descriptive study of recurrence patterns in patients with locally advanced esophageal squamous cell carcinoma. The data were collected from a large randomized trial (NEOCRTEC5010) conducted by the same authors, and the results show better patient outcomes with neoadjuvant chemoradiotherapy followed by surgery than with surgery alone. The authors should be congratulated for contributing data on a large cohort of patients to a robust body of published evidence, confirming previously described patterns and risk factors for recurrence (ie, greater T and N stage, lack of neoadjuvant treatment, absence of complete pathologic response). In addition, the median time to recurrence of approximately 1 year is consistent with previous reports.

The main goal of this study was to describe postrecurrence survival patterns, although it has the significant limitation of lacking information on posttreatment treatment. The data should be evaluated carefully, as the benefit of posttreatment therapy is well documented but was not evaluated in this population. The receipt of any posttreatment therapy is associated with longer survival, and the use of surgery or multimodal intensive therapy is associated with the best outcomes. Oligometastatic disease and nodal metastasis are known to be associated with better prognosis, and specific characteristics of metastases, such as large size, rapid rate of growth, and hepatic location, are associated with a poorer prognosis. This study accrued patients well before publication of the results from CheckMate577; therefore, it is safe to assume that none of the participants received adjuvant nivolumab. Adjuvant nivolumab has become the standard of care in the United States for patients with a high risk of recurrence, as it was associated with 2.7-fold longer disease-free survival, compared with placebo, in patients with squamous cell histology.

The recurrence rate among patients who received neoadjuvant therapy in this study was 36.9%, which is consistent with the rate (34.7%) among similar patients in CROSS (Chemoradiotherapy for Oesophageal Cancer Followed by Surgery Study). In both trials, the recurrence rate in the surgery-only arm was >50%.

This study, comprising a large randomized population in Asia, has soundly confirmed that neoadjuvant chemoradiotherapy leads to better outcomes in the short and long term in patients with esophageal cancer, and it will hopefully convince surgeons that upfront esophagectomy for locally advanced esophageal cancer belongs in the past. What this study showed that CROSS could not is that a greater number of lymph nodes removed during the initial operation (>20) is an important factor for lowering the risk of recurrence. This has been reported in other studies and should remind us all that, while chemotherapy and radiation are important, an oncologically sound operation cannot be replaced.
Esophagectomy remains the mainstay of treatment for patients with esophageal cancer, and all patients with esophageal squamous cell cancer should receive neoadjuvant chemoradiotherapy. As we close the curtain on upfront surgery, we can move forward with the knowledge that radical resection remains crucial and chemoradiation is a complementary tool and not a replacement for optimal oncologic resection.

References