Editorial Commentary

Role of adjuvant therapy in esophageal cancer patients after neoadjuvant therapy and esophagectomy

Stuart Campbell[1,2], **Thomas Bauer**[1,2]

[1]Hackensack Meridian Health School of Medicine, Nutley, NJ, USA; [2]Jersey Shore University Medical Center, Hackensack Meridian Health, Neptune, NJ, USA

Correspondence to: Thomas Bauer, MD, MBA. Hackensack Meridian Health School of Medicine, Nutley, NJ, USA. Email: thomas.bauer@hmhn.org.

Comment on: Lee Y, Samarasinghe Y, Lee MH, *et al.* Role of Adjuvant Therapy in Esophageal Cancer Patients After Neoadjuvant Therapy and Esophagectomy: A Systematic Review and Meta-analysis. Ann Surg 2022;275:91-8.

Received: 11 June 2022; Accepted: 30 June 2022; Published: 30 September 2022.

doi: 10.21037/dmr-22-43

View this article at: https://dx.doi.org/10.21037/dmr-22-43

Esophageal cancer is the seventh most common cancer globally with a steadily increasing rate of incidence, mortality (1), and proportion of adenocarcinoma over squamous cell carcinoma (2). Despite advances in screening, staging, and treatment; morbidity and mortality of esophageal cancer remains a major concern with an overall five-year survival of 20% (3). Treatment modalities include surgical resection, chemotherapy, and/or radiation therapy. Several studies, including the CROSS trial, demonstrated significant improvement in survival using neoadjuvant therapy which is now the standard of care for Stage II and III esophageal cancer (4). In the United States, National Comprehensive Cancer Network (NCCN) guidelines recommend neoadjuvant therapy consisting of chemotherapy and radiation therapy prior to surgery, whereas, in Japan and the United Kingdom neoadjuvant therapy consists of chemotherapy alone (5,6). Following surgical resection, adjuvant therapy depends on resection margin and tumor response with some patients being observed and others receiving adjuvant chemotherapy or immunotherapy (6).

Lee and colleagues in their meta-analysis attempt to determine the role for adjuvant therapy in patients who have undergone neoadjuvant therapy with surgically negative margins (7). Their study looked at 10 cohort studies and 1 randomized control trial aiming to compare overall survival at 1 year and 5 years in patients treated with neoadjuvant therapy and surgery *vs.* patients treated with neoadjuvant therapy, surgery and adjuvant therapy (7). The results of their meta-analysis claim improvement in overall survival at 1 and 5 years in those patients who received adjuvant therapy, however, this seems limited to the patients who received neoadjuvant chemotherapy. There did not appear to be an increased survival advantage of adjuvant chemotherapy in patients who received neoadjuvant chemoradiation therapy or those with squamous cell carcinoma. In addition, they saw increased survival advantage of adjuvant chemotherapy in the mixed node group compared to node positive group, suggesting responders to preoperative chemotherapy were more likely to benefit from adjuvant chemotherapy. Their results do suggest that adjuvant chemotherapy could have a role in specific circumstances. More recent trials using adjuvant immunotherapy, which they do mention, have very promising results and adjuvant immunotherapy will likely play a much larger role in esophageal cancer treatment in the future (8-10).

The advances in genetic profiling and immunologics will hopefully continue to provide additional information and targets for adjuvant chemotherapy. Kelly and colleagues show improved survival using adjuvant Nivolumab in a subset of esophageal cancer patients after neoadjuvant chemoradiation therapy and surgery (9). NCCN guidelines now recommend Nivolumab as adjuvant therapy after surgical resection in patients with residual disease (6). Ruhstaller and colleagues also had some promising results using cetuximab as an adjunct to chemoradiation therapy and surgery (10). As more immunotargets are discovered

(i.e., CTLA-4 inhibitors and those yet to be discovered) the ability to personalize chemotherapy will likely soon be a reality and standard of care.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the editorial office, *Digestive Medicine Research*. The article did not undergo external peer review.

Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at https://dmr.amegroups.com/article/view/10.21037/dmr-22-43/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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doi: 10.21037/dmr-22-43
Cite this article as: Campbell S, Bauer T. Role of adjuvant therapy in esophageal cancer patients after neoadjuvant therapy and esophagectomy. Dig Med Res 2022;5:48.