Commentary: “Neoadjuvant Immunochemotherapy for Locally Advanced Esophageal Squamous Cell Carcinoma: Beginning of a Paradigm Shift”

Monisha Sudarshan, MD, MPH, Snigdha Gulati, MD

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Commentary: "Neoadjuvant Immunochemotherapy for Locally Advanced Esophageal Squamous Cell Carcinoma: Beginning of a Paradigm Shift"

Monisha Sudarshan, MD, MPH
Department of Thoracic and Cardiovascular Surgery, Heart, and Vascular Institute
Cleveland Clinic, Cleveland, Ohio.

Snigdha Gulati, MD
Department of Thoracic and Cardiovascular Surgery, Heart, and Vascular Institute
Cleveland Clinic, Cleveland, Ohio.

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Correspondence:
Address reprint requests to Monisha Sudarshan MD, MPH, Department of Thoracic and Cardiovascular Surgery, Heart and Vascular Institute, Cleveland Clinic
9500 Euclid Ave J4-1, Cleveland, OH 44195
E-mail: Sudarsm2@ccf.org

Central Message:
Neoadjuvant immunochemotherapy may be associated with better progression free survival as compared to neoadjuvant chemoradiotherapy in a selected group of patients with locally advanced esophageal SCC.

Central Picture Legend:
Dr. Snigdha Gulati, Dr. Monisha Sudarshan

Main text (<500 words): 537 words
The most used regimen for locally advanced esophageal squamous cell carcinoma (LA-SCC) [cT2-4 and/or cN+] is neoadjuvant chemoradiotherapy, followed by surgical resection [1]. However, the rates of locoregional relapse (13.7%), distant relapse (25.3%), synchronous distant and locoregional relapse (4.4%), and a 5-year survival rate of 59.9% presents much to be improved [2]. Better systemic control will be key in improving outcomes for esophageal cancer, especially understanding potential benefits, risks, and how to integrate immunotherapy into treatment protocols.

In this month’s issue of the Journal, Dr Yang and authors retrospectively review and compare the use of neoadjuvant immunochemotherapy (nICT) and neoadjuvant chemoradiotherapy (nCRT) for LA-SCC [3].

The patients in the nICT group received 1-4 cycles of a single checkpoint inhibitor combined with a two-drug (platinum/taxane) immunotherapy regimen. In contrast, the nCRT group received the same two-drug combination, with 40 Gy of radiation. Both treatments were followed by surgical procedures (McKeown, Ivor Lewis, or Sweet) after 4-8 weeks.

With the median follow up of 26.2 months, both groups exhibited comparable outcomes in complete pathological response rate (cPR: 20.2% vs. 29.0%, p=0.140), overall survival (HR=0.62; 95%CI: 0.36-1.09; p=0.094), and complication-related death (0.8% vs. 3.2%, p=0.366). The nICT group had lower rates of distant metastasis (6.5% vs. 16.1%, p=0.027) and overall recurrence (11.3% vs. 23.4%, p=0.019) within the first postoperative year. Notably, the nICT group also exhibited better prognosis-free survival (HR 0.50, 95% CI: 0.26-0.96, p=0.040) especially for patients with T3/T4 tumors.

Despite the retrospective nature of the study, small sample size and short follow-up period, the authors raise the important question about the role of immunotherapy in the neoadjuvant setting. Currently, the checkmate 577 trial [4] has established checkpoint inhibitors as adjuvant therapy when residual disease is identified after surgery; however, immunotherapy use in the neoadjuvant setting is not well established. Due to the retrospective nature of the current study, the criteria of patient selection for either treatment is not defined. The Programmed Cell Death Ligand 1 (PD-L1) status, microsatellite instability high (MSI-H), mismatch repair (MMR) deficient and tumor mutational burden high (TMB-H) statuses [5]-that could determine the response to immunotherapy and chemotherapy, were unknown for most patients, further limiting the study’s generalizability. Significant heterogeneity also existed within the nICT group regarding the type, dose, and duration of the immune checkpoint inhibitors.

We congratulate the authors on this study with its remarkable results which highlights the need for personalized medicine in esophageal cancer rather than a uniform approach for all. Although the study does not establish the role of neoadjuvant ICT, it does suggest that certain selected patients will have an oncologic benefit. Future larger prospective studies with well-defined treatment protocol, molecular characterization of tumors, and longer follow-up are needed to establish the role of neoadjuvant immunotherapy in esophageal cancer.

References (MLA format):


