

### Transcript Details

This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: <https://reachmd.com/programs/project-oncology/overall-survival-with-neoadjuvant-therapy-in-hnsc/32999/>

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## Overall Survival with Neoadjuvant Therapy in HNSCC: Examining Real-World Data

### Announcer:

You're listening to *Project Oncology* on ReachMD. On this episode, we'll hear from Dr. Vanessa Helou, who's a Postdoctoral Research Associate in the Department of Otolaryngology - Head and Neck Surgery at the University of Pittsburgh. She'll be discussing a poster she presented at the 2025 American Society of Clinical Oncology Annual Meeting, which compared survival outcomes among patients with head and neck squamous cell carcinoma who were treated with versus without neoadjuvant systemic therapy. Here's Dr. Helou now.

### Dr. Helou:

Despite advances in surgery, radiation, and adjuvant therapies, long-term survival in head and neck squamous cell carcinoma remains suboptimal. Neoadjuvant systemic therapy, which is delivering therapy prior to surgery, has been explored as a promising approach to reduce the risk of distant metastasis and enable organ preservation. In head and neck cancer, neoadjuvant chemotherapy has been used preoperatively to shrink tumors and improve resectability. However, its use has not translated into consistent survival benefits.

The treatment paradigm began to shift with the introduction of immunotherapy—particularly anti-PD-1 agents, which have changed outcomes across several solid tumors, including head and neck cancer. Since 2019, anti-PD-1 therapy has been approved as a first-line treatment for patients with recurrent metastatic head and neck squamous cell carcinoma, and interest has grown in moving these agents earlier in the treatment course. More recently, KEYNOTE-689, which is a phase III trial, demonstrated improved event-free survival in patients who received neoadjuvant and adjuvant pembrolizumab with surgery compared to surgery alone. While these results are promising, overall survival at the time of analysis did not reach significance, and longer follow-up is needed to determine its full impact. Given this evolving landscape, real-world data on the survival impact of neoadjuvant systemic therapy in head and neck cancer are still limited.

Our main objective was to assess overall survival outcomes associated with neoadjuvant systemic therapy, whether immunotherapy, chemotherapy, or a combination of both in patients with resectable head and neck squamous cell carcinoma. In order to do this, we conducted a retrospective cohort study using the National Cancer Database, which is a comprehensive hospital-based cancer registry in the United States. We included patients treated surgically for tumors of the oral cavity, oropharynx, larynx, hypopharynx, and other mucosal sites between 2004 and 2022. We defined neoadjuvant therapy as systemic treatment delivered within eight weeks prior to surgery. We then categorized patients based on the treatment they received before surgery, neoadjuvant immunotherapy alone, neoadjuvant chemotherapy alone, and the combination of both.

Then, each neoadjuvant group was matched to a controlled group of patients who had surgery without neoadjuvant therapy using a 10:1 ratio propensity score matching. We matched patients on a broad range of patient demographics and clinical variables, including overall tumor stage, tumor site, treatment facility type, and other socioeconomic factors. Our primary outcome was overall survival, which was measured from the date of diagnosis to death or to the last follow-up date. We compared overall survival among patients treated with versus without neoadjuvant therapy using Cox regression models.

We identified a total of 1,570 patients with mucosal head and neck squamous cell carcinoma who received neoadjuvant systemic therapy followed by surgery. Of these, about 65 percent received chemotherapy alone, 29 percent received immunotherapy alone, and just over 5 percent received a combination therapy of both. These groups were then matched to over 15,000 controls who had surgery without neoadjuvant therapy. In terms of patient characteristics, the average age ranged from about 58 to 62 years, and around three-quarters were male across all groups. The tongue was the most common primary site across all treatment groups, and the majority of patients presented with stage IVA and IVB, which reflects more advanced presentations.

Now, looking at survival outcomes, compared to patients treated surgically, neoadjuvant immunotherapy was significantly associated with 18 percent improved overall survival with a five-year survival significantly higher at 69 percent versus 63 percent in patients who received surgery alone. On the other hand, neoadjuvant chemotherapy was associated with the 20 percent worse overall survival, with a five-year survival of 52 percent versus 58 percent. Combination therapy showed no statistically significant difference in overall survival compared to matched patients with similar five-year survival rates.

Our study provides evidence that neoadjuvant immunotherapy may offer a survival advantage for patients with resectable mucosal head and neck squamous cell carcinoma, while neoadjuvant chemotherapy alone may be associated with inferior outcomes. However, as with all retrospective analyses, we have limitations. The results underscore the promising role for neoadjuvant immunotherapy and highlight the urgent need for large-scale randomized trials with long-term follow-up to validate the observed survival benefits and inform clinical practice in the treatment of head and neck cancer.

**Announcer:**

That was Dr. Vanessa Helou talking about the poster she presented at the 2025 American Society of Clinical Oncology Annual Meeting that examined the impacts of neoadjuvant systemic therapy on survival outcomes in head and neck squamous cell carcinoma. To access this and other episodes in our series, visit *Project Oncology* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!