Systemic Treatment for Squamous Cell Carcinoma of the Head and Neck

Aditya V. Shetty, MD, Deborah J. Wong, MD, PhD*

KEYWORDS

• Chemoradiation • Cisplatin • Erbitux • PD-1 inhibition

KEY POINTS

- Head and neck cancers represent a diverse group of diseases with varied histopathologic features and outcomes.
- In patients with locally advanced squamous cell cancer of the head and neck, a multimodality treatment approach is recommended.
- The addition of platinum-based systemic therapy concurrently with radiation has been shown to be superior to radiation alone and is considered standard therapy for locally advanced disease.
- In the recurrent or metastatic setting, systemic treatment with chemotherapy is palliative.
- A subset of patients treated with PD-1 immunotherapy, however, may achieve durable responses.

INTRODUCTION

Head and neck cancer is a heterogeneous group of neoplasms arising in the oral cavity, nasopharynx, pharynx, larynx, or salivary glands. Although head and neck cancer can present with a variety of different histologic variants, squamous cell carcinomas of the head and neck (SCCHN) account for nearly 95% of the cases. A multidisciplinary treatment approach is recommended in all patients with head and neck cancer. The choice of treatment modality largely depends on the site and extent of the disease and the feasibility of organ preservation. Although stage I and II SCCHN is typically treated with radiotherapy or surgery, a multimodality treatment approach, including systemic therapy, is recommended for more advanced stages of the disease. The optimal sequencing of chemotherapy, radiotherapy, and surgery is still unclear. Although many chemotherapeutic agents have shown activity in SCCHN,

Division of Hematology-Oncology, UCLA Medical Center, 2825 Santa Monica Boulevard suite 200, Santa Monica, Los Angeles, CA 90404, USA
* Corresponding author.
E-mail address: DeWong@mednet.ucla.edu

Otolaryngol Clin N Am 50 (2017) 775–782
http://dx.doi.org/10.1016/j.otc.2017.03.013
0030-6665/17/Published by Elsevier Inc.

platinum-based therapy with either cisplatin or carboplatin is considered standard frontline therapy in inoperable or metastatic disease.

CONCURRENT CHEMORADIATION

The superiority of concurrent chemoradiation versus radiotherapy alone was first demonstrated in a study published in 1992. A total of 157 patients with previously untreated, unresectable advanced SCCHN were assigned to treatment with either alternating chemotherapy and radiotherapy or radiotherapy alone.[1] The median survival was noted to be 16.5 months in the combination arm and 11.7 months in the radiotherapy group. The 3-year survival was 41% in the combination arm and 23% in the radiotherapy arm. In a 5-year update to this study, overall survival (OS) was noted to be 24% in the combination group versus 10% in the radiotherapy group.[2] Five-year progression-free survival (PFS) was also noted to be significantly improved in the combination group at 21% and 9% in the radiotherapy group. In another trial, 295 unresectable patients were randomly to single daily radiation; to single daily radiation plus three cycles of concurrent cisplatin on Days 1, 22, and 43; or to a split course of single daily fractionated radiotherapy and three cycles of concurrent fluorouracil and cisplatin (CF) chemotherapy.[3] The 3-year OS rate was significantly improved with concurrent cisplatin and radiotherapy arms (37% vs 23%; $P = .014$) versus radiotherapy alone. No statistically significant differences in survival were observed with split course concurrent arm versus the radiotherapy arm (27% vs 23%).

Evidence also suggests that concurrent chemoradiotherapy leads to improved disease control versus radiotherapy not only in unresectable head and neck cancer but also in resectable cases of advanced head and neck cancer. A phase III study comparing the radiotherapy versus combination chemotherapy and radiotherapy in resectable stage III and IV head and neck cancer was undertaken.[4] A total of 100 resectable stages III and IV patients were randomized to either radiotherapy alone, 68 to 72 Gy at 1.8 to 2.0 Gy per day, or to radiotherapy with concurrent chemotherapy, consisting of 5-fluorouracil, 1000 mg/m^2/day and cisplatin 20 mg/m^2/day, both given as continuous intravenous infusions over 4 days beginning on Day 1 and Day 22 of the radiotherapy. Three-year relapse-free survival was noted to be higher in the combination arm at 67% versus 52% in the radiotherapy-alone arm. Successful primary site preservation was also noted to be improved in the combination arm at 57% versus 35% in the radiotherapy-alone arm. Development of metastases was also significantly lower in the combination arm compared with the radiotherapy arm alone (10% vs 2%). In a 5-year follow-up study, relapse-free survival (62% vs 51%) and development of metastasis (84% vs 75%) were noted to be improved in the combination arm.[5] No significant differences in OS were noted; however, 5-year OS was improved in patients who successfully achieved primary site preservation in the chemoradiotherapy arm.

The benefits of concurrent chemoradiation can also be seen in organ-preservation treatment of larynx and nasopharyngeal cancers. In the Intergroup RTOG 91-11 trial, 547 patients with locally advanced larynx cancer were randomly assigned to either induction cisplatin plus fluorouracil followed by radiotherapy, radiotherapy with concurrent administration of cisplatin, or radiotherapy alone.[6] At the 2-year mark larynx preservation was achieved in 88% in radiotherapy with concurrent cisplatin arm, 75% in the induction chemotherapy followed by radiotherapy arm, and 70% in radiotherapy arm alone. Locoregional control was also significantly better with concurrent chemoradiation (78% vs 61% in induction