

Chemotherapy for Oral Cancer

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KEYWORDS

- Chemotherapy • Oral cancer • Chemoradiation • Cisplatin • Cetuximab
- Nivolumab • Pembrolizumab

KEY POINTS

- Adjuvant chemotherapy has not been shown to improve treatment outcomes in patients with oral cancer after surgery and should not be used.
- Adjuvant combined chemotherapy and radiation improves survival for patients with extracapsular extension in nodal metastases and positive resection margins. Cisplatin should be used.
- Patients with oral cancer can be treated with primary chemoradiation, although the impact on survival is unclear. Cisplatin is the standard agent to combine with radiation. Cetuximab has not been well-studied.
- Induction chemotherapy can be used selectively, but its impact on overall survival remains unclear and is associated with significant toxicity.
- Anti-programmed cell death-ligand 1 antibodies have been shown to improve survival for patients with metastatic disease after treatment with platinum-based chemotherapy.

INTRODUCTION

The past several years have seen major advances in the use of systemic therapy for treatment of patients with oral cancer. Systemic therapy refers to chemotherapy and immunotherapy drugs, which are playing an increasingly important role in treatment. Chemotherapy has classically been used either as a primary treatment modality or in combination with radiation, where it is used as a radiation sensitizer. Based on the results of pivotal trials during the past decade, the use of systemic therapy has expanded in scope and has resulted in meaningful improvements in patient outcomes. This article discusses the different uses for systemic therapy in the treatment of patients with oral squamous cell carcinoma and reviews the current state of practice and areas of future investigation. In discussing studies, the relevance to patients with oral cancer are highlighted. It is important to remember that studies in patients

Conflicts of Interest: None to report.

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with squamous cell carcinoma of the head and neck include patients with different primary sites and they are not always represented in the same relative amounts. Despite that, however, the results of these studies are in most cases applied to patients with primary tumors of all different subsites.

ADJUVANT CHEMOTHERAPY

The primary treatment modality for patients with oral cancer is surgery when possible without undue morbidity. Adjuvant chemotherapy is given after surgery in many types of cancer for reducing the incidence of metastatic recurrence. At the present time, adjuvant chemotherapy has no established role in the treatment of patients after surgery for oral cancer. The most recent update of a very large metaanalysis examining the role of chemotherapy in treatment of patients with head and neck cancer found no evidence of benefit.¹ It included a total of 2567 patients taken from 6 studies that included patients with oral cancer. Therefore, adjuvant chemotherapy should only be used in the context of a clinical trial.

ADJUVANT CHEMORADIOTHERAPY

In addition to studies of chemotherapy as a standalone adjuvant treatment modality, multiple studies have examined the use of concurrent chemotherapy and radiation. In this setting, chemotherapy is given as a radiation sensitizer with the goal of reducing radiation resistance. Multiple studies have found this approach is superior to radiation alone in patients with an increased risk of recurrence. The 2 largest trials examining this question, unfortunately, came to different conclusions. In the EORTC trial 22,931, a total of 334 patients were treated with either radiation alone or radiation combined with cisplatin 100 mg/m² given on days 1, 22, and 43.² The same treatments were compared in RTOG 9501, which enrolled a total of 459 patients.^{3,4} However, these 2 studies had different enrollment criteria, defining high-risk disease differently (Table 1). As a result, they unfortunately came to different conclusions regarding the benefit of adjuvant chemoradiation. Based on analysis of these 2 studies, adjuvant chemoradiation seems to improve outcomes in patients with extracapsular extension

Table 1
Adjuvant chemoradiation: comparison between EORTC 22931 and RTOG 9501

	EORTC 22931	RTOG 9501
Number of patients	334	459
Oral cavity patients	87	112
Stage	pT3 or pT4/any N or pT1 or pT2/N2 or N3	Any T stage, N2b or higher N stage
Unfavorable pathologic findings	ECE, positive margins, PNI, VTE	2 or more positive nodes, ECE, positive margins
Radiation	54 Gy with boost to 66 Gy	60 Gy with boost to 66 Gy
Chemotherapy	Cisplatin 100 mg/m ² days 1, 22, and 43	Cisplatin 100 mg/m ² days 1, 22, and 43
Findings	Improved 5 y PFS and OS	Improved DFS only for ECE, positive margins

Abbreviations: ECE, extracapsular extension; OS, overall survival; PFS, progression-free survival; PNI, perineural invasion; VTE, vascular tumor embolism.

*Data from Refs.*²⁻⁴

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