

Oral Cavity Cancer Treatment Protocols

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Treatment Protocols

Treatment protocols for oral cavity cancers are provided below, including generalized first-line therapy based on stage; chemoradiation therapy and induction chemotherapy for locally advanced disease; and first-, second-, and third-line chemotherapy for metastatic or recurrent disease.

Generalized treatment recommendations for oral cavity cancers

See the list below:

- Treatment plans for all disease stages should be discussed at a multidisciplinary tumor conference involving ear, nose, throat (ENT) surgeons; radiation oncologists; and medical oncologists
- Selected patients with advanced or metastatic disease may receive surgical resection of their primary tumors, depending on their response to first-line therapy

Surgery or radiation therapy for early or localized oral cavity cancers

Stages I-II^[1, 2]:

- Primary treatment for oropharyngeal cancers is surgical resection or definitive radiation therapy
- Surgery is the preferred approach, except for some patients who may have early lip, retromolar trigone, and soft palate cancers
- Radiation therapy is preferred for patients who may not be able to tolerate surgery
- The radiation dose depends on tumor size; however, for early stage disease, doses of 66-74 Gy (2.0 Gy/fraction; daily Monday-Friday in 7wk) may be used with adequate results

Chemotherapy with radiation therapy for locally advanced oral cavity cancers

Stages III-IVB^[1, 2]:

- Surgery should be considered for locally advanced disease; however, definitive radiation therapy, concurrent chemoradiation, and induction therapy are alternative options for patients who are not candidates for surgery^[3]
- Concurrent chemoradiation therapy is the current standard of care for patients with locally advanced squamous cell carcinoma of the head and neck
- Chemotherapy is given for the duration of radiation therapy unless otherwise stated; definitive radiation doses used are 66-74 Gy (2.0 Gy/fraction; daily Monday-Friday in 7wk)
- Conventional fractionation for concurrent chemoradiation is up to 70 Gy (2.0 Gy/fraction)
- Postoperative radiation dose is 60-66 Gy (2.0 Gy/fraction); preferred interval between resection and postoperative radiation therapy is = 6wk
- The decision to treat the patient with concurrent chemoradiation therapy rather than surgery, radiation, or chemotherapy individually should be made by a multidisciplinary tumor board (including a medical oncologist, a radiation therapist, and an ENT surgeon)

Acceptable chemotherapy regimens for primary systemic therapy with concurrent radiation:

- **Cisplatin** 100 mg/m² IV on days 1, 22, and 43^[1, 2, 4, 5] **or** 40-50 mg/m² IV weekly for 6-7wk^[6] **or**
- **Cetuximab** 400 mg/m² IV loading dose 1wk before the start of radiation therapy, **then** 250 mg/m² weekly (premedicate with dexamethasone, diphenhydramine, and **ranitidine**)^[7, 8]; **or**
- **Cisplatin** 20 mg/m² IV on day 2 weekly for up to 7wk **plus** **paclitaxel** 30 mg/m² IV on day 1 weekly for up to 7wk^[9] **or**
- **Cisplatin** 20 mg/m²/day IV on days 1-4 and 22-25 **plus** **fluorouracil** (5-FU) 1000 mg/m²/day by continuous IV infusion on days 1-4 and 22-25^[10, 11, 12] **or**

- 5-FU 800 mg/m² by continuous IV infusion on days 1-5 given on the days of radiation **plus** hydroxyurea 1 g PO q12h (11 doses per cycle); chemotherapy and radiation given every other week for a total of 13wk^[9] **or**
- Carboplatin 70 mg/m²/day IV on days 1-4, 22-25, and 43-46 **plus** 5-FU 600 mg/m²/day by continuous IV infusion on days 1-4, 22-25, and 43-46^[13] **or**
- Carboplatin area under the curve (AUC; see the [Carboplatin AUC Dose Calculation \[Calvert formula\] calculator](#)) 1.5 IV on day 1 weekly **plus** paclitaxel 45 mg/m² IV on day 1 weekly^[14]

Acceptable chemotherapy regimens for patients receiving postoperative concurrent chemoradiation:

- Cisplatin 100 mg/m² IV on days 1, 22, and 43^[4, 5] **or** 40-50 mg/m² IV weekly for 6-7wk^[6, 15]

Induction chemotherapy for locally advanced oral cavity cancers

Stages III-IVB:

- Induction chemotherapy is typically given to patients with stage III-IVB disease in order to shrink a primary tumor to reduce its bulkiness in preparation for future surgery or radiation therapy
- The decision to treat the patient with induction chemotherapy rather than concurrent chemoradiation or surgery, radiation, or chemotherapy alone should be made by a multidisciplinary tumor board (including a medical oncologist, a radiation therapist, and an ENT surgeon)^[1, 2]

Acceptable chemotherapy regimens for induction chemotherapy:

- Docetaxel 75 mg/m² IV on day 1 **plus** cisplatin 100 mg/m² IV on day 1 **plus** 5-FU 100 mg/m²/day by continuous IV infusion on days 1-4 every 3wk for 3 cycles; **then** 3-8wk later, carboplatin AUC 1.5 IV weekly for up to 7wk during radiation therapy; **then** 6-12wk later, pursue surgery, if applicable^[16, 17]; **or**
- Docetaxel 75 mg/m² IV on day 1 **plus** cisplatin 75 mg/m² IV on day 1 **plus** 5-FU 750 mg/m²/day by continuous IV infusion on days 1-4 every 3wk for 4 cycles; **then** 4-7wk later, radiation; surgical resection can be pursued before or after chemotherapy^[18]
- Paclitaxel 175 mg/m² IV on day 1 **plus** cisplatin 100 mg/m² IV on day 2 **plus** 5-FU 500 mg/m²/day by continuous IV infusion on days 2-6 every 3wk for 3 cycles; **then** radiation with cisplatin 100 mg/m² IV on days 1, 22, and 43^[19]

First-line chemotherapy for metastatic or recurrent oral cavity cancers

Stage IVC:

- Treatment recommendations include the use of single-agent or combination chemotherapy
- Platinum-based chemotherapy regimens are preferred if these agents can be tolerated by the patient; if they cannot be tolerated, single agents have been used in this setting^[1, 2]
- Below are first-line chemotherapy options for metastatic disease or recurrent squamous head and neck cancers (after surgery and/or radiation)

Acceptable chemotherapy regimens in patients with metastatic (incurable) head and neck cancers (unless otherwise stated, goal is to complete at least 6 cycles):

- Cisplatin 100 mg/m² IV on day 1 every 3wk for 6 cycles **plus** 5-FU 1000 mg/m²/day by continuous IV infusion on days 1-4 every 3wk for 6 cycles **plus** cetuximab 400 mg/m² IV loading dose on day 1, **then** 250 mg/m² IV weekly until disease progression (premedicate with dexamethasone, diphenhydramine, and ranitidine)^[20]; **or**
- Carboplatin AUC 5 IV on day 1 every 3wk for 6 cycles **plus** 5-FU 1000 mg/m²/day by continuous IV infusion on days 1-4 every 3wk for 6 cycles **plus** cetuximab 400 mg/m² IV loading dose on day 1, **then** 250 mg/m² IV weekly until disease progression (premedicate with dexamethasone, diphenhydramine, and ranitidine)^[20]; **or**
- Cisplatin 75 mg/m² IV on day 1 **plus** docetaxel 75 mg/m² IV on day 1 every 3wk^[21, 22] **or**
- Cisplatin 75 mg/m² IV on day 1 **plus** paclitaxel 175 mg/m² IV on day 1 every 3wk^[23, 24] **or**
- Carboplatin AUC 6 IV on day 1 **plus** docetaxel 65 mg/m² IV on day 1 every 3wk^[25] **or**
- Carboplatin AUC 6 IV on day 1 **plus** paclitaxel 200 mg/m² IV on day 1 every 3wk^[26] **or**
- Cisplatin 75-100 mg/m² IV on day 1 every 3-4wk **plus** cetuximab 400 mg/m² IV loading dose on day 1, **then** 250 mg/m² IV weekly (premedicate with dexamethasone, diphenhydramine, and ranitidine)^[27, 28, 29]; **or**
- Cisplatin 100 mg/m² IV on day 1 **plus** 5-FU 1000 mg/m²/day by continuous

IV infusion on days 1-4 every 3wk^[12, 24, 30, 31, 32] **or**

- Cisplatin 75 mg/m² IV on day 1 **plus** docetaxel 75 mg/m² IV on day 1 **plus** cetuximab (400 mg/m² IV on day 1, then 250 mg/m² IV weekly) every 21 days for 4 cycles followed by cetuximab maintenance (500 mg/m² IV every 2 weeks) until disease progression or unacceptable toxicity^[33] **or**
- **Methotrexate** 40 mg/m² IV weekly (3wk equals 1 cycle)^[12, 30] **or**
- Paclitaxel 200 mg/m² IV every 3wk^[34, 35] **or**
- Docetaxel 75 mg/m² IV every 3wk^[36, 37, 38] **or**
- Cetuximab 400 mg/m² IV loading dose on day 1, **then** 250 mg/m² IV weekly until disease progression (premedicate with dexamethasone, diphenhydramine, and ranitidine)^[39]

Second- and third-line chemotherapy for metastatic or recurrent oral cavity cancers

Stage IVC:

- Second-line chemotherapy is given after disease progression or recurrence following completion of first-line therapy
- Third-line therapies are given after disease progression or recurrence following completion of first-line and second-line therapies
- Second- and third-line regimens are similar to regimens used as first-line therapy but usually offer lower response rates and survival benefits
- Patients should be treated with platinum-based chemotherapy regimens if they have not previously received a platinum-based drug

Acceptable chemotherapy regimens in patients with recurrent head and neck cancers (unless otherwise stated, goal is to complete at least 6 cycles):

- Cisplatin 100 mg/m² IV on day 1 every 3wk for 6 cycles **plus** 5-FU 1000 mg/m²/day by continuous IV infusion on days 1-4 every 3wk for 6 cycles **plus** cetuximab 400 mg/m² IV loading dose on day 1, **then** 250 mg/m² IV weekly until disease progression (premedicate with dexamethasone, diphenhydramine, and ranitidine)^[20]; **or**
- Carboplatin AUC 5 IV on day 1 every 3wk for 6 cycles **plus** 5-FU 1000 mg/m²/day by continuous IV infusion on days 1-4 every 3wk for 6 cycles **plus** cetuximab 400 mg/m² IV loading dose on day 1, **then** 250 mg/m² IV weekly until disease progression (premedicate with dexamethasone, diphenhydramine, and ranitidine)^[21]; **or**
- Cisplatin 75 mg/m² IV on day 1 **plus** docetaxel 75 mg/m² IV on day 1 every 3wk^[21] **or**
- Cisplatin 75 mg/m² IV on day 1 **plus** paclitaxel 175 mg/m² IV on day 1 every 3wk^[23, 24] **or**
- Carboplatin AUC 6 IV on day 1 **plus** docetaxel 65 mg/m² IV on day 1 every 3wk^[25] **or**
- Carboplatin AUC 6 IV on day 1 **plus** paclitaxel 200 mg/m² IV on day 1 every 3wk^[26] **or**
- Cisplatin 75-100 mg/m² IV on day 1 every 3-4wk **plus** cetuximab 400 mg/m² IV loading dose on day 1, **then** 250 mg/m² IV weekly (premedicate with dexamethasone, diphenhydramine, and ranitidine)^[27, 28, 29]; **or**
- Cisplatin 100 mg/m² IV on day 1 **plus** 5-FU 1000 mg/m²/day by continuous IV infusion on days 1-4 every 3wk^[12, 24, 30, 31, 32] **or**
- Cisplatin 75 mg/m² IV on day 1 **plus** docetaxel 75 mg/m² IV on day 1 **plus** cetuximab (400 mg/m² IV on day 1, then 250 mg/m² IV weekly) every 21 days for 4 cycles followed by cetuximab maintenance (500 mg/m² IV every 2 weeks) until disease progression or unacceptable toxicity^[33] **or**
- Methotrexate 40 mg/m² IV weekly (3wk equals 1 cycle)^[12, 30] **or**
- Paclitaxel 200 mg/m² IV every 3wk^[2, 35] **or**
- Docetaxel 75 mg/m² IV every 3wk^[36, 37, 38] **or**
- Cetuximab 400 mg/m² IV loading dose on day 1, **then** 250 mg/m² IV weekly until disease progression (premedicate with dexamethasone, diphenhydramine, and ranitidine)^[39]

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