Oncology Clinical Pathways
Head and Neck Cancer
April 2022 – V1.2022
Head and Neck Cancer – Oral Cavity T1-2, N0, M0

Evaluate need for support regarding tobacco use/smoking cessation, dental health, nutrition, audiology, speech/swallowing

Resection consider neck dissection if depth of invasion is >3mm; always consider neck dissection with perineural or perivascular/vascular invasion

Adverse features include extranodal extension, positive margins, close margins, pT3 or pT4 primary, pN2 or pN3 nodal disease, nodal disease in levels IV or V, perineural invasion, perivascular/vascular invasion, or lymphatic invasion

Plan for total cisplatin dose > 200 mg/m² (either as 100 mg/m² IV every 3 weeks for 3 cycles or 40 mg/m² IV weekly with concurrent radiation); candidates for high-dose cisplatin should be ECOG PS 0-1 with minimal comorbidities, as toxicities may be anticipated (i.e. nephrotoxicity, neutropenia, nausea/vomiting, etc.);

If not cisplatin-eligible, prescribe carboplatin-fluorouracil or carboplatin-paclitaxel

Clinical trial(s) always considered on pathway.

Yes

Oral Cavity T1-2, N0, M0 *

Patient candidate for surgery?

No

T1

Resection b

Radiation to primary site

Adverse features? c

No

T2

Resection with nodal-basin dissection

T1

Resection with nodal-basin dissection

T2

Radiation to primary site and nodal-basin

Radiation to primary site

Extranodal extension or positive margins?

No

No

Surveillance

Yes

Yes

Reresection feasible?

Yes

Extranodal extension

Cisplatin with radiation d

No

Positive margin

Reresection

No

Cisplatin with radiation d

* Evaluate need for support regarding tobacco use/smoking cessation, dental health, nutrition, audiology, speech/swallowing

b Resection consider neck dissection if depth of invasion is >3mm; always consider neck dissection with perineural or perivascular/vascular invasion

c Adverse features include extranodal extension, positive margins, close margins, pT3 or pT4 primary, pN2 or pN3 nodal disease, nodal disease in levels IV or V, perineural invasion, perivascular/vascular invasion, or lymphatic invasion

d Plan for total cisplatin dose > 200 mg/m² (either as 100 mg/m² IV every 3 weeks for 3 cycles or 40 mg/m² IV weekly with concurrent radiation); candidates for high-dose cisplatin should be ECOG PS 0-1 with minimal comorbidities, as toxicities may be anticipated (i.e. nephrotoxicity, neutropenia, nausea/vomiting, etc.);

If not cisplatin-eligible, prescribe carboplatin-fluorouracil or carboplatin-paclitaxel
Head and Neck Cancer – Oral Cavity T1-4, N1-3, M0 and T3-4, N0, M0

Clinical trial(s) always considered on pathway.

**Oral Cavity T1-4, N1-3, M0 and T3-4, N0, M0**

- **Patient candidate for surgery?**
  - Yes ➔ Resection of primary and nodal-basin dissection
  - No ➔ Cisplatin with radiation

- **Extranodal extension or positive margins?**
  - Yes ➔ Positive margin
  - No ➔ Extranodal extension

- **Reresection feasible?**
  - Yes ➔ Reresection
  - No ➔ Cisplatin with radiation

**Plan for total cisplatin dose > 200 mg/m^2** (either as 100 mg/m^2 IV every 3 weeks for 3 cycles or 40 mg/m^2 IV weekly with concurrent radiation); candidates for high-dose cisplatin should be ECOG PS 0-1 with minimal comorbidities, as toxicities may be anticipated (i.e. nephrotoxicity, neutropenia, nausea/vomiting, etc.); **if not cisplatin-eligible**, prescribe carboplatin-fluorouracil or carboplatin-paclitaxel

**Radiation** forgo radiation for N1 disease with a single lymph node if the only adverse pathological feature

---

**Evaluate need for support regarding** tobacco use/smoking cessation, dental health, nutrition, audiology, speech/swallowing

---

**ChooseVA**

**U.S. Department of Veterans Affairs**
Clinical trial(s) always considered on pathway.

**Head and Neck Cancer – Oral Cavity Recurrence**

Oral Cavity Recurrence® → Multidisciplinary discussion → Candidate for salvage resection?

- **Yes** → Surgery and reconstruction → Candidate for radiation +/- chemotherapy?
  - **Yes** → Radiation +/- cisplatin
  - **No** → Candidate for systemic therapy?
    - **Yes** → Systemic therapy
    - **No** → Observation +/- Palliative Care

**Evaluate need for support regarding** tobacco use/smoking cessation, dental health, nutrition, audiology, speech/swallowing

**Plan for total cisplatin** dose $\geq 200$ mg/m$^2$ (either as $100$ mg/m$^2$ IV every 3 weeks for 3 cycles or $40$ mg/m$^2$ IV weekly with concurrent radiation); candidates for high-dose cisplatin should be ECOG PS 0-1 with minimal comorbidities, as toxicities may be anticipated (i.e. nephrotoxicity, neutropenia, nausea/vomiting, etc.); **if not cisplatin-eligible**, prescribe carboplatin-flourouracil or carboplatin-paclitaxel
**Head and Neck Cancer – Oropharynx HPV Positive or Negative T1-2, N0, M0**

Clinical trial(s) always considered on pathway.

**a Pathway takes into consideration** the difference in staging between HPV negative and positive disease

**b Adverse features include** extranodal extension, positive margins, close margins, pT3 or pT4 primary, pN2 or pN3 nodal disease, nodal disease in levels IV or V, perineural invasion, perivascular/vascular invasion, or lymphatic invasion

**c Plan for total cisplatin** dose ≥ 200 mg/m² (either as 100 mg/m² IV every 3 weeks for 3 cycles or 40 mg/m² IV weekly with concurrent radiation); candidates for high-dose cisplatin should be ECOG PS 0-1 with minimal comorbidities, as toxicities may be anticipated (i.e. nephrotoxicity, neutropenia, nausea/vomiting, etc.); **if not cisplatin-eligible**, prescribe carboplatin-fluorouracil or carboplatin-paclitaxel
Head and Neck Cancer – Oropharynx HPV Positive or Negative T1-2, N1

Clinical trial(s) always considered on pathway.

- **Pathway takes into consideration** the difference in staging between HPV negative and positive disease
- **Adverse features include** extranodal extension, positive margins, close margins, pT3 or pT4 primary, pN2 or pN3 nodal disease, nodal disease in levels IV or V, perineural invasion, perivascular/vascular invasion, or lymphatic invasion
- **Plan for total cisplatin** dose ≥ 200 mg/m² (either as 100 mg/m² IV every 3 weeks for 3 cycles or 40 mg/m² IV weekly with concurrent radiation); candidates for high-dose cisplatin should be ECOG PS 0-1 with minimal comorbidities, as toxicities may be anticipated (i.e. nephrotoxicity, neutropenia, nausea/vomiting, etc.); if not **cisplatin-eligible**, prescribe carboplatin-fluorouracil or carboplatin-paclitaxel
- **If not platinum eligible**, prescribe cetuximab

Patient preference after shared decision making?

- Oropharynx HPV Positive or Negative T1-2, N1
- Resection of the primary and neck dissection of nodal basin
- Adverse features? b
  - Yes
    - Extramodal extension or positive margins?
      - Yes
        - Cisplatin with radiation c d
      - No
        - Surveillance
    - No
      - Multiple nodes; or one node ≥ 3cm?
        - Yes
          - Cisplatin with radiation c d
        - No
          - Radiation
      - Radiation
  - No
    - Surveillance

---

- Clinical trial(s) always considered on pathway.
- Pathway takes into consideration the difference in staging between HPV negative and positive disease
- Adverse features include extranodal extension, positive margins, close margins, pT3 or pT4 primary, pN2 or pN3 nodal disease, nodal disease in levels IV or V, perineural invasion, perivascular/vascular invasion, or lymphatic invasion
- Plan for total cisplatin dose ≥ 200 mg/m² (either as 100 mg/m² IV every 3 weeks for 3 cycles or 40 mg/m² IV weekly with concurrent radiation); candidates for high-dose cisplatin should be ECOG PS 0-1 with minimal comorbidities, as toxicities may be anticipated (i.e. nephrotoxicity, neutropenia, nausea/vomiting, etc.); if not cisplatin-eligible, prescribe carboplatin-fluorouracil or carboplatin-paclitaxel
- If not platinum eligible, prescribe cetuximab
Head and Neck Cancer – Oropharynx HPV Positive or Negative T1-2, N2-3 and T3-4, N0-3

Clinical trial(s) always considered on pathway.

**Pathway takes into consideration** the difference in staging between HPV negative and positive disease

**Plan for total cisplatin** dose ≥ 200 mg/m² (either as 100 mg/m² IV every 3 weeks for 3 cycles or 40 mg/m² IV weekly with concurrent radiation); candidates for high-dose cisplatin should be ECOG PS 0-1 with minimal comorbidities, as toxicities may be anticipated (i.e. nephrotoxicity, neutropenia, nausea/vomiting, etc.);

**If not cisplatin-eligible**, prescribe carboplatin-fluorouracil or carboplatin-paclitaxel
Head and Neck Cancer – Hypopharynx T1-2, N0, M0

Hypopharynx T1-2, N0, M0

Patient preference after shared decision making?

- Surgery
  - Resection with nodal-basin dissection
  - Adverse features? b
    - Yes → Extraneous extension or positive margins?
      - Yes → Cisplatin with radiation c
      - No → Surveillance
    - No → Radiation

- Radiation
  - Radiation to primary site and nodal-basin

Clinical trial(s) always considered on pathway.

a Evaluate need for support regarding tobacco use/smoking cessation, dental health, nutrition, audiology, speech/swallowing.

b Adverse features include extranodal extension, positive margins, close margins, pT3 or pT4 primary, pN2 or pN3 nodal disease, nodal disease in levels IV or V, perineural invasion, perivascular/vascular invasion, or lymphatic invasion.

c Plan for total cisplatin dose ≥ 200 mg/m² (either as 100 mg/m² IV every 3 weeks for 3 cycles or 40 mg/m² IV weekly with concurrent radiation); candidates for high-dose cisplatin should be ECOG PS 0-1 with minimal comorbidities, as toxicities may be anticipated (i.e. nephrotoxicity, neutropenia, nausea/vomiting, etc.); if not cisplatin-eligible, prescribe carboplatin-fluorouracil or carboplatin-paclitaxel.
Head and Neck Cancer – Hypopharynx T1-4, N1-3 and T3-4, N0, M0

Hypopharynx T1-4, N1-3 and T3-4, N0, M0 a

Candidate for functional organ preservation?

Yes

Evaluate need for support regarding tobacco use/smoking cessation, dental health, nutrition, audiology, speech/swallowing

No

Resection with nodal-basin dissection

Adverse features? c

Yes

Extranodal extension or positive margins?

Yes

Docetaxel, cisplatin, and fluorouracil

Radiation with carboplatin

No

Surveillance

No

High risk for distant metastases or bulky nodal disease? b

Yes

Surveillance

No

Radiation and cisplatin

Clinical trial(s) always considered on pathway.

a Evaluate need for support regarding tobacco use/smoking cessation, dental health, nutrition, audiology, speech/swallowing

b Bulky nodal disease includes N2, N3

c Adverse features include extranodal extension, positive margins, close margins, pT3 or pT4 primary, pN2 or pN3 nodal disease, nodal disease in levels IV or V, perineural invasion, perivascular/vascular invasion, or lymphatic invasion

d Plan for total cisplatin dose ≥ 200 mg/m² (either as 100 mg/m² IV every 3 weeks for 3 cycles or 40 mg/m² IV weekly with concurrent radiation); candidates for high-dose cisplatin should be ECOG PS 0-1 with minimal comorbidities, as toxicities may be anticipated (i.e. nephrotoxicity, neutropenia, nausea/vomiting, etc.); if not cisplatin-eligible, prescribe carboplatin-fluorouracil or carboplatin-paclitaxel
Head and Neck Cancer – Larynx Supraglottis T1-2, N0, M0

Clinical trial(s) always considered on pathway.

Larynx Supraglottis T1-2, N0, M0

Patient preference after shared decision making?

- Radiation to primary site and nodal-basin
- Surgery
- Resection with nodal-basin dissection

Adverse features? b

- Yes
- No

Extranodal extension or positive margins?

- Yes
- No

Surveillance

- Radiation
- Cisplatin with radiation c

Evaluate need for support regarding tobacco use/smoking cessation, dental health, nutrition, audiology, speech/swallowing a

Adverse features include extranodal extension, positive margins, close margins, pT3 or pT4 primary, pN2 or pN3 nodal disease, nodal disease in levels IV or V, perineural invasion, perivascular/vascular invasion, or lymphatic invasion b

Plan for total cisplatin dose ≥ 200 mg/m² (either as 100 mg/m² IV every 3 weeks for 3 cycles or 40 mg/m² IV weekly with concurrent radiation); candidates for high-dose cisplatin should be ECOG PS 0-1 with minimal comorbidities, as toxicities may be anticipated (i.e. nephrotoxicity, neutropenia, nausea/vomiting, etc.); if not cisplatin-eligible, prescribe carboplatin-fluorouracil or carboplatin-paclitaxel c
Head and Neck Cancer – Larynx Supraglottis T1-4, N1-3 and T3-4, N0, M0

Clinical trial(s) always considered on pathway.

**a** Evaluate need for support regarding tobacco use/smoking cessation, dental health, nutrition, audiology, speech/swallowing

**b** Adverse features include extranodal extension, positive margins, close margins, pT3 or pT4 primary, pN2 or pN3 nodal disease, nodal disease in levels IV or V, perineural invasion, perivascular/vascular invasion, or lymphatic invasion

**c** Plan for total cisplatin dose ≥ 200 mg/m² (either as 100 mg/m² IV every 3 weeks for 3 cycles or 40 mg/m² IV weekly with concurrent radiation); candidates for high-dose cisplatin should be ECOG PS 0-1 with minimal comorbidities, as toxicities may be anticipated (i.e. nephrotoxicity, neutropenia, nausea/vomiting, etc.); if not cisplatin-eligible, prescribe carboplatin-fluorouracil or carboplatin-paclitaxel

---

Larynx Supraglottis T1-4, N1-3 and T3-4, N0, M0

Candidate for functional organ preservation and no significant cartilage invasion?

- **Yes**
  - Candidate for partial laryngectomy with nodal basin dissection?
    - **Yes**
      - Total laryngectomy with nodal-basin dissection
    - **No**
      - Adverse features?
        - **Yes**
          - Radiation to primary site and nodal-basin with cisplatin
        - **No**
          - Surveillance

- **No**
  - Candidate for partial laryngectomy with nodal basin dissection?
    - **Yes**
      - Total laryngectomy with nodal-basin dissection
    - **No**
      - Adverse features?
        - **Yes**
          - Radiation to primary site and nodal-basin with cisplatin
        - **No**
          - Surveillance

Extranodal extension or positive margins?

- **Yes**
  - Cisplatin with radiation
- **No**
  - Radiation
**Head and Neck Cancer – Larynx Glottis T1-2, N0, M0**

- **Patient preference after shared decision making?**
  - Resection
  - Radiation to primary site

- **Positive margins?**
  - Yes
  - No
    - Surveillance
    - Further surgery?
      - Yes
      - No

Clinical trial(s) always considered on pathway.

- **Evaluate need for support regarding** tobacco use/smoking cessation, dental health, nutrition, audiology, speech/swallowing
- **Consider** voice quality, swallowing function, and ability to adhere to radiation protocols
- **Surgical options include** cold steel versus laser
Head and Neck Cancer – Larynx Glottis T1-4, N1-3 and T3-4, N0, M0

Clinical trial(s) always considered on pathway.

- **Evaluate need for support regarding** tobacco use/smoking cessation, dental health, nutrition, audiology, speech/swallowing
- **If patient T4** with obvious cartilage invasion, laryngectomy with nodal basis dissection is preferred
- **Adverse features include** extranodal extension, positive margins, close margins, pT3 or pT4 primary, pN2 or pN3 nodal disease, nodal disease in levels IV or V, perineural invasion, perivascular/vascular invasion, or lymphatic invasion
- **Plan for total cisplatin** dose ≥ 200 mg/m² (either as 100 mg/m² IV every 3 weeks for 3 cycles or 40 mg/m² IV weekly with concurrent radiation); candidates for high-dose cisplatin should be ECOG PS 0-1 with minimal comorbidities, as toxicities may be anticipated (i.e. nephrotoxicity, neutropenia, nausea/vomiting, etc.); if **not cisplatin-eligible**, prescribe carboplatin-fluorouracil or carboplatin-paclitaxel
Head and Neck Cancer – Larynx Subglottis T1-2, N0, M0

Patient preference after shared decision making? b

Larynx Subglottis T1-2, N0, M0 a

Surgery

Resection with nodal-basin dissection

Extranodal extension or positive margins?

No

Yes

Positive margin

Reresection feasible?

Yes

Reresection

No

Extranodal extension

Cisplatin with radiation c

Surveillance

Cisplatin with radiation c

Clinical trial(s) always considered on pathway.

a Evaluate need for support regarding tobacco use/smoking cessation, dental health, nutrition, audiology, speech/swallowing

b Patient preference and positive margins: consider voice quality, swallowing function, ability to adhere to radiation protocols, and patient preference

c Plan for total cisplatin dose ≥ 200 mg/m^2 (either as 100 mg/m^2 IV every 3 weeks for 3 cycles or 40 mg/m^2 IV weekly with concurrent radiation); candidates for high-dose cisplatin should be ECOG PS 0-1 with minimal comorbidities, as toxicities may be anticipated (i.e. nephrotoxicity, neutropenia, nausea/vomiting, etc.); if not cisplatin-eligible, prescribe carboplatin-fluorouracil or carboplatin-paclitaxel
Head and Neck Cancer – Larynx Subglottis T1-4, N1-3 and T3-4, N0, M0

Clinical trial(s) always considered on pathway.

**a** Evaluate need for support regarding tobacco use/smoking cessation, dental health, nutrition, audiology, speech/swallowing

**b** Consider consultation with thoracic surgery

**c** Adverse features include extranodal extension, positive margins, close margins, pT3 or pT4 primary, pN2 or pN3 nodal disease, nodal disease in levels IV or V, perineural invasion, perivascular/vascular invasion, or lymphatic invasion

**d** Plan for total cisplatin dose > 200 mg/m² (either as 100 mg/m² IV every 3 weeks for 3 cycles or 40 mg/m² IV weekly with concurrent radiation); candidates for high-dose cisplatin should be ECOG PS 0-1 with minimal comorbidities, as toxicities may be anticipated (i.e. nephrotoxicity, neutropenia, nausea/vomiting, etc.). If not cisplatin-eligible, prescribe carboplatin-fluorouracil or carboplatin-paclitaxel
Head and Neck Cancer – Nasopharynx T1, N0, M0

Nasopharynx T1, N0, M0 \(^a\) → EBV testing, PET/CT, and MRI to include skull base → Radiation to primary site and nodal basin

Clinical trial(s) always considered on pathway.

\(^a\) Evaluate need for support regarding tobacco use/smoking cessation, dental health, nutrition, audiology, speech/swallowing
Head and Neck Cancer – Nasopharynx T0-1, N1, M0; T2, N0, M0; and T2, N1, M0

Nasopharynx T0-1, N1, M0; T2, N0, M0; and T2, N1, M0

EBV testing, PET/CT, and MRI to include skull base

High risk features? b

Yes → Cisplatin with radiation c

No → Radiation

Clinical trial(s) always considered on pathway.

a Evaluate need for support regarding tobacco use/smoking cessation, dental health, nutrition, audiology, speech/swallowing

b High risk features include bulky disease and elevated EBV titers

c Plan for total cisplatin dose ≥ 200 mg/m² (either as 100 mg/m² IV every 3 weeks for 3 cycles or 40 mg/m² IV weekly with concurrent radiation); candidates for high-dose cisplatin should be ECOG PS 0-1 with minimal comorbidities, as toxicities may be anticipated (i.e. nephrotoxicity, neutropenia, nausea/vomiting, etc.); if not cisplatin-eligible, prescribe carboplatin-fluorouracil or carboplatin-paclitaxel
Head and Neck Cancer – Nasopharynx T3-4, N0-3, M0

Nasopharynx T3-4, N0-3, M0 → Adequate performance status?
  Yes → EBV associated disease?
    Yes → Cisplatin with gemcitabine
    No → Docetaxel, cisplatin, and fluorouracil
  No → Cisplatin with radiation

Clinical trial(s) always considered on pathway.

Plan for total cisplatin dose ≥ 200 mg/m² (either as 100 mg/m² IV every 3 weeks for 3 cycles or 40 mg/m² IV weekly with concurrent radiation); candidates for high-dose cisplatin should be ECOG PS 0-1 with minimal comorbidities, as toxicities may be anticipated (i.e. nephrotoxicity, neutropenia, nausea/vomiting, etc.); if not cisplatin-eligible, prescribe carboplatin-fluorouracil or carboplatin-paclitaxel

EBV Epstein-Barr Virus
Head and Neck Cancer – Local or Regional Recurrent Disease

Clinical trial(s) always considered on pathway.
Head and Neck Cancer – Metastatic or Recurrent Disease

**Metastatic or Recurrent Disease**

- **Candidate for systemic therapy?**
  - Yes: PD-L1 by CPS via IHC 22C3 pharmDx
  - No: Palliative care

**≥ 1?**

- Yes: Candidate for platinum? (a)
  - Yes: Candidate for immunotherapy?
    - Yes: Pembrolizumab, platinum, and fluorouracil
    - No: Pembrolizumab
  - No: Pembrolizumab, platinum, and fluorouracil

- No: Progression?
  - No: Surveillance
  - Yes: Docetaxel

---

**Clinical trial(s) always considered on pathway.**

- **Patient not eligible** for localized therapies
- **Palliative Care**, consider palliative radiation
- **Candidacy** based on platinum toxicities such as adequate cell counts, severe neuropathy, hearing loss/tinnitus, renal failure toxicity, and/or need for rapid cytoreduction
- **Pembrolizumab**, duration maximum of two years
- **If not docetaxel eligible**, prescribe cetuximab
- CPS Combined Positive Score
Head and Neck Cancer – Unknown Primary

- **Unknown Primary** (based on needle biopsy of nodes)
- **HPV and EBV testing and PET/CT**
- **Direct laryngoscopy with directed biopsy**
- **Primary found?**
  - Yes
    - Follow appropriate pathway
  - No
    - **N1**
      - Patient preference after shared decision making?
        - Yes
          - Neck dissection
        - No
          - Radiation and cisplatin
    - **N2-3**
      - Radiation and cisplatin

**Clinical trial(s) always considered on pathway.**

- **Directed biopsy** of bilateral base of tongue, lingual tonsils, palatine tonsils; if Level 5 node positive, include nasopharynx
- **Tonsillectomy** should be considered unless patient has very small, soft palatine tonsils
- **Appropriate Pathway** if HPV positive follow oropharynx pathway; if EBV positive follow the nasopharynx pathway
- **Plan for total cisplatin dose > 200 mg/m^2** (either as 100 mg/m^2 IV every 3 weeks for 3 cycles or 40 mg/m^2 IV weekly with concurrent radiation); candidates for high-dose cisplatin should be ECOG PS 0-1 with minimal comorbidities, as toxicities may be anticipated (i.e. nephrotoxicity, neutropenia, nausea/vomiting, etc.). **If not cisplatin-eligible**, prescribe carboplatin-fluorouracil or carboplatin-paclitaxel.
Questions?

Contact VHAOncologyPathways@va.gov