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### Section Name: Workup

The workup section outlines the initial steps for diagnosing glottic larynx cancer. It includes a comprehensive history and physical examination (H&P), which should document tobacco and alcohol use, and provide counseling for smoking cessation. A biopsy of the primary site is required, and direct laryngoscopy under anesthesia is generally recommended. Imaging studies such as CT scans with contrast and possibly MRI are used to evaluate the larynx and neck. Additional evaluations may include chest CT, FDG-PET/CT, pulmonary function tests, dental evaluation, and nutrition, speech, and swallowing therapy. Multidisciplinary consultation is advised as clinically indicated.

### Section Name: Clinical Staging

Clinical staging involves categorizing the cancer based on its aggressiveness. It starts with carcinoma in situ, which is non-invasive, and progresses through stages T1-T4. Staging is based on H&P, biopsy, and imaging studies. For T1-T2, larynx-preserving surgeries are considered, while more advanced stages like T3 or T4 may require total laryngectomy. Additional evaluations such as videostrobe, audiogram, and fertility counseling may be considered.

### Section Name: Treatment

Treatment recommendations vary by stage. Carcinoma in situ may be treated with larynx-preserving surgery. T1-T2 stages may also be amenable to conservation surgery. T3 stages may require total laryngectomy, especially if nodal involvement is present. T4a disease and unresectable or metastatic cases require more complex interventions. The guidelines emphasize the importance of multidisciplinary consultations and consider clinical trials as the best management option.

### Section Name: Additional Notes

Additional notes include the use of image-guided needle biopsy for better diagnostic yield, principles of imaging, dental evaluation, and nutrition management. The guidelines also address fertility and reproductive considerations, and note that nodal disease in glottic tumors is rare.

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### Section Name: Clinical Staging

**Clinical Staging**: The flowchart begins with “Carcinoma in situ” and progresses to determine the amenability of the patient to larynx-preserving surgery, specifically for tumors classified as T1 to T2, N0, or select T3, N0. This initial assessment is critical as it drives treatment decisions. In SOURCE2, it is noted that nodal disease in such glottic tumors is rare.

### Section Name: Treatment of Primary and Neck

**Treatment of Primary and Neck**: If the condition allows for larynx-preserving options, the preferred treatment is endoscopic resection or radiation therapy (RT). Alternative options include partial laryngectomy or a more extensive endoscopic/open resection

with neck dissection, depending on the specific characteristics of the tumor. SOURCE2 specifies that endoscopic resection is preferred, and RT or partial laryngectomy/endoscopic or open resection is indicated as needed.

### Section Name: Adjuvant Treatment

**Adjuvant Treatment**: Following surgical intervention, the presence of adverse pathologic features (such as extranodal extension or positive margins) necessitates different adjuvant strategies. For cases without adverse features, the protocol may involve simple observation, while those exhibiting high-risk characteristics may require systemic therapy or additional radiation. SOURCE2 lists adverse pathologic features including extranodal extension, positive margins, and other risk features.

### Section Name: Follow-Up

**Follow-Up**: The flowchart concludes with follow-up strategies which are essential for monitoring recurrence or persistent disease. This part of the chart emphasizes the importance of continual assessment post-treatment to ensure any signs of recurrence are addressed promptly. SOURCE2 mentions observation, systemic therapy/RT, re-resection if feasible, and follow-up for recurrent or persistent disease.

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### Section Name: Flowchart Structure

1. **Clinical Staging**: The flow begins with the clinical staging of T3 tumors that require total laryngectomy (N2–3). This staging is crucial for determining the appropriate therapeutic approach.
2. **Treatment Options**:
    - The flowchart provides multiple pathways for treatment, indicating that patients may undergo either "Concurrent systemic therapy/RT" or "Surgery."
    - There is also an option for "Induction chemotherapy," leading to further imaging (CT or MRI) to assess the primary site and neck status.
3. **Adverse Pathologic Features**: For patients who have surgery, the flowchart distinguishes between those with adverse pathologic features and those without. Patients with adverse features—such as extranodal extension or positive margins—are directed toward systemic therapy or radiation treatment, while those without may follow a different management path.
4. **Follow-up and Recurrence**: The flowchart concludes by outlining follow-up procedures for recurrent or persistent disease, suggesting additional assessments and treatments based on the risk features identified during earlier stages.

### Section Name: Detailed Explanation

The flowchart is designed to provide healthcare professionals with a systematic pathway for managing glottic larynx cancer. Each step is meticulously organized to ensure that important factors are considered, such as the presence of adverse pathological features, which strongly influence treatment decisions.
The emphasis on concurrent treatments, such as systemic therapy combined with radiation, reflects current best practices in oncology, where multimodal approaches are often necessary to achieve better outcomes. The inclusion of clinical trials

indicates an emphasis on maintaining up-to-date practices and personalized treatment plans as part of patient management strategies.
Furthermore, the chart's organization into treatment and follow-up segments allows for a straightforward interpretation, guiding oncologists through complex decisions in a logical manner. This can improve consistency in care and enhance patient safety through meticulous monitoring and responses to treatment efficacy or disease progression.
In summary, this flowchart serves as an essential resource for oncologists, facilitating a better understanding of treatment protocols for glottic larynx cancer while promoting a patient-centered approach to oncological care.

### Section Name: Principles of Treatment

- **Principles of Radiation Therapy (GLOT-A)**
- **Principles of Surgery (SURG-A)**
- **Adverse Pathologic Features:**
  - Extranodal extension
  - Positive margins
  - Close margins
  - pT4 primary
  - pN2 or pN3 nodal disease
  - Perineural invasion
  - Vascular invasion
  - Lymphatic invasion
  - Subglottic extension

### Section Name: Clinical Staging

- **Adjuvant Treatment**
- **Treatment of Primary and Neck**
- **Follow-up (FOLL-A, 1 of 2)**
- **Recurrent or Persistent Disease (ADV-3)**

### Section Name: Treatment Options

- **T3 requiring (amenable to) total laryngectomy (N2–3):**
  - Concurrent systemic therapy/RT
  - Surgery
  - Induction chemotherapy
  - Clinical trials
- **Response Assessment (GLOT-5)**

### Section Name: Surgical Considerations

- **Laryngectomy with thyroidectomy as indicated, ipsilateral or bilateral neck dissection, and pretracheal and ipsilateral paratracheal lymph node dissection**

### Section Name: Pathologic Features

- **No adverse pathologic features**
- **Adverse pathologic features:**
  - Extranodal extension and/or positive margin
  - Other risk features

### Section Name: Systemic Therapy

- **Systemic therapy/RT (category 1)**

- **RT**
- **Consider systemic therapy/RT**

### Section Name: Imaging

- **CT (with contrast) or MRI (with and without contrast) of primary and neck**

### Section Name: Post-Treatment Evaluation

- **Post Systemic Therapy/RT or RT Neck Evaluation (FOLL-A, 2 of 2)**
- **pN1 without other risk features**
- **Consider RT**

### Section Name: Additional Notes

- **Principles of Systemic Therapy for Non-Nasopharyngeal Cancers (SYST-A)**
- **When using concurrent systemic therapy/RT, the preferred agent is cisplatin (category 1). See Principles of Systemic Therapy for Non-Nasopharyngeal Cancers (SYST-A).**
- **See Discussion on induction chemotherapy.**

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### Section Name: Introduction

The image depicts a flowchart outlining the treatment guidelines for cancer of the glottic larynx, as provided by the National Comprehensive Cancer Network (NCCN). The flowchart is structured to guide healthcare professionals through clinical decision-making related to both primary and neck treatment, as well as adjuvant therapy, based on various clinical stages and specific patient conditions.

### Section Name: Clinical Staging and Treatment

At the top, the flowchart begins with a clinical staging indicator labeled "T4a,N0–3," which relates to the severity of the cancer and the involvement of lymph nodes. It emphasizes the importance of surgical intervention, highlighting procedures such as bilateral neck dissection and the need to address certain pathologic features.

- **Clinical Staging:**
    - T4a, N0–3
    - Selected T4a patients who decline surgery
- **Treatment of Primary and Neck:**
    - Consider concurrent systemic therapy/RT or clinical trial for function-preserving surgical or RT management or induction chemotherapy.

### Section Name: Principles of Treatment

**Principles of Treatment**

- **Principles of Radiation Therapy (GLOT-A):**
    - Adverse pathologic features: extranodal extension, positive margins, close margins, pT4 primary, pN2 or pN3 nodal disease, perineural

invasion, vascular invasion, lymphatic invasion, and subglottic extension (Discussion).

- **Principles of Surgery (SURG-A):**
    - Surgery, including ipsilateral or bilateral neck dissection; thyroidectomy to clear central compartment nodes, especially when there is thyroid cartilage with gross invasion of the thyroid gland and significant subglottic extension.

### Section Name: Adjuvant Treatment and Follow-up

In cases where adverse features such as extralateral extension or positive margins are present, specific treatments are suggested. The guidelines recommend considering options like concurrent systemic therapy or clinical trials for patients who decline surgery.

- **Adjuvant Treatment:**
    - CT (with contrast) or MRI (with and without contrast) of primary and neck.
- **Follow-up (FOLL-A, 1 of 2):**
    - Recurrent or persistent disease (ADV-3).
- **Post Systemic Therapy/RT or RT Neck Evaluation (FOLL-A, 2 of 2):**
    - pN1 without other risk features: Consider RT.

### Section Name: Response Assessment

As the flowchart progresses to the adjuvant treatment section, it depicts further decision points based on treatment responses and disease recurrence. The inclusion of references to follow-up assessments, such as CT or MRI scans, underscores the emphasis on continuous monitoring and evaluation of treatment efficacy.

- **Response Assessment (GLOT-5):**
    - Recurrent or persistent disease (ADV-3).

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### Section Name: Overview of Radiation Therapy Guidelines

The image presents a detailed flowchart outlining the principles of radiation therapy specifically for the treatment of cancer in the glottic larynx, as per the National Comprehensive Cancer Network (NCCN) guidelines (version 2.2024). This structured guidance delineates various treatment protocols, stratified by risk levels and therapeutic approaches.

### Section Name: Principles of Radiation Therapy

**Definitive: RT Alone**

- **Tis, N0:** 60.75 Gy (2.25 Gy/fraction) to 66 Gy (2.0 Gy/fraction)
- **T1, N0:**
    - 63 Gy (2.25 Gy/fraction, preferred) to 66 Gy (2.0 Gy/fraction) or

    - 50 Gy (3.12 Gy/fraction) to 52 Gy (3.28 Gy/fraction)
- **T2, N0:** 65.25 Gy (2.25 Gy/fraction) to 70 Gy (2.0 Gy/fraction)
- **≥T2, N1:**
    - **PTV High risk:** Primary tumor and involved lymph nodes (includes possible local subclinical infiltration at the primary site and at the high-risk level lymph node(s))
        - Fractionation: 66 Gy (2.2 Gy/fraction) to 70 Gy (2.0 Gy/fraction); daily Monday–Friday in 6–7 weeks
        - Concomitant boost accelerated RT:
            - 72 Gy/6 weeks (1.8 Gy/fraction, large field; 1.5 Gy boost as second daily fraction during last 12 treatment days)
            - 66–70 Gy (2.0 Gy/fraction; 6 fractions/wk accelerated)
        - Hyperfractionation: 79.2–81.6 Gy/7 weeks (1.2 Gy/fraction, twice daily)
    - **Low to intermediate risk:** Sites of suspected subclinical spread
        - 44–50 Gy (2.0 Gy/fraction) to 54–63 Gy (1.6–1.8 Gy/fraction)

### Section Name: Concurrent Systemic Therapy/RT

- **PTV High risk:** Typically 70 Gy (2.0 Gy/fraction)
- **Low to intermediate risk:** 44–50 Gy (2.0 Gy/fraction) to 54–63 Gy (1.6–1.8 Gy/fraction)

Based on published data, concurrent systemic therapy/RT most commonly uses conventional fractionation at 2.0 Gy per fraction to a typical dose of 70 Gy in 7 weeks with single-agent cisplatin given every 3 weeks at 100 mg/m$^2$; 2–3 cycles of chemotherapy are used depending on the radiation fractionation scheme (RTOG 0129). When carboplatin and 5-FU are used, the recommended regimen is standard fractionation plus 3 cycles of chemotherapy. Other fraction sizes (e.g., 1.8 Gy, conventional), multiagent chemotherapy, other dosing schedules of cisplatin, or altered fractionation with chemotherapy are efficacious, and there is no consensus on the optimal approach.

In general, the use of concurrent systemic therapy/RT carries a high toxicity burden; multiagent chemotherapy will likely further increase the toxicity burden. For any systemic therapy/RT approach, close attention should be paid to published reports for the specific chemotherapy agent, dose, and schedule of administration. Systemic therapy/RT should be performed by an experienced team and should include substantial supportive care.

### Section Name: Treatment Modalities

Further breakdown in the guidelines suggests either Intensity-Modulated Radiation Therapy (IMRT) or 3D Conformal Radiation Therapy (3D-CRT) as delivery methods, contingent upon patient-specific considerations. These advanced techniques are employed to optimize treatment accuracy, preserving surrounding healthy tissue and improving overall patient outcomes. Moreover, a focus on concurrent systemic therapies underlines the importance of integrating chemotherapy, particularly for patients with more aggressive forms of cancer or those demonstrating advanced disease characteristics.

### Section Name: Additional Information

All recommendations are category 2A unless otherwise indicated. Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged. Either IMRT (preferred) or 3D-CRT is recommended.

### Section Name: Conclusion

In summary, the flowchart succinctly encapsulates multifaceted treatment paradigms for glottic larynx cancer. It underscores the necessity of personalized treatment plans that adapt to the nuances of each patient's condition, promoting effective management and improved prognosis. This structured guideline aims to help healthcare professionals deliver clear, evidence-based interventions while considering the complexities involved in cancer treatment.

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### Section Name: SUPRA-1

- **a** H&P should include documentation and quantification (pack years smoked) of tobacco use history, as well as alcohol use and counseling. All patients who currently smoke should be advised to quit smoking, and those who formerly smoked should be advised to remain abstinent from smoking. For additional cessation support, refer to the Patient/Provider Smoking Cessation and Treatment Resources in the NCCN Guidelines for Smoking Cessation.
- **b** Screen for depression (NCCN Guidelines for Distress Management).
- **c** Image-guided (US or CT) needle biopsy of cystic neck nodes may offer better diagnostic yield than FNA by palpation alone for initial diagnosis in this setting. For unresectable or metastatic disease where there is a plan for systemic therapy, a core biopsy would allow for ancillary immune-genomic testing.

### Section Name: WORKUP

#### WORKUP

The "WORKUP" section details the essential initial assessments and procedures that must be conducted. It begins with a comprehensive history and physical examination, emphasizing the need for an exhaustive evaluation of both the head and neck, including any necessary biopsies of the primary tumor site or fine-needle aspiration (FNA) of cervical lymph nodes. Additional imaging techniques, such as chest CT scans and contrast-enhanced imaging (CT or MRI), are recommended to assess the extent of the disease. The guideline suggests considering advanced imaging methods like FDG-PET/CT and endoscopic examinations when clinically indicated.

#### Clinical Staging

- **Amenable to larynx-preserving (conservation) surgery**
  (Most T1–2, N0; selected T3)
    - **Treatment of Primary and Neck (SUPRA-2)**
    - **H&P** including a complete head and neck exam; mirror and/or fiberoptic examination as clinically indicated
    - **Biopsy of primary site or FNA of the neck**
    - **Chest CT (with or without contrast) as clinically indicated**

    - **CT with contrast and thin angled cuts through larynx and/or MRI with and without contrast of primary and neck**
    - **Consider FDG-PET/CT**
    - **EUA with endoscopy**
    - **As clinically indicated:**
        - Preanesthesia studies
        - Consider PFTs for conservation surgery candidates
        - Consider videostrobe for select patients
        - Dental evaluation
        - Nutrition, speech and swallowing evaluation/therapy
        - Audiogram
        - Smoking cessation counseling
        - Fertility/reproductive counseling
        - Screening for hepatitis B
    - **Multidisciplinary consultation as clinically indicated**
- **Requiring (amenable to) total laryngectomy (T3, N0)**
    - T4a, N0
    - Node-positive disease
    - T4b, N0–3
    - or Unresectable nodal disease or Unfit for surgery
    - Metastatic (M1) disease at initial presentation
    - **Treatment of Primary and Neck (SUPRA-3)**
    - **Treatment of Primary and Neck (SUPRA-8)**
    - **Clinical Staging (SUPRA-4)**
    - **Treatment of Very Advanced Head and Neck Cancer (ADV-1)**
    - **Treatment of Very Advanced Head and Neck Cancer (ADV-2)**

### Section Name: Principles

**Principles**

- **Principles of Imaging (IMG-A)**
- **Principles of Dental Evaluation and Management (DENT-A)**
- **Principles of Nutrition: Management and Supportive Care (NUTR-A)**
- **See fertility and reproductive endocrine considerations in the NCCN Guidelines for Adolescent and Young Adult (AYA) Oncology.**

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### Section Name: Introduction

The provided image is a detailed flowchart from the National Comprehensive Cancer Network (NCCN) guidelines regarding the clinical staging and treatment protocols for cancer of the supraglottic larynx. This flowchart is structured to guide healthcare professionals through the stages of treatment based on clinical findings, emphasizing the complexity and systematic approach required in managing this type of cancer.

### Section Name: Clinical Staging

The flowchart begins with the clinical staging criteria, specifically focusing on cases that require total laryngectomy, denoted as requiring (amenable to) total

laryngectomy (T3, N0). This categorization is crucial as it forms the basis for determining the appropriate treatment strategy.

### Section Name: Treatment of Primary and Neck

Once clinical staging is established, the chart outlines various treatment options. The initial step may involve either concurrent systemic therapy combined with radiation therapy (RT) or opting for RT alone, especially if the patient is not a medical candidate for both therapies. Laryngectomy, thyroidectomy, and neck dissection are considered based on the extent of lymph node involvement.

### Section Name: Surgical Options

If concurrent therapies are not suitable, the chart presents laryngectomy combined with thyroidectomy, depending on the extent of lymph node dissection required. This highlights surgical intervention as a viable option in the management of advanced cases.

### Section Name: Induction Chemotherapy

The flowchart also considers the option of induction chemotherapy in cases where immediate surgical intervention is either not feasible or considered insufficient. This step is particularly key for tailoring therapeutic approaches tailored to individual patient needs.

### Section Name: Adjuvant Treatment

Following primary treatment, the flowchart addresses the potential for adjuvant treatment pathways. This may include systemic therapy, RT, or further evaluations based on the patient's response and any recurrence or persistent disease. It emphasizes the need for follow-up assessments to evaluate treatment efficacy.

### Section Name: Risk Features and Response Assessment

The chart incorporates a segment that takes into account adverse pathologic features, such as extramural extension or positive margins, which could influence subsequent treatment decisions. This highlights the importance of ongoing assessment in the management of cancer, leading to response evaluation and adjustments to treatment as necessary.

### Section Name: SUPRA-3

- **Requiring (amenable to) total laryngectomy (T3,N0)**
  - Concurrent systemic therapy/RT[i,k,l] or RT[i] if patient not medical candidate for concurrent systemic therapy/RT
  - Laryngectomy, thyroidectomy and with ipsilateral, central, or bilateral neck dissection[h]
  - or
  - Induction chemotherapy[k,m]
  - or
  - Clinical trials

### Section Name: Follow-up

- **Follow-up (FOLL-A, 1 of 2)**

- Recurrent or persistent disease (ADV-3)

### Section Name: Adverse Pathologic Features

- **pN1 without other risk features**[j]
  - Adverse pathologic features[j]
  - Consider RT[h]
  - Extranodal extension and/or positive margin
  - Other risk features
  - Systemic therapy/RT[i,k] (category 1)
  - RT[i] or Consider systemic therapy/RT[i,k]

### Section Name: Response Assessment

**Response Assessment (SUPRA-7)**

### Section Name: Principles of Surgery and Radiation Therapy

**Principles of Surgery (SURG-A).**

**Principles of Radiation Therapy (SUPRA-A).**

### Section Name: Principles of Systemic Therapy

**Principles of Systemic Therapy for Non-Nasopharyngeal Cancers (SYST-A).**

**When using concurrent systemic therapy/RT, the preferred agent is cisplatin (category 1).** See Principles of Systemic Therapy for Non-Nasopharyngeal Cancers (SYST-A).

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### Section Name: Introduction

The provided image is a flowchart outlining the NCCN (National Comprehensive Cancer Network) guidelines for the treatment of cancers of the supraglottic larynx. This flowchart utilizes a highly structured approach to convey clinical staging and treatment strategies, indicating the various pathways based on patient conditions and disease features.

## Cancer of the Supraglottic Larynx

### Note

- All recommendations are category 2A unless otherwise indicated.
- **Clinical Trials**: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

### Section Name: Key Components of the Flowchart

**Key Components of the Flowchart**

1. **Clinical Staging**: The flowchart starts with clinical staging, indicating that patients must first be evaluated to determine the extent of cancer. This is essential for deciding on appropriate treatment options.

2. **Treatment of Primary and Neck**: The flowchart details multiple treatment strategies, including:
    - **Concurrent systemic therapy/RT**: This suggests a combination approach for patients eligible for such treatment.
    - **Definitive Radiation Therapy (RT)**: Recommended for low-volume diseases or patients who cannot tolerate systemic therapy.
    - **Surgical Options**: It highlights options such as endoscopic or open partial laryngectomy and neck dissection, which are contingent on clinical evaluations.
3. **Evaluation and Follow-Up**: After initial treatment approaches, the chart directs clinicians to perform a "Post Systemic Therapy/RT or RT Neck Evaluation." This step assesses whether there are adverse pathologic features, guiding subsequent treatment decisions.
4. **Adverse and No Adverse Features**: The decision pathway diverges based on findings:
    - Patients with **adverse pathologic features** may have additional diagnostic imaging (CT or MRI) and may require further systemic treatment.
    - Patients with **no adverse features** may be directed towards considerations for radiation therapy.
5. **Adjuvant Treatment and Recurrence**: The chart also addresses management of any recurrent or persistent disease, emphasizing the importance of regular follow-up assessments. Various options for adjuvant treatment are mentioned, focusing on tailored approaches towards ongoing management of the disease.
6. **Clinical Trials**: The flowchart encourages participation in clinical trials, indicating a commitment to exploring new treatments and improving patient outcomes.

## Section Name: Principles

**Principles**

- **Principles of Imaging (IMG-A)**
- **Principles of Surgery (SURG-A)**
- **Principles of Radiation Therapy (SUPRA-A)**
- **Principles of Systemic Therapy for Non-Nasopharyngeal Cancers (SYST-A)**

## Section Name: Adverse Pathologic Features

**Adverse Pathologic Features**

- Extranodal extension
- Positive margins
- Close margins
- pT3 or pT4 primary
- pN2 or pN3 nodal disease
- Perineural invasion
- Vascular invasion
- Lymphatic invasion

## Section Name: Clinical Staging and Treatment of Primary and Neck

**Clinical Staging**

**Treatment of Primary and Neck**

- **Adjuvant Treatment**
- **Follow-up** (FOLL-A, 1 of 2)

- **Recurrent or Persistent Disease** (ADV-3)

**Treatment Options**

- **Amenable to Larynx-Preserving (Conservation) Surgery**: T1–2, N+ and selected T3, N1
- **Concurrent Systemic Therapy/RT**: i, k, l
- **Clinical Trials or Definitive RT**: i
- **Endoscopic or Open Partial Laryngectomy and Neck Dissection(s)**: h
- **Induction Chemotherapy**: k, m

### Section Name: Pathologic Features and Response Assessment

**Pathologic Features**

- **No Adverse Pathologic Features**: j
  - Consider RT: i
- **Adverse Pathologic Features**: j
  - Extranodal extension and/or positive margin: n
  - Other risk features
  - Systemic therapy/RT: i, k (category 1)
  - Consider systemic therapy/RT: i, k

**Response Assessment**

- **Response Assessment** (SUPRA-7)

### Section Name: Imaging and Recurrent or Persistent Disease

**Imaging**

- CT (with contrast) or MRI (with and without contrast) of primary and neck: d

**Recurrent or Persistent Disease**

- **Post Systemic Therapy/RT or RT Neck Evaluation** (FOLL-A, 2 of 2)

### Section Name: Conclusion

**Conclusion**

The flowchart serves as a comprehensive guide for oncologists and healthcare providers, facilitating informed decision-making in the treatment of supraglottic larynx cancer. By visualizing the complex interactions between clinical staging, treatment strategies, and follow-up evaluations, it streamlines the management process, ensuring that patients receive appropriate care tailored to their specific needs. The detailed pathways not only enhance clinical efficacy but also underscore the importance of ongoing research and adaptation of treatment paradigms in oncology.

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### Section Name: Principles

**Principles**

- **Principles of Surgery (SURG-A)**
- **Principles of Radiation Therapy (SUPRA-A)**
- **Principles of Systemic Therapy for Non-Nasopharyngeal Cancers (SYST-A)**

### Section Name: Adverse Pathologic Features

**Adverse Pathologic Features**

- Extranodal extension
- Positive margins
- Close margins
- pT3 or pT4 primary
- pN2 or pN3 nodal disease
- Perineural invasion
- Vascular invasion
- Lymphatic invasion

## Section Name: Response Assessment

**Response Assessment**

- **Response after induction chemotherapy**:
    - **Primary site: CR**
    - **Primary site: PR**
    - **Primary site: < PR**
- **Treatment Options**:
    - **Definitive RT** (category 1)
    - **RT** (category 1) or systemic therapy/RT (category 2B)
    - **Surgery** or unresectable nodal disease

## Section Name: Follow-up

**Follow-up**

- **Follow-up** (FOLL-A, 1 of 2)
- **Recurrent or persistent disease** (ADV-3)

## Section Name: Risk Features

**Risk Features**

- **No adverse pathologic features**
- **Other risk features**
- **Adverse pathologic features**:
    - Extranodal extension and/or positive margin
    - **RT** or consider systemic therapy/RT

## Section Name: Post-Therapy Evaluation

**Post-Therapy Evaluation**

- **Post Systemic Therapy/RT or RT Neck Evaluation** (FOLL-A, 2 of 2)

## Section Name: Flowchart Overview

The image presented is a detailed flowchart from the NCCN Guidelines Version 2.2024 concerning the assessment and management of cancer of the supraglottic larynx. This flowchart serves as a systematic guide for healthcare professionals to evaluate patient responses following treatment, particularly focusing on the evaluation of the primary site and determining subsequent steps based on observed outcomes.

## Section Name: Assessment and Treatment Decisions

At the top of the flowchart, the assessment begins with the definition of responses to initial treatments such as induction chemotherapy. Three main response categories are recognized: Complete Response (CR), Partial Response (PR), and less than Partial Response (< PR). These categories are pivotal in determining the next steps. CR indicates full resolution of the disease at the primary site, leading to the consideration of definitive radiation therapy or the likelihood of surgery. Conversely, PR suggests that the disease has improved but not completely resolved, which directs the pathway towards either systemic therapy or continued radiation therapy, with further evaluation necessary.

### Section Name: Adverse Pathologic Features and Follow-up

The flowchart also accounts for the presence of adverse pathologic features — such as extranodal extension or positive margins — that can directly influence treatment decisions. If adverse features are found, surgical intervention is recommended. In cases where there are no adverse features, the patient may proceed directly to radiation therapy or continued systemic treatment, emphasizing the tailored approach based on the individual patient's disease characteristics.

Furthermore, the chart includes a section addressing the follow-up process after initial treatment. If there are signs of recurrent or persistent disease, additional evaluations and treatment modalities may be necessary. These evaluations lead to specific recommendations for advanced disease management, denoted as ADV-3 on the chart, emphasizing the importance of continuous monitoring and assessment in cancer care.

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### Section Name: Definitive Treatment

The document begins by defining the definitive radiation therapy (RT) approach for patients classified as T1–3, N0–1, with a specific focus on high-risk patients. It suggests a regimen involving conventional RT, particularly highlighting a total dose of 66 to 70 Gray (Gy) delivered in fractions of 2.0 Gy each. The schedule emphasizes daily treatments, indicating a typical 7-week plan.

### Section Name: Concurrent Therapy

It further elaborates on concurrent systemic therapy in combination with radiation treatment. High-risk patients may receive up to 70 Gy, while those with lower risks are advised to receive between 44 to 63 Gy, depending on their specific case. This section recommends careful consideration of systemic therapies like cisplatin, particularly every three weeks or in combination with pre-existing chemotherapy protocols.

### Section Name: Additional Techniques and Research

The document suggests employing either Intensity-Modulated Radiation Therapy (IMRT) or 3D-Conformal Radiation Therapy (3D-CRT) as preferred treatment modalities. It mentions that proton therapy could be beneficial under specific conditions and stresses the importance of minimizing treatment toxicity. This part indicates ongoing research into the efficacy and safety of various radiation techniques.

## Section Name: Practical Recommendations

It includes practical recommendations for treatment sequencing, emphasizing a tailored approach based on individual patient circumstances, and highlights the importance of multi-disciplinary collaboration in treatment planning. There’s an implicit suggestion for careful patient management due to the complexity and risks of concurrent systemic therapies.

## Section Name: SUPRA-A 1 OF 2

1. **See Principles of Radiation Techniques (RAD-A) and Discussion.**
2. For select T1–2, N0 tumors, accelerated fractionation may be used.
3. For doses >70 Gy, some clinicians feel that the fractionation should be slightly modified (e.g., <2.0 Gy/fraction for at least some of the treatment) to minimize toxicity. An additional 2–3 doses can be added depending on clinical circumstances.
4. Suggest 44–50 Gy in 3D-CRT and sequentially planned IMRT or 54–63 Gy with IMRT dose painting technique (dependent on dose per fraction).
5. **Principles of Systemic Therapy for Non-Nasopharyngeal Cancers (SYST-A).**
6. Based on published data, concurrent systemic therapy/RT most commonly uses conventional fractionation at 2.0 Gy per fraction to a typical dose of 70 Gy in 7 weeks with single-agent cisplatin given every 3 weeks at 100 mg/m$^2$; 2–3 cycles of chemotherapy are used depending on the radiation fractionation scheme (RTOG).
    - When carboplatin and 5-FU are used, the recommended regimen is standard fractionation plus 3 cycles of chemotherapy.
    - Other fraction sizes, multiagent chemotherapy, other dosing schedules of cisplatin, or altered fractionation with chemotherapy are efficacious, and there is no consensus on the optimal approach.
    - In general, the use of concurrent systemic therapy/RT carries a high toxicity burden; multiagent chemotherapy will likely further increase the toxicity burden. For any systemic therapy/RT approach, close attention should be paid to published reports for the specific chemotherapy agent, dose, and schedule of administration. Systemic therapy/RT should be performed by an experienced team and should include substantial supportive care.

## Section Name: Principles of Radiation Therapy

1. **DEFINITIVE: RT Alone**
    - T1–3, N0–1: 66–70 Gy conventional (2.0 Gy/fraction)
    - **PTV**
        - High risk: Primary tumor and involved lymph nodes [this includes possible local subclinical infiltration at the primary site and at the high-risk level lymph node(s)]
            - Fractionation: 66 Gy (2.2 Gy/fraction) to 70 Gy (2.0 Gy/fraction); daily Monday–Friday in 6–7 weeks
            - Concomitant boost accelerated RT:
                - 72 Gy/6 weeks (1.8 Gy/fraction, large field; 1.5 Gy boost as second daily fraction during last 12 treatment days)
                - 66–70 Gy (2.0 Gy/fraction; 6 fractions/wk accelerated)

        - Hyperfractionation: 79.2–81.6 Gy/7 weeks (1.2 Gy/fraction twice daily)
    - Low to intermediate risk: Sites of suspected subclinical spread
        - 44–50 Gy (2.0 Gy/fraction) to 54–63 Gy (1.6–1.8 Gy/fraction)

2. **CONCURRENT SYSTEMIC THERAPY/RT:**

    - **PTV**
        - High risk: Typically 70 Gy (2.0 Gy/fraction)
        - Low to intermediate and low risk: 44–50 Gy (2.0 Gy/fraction) to 54–63 Gy (1.6–1.8 Gy/fraction)
    - Either IMRT (preferred) or 3D-CRT is recommended.
    - Use of proton therapy is an area of active investigation. Proton therapy may be considered when normal tissue constraints cannot be met by photon-based therapy, or when photon-based therapy causes compromise of standard radiation dosing to tumor or postoperative volumes.

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### Section Name: Diagnosis Section

At the top of the flowchart, the diagnosis segment is highlighted, initiating the decision-making process. It notes that for patients presenting with metastatic disease, a clinical trial is the preferred pathway, emphasizing the critical nature of innovative therapies in advanced cancer care. The option to "Consider locoregional treatment based on primary site algorithms" suggests that specific treatment strategies may be tailored depending on the exact location and characteristics of the cancer.

### Section Name: Treatment Pathways

The treatment section branches into various pathways depending on the patient’s performance status (PS), which is a measure of their general well-being and ability to function.

- **For PS 0–1 Patients:**
  The flowchart indicates several treatment options, including combination systemic therapy, single-agent systemic therapy, surgery, and radiation therapy (RT). This group is highlighted as those who are most capable of handling intensive treatments and may benefit significantly from combination therapies.
- **For PS 2 Patients:**
  The recommended approach varies slightly, with a continued emphasis on systemic therapies, palliative radiation therapy, or best supportive care. This indicates a level of compromise in treatment options, suggesting that while aggressive treatment is still possible, the focus might shift more towards quality of life.
- **For PS 3 Patients:**
  The treatment options further narrow, still recommending systemic therapy or supportive care but highlighting palliative approaches, reflecting a

recognition of the more advanced disease and potentially limited treatment efficacy.

### Section Name: Principles of Treatment

- **Principles of Systemic Therapy for Non-Nasopharyngeal Cancers (SYST-A)**
- **Principles of Radiation Therapy (ADV-A)**
- **Principles of Surgery (SURG-A)**

### Section Name: Diagnosis and Treatment of Head and Neck Cancer

- **Metastatic (M1) disease at initial presentation:**
  - Clinical trial preferred
  - Distant metastases
  - Consider locoregional treatment based on primary site algorithms (Table of Contents)

**Performance Status (PS)**

- **PS 0–1:**
  - Combination systemic therapy or Single-agent systemic therapy or Surgery or RT or systemic therapy/RT for selected patients with limited metastases or Best supportive care
- **PS 2:**
  - Single-agent systemic therapy or Best supportive care ± Palliative RT or Palliative surgery
- **PS 3:**
  - Systemic therapy, clinical trial preferred or Palliative RT or Best supportive care

### Section Name: Persistent Disease or Progression

- Best supportive care or Alternate single-agent systemic therapy or Palliative RT

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### Section Name: Diagnosis

The diagnosis process for very advanced head and neck cancer involves categorizing patients based on their disease status. The guidelines differentiate between 'Recurrent or persistent disease' and 'Locoregional recurrence or persistent disease without prior RT (radiation therapy)'. This distinction is crucial as it influences subsequent treatment decisions. In cases of locoregional recurrence or persistent disease without prior RT, the disease can be classified as 'Resectable' or 'Unresectable'. If resectable, surgery is the preferred treatment. If unresectable, options include reirradiation with or without systemic therapy, and clinical trials are preferred.

### Section Name: Treatment of Very Advanced Head and Neck Cancer

The treatment of very advanced head and neck cancer involves several strategies. For resectable disease, surgery with or without postoperative reirradiation is recommended, and systemic therapy or RT is considered, with clinical trials preferred.

For unresectable disease, reirradiation with or without systemic therapy is recommended, and best supportive care is considered. The guidelines emphasize the importance of clinical trials and suggest that the best management of any patient with cancer is in a clinical trial.

### Section Name: Pathologic Features

Pathologic features play a significant role in determining the treatment approach. If no adverse pathologic features are present, observation and follow-up are recommended. However, if adverse pathologic features such as extranodal extension or positive margins are present, systemic therapy with RT is recommended. Other risk features may also warrant RT or systemic therapy with RT. The guidelines highlight the importance of considering these features in treatment planning.

### Section Name: Therapy for Persistent Disease

For persistent disease, the guidelines recommend therapy as indicated by the specific clinical scenario. This may include systemic therapy, RT, or a combination of both, depending on the presence of adverse pathologic features and other risk factors. The guidelines also suggest considering next-generation sequencing genomic profiling for biomarker identification to tailor treatment strategies.

### Section Name: Conclusion

The NCCN guidelines provide a comprehensive framework for the diagnosis and treatment of very advanced head and neck cancer. They emphasize evidence-based practices and the importance of clinical trials, advocating for an individualized approach to patient care. The guidelines serve as a critical resource for healthcare providers, ensuring that all potential treatment avenues are explored while considering patient-specific factors.

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### Section Name: Diagnosis

In the **Diagnosis** section, the focus is on recurrent or persistent disease with distant metastases. Clinical trials are preferred for patients diagnosed at this stage. If there is locoregional failure, locoregional treatment should be considered based on the extent of the disease and symptoms presented. This highlights the importance of personalized treatment approaches, taking into account the unique circumstances of each patient.

### Section Name: Treatment

The **Treatment** section outlines pathways based on performance status (PS).

- For **PS 0–1** patients, options include combination systemic therapy, single-agent systemic therapy, surgery, or best supportive care for those with limited metastases.
- For **PS 2** patients, recommendations include single-agent systemic therapy, supportive care, or palliative treatments.
- For **PS 3** patients, the focus is on single-agent therapy and best supportive care, with consideration of palliative radiation therapy (RT) and palliative

surgery.

This section addresses the evolving needs of patients as their performance status declines.

### Section Name: Persistent Disease or Progression

In the **Persistent Disease or Progression** section, the importance of continued evaluation of treatment efficacy is reiterated. Options include systemic therapy, clinical trials, or palliative care based on the specific patient condition. Best supportive care is emphasized, prioritizing the patient's quality of life, particularly in the context of advanced illness.

### Section Name: Principles and Considerations

- **Principles of Radiation Therapy (ADV-A).**
- **Principles of Surgery (SURG-A).**
- Consider NGS genomic profiling for biomarker identification.
- Consider palliative RT as clinically indicated (e.g., bone metastases) (RAD-A).
- See Principles of Systemic Therapy for Non-Nasopharyngeal Cancers (SYST-A) or Systemic Therapy for Nasopharyngeal Cancers (NASO-B).

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### Section Name: NCCN Guidelines Overview

The image presents a flowchart from the National Comprehensive Cancer Network (NCCN) Guidelines Version 2.2024, especially focusing on follow-up recommendations for patients with head and neck cancers after systemic therapy or radiation therapy (RT).

All recommendations are categorized as level A unless stated otherwise, highlighting the importance of clinical trials in cancer management.

### Section Name: Imaging and Assessment Protocols

1. After systemic therapy or RT, a clinical assessment should occur 4 to 8 weeks later. If there is a response, it is necessary to assess the extent of disease or distant metastases, preferably through a FDG-PET/CT scan at a minimum of 12 weeks post-treatment.
    - If the FDG-PET/CT results are negative, the patient may continue with monitoring through observation.
    - If the results are equivocal, observation or repeat FDG-PET/CT within 3 to 6 months is prescribed.
2. In cases where the FDG-PET/CT results are strongly positive, further imaging via CT scan with contrast of the primary site and neck, or MRI with and without contrast, becomes necessary.
    - If these imaging results confirm positive findings, neck dissection may be considered, depending on the evidence of residual or persistent disease.
    - If the imaging findings are negative, the patient might continue in observation.

### Section Name: Outcomes Based on Disease Resectability

The flowchart delineates different pathways based on whether the disease is resectable or unresectable:

- If there is confirmed residual or persistent disease, the options split into two pathways: **'Unresectable'** or **'Resectable.'**
  - **Unresectable:** Advances in treatment plans (labeled ADV-3) are called for.
  - **Resectable:** A resection of the primary and/or neck dissection may occur, contingent upon the disease status.

### Section Name: Important Notes

- NCCN emphasizes that the best management for any cancer patient is participation in clinical trials, which is especially encouraged for all patients.
- Additional notes clarify that if the FDG-PET/CT is negative for persistent cancer, further cross-sectional imaging is optional.
  - **PET Negative:** Defined as no or low-grade uptake not suspicious for disease.
  - **PET Positive:** Implies suspicion for disease.

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### Section Name: PRINCIPLES OF IMAGING

Imaging plays an essential role in the clinical care of patients with head and neck cancer. The proper selection and utilization of imaging studies is critical in caring for patients with head and neck cancer.

- **CT**: Performed with contrast, while CT imaging of the chest can be performed with or without contrast, as clinically indicated.
- **MRI**: Performed with and without contrast, unless contraindicated.

### Section Name: Initial Workup - Primary Site

Imaging assessment of the primary site can be performed with:

- **CT** of the soft tissues of the neck
- **MRI** of the neck

**CT** is complementary to MRI for head and neck cancers and is utilized to evaluate:

- Cortical bone erosion or periosteal invasion
- Cartilage invasion
- Bony erosion or destruction

**MRI** is preferred over CT in certain conditions, such as:

- Evaluating the extent of bone marrow invasion
- Patients with extensive dental amalgam obscuring anatomy on CT
- Assessing skull base invasion and cranial nerve involvement
- Differentiating tumor from obstructed sinuses

Complete evaluation of primary and nodal disease requires imaging from the skull base to the thoracic inlet, extending to the carina when involved lymph nodes or upper mediastinal cancers are present.

### Section Name: PET/CT and Biopsy

- If imaging does not reveal an obvious primary cancer, a **PET/CT** should be ordered before EUA, biopsies, and tonsillectomy. This helps identify potential primary sites before any interventions.
- **Fine Needle Aspiration (FNA)** biopsy of metastatic nodes may provide pathologically informative results.
- For initial diagnosis in cystic neck nodes, **image-guided needle biopsy** (ultrasound or CT) may yield better results than FNA by palpation alone.

### Section Name: Postoperative Imaging Advice

A **panoramic dental x-ray** is recommended for oral cavity cancers requiring mandibulotomy and/or mandibulectomy.

- When postoperative radiotherapy (RT) is anticipated for areas like the lip, oral cavity subsites, or oropharynx, panoramic x-ray is essential for a comprehensive pre-radiation dental evaluation.
- This evaluation helps assess the health of affected teeth and determine if pre-radiation dental procedures or extractions are necessary.

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### Section Name: Head and Neck Cancers - Principles of Imaging

**Principles of Imaging**

1. **PET/CT** is preferred over PET scan alone (i.e., without superimposed CT scan). PET/CT provides more accurate anatomical localization of abnormalities.
2. Pantvaidya GH, Agarwal JP, Deshpande MS, et al. PET-CT in recurrent head neck cancers: a study to evaluate impact on patient management. J Surg Oncol 2009;100:401-403.

### Section Name: Initial Workup - Nodal Metastases

**Nodal Metastases**

- Evaluation of lymph node metastases should be conducted with **CT or MRI** of the neck, using whichever imaging study is suitable for primary site evaluation (**IMG-A, 1 of 4**).
- For patients with multistation or lower neck nodal involvement or high-grade tumor histology:
  - **CT of the chest** may be performed to assess for mediastinal lymph node metastases.
  - **FDG-PET/CT** is preferred due to its higher sensitivity for both nodal and distant metastases.
- For patients under consideration for a **surgical primary approach**, the higher sensitivity of FDG-PET/CT is warranted for tumors near the midline to determine the surgical approach to the contralateral neck.
- Patients scheduled for **definitive RT** may also benefit from FDG-PET/CT for identifying involved lymph nodes.

### Section Name: Initial Workup - Distant Metastases

**Distant Metastases**

- For patients with locoregionally advanced cancer (e.g., **T3–T4 primary or ≥N1 nodal staging**), **FDG-PET/CT** is preferred for evaluating distant disease and thoracic metastases.
- **Limitations of FDG-PET/CT**:
    - It cannot rule out brain metastasis. For concerns such as mucosal melanoma or high-grade neuroendocrine carcinomas or adenocarcinomas, a contrast-enhanced brain MRI should also be obtained.
- If **FDG-PET/CT** is not performed:
    - **CT of the chest** is used to assess for pulmonary metastases and mediastinal lymph node involvement.
    - Non-contrast chest CT can screen for lung parenchymal metastases but is not adequate for assessing mediastinal adenopathy.
- **Screening for Lung Metastases:**
    - Following primary definitive treatment (surgery, RT, or systemic therapy/RT), the role of annual **CT screening** for lung metastases is debated.
    - Annual chest CT may be considered for patients with a substantial smoking history or high risk for lung metastases. Historically, annual chest x-rays have been used but are less sensitive than CT.
- **Directed Imaging for Specific Concerns:**
    - If metastatic disease is suspected in specific anatomical areas, directed imaging can be performed, such as:
        - **Non-contrast chest CT** for pulmonary metastasis
        - **Contrast-enhanced spine MRI** for spinal metastasis
    - Frequency of imaging depends on the treatment regimen and cancer type.
- **Role of FDG-PET/CT in Recurrent Disease Staging:**
    - FDG-PET/CT may complement or replace other imaging modalities when staging recurrent disease before therapy for relapsed/refractory disease. It is used to explore distant disease or second primaries that could significantly impact therapy choice.

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### Section Name: Locoregionally Advanced Disease: <6 Months Post-Treatment (Short-Term)

**Locoregionally Advanced Disease: <6 Months Post-Treatment (Short-Term)**

- Following surgery in patients with locoregionally advanced cancer, short-term post-treatment imaging is recommended for those who show signs of early recurrence or who are at high risk of early recurrence prior to starting adjuvant postoperative therapy.

- Obtain **CT and/or MRI** within 3–4 months after surgical treatment for patients with locoregionally advanced disease or with altered anatomy causing challenging physical exam assessment, in order to establish a new baseline for future comparisons.
- In cases of concern for incomplete response, a CT or MRI scan may be obtained much earlier, such as **4–8 weeks post-treatment** or even immediately based on the specific clinical situation. Ultrasound (US) of the neck for targeted sampling of any suspicious tissues may also be helpful, but results can be variably interpreted depending on the specific clinical situation.
- **FDG-PET/CT** should be performed within **3–6 months** of definitive radiation or systemic therapy/RT for assessment of treatment response and to identify any residual tumor:
  - Early FDG-PET/CT scans before 12 weeks are associated with significant false-positive rates and should be avoided in the absence of signs of recurrence or progression.
  - The optimal timing of PET scans after radiation treatment appears to be at the **3- to 6-month window**. A negative PET at this time point predicts improved overall survival at 2 years.
- In patients receiving definitive RT-based treatment of mucosal squamous cell carcinoma with **AJCC 7th edition N2–N3 nodal disease**, an FDG-PET/CT surveillance approach led to fewer neck dissections and considerable cost savings compared to a routine approach of planned post-treatment neck dissection. The majority of cases studied were **p16-positive oropharyngeal cancers**.
- In the special case of patients who are treated initially with induction chemotherapy prior to the initiation of definitive therapy, either **CT or MRI** has typically been obtained after 2–3 cycles of induction. **Chest CT and/or FDG-PET/CT** (with diagnostic-quality imaging of the regions of the body at risk) may be obtained if there is concern for locoregional or distant metastatic progression.

### Section Name: PRINCIPLES OF IMAGING

**Principles of Imaging**


1. Cheung PK, Chin RY, Eslick GD. Detecting residual/recurrent head neck squamous cell carcinomas using PET or PET/CT: Systematic review and meta-analysis. Otolaryngol Head Neck Surg 2016;154:421-432.
2. Heineman TE, Kuan EC, St John MA. When should surveillance imaging be performed after treatment for head and neck cancer? Laryngoscope 2017;127:533-534.
3. Mehanna H, Wong WL, McConkey CC, et al. PET-CT surveillance versus neck dissection in advanced head and neck cancer. N Engl J Med 2016;374:1444-1454.
4. Ng SP, Pollard C, 3rd, Berends J, et al. Usefulness of surveillance imaging in patients with head and neck cancer who are treated with definitive radiotherapy. Cancer 2019;125:1823-1829.


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### Section Name: Head and Neck Cancers

**Locoregionally Advanced Disease: ≥6 Months to 5 Years Post-Treatment (Long-Term)**

- The majority of recurrences after treatment of head and neck cancer occur in the first 2 years. Surveillance can be challenging due to altered anatomy

and/or fibrosis from surgery, radiation, and/or chemotherapy.
- There are no consensus guidelines on the frequency and modality of routine post-treatment imaging in the asymptomatic patient, leading to wide variations in practice across institutions.

**Imaging Modalities:**

- **US, CT, MRI, and PET/CT** each have unique advantages and disadvantages for surveillance imaging.
- Evidence suggests that **FDG-PET/CT** may be the most sensitive modality:
  - A 12-month PET revealed recurrent or second primary cancers in ~10% of treated patients.
  - A 24-month FDG-PET/CT revealed these findings in ~5% of treated cases.

**Challenges and Considerations:**

- Whether earlier detection through PET/CT leads to improved disease-specific survival is not established.
- Standardized multi-institutional imaging-based trials are needed to assess the value of routine imaging in asymptomatic patients.
- **Ho et al. findings:** No significant difference in 3-year disease-free survival between imaging surveillance and clinical surveillance (41% vs. 46%, P = .91).
- If an FDG-PET/CT at 3 months post-treatment is negative, further routine imaging in asymptomatic patients may not provide substantial benefit.

**Tailored Surveillance:**

- A tailored approach to surveillance should consider:
  - Tumor type, stage, prognostic factors, symptomatology, and physical exam changes or restrictions.
- **US of the neck:** A well-established tool for nodal surveillance—safe, fast, inexpensive, and effective for detecting suspicious nodal disease.

**Indications for Additional Imaging:**

- Worrisome or equivocal signs/symptoms.
- Routine annual imaging may be indicated to visualize areas inaccessible to routine clinical examination (deep-seated locations or areas obscured by treatment changes).

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## Section Name: Principles of Imaging

**PRINCIPLES OF IMAGING**


1. Heineman TE, Kuan EC, St John MA. When should surveillance imaging be performed after treatment for head and neck cancer? Laryngoscope 2017;127:533-534.
2. Dunsky KA, Wehrmann DJ, Osman MM, et al. PET-CT and the detection of the asymptomatic recurrence or second primary lesions in the treated head and neck cancer patient. Laryngoscope 2013;123:2161-2164.
3. Ho AS, Tsao GJ, Chen FW, et al. Impact of positron emission tomography/computed tomography surveillance at 12 and 24 months for detecting head and neck cancer recurrence. Cancer 2013;19:1349-1356.
4. Paleri V, Urbano TG, Mehanna H, et al. Management of neck metastases in head and neck cancer: United Kingdom National Multidisciplinary Guidelines. J Laryngol Otol 2016;130:S161-S169.


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### Section Name: Head and Neck Cancers - Principles of Surgery

**Head and Neck Cancers**

**PRINCIPLES OF SURGERY**

**Discussion**

**Evaluation**

All patients should be evaluated by a head and neck surgical oncologist prior to treatment to ensure the following:

- **Review biopsy material, staging, and imaging** to determine the extent of disease, exclude the presence of a synchronous primary tumor, assess current functional status, and evaluate potential surgical options, including those applicable if initial non-surgical treatment is unsuccessful.
- **Pre-treatment evaluation** should include consultations with a medical oncologist, radiation oncologist, dentist or oral maxillofacial surgeon, speech-language pathologist, dietitian, and reconstructive surgeon as appropriate.
- **Tumor staging for untreated patients** is essential, based on diagnostic imaging studies and chest imaging as appropriate.
- **Office-based head and neck examination** should include fiberoptic nasopharyngolaryngoscopy, and an EUA to assess tumor extent and obtain a biopsy. For metastatic carcinoma to the neck, an EUA is crucial to search for the putative primary site for diagnosis and treatment planning.
- **Participate in multidisciplinary team discussions** to maximize survival while preserving form and function.
- **Develop a surveillance plan** that includes:
  - Adequate dental, nutritional, and health behavioral evaluations and interventions.
  - Ancillary evaluations for comprehensive rehabilitation.

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### Section Name: Integration of Therapy

**Integration of Therapy**

- Multidisciplinary evaluation and treatment must be coordinated and integrated prospectively by all disciplines involved before initiating any treatment.
- For surgical patients:
  - Surgical procedures, margins, and reconstructive plans should ensure resection of all gross tumors with adequate tumor-free surgical margins.
  - Surgical procedures should rarely be modified based on response to prior therapy, except in cases of tumor progression necessitating a more extensive procedure for definitive resection.
- Multidisciplinary team decisions:
  - The treatment regimen should be thoroughly discussed with the patient, covering risks, benefits, and potential outcomes.
  - Shared decision-making should be encouraged, allowing the patient to participate in the final decision.

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### Section Name: Clinical Trials

**Clinical Trials:**
NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

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### Section Name: Head and Neck Cancers - Principles of Surgery

**Principles of Surgery**

The surgical management of regional lymphatics is dictated by the extent of the tumor at initial tumor staging. These guidelines apply to the performance of neck dissections as part of treatment of the primary tumor.

- In general, patients undergoing surgery for resection of the primary tumor will undergo dissection of the **ipsilateral side of the neck** that is at greatest risk for metastases.

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### Section Name: Neck Management

**Neck Management**

- **Tumor sites with bilateral lymphatic drainage** (e.g., base of tongue, palate, supraglottic larynx, hypopharynx, nasopharynx, deep pre-epiglottic space involvement) often require dissection of **both sides of the neck**.
    - For tumors at or approaching the midline, both sides of the neck are at risk, necessitating **bilateral neck dissections**.
- Advanced lesions involving the anterior tongue, floor of the mouth, or alveolus that cross the midline should undergo **contralateral selective/modified neck dissection** to ensure adequate tumor resection.
- **Elective Neck Dissection:**
    - Based on the **risk of occult metastasis** in the appropriate nodal basin.
    - For oral cavity squamous cell carcinoma, **sentinel lymph node biopsy (SLN)** or the **primary tumor depth of invasion** is the best predictor of occult metastatic disease.
    - For tumors with a depth greater than 3 mm, **elective dissection is strongly recommended** if RT is not already planned.
    - Depth-based recommendations:
        - **<2 mm:** Elective dissection only in highly selective cases.
        - **2–4 mm:** Clinical judgment should guide decision-making, considering factors such as reliability of follow-up and clinical suspicion.
        - Elective dissections are generally selective, preserving major structures unless dictated otherwise by operative findings.

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### Section Name: Types of Neck Dissection

**Types of Neck Dissection**

The type of neck dissection (comprehensive or selective) is determined by **preoperative clinical staging** and the surgeon's discretion based on tumor extent:

- **N0 (No regional lymph node metastasis):**
  - **Selective neck dissection:**
    - Oral cavity: At least levels I–III
    - Oropharynx: At least levels II–IV
    - Hypopharynx: At least levels II–IV and level VI (as appropriate)
    - Larynx: At least levels II–IV and level VI (as appropriate)
- **N1–N2a–c (Regional lymph node metastasis):**
  - Selective or comprehensive neck dissection (Discussion)
- **N3 (Large nodal metastasis):**
  - Comprehensive neck dissection
- **Level VI neck dissections** are performed for certain primary sites (e.g., larynx and hypopharynx):
  - Includes pretracheal lymph nodes, the Delphian lymph node, and unilateral or bilateral paratracheal lymph nodes.
  - **Hemithyroidectomy or total thyroidectomy** may also be appropriate.
- For **subglottic tumors or glottic cancers with significant subglottic extension:**
  - Level VI dissection with **unilateral or total thyroidectomy** is advised, based on tumor extent.
  - Example: A **T4a glottic tumor** with cricothyroid membrane and subglottic extension should include thyroidectomy and pretracheal and bilateral paratracheal lymph node dissection.
- **Parathyroid glands** should be preserved in situ or autotransplanted as necessary.

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### Section Name: TNM Staging System for the Larynx - Regional Lymph Nodes (N)

The **NCCN Guidelines Version 2.2024** and the **AJCC TNM Staging System for the Larynx (8th ed., 2017)** provide a detailed classification of the **Regional Lymph Nodes (N)** for head and neck cancers. This classification is crucial for determining the presence and extent of lymph node metastases, which are critical in establishing the severity and appropriate treatment strategies.

**Clinical N (cN)**

- **NX**: Regional lymph nodes cannot be assessed.
- **N0**: No regional lymph node metastasis.
- **N1**: Metastasis in a single ipsilateral lymph node, 3 cm or smaller in greatest dimension, ENE(–).

- **N2**:
  - Metastasis in a single ipsilateral node, larger than 3 cm but not larger than 6 cm in greatest dimension and ENE(–);
  - *or* metastases in multiple ipsilateral lymph nodes, none larger than 6 cm in greatest dimension and ENE(–);
  - *or* metastasis in bilateral or contralateral lymph nodes, none larger than 6 cm in greatest dimension and ENE(–).
  - **N2a**: Metastasis in a single ipsilateral lymph node, larger than 3 cm but not larger than 6 cm in greatest dimension and ENE(–).
  - **N2b**: Metastases in multiple ipsilateral lymph nodes, none larger than 6 cm in greatest dimension and ENE(–).
  - **N2c**: Metastases in bilateral or contralateral lymph nodes, none larger than 6 cm in greatest dimension and ENE(–).
- **N3**:
  - Metastasis in a lymph node, larger than 6 cm in greatest dimension and ENE(–);
  - *or* metastasis in any lymph node(s) with clinically overt ENE(+).
  - **N3a**: Metastasis in a lymph node, larger than 6 cm in greatest dimension and ENE(−).
  - **N3b**: Metastasis in any lymph node(s) with clinically overt ENE(+).

**Note**:

- A designation of **“U” or “L”** may be used for any N category to indicate metastasis above the lower border of the cricoid (**U**) or below the lower border of the cricoid (**L**).
- Clinical and pathological ENE should be recorded as **ENE(−)** or **ENE(+)**.

This structured classification is vital for clinicians for accurate staging and subsequent treatment planning in patients diagnosed with head and neck cancers.

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### Section Name: Pathological N (pN)

**Pathological N (pN)**

- **NX**: Regional lymph nodes cannot be assessed
- **N0**: No regional lymph node metastasis
- **N1**: Metastasis in a single ipsilateral lymph node, 3 cm or smaller in greatest dimension ENE(–)
- **N2**:
  - Metastasis in a single ipsilateral lymph node, 3 cm or smaller in greatest dimension and ENE(+);
  - Or larger than 3 cm but not larger than 6 cm in greatest dimension and ENE(−);
  - Or metastases in multiple ipsilateral lymph nodes, none larger than 6 cm in greatest dimension and ENE(−);
  - Or in bilateral or contralateral lymph node(s), none larger than 6 cm in greatest dimension and ENE(−)
  - **N2a**: Metastasis in a single ipsilateral node, 3 cm or smaller in greatest dimension and ENE(+); or metastasis in a single ipsilateral

node, larger than 3 cm but not larger than 6 cm in greatest dimension and ENE(−)
    - **N2b**: Metastases in multiple ipsilateral nodes, none larger than 6 cm in greatest dimension and ENE(−)
    - **N2c**: Metastases in bilateral or contralateral lymph node(s), none larger than 6 cm in greatest dimension and ENE(−)
- **N3**:
    - Metastasis in a lymph node, larger than 6 cm in greatest dimension and ENE(−);
    - Or metastasis in a single ipsilateral node, larger than 3 cm in greatest dimension and ENE(+);
    - Or multiple ipsilateral, contralateral, or bilateral lymph nodes and any with ENE(+);
    - Or a single contralateral node of any size and ENE(+)
    - **N3a**: Metastasis in a lymph node, larger than 6 cm in greatest dimension and ENE(−)
    - **N3b**:
        - Metastasis in a single ipsilateral node, larger than 3 cm in greatest dimension and ENE(+);
        - Or multiple ipsilateral, contralateral, or bilateral lymph nodes any with ENE(+);
        - Or a single contralateral node of any size and ENE(+)

*Note: A designation of “U” or “L” may be used for any N category to indicate metastasis above the lower border of the cricoid (U) or below the lower border of the cricoid (L). Similarly, clinical and pathological ENE should be recorded as ENE(−) or ENE(+).*

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### Section Name: Distant Metastasis (M)

**Distant Metastasis (M)**

- **M0**: No distant metastasis
- **M1**: Distant metastasis

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### Section Name: Histologic Grade (G)

**Histologic Grade (G)**

- **GX**: Grade cannot be assessed
- **G1**: Well differentiated
- **G2**: Moderately differentiated
- **G3**: Poorly differentiated

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### Section Name: Prognostic Stage Groups

**Prognostic Stage Groups**

- **Stage 0**: Tis N0 M0
- **Stage I**: T1 N0 M0
- **Stage II**: T2 N0 M0
- **Stage III**:
    - T3 N0 M0
    - T1 N1 M0

    - T2 N1 M0
    - T3 N1 M0
- **Stage IVA**:
    - T1 N2 M0
    - T2 N2 M0
    - T3 N2 M0
    - T4a N0,N1,N2 M0
- **Stage IVB**:
    - Any T N3 M0
    - T4b Any N M0
- **Stage IVC**: Any T Any N M1

*Used with permission of the American College of Surgeons, Chicago, Illinois. The original source for this information is the AJCC Cancer Staging Manual, Eighth Edition (2017) published by Springer International Publishing. For complete information and data supporting the staging tables, visit [www.springer.com](http://www.springer.com).*

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### Section Name: Head and Neck Cancers - Management Approaches

**Management Approaches**

- Treatment decisions for head and neck cancers are guided by the **site of disease**, **histology**, **stage**, and **baseline comorbid conditions**.
- **Single-modality treatment** with surgery or RT is typically recommended for **30% to 40% of patients** with early-stage disease (stage I or II) HPV-unrelated cancers.
    - **Surgery** is usually preferred for oral cavity and paranasal sinus cancers.
    - **RT (with or without chemotherapy)** is nearly always preferred for all stages of nasopharyngeal carcinoma (NPC) and advanced HPV-associated oropharyngeal cancer.
- The choice between surgery or RT as a primary treatment modality often depends on local **institutional expertise** and the perceived relative morbidity of the options.

**Evolving Treatment Techniques:**

- Improvements in conformal RT techniques, less invasive surgery, and supportive care for systemic therapy have made morbidity a moving target.

**Combined Modality Therapy:**

- Generally recommended for the **60% of patients** with **locally or regionally advanced disease**.
- Participation in **clinical trials** is a preferred option in many scenarios.

**Guideline Development:**

- These NCCN Guidelines are evidence-based while reflecting a consensus on an acceptable range of treatment options.
- Population-based studies show better outcomes for patients treated at **high-volume centers**.

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### Section Name: Head and Neck Cancers - Prognostic Factors

**Prognostic Factors**

- **p16 Positivity and HPV Status:**
  Distinguishing patients by p16 positivity and HPV tumor status informs prognosis.
    - **5-year Overall Survival (OS):**
        - **p16-negative/HPV-positive:** 53.2% (95% CI, 46.6%–60.8%)
        - **p16-positive/HPV-negative:** 54.7% (95% CI, 49.2%–60.9%)
        - **Concordant p16-positive/HPV-positive:** 81.1% (95% CI, 79.5%–82.7%)
        - **Concordant p16-negative/HPV-negative:** 40.4% (95% CI, 38.6%–42.4%)

- **HPV and Survival:**
    - Retrospective analysis (N = 1070) found better OS in patients with **HPV 16/18 positive sinonasal cancer** compared to HPV-negative disease (adjusted HR, 0.63; 95% CI, 0.48–0.82).
    - Smoking and cancer stage significantly impact survival for patients with HPV-positive SCCHN.
        - **Non-smokers** have a 51% (HR, 0.40; 95% CI, 0.33–0.75) reduction in risk of cancer progression compared to smokers.

- **Distant Metastasis and Prognosis:**
    - No difference in the rate of distant metastasis in p16-positive vs. p16-negative patients was observed in RTOG 0129.
    - Patients with **T4 or N3 disease** or radiographically detectable matted lymph nodes may have worse prognosis and are excluded from **deintensification trials**.

**Implications for Treatment:**

- Prognostic factors form the basis for **RT deintensification studies** in HPV-positive cancers.
- The difference in prognosis between HPV-positive and HPV-negative SCCHN led to the creation of new **AJCC staging criteria (2018)** for oropharyngeal cancers.
    - Further details available in the NCCN Guidelines for Head and Neck Cancers at www.NCCN.org.

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### Section Name: Head and Neck Cancers Imaging

**Imaging of Head and Neck Cancers**

- Proper selection and utilization of imaging studies are essential for effective care:
    - **CT and/or MRI** are used for initial imaging of the primary site.
    - **MRI** is preferred for:
        - Symptoms involving cranial nerves or tumors near the skull base.

        - Differentiating tumor extent from obstructed sinuses or secretions.
        - Evaluating intracranial/dural involvement.
    - **CT** is complementary to MRI for:
        - Evaluating bony erosion or cartilage invasion (e.g., laryngeal cancer).
        - Assessing cortical bone erosion or periosteal invasion in bone-involved cancers.
    - **MRI** is used to evaluate bone marrow invasion and to delineate tumor boundaries (e.g., at the base of the tongue).
- **Lymph Node Metastases:**
    - CT or MRI can evaluate lymph node involvement, though **FDG-PET/CT** has superior accuracy.
    - **FDG-PET/CT Evidence:**
        - Meta-analysis (18 studies):
            - **PPV:** 0.62 (95% CI, 0.55–0.69).
            - **NPV:** 0.83 (95% CI, 0.79–0.86).
        - ACRIN 6685 study (cN0 patients):
            - 87% of negative PET scans were confirmed pathologically negative at neck dissection.
        - German study (N = 150):
            - **NPV:** 93.3% (95% CI, 88.2%–98.5%).
        - PET/CT findings altered surgical plans in 22% of cases.
- If metastasis to specific areas is suspected, directed imaging (e.g., contrast-enhanced chest CT, brain MRI) should be performed:
    - Head and neck cancers rarely metastasize to the brain hematogenously, so routine brain studies are not necessary during initial workup.
- **Panoramic Dental X-Ray:**
    - Required before postoperative RT for dentulous patients as part of dental evaluation.
    - Also useful for assessing dentition and mandibular height if marginal resection is planned.

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## Section Name: Quality of Life and Patient-Reported Outcomes

**Quality of Life and Patient-Reported Outcomes**

- **Patient-completed scales** are critical for measuring Quality of Life (QOL) in head and neck cancer patients:
    - **Validated Measures:**
        1. **University of Washington Quality of Life Questionnaire (UW-QOL)**
        2. **EORTC-QLQ-H&N35** (European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Head and Neck Module)
        3. **FACT-H&N** (Functional Assessment of Cancer Therapy Head and Neck scale)
- **Performance Status Scale:**

    - A clinician-rated scale widely used for evaluating patients' functional performance.
- **Oral Mucositis Weekly Questionnaire HN (OMWQ-HN):**
    - A validated patient-reported tool measuring oral mucositis symptoms, including pain and its impact on well-being and function.
- Use of the **Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE)** is encouraged to assess symptomatic toxicity in clinical trials.

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### Section Name: Head and Neck Cancers

**Head and Neck Cancers**

**MS-13**

- The **College of Radiology** provides basic technical specifications for imaging and radiation techniques (source).
- Consensus contouring guidelines for treating head and neck (H&N) cancers are especially useful for patients treated without surgery. [143,144]

**Radiation Dosages:**

- When radiation is used with definitive intent:
    - A standard dose of **70 Gy (2 Gy/fraction/day)** is prescribed for gross disease at primary sites like the lip, oral cavity, nasopharynx, oropharynx, hypopharynx, glottic larynx, supraglottic larynx, occult primary, salivary gland tumors, and MM.
    - A secondary dose (e.g., **60 Gy**) covers areas at higher risk for microscopic spread.
    - Elective low-risk areas may receive lower doses (**~50 Gy**).

**Palliative RT:**

- Various regimens exist, but no single regimen is preferred. [145,146]
- Hypofractionated regimens are suitable for patients with limited life expectancy.
    - Example: **QUAD SHOT regimen** delivers **44.4 Gy** in 12 fractions over three cycles, with 2–3 weeks between cycles. [147]

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### Section Name: Radiation Doses

**Radiation Doses**

- **Radiation dose prescription and delivery schedule** depend on:
    - Primary tumor and neck node size.
    - Use of altered fractionation.
    - Clinical circumstances, including concurrent systemic therapy.
- **Considerations for dose adjustments:**

    - Proximity to organs at risk (e.g., brain, cochlea, optic chiasm/nerves, spinal cord).
    - Precise target definition and on-treatment imaging are critical for accurate radiation delivery.
    - Anatomical changes (e.g., tumor shrinkage, weight loss) may necessitate repeat imaging and treatment replanning.

- **Definitive RT with conventional fractionation:**

    - High-risk sites (primary tumor and lymph nodes): **66–70 Gy** (2.0–2.2 Gy/fraction). [148-151]
    - Sensitive sites (e.g., neural structures): Modified fractionation (e.g., <2.0 Gy/fraction) may reduce toxicity, with additional fractions added if needed.
    - Hyperfractionation for gross disease: Up to **81.6 Gy** (1.2 Gy/fraction) for tumors near sensitive areas like the brain or optic structures. [148,149]
    - Care must be taken with doses >72 Gy to avoid normal tissue injury, though modern techniques (e.g., IMRT, IMPT) mitigate some risks. [148,152]

- **Elective irradiation to low- and intermediate-risk sites:**

    - **3D-CRT or IMRT:** Typically **44–50 Gy** (2.0 Gy/fraction).
    - **Simultaneous Integrated Boost (SIB) IMRT: 54–63 Gy** (1.6–1.8 Gy/fraction), depending on fractionation schedule and tumor risk in the area. [154-156]

- **Mildly accelerated schedules:**

    - Six fractions per week are commonly used in definitive RT, especially when chemotherapy is not given concurrently. [150]

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### Section Name: JUPITER-02 Trial

**JUPITER-02 Trial**

- **Patients**: 553 from China, Taiwan, and Singapore (N = 289).
- **Treatment**: Randomized to receive **toripalimab** or a placebo.
- **Results**:
    - **Progression-Free Survival (PFS)**: HR, 0.52; 95% CI, 0.37–0.73.
    - **Overall Survival (OS)**: HR, 0.63; 95% CI, 0.45–0.89.
    - **Median PFS**: 21.4 months (toripalimab) vs. 8.2 months (placebo).
    - **Median OS**: Not reached (toripalimab) vs. 33.7 months (placebo).
- **Adverse Events**: More frequent in the toripalimab arm, but the overall incidence did not differ significantly between arms.

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### Section Name: Toripalimab Monotherapy

**Toripalimab Monotherapy**

- **Study**: Nonrandomized phase II study from China (N = 190).
- **Results**:

- **Overall Response Rate (ORR)**: 20.5%.
- **Median Duration of Response (DOR)**: 12.8 months.
- **Median PFS**: 1.9 months.
- **Median OS**: 17.4 months.

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## Section Name: NCCN Guidelines Recommendations

**NCCN Guidelines Recommendations**

- **Toripalimab-tpzi**: Preferred option for recurrent or metastatic nasopharyngeal carcinoma (NPC) after platinum-containing therapy.
- **Other Anti-PD-1 Antibodies**: Camrelizumab and tislelizumab evaluated in phase III trials in China but are not available in the US.
- **Pembrolizumab and Nivolumab**: Used based on extrapolation where toripalimab is unavailable.

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## Section Name: Pembrolizumab

**Pembrolizumab**

- **Trial**: KEYNOTE-028 (N = 27).
- **Results**:
  - **Objective Response Rate (ORR)**: 26%.
  - **Median Duration of Response (DOR)**: 17.1 months.
  - **6-month OS**: 85%.
  - **12-month OS**: 63%.
  - **6-month PFS**: 39%.
  - **12-month PFS**: 34%.
  - **Adverse Events**: 30% experienced grade 3–5 drug-related adverse events.
- **Recommendation**: Category 2B option for **PD-L1–positive recurrent or metastatic NPC**.

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## Section Name: Nivolumab

**Nivolumab**

- **Trials**: CheckMate 358 and others.
- **Results**:
  - **ORR**: 20.8% in CheckMate 358.
  - **Disease Control Rate (DCR)**: 45.8%.
  - **Japanese Study**: ORR of 16.7%, DCR of 41.7%.
  - **NCI Sponsored Trial**: ORR of 20.5%, 1-year OS of 59%, 1-year PFS of 19.3%.
- **Recommendation**: Category 2B treatment option for **recurrent or metastatic non-keratinizing NPC**.

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## Section Name: Radiation Therapy Fractionation

**Radiation Therapy Fractionation**

- **Recommendation**: Radiation doses of approximately **70 Gy in standard fractions of 2.0 Gy/fraction** for control of the gross primary tumor and involved lymph nodes.

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### Section Name: Follow-up

**Follow-up**

- Recommendations for surveillance are outlined in the algorithm (see *Follow-up Recommendations* in the NCCN Guidelines for Head and Neck Cancers).

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### Section Name: Very Advanced Head and Neck Cancers

**Very Advanced Head and Neck Cancers**

- **Algorithms for very advanced H&N cancers** include:

    1. Newly diagnosed locally advanced T4b (M0).
    2. Newly diagnosed unresectable regional nodal disease (typically N3).
    3. Metastatic disease at initial presentation (M1).
    4. Recurrent or persistent disease.

- **Treatment Goals**:
    - **Locoregional unresectable disease**: Cure.
    - **Recurrent disease**: Cure (if surgery or radiation remains feasible) or palliation (if unresectable after prior RT).
    - **Widely metastatic disease**: Palliation or life prolongation.

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### Section Name: Treatment

**Treatment**

- **Treatment Options** depend on:
    - **Performance Status (PS)**: Patients with good PS can tolerate a wide range of treatments, while those with reduced PS may require more limited approaches.
    - **Intent of Treatment**: Palliative vs. curative.

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### Section Name: Newly Diagnosed Locoregionally Advanced Disease

**Newly Diagnosed Locoregionally Advanced Disease**

- **For PS 0–1 Patients**:
    - Recommended treatment: **Concurrent systemic therapy/RT**.
    - **High-dose cisplatin**: Preferred category 1 recommendation based on substantial phase III data.
    - **Carboplatin/5-FU with RT**: Supported by phase III European data, also category 1.

- **Induction Therapy**:
    - Cisplatin-based induction therapy followed by RT alone or chemoradiation has been studied but does not show OS improvement over state-of-the-art concurrent systemic therapy/RT in randomized studies.

- **Cetuximab with RT**:

    - Category 2B option (based on phase II and phase III data).
    - Inferior to cisplatin with RT, especially in HPV-positive disease.
- **Other Chemoradiation Options**:
    - **Category 2B options**: Carboplatin/paclitaxel, weekly cisplatin (40 mg/m²), docetaxel for cisplatin-ineligible patients.
    - Useful only in select circumstances: 5-FU/hydroxyurea, cisplatin with infusional 5-FU, cisplatin/paclitaxel.
- **For PS 2–3 Patients**:
    - See the algorithm in the NCCN Guidelines (*Very Advanced Head and Neck Cancer: Treatment of Newly Diagnosed (M0) T4b, N0–3 or Unresectable Nodal Disease or Unfit for Surgery*).
- **Radiation Therapy Fractionation**:
    - Described in the *Principles of Radiation Therapy* in the NCCN Guidelines for Very Advanced Head and Neck Cancers.

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## Section Name: Metastatic Disease

**Metastatic Disease**

- For patients with **metastatic (M1) disease** at initial presentation:
    - **Palliative adjunctive measures**: RT, surgery, analgesics, and other therapies to manage disease manifestations (e.g., pain, hypercalcemia).

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