NCG Guidelines Version.3

Management of
Head and Neck Cancers
INITIAL REMARKS

• The guidelines have been formulated in line with the latest evidence available at the time they were laid out.

They incorporate available evidence and also the considered opinion of the Expert group.

• All the available treatment options have been considered and resource stratified as Essential, Optimal, and Optional. The definition of the same are given below.

**Essential:** This would be considered as the minimum treatment that should be provided. The recommendation is based on evidence, practicality (wide availability of expertise and infrastructure), as well as the cost of treatment and the value it offers. If centers do not have the capabilities to implement these, they should refer patients to a higher center.

**Optimal:** Based on both evidence as well as cost effectiveness.

**Optional:** Based on the available evidence (some could be standard of care) with no consideration for cost effectiveness. These options should be considered and undertaken when affordable (employer insurance scheme, personal insurance scheme etc.)

• For most situations more than one treatment option is listed.

• It is strongly recommended that Optimal Care includes the constitution of a Tumor Board/ Joint Cancer Clinic with mechanisms for cross-specialty inputs at the basic minimum from Surgical and Radiation specialists, and optimally from Medical oncology specialists and other specialties.

The current guidelines may be taken as guiding principles, but treatment decisions may need to be individualized and to be based on disease status, patient’s general health and co-morbidities, social support, treatment center feasibility, circumstances and expertise, and consideration to the patient’s expectations and desires.
• Decisions regarding intent of treatment (Curative/ Curative & Organ Preserving / Palliative / Response Assessment and reassess) need to be taken early and communicated to patients. Integration of palliative care must be considered at the earliest for cases where it is deemed appropriate.

• Clinicians must encourage patients to participate in clinical trials. The option of participating in these trials must also be provided to the patients whenever appropriate.

• Post completion of initial treatment, focus should be directed to rehabilitation and survivorship issues for patients.
ORAL CANCER

ORAL CANCER - ASSESSMENT/ Workup-
Non–healing ulcer over the lip/tongue/cheek/gums/palate

Loose teeth/ Earache/ Metastatic Lymph nodes

Clinical Evaluation

Biopsy for the tissue diagnosis

Imaging for assessing primary /neck nodes/distant metastasis

Dental/ Nutrition/ speech-swallowing Assessment & appropriate intervention

ORAL CANCERS Rx

Stage I/ II (Early)

Single modality

1. SURGERY %
2. RT *** (rarely preferred)

Stage III, IVa Resectable

1. SURGERY%+PORT/ POCTRT $ (If Patient unwilling/unfit for Surgery follow Unresectable algorithm****)

Stage IVb

Borderline resectable®, Good GC

NACT#

Good GC

Unresectable

Poor GC

Symptomatic Treatment /Best Supportive Care

Good Response → Re-evaluate for Curative Rx (Surgery & POCTRT)

Inadequate Response → Follow algorithm as for Unresectable

PALLIATIVE RT / CT*/ RT+CT**

If Good Responder → Re-evaluate for Curative Rx
Optimal Imaging modality for tongue lesion is a MRI and for other sites a Contrast enhanced CT scan. Loco
tional imaging is for assessment of the primary and the neck. Early stage oral cavity that is amenable to
adequate clinical evaluation may not warrant imaging studies of the primary and Ultrasound examination of
the neck is an optional alternative to CECT/MRI in this situation.

Chest X-ray is an essential investigation for ruling out lung metastasis and possible aspiration. Either a PET
CT(Optional) or CECT Thorax (Optimal) should be preferred in patients being considered for curative therapy
but with a high risk for distant metastasis (N3 node (size > 6 cm), multiple bilateral neck nodes, Lower cervical
neck nodes , large primary ( T4b) and in patients who have symptoms suggestive of distant metastasis.

Surgery - Primary tumor- Wide local excision (at least 1 cm gross margin so as to achieve > 5 mm
histological tumor free margin) with appropriate Neck Dissection and appropriate reconstruction. For N0
Neck- Selective neck dissection addressing Level I-III (Essential)+/- Level IV. For N+ Neck – Modified neck
dissection (Level I-V) with sparing of the XI nerve, IJV, SCM Muscle whenever oncologically feasible
(Essential). The minimum optimal number of lymph nodes included in a SND should be >10 and in a MND
>14.

The option of Radiation therapy for early oral cancers is preferred only for lip tumors and selected other
sub sites. Tumors abutting the mandible risk osteoradioneerosis. The treatment should preferably include
brachytherapy as a part of treatment. Either complete dose or partial dose should be delivered by
brachytherapy.

The option of Radiation Rx/ Chemo radiation Rx for advanced tumors is applicable only for patients who
are unfit and unwilling for surgery, and target volumes that can be safely encompassed by a tumoricidal dose
of 70 Gy. Patients with gross mandibular erosion risk osteoradioneerosis and are not suitable for this modality.
Tumors abutting the mandible and tumors with gross skin ulceration are also at greater risk of complications.
$- Indication for adjuvant post-op radiotherapy are T3-T4 primary, Node positivity, perineural invasion, lymphovascular invasion, and poorly differentiated disease. IMRT may be considered (Optional) if affordable (employer insurance scheme, personal insurance schemes) and available. Adjuvant post-op concurrent chemoradiation is indicated for positive margin and presence of extra nodal extension/extracapsular spread and presence of nodal positivity of 2 or more lymph nodes. The options for adjuvant concurrent chemotherapy are- Cisplatin 100 mg/m2 (preferred option) or weekly cisplatin 30-40 mg/m2. Audiometry is preferred prior to administration of cisplatin.

@- Borderline Resectable - This is broadly a situation wherein the primary tumor is grossly resectable, but significant concern exists regarding the probability of a positive resection margin or excessive surgical morbidity. The decision regarding borderline resectability should be taken by a surgeon (preferably in a multidisciplinary tumor board). Situations which may be deemed as borderline resectable are-

1. Soft tissue swelling up to the zygoma in case of a BM-GBS primary.
2. Disease close to hyoid or valleculae in case of a Tongue primary.
3. Some situations with Extensive skin infiltration and Involvement of (Supra-notch) infratemporal fossa.

Radiological involvement of the infratemporal fossa which is inferior to the level of the mandibular notch is deemed as resectable by current surgical techniques.

If the treating team (surgeon) considers the lesion to be resectable then surgery should be offered as per the algorithm for operable oral cancers.

*Options for first line palliative chemotherapy include-

- Cytotoxic chemotherapy (single agent or combination)- metronomic chemotherapy consisting of weekly methotrexate-celecoxib; or combination Chemotherapy (Platinum, 5-FU, Taxane)
- 5FU– Platinum –Cetuximab - or Paclitaxel -Platinum-Cetuximab - (Optional);
- Pembrolizumab (if deemed appropriate with genetic testing for PDL1 and mutation load) – Optional
Oropharynx/Hypopharynx/Larynx

Symptomatology
Odynophagia / Dysphagia
Hoarseness / hot potato speech
Referred otalgia
Difficulty breathing / Stridor

Clinical evaluation
Indirect Laryngoscopy
Direct Laryngoscopy OR
Examination Under Anesthesia (Optional)
(To delineate the mucosal extent, vocal cord mobility and arytenoid status)
Assessment of laryngeal functionality

Imaging for assessing primary /neck nodes/distant metastasis\(^\wedge\)
HPV Testing for Oropharyngeal Cancer\(^%\)
Dental, Nutrition, Swallowing Assessment & Appropriate Intervention\(^**\)

Primary in oropharynx
Primary in hypopharynx
Primary in Larynx

Refer algorithm for oropharynx
Refer algorithm for Hypopharynx
Refer algorithm for Larynx
Optimal Imaging modality for the primary and the neck may be by a CECT or MR. A MRI may be preferred for the Oropharynx and a CECT for the larynx and hypopharynx.

Chest X-ray is an essential investigation for ruling out lung metastasis and possible aspiration. Either a PET CT(Optional) or CECT Thorax (Optimal) should be preferred in patients being considered for curative therapy but with a high risk for distant metastasis (N3 node (size > 6 cm), multiple bilateral neck nodes, Lower cervical neck nodes, large primary (T4b), advanced hypopharyngeal cancer, and in patients who have symptoms suggestive of distant metastasis.

HPV testing is Optimal for all Oropharyngeal Cancers. This may be by p16 (Optimal). If expertise and facilities are available, then HPV mRNA testing is more specific (Optional). HPV+Ve Oropharyngeal Cancer is however currently noted in < 20% as per Indian studies and testing is not yet routine.

Assessment for speech and swallowing to evaluate for aspiration is considered Optimal. At least a 100 ml Bed side water swallowing test should be considered (Optimal). If facility available, Fiber optic endoscopic evaluation of swallowing or Videofluoroscopy evaluation of swallowing to be undertaken (Optional)
Ca Oropharynx-Base of Tongue, Tonsil, Soft palate, Pharyngeal wall

Stage I-II
T1-T2 NO

1. RADIOThERAPY
2. SURGERY (+/- adjuvant Rx if pathological upstaging)~

Stage III-V
T3-T4 N0 or any T N1-3

RADICAL INTENT

PALLIATIVE INTENT**

CISPLATIN FIT+

CISPLATIN UNFIT+

PALLIATIVE RT/ CT/ RT+CT$

1. RADICAL RADIATION 70 Gy (Essential)
2. RADIATION + CYTOTOXIC SENSITIZER@ (Optimal)
3. RADIATION + BIOLOGICALS# (Optional)

10 – 12 Weeks Assessment for Residual Disease

No Residual disease

Observe
First one year: 3 monthly
After one year: 4 monthly
After three years: 6 monthly

Residual disease

Surgery feasible

Surgery

Surgery not feasible

t Palliative Systemic therapy*

Tany Nany M1
Selected T1-2N0 lesion of tonsil – Base Tongue can be considered for minimally invasive Trans Oral Surgery (Laser/Robotic) surgery (Optional) to achieve a margin negative resection of the primary (tumour free margin of 3-5 mm). This needs to be accompanied with selective neck dissection and appropriate adjuvant RT/CTRT as indicated by surgical histology.

$- carboplatin -5FU or 5FU-Hydroxyurea or paclitaxel-cisplatin. These options were tested in platinum fit patients. Expertise in delivering chemotherapy is required for these regimens.

@$- The options in non-cisplatin fit are carboplatin -5FU or 5FU-Hydroxyurea. These options were tested in platinum fit patients and hence while administering them in cisplatin unfit patients caution is mandated. Expertise in delivering chemotherapy is required for these regimens.

#$- Either Cetuximab or Nimotuzumab can be used in this setting, Optimal if affordable (employer insurance scheme, personal insurance schemes) and available. However, these options were tested in platinum fit patients and hence while administering them in cisplatin unfit patients caution is mandated. Expertise in delivering chemotherapy is required for these regimens.

^^- Indications for neoadjuvant chemotherapy are N3 lymph node (> 6 cm) and extensive soft tissue extension, which is difficult to encompass safely in radiation portals. Post induction chemotherapy patients may be routed to Curative therapy or Palliative therapy as per clinical response and reassessment of General Condition.

**- Large T4b lesions or large multiple N3 nodes (> 6 cm) could be considered for palliative therapy. In case of elderly patients or those with poor social support with very advanced disease this option can be considered.

+- The criteria for cisplatin fitness can be adopted from Ahn et al Oral Oncol. 2016 Feb;53:106. doi: 10.1016/j.oraloncology.2015.11.019

$Options for palliative chemotherapy - As listed in section for Oral Cancer
*At least a 16 slice CT scan with 3 mm cut should be preferred to evaluate involvement of cartilage.

**- Tumor free margin of at least 1-2 mm should be achieved.

*** The risk of occult metastasis to the neck needs to be addressed in all treatments for Supraglottic Cancer.
Glottis/Supraglottis T1-2 N1-3
Normal Cord Mobility

Non-Surgical Option***

Surgical Option for Primary

Cisplatin Fit+

1. RADICAL RADIATION
   (Essential)
2. RADIATION + CYTOTOXIC SENSITIZER® (Optimal)
3. RADIATION + BIOLOGICALS# (Optional)

Cisplatin Unfit+

1. Trans oral Surgery with laser or Robot and appropriate neck dissection. Pathology directed adjuvant post op therapy (RT/CT-RT)
2. Open Partial laryngectomy* with appropriate neck dissection and pathology directed adjuvant post op therapy (RT/CT-RT)**

1 Concurrent CHEMORADIATION
   RADIATION 70 Gy + CISPLATIN 100 MG/M² 3 WEEKLY (Optimal)
   RADIATION 70 Gy + CISPLATIN 40 MG/M² WEEKLY (Essential)
   RADIATION 70 Gy + CISPLATIN 30-40 MG/M²+ NIMOTUZUMAB 200 MG WEEKLY (Optimal)
   OTHER REGIMENS$ (Optional)

2. NACT FOLLOWED BY CTRT / RT^^ (Optional)
*Conservative laryngeal surgeries (Open partial laryngectomy) for Glottic growth / Supraglottic Laryngectomy for Supraglottic growth. Case selection should include considerations of anatomical spread to warrant a reasonable expectation of a R0 resection, and also physiological considerations with regard to pulmonary and swallowing function to minimize post-surgical swallowing dysfunction and aspiration.

** Indication for adjuvant post-op radiotherapy are T3-T4 primary, Node positivity, perineural invasion, lymphovascular invasion, and poorly differentiated disease. Adjuvant post-op concurrent chemoradiation is indicated for positive margin, and presence of extra nodal extension/extracapsular spread. The options for adjuvant concurrent chemotherapy are- Cisplatin 100 mg/m2 on day 1,22, 43 or weekly cisplatin 30-40 mg/m2. Audiometry is preferred prior to administration of cisplatin.

+- The criteria for cisplatin fitness can be adopted from Ahn et al Oral Oncol. 2016 Feb;53:10-6. doi: 10.1016/j.oraloncology.2015.11.019

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#- Either Cetuximab or Nimotuzumab can be used in this setting, Optimal if affordable (employer insurance scheme, personal insurance schemes) and available. However, these options were tested in platinum fit patients and hence while administering them in cisplatin unfit patients caution is mandated. Expertise in delivering chemotherapy is required for these regimens.

^^- Post induction chemotherapy the options for concurrent are weekly cisplatin (30 mg/m2), weekly carboplatin or weekly Cetuximab or weekly Nimotuzumab.
Supra Glottis/ Glottis T3 N0-3
Impaired Cord Mobility / Fixed cord
CT - SCAN Larynx – Paraglottic Space / Pre-epiglottic
Space Involvement
Operable Neck nodes

Laryngeal function intact & Cisplatin fit+

1. CHEMORADIATION
   A) Concurrent CHEMORADIATION
      • RADIATION 70 Gy + CISPLATIN
        100 MG/M² 3 WEEKLY (Optional)
      • RADIATION 70 Gy + CISPLATIN
        40 MG/M² WEEKLY (Essential)
      • RADIATION 70 Gy + CISPLATIN
        30-40 MG/M²+ NIMOTUZUMAB
        200 MG WEEKLY (Optimal)
      • OTHER REGIMENS$ (Optional)
   B) NACT FOLLOWED BY RT / CTRT^^
      (Optimal)
*If CR/PR – consider RT/ CTRT
*If <PR / stable disease -> surgery
   followed by RT/CTRT

2. Open Partial laryngectomy* with appropriate neck dissection and pathology directed adjuvant post op therapy
   (RT/CT-RT) ** (Occasionally appropriate)*

Laryngeal function intact & cisplatin unfit+

- RADICAL RADIATION(Essential)
- RADIATION + CYTOTOXIC SENTIZER@ (Optional)
- RADIATION + BIOLOGICALS# (Optional)
- Open Partial Laryngectomy* with appropriate neck dissection with adjuvant therapy (RT/CT-RT)
  (Occasionally appropriate/Optional)*

Laryngeal Function Compromised

Near-Total Laryngectomy / Total Laryngectomy with TEP* & bilateral appropriate neck dissection with adjuvant therapy (RT/CT-RT)
   (Optimal)**
*Conservative laryngeal surgery (Supracricoid Laryngectomy) for Glottic growth / Supraglottic Laryngectomy for Supraglottic growth is occasionally appropriate in the situation of mobile cords but T3 staging in view of paraglottic space/ pre-epiglottic space involvement.

# A Tracheo-Esophageal Prosthesis (TEP) for speech rehabilitation is appropriate and optimal for most patients undergoing a Total Laryngectomy

**- Indication for adjuvant post-op radiotherapy are T3-T4 primary, Node positivity, perineural invasion, lymphovascular invasion, and poorly differentiated disease. Adjuvant post-op concurrent chemoradiation is indicated for positive margin, and presence of extra nodal extension/extracapsular spread. The options for adjuvant concurrent chemotherapy are - Cisplatin 100 mg/m2 on day 1,22, 43 or weekly cisplatin 30-40 mg/m2. Audiometry is preferred prior to administration of cisplatin.

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Glottis / Supraglottis T\textsubscript{4} any N
Operable Neck Nodes

Intact Laryngeal Function and framework
[exolaryngeal without cartilage involvement]

Laryngeal cartilage infiltration /
Laryngeal function comprised
[Aspiration/ Tracheostomy]

1. Near total Laryngectomy/ Total Laryngectomy with TEP\# &
bilateral appropriate neck dissection with adjuvant Therapy
(RT/ CTRT)*/** (Optimal)
2. Organ preservation can be attempted in patients with
preserved laryngeal function by -
   A) NACT FOLLOWED by Response evaluation^^ (Optimal)
      ➢ If CR/PR – consider RT/ CTRT
      ➢ If <PR / stable disease –> surgery followed by
         RT/CTRT
   B) Concurrent CHEMORADIATION regimes as detailed
      previously
   C) Radical Radiation (Optional) ( & salvage if appropriate)

Near total Laryngectomy/ Total Laryngectomy with TEP\# &
bilateral appropriate neck dissection with
adjuvant Therapy (RT/ CT-RT)* (Optimal)
*- Surgery remains the preferred option. Non-surgical options are likely to compromise cure rates especially in the setting of cartilage erosion. Patients may however choose for a laryngeal preserving non-surgical option despite the risks towards cure.

Some situations with anterior commissure related Thyroid cartilage erosion with mobile cords may be appropriate for surgical organ preservation with partial laryngectomy rather than Total/Near-total laryngectomy.

# For patients undergoing Total Laryngectomy, a Tracheo-Esophageal Prosthesis (TEP) for speech rehabilitation is appropriate and optimal

**- Indication for adjuvant post-op radiotherapy are T3-T4 primary, Node positivity, perineural invasion, lymphovascular invasion, and poorly differentiated disease. Adjuvant post-op concurrent chemoradiation is indicated for positive margin, and presence of extra nodal extension/extracapsular spread. The options for adjuvant concurrent chemotherapy are- Cisplatin 100 mg/m2 on day 1,22, 43 or weekly cisplatin 30-40 mg/m2. Audiometry is preferred prior to administration of cisplatin.

^^- Post induction chemotherapy the options for concurrent are weekly cisplatin (30 mg/m2), weekly carboplatin or weekly Cetuximab or weekly Nimotuzumab
Hypopharynx T₁ / T₂
Both Cords Mobile

Clinicoradiological N₀

- Radical Radiotherapy (Optimal)
- Trans oral Laser Microsurgery with selective neck dissection.
  * (Optional)

Clinicoradiological N+:

- NACT FOLLOWED BY Response Evaluation^^ (Optimal)
  If CR/ PR → Radical RT/ CTRT
  If <PR / stable disease → Surgery & post op RT/CTRT^^

- Concurrent CHEMORADIATION

Cisplatin Fit

- RADIATION 70 Gy + CISPLATIN 40 MG/M² WEEKLY (Essential)
- RADIATION 70 Gy + CISPLATIN 100 MG/M² 3 WEEKLY (Optimal)
- RADIATION 70 Gy + CISPLATIN 30-40 MG/M²+ NIMOTUZUMAB 200 MG WEEKLY (Optimal)
- Other Regimens (Optional)

Cisplatin unfit+

1. Radical Radiation (Essential)
2. Concurrent RT with Biologicals # or other regimes@ (Optional)
3. Conservation laryngeal surgery with appropriate neck dissection & Post op RT/CTRT as appropriate */** (Optional)
Surgical Organ preservation should be considered in select cases as expertise for the same is not widely available.

Case selection should include considerations of anatomical spread to warrant a reasonable expectation of a R0 resection, and also physiological considerations with regard to pulmonary and swallowing function to minimize post-surgical swallowing dysfunction and aspiration.

** Indication for adjuvant post-op radiotherapy are T3-T4 primary, Node positivity, perineural invasion, lympho-vascular invasion, and poorly differentiated disease. Adjuvant post-op concurrent chemoradiation is indicated for positive margin, and presence of extra nodal extension/extracapsular spread.

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@- The options in non-cisplatin fit are carboplatin -5FU or 5FU-Hydroxyurea. These options were tested in platinum fit patients and hence while administering them in cisplatin unfit patients caution is mandated. Expertise in delivering chemotherapy is required for these regimens.
Hypopharynx T3 Any N
Impaired cord Mobility/ Fixed cord
CT – SCAN Larynx – Paraglottic space / Pre-epiglottis space involvement
Operable Neck Nodes

Laryngeal function intact and Cisplatin fit

- NACT FOLLOWED BY Response Evaluation\^\^ (Optimal)
  - If CR/ PR \(\rightarrow\) Radical RT/ CTRT
  - If <PR / stable disease \(\rightarrow\) Sx & post op RT/CTRT\^\^\^\^*
- Concurrent CHEMORADIATION
  - RADIATION 70 Gy + CISPLATIN 100 MG/M² 3 WEEKLY (Optimal)
  - RADIATION 70 Gy + CISPLATIN 40 MG/M² WEEKLY (Essential)
  - RADIATION 70 Gy + CISPLATIN 30-40 MG/M2+ NIMOTUZUMAB 200 MG WEEKLY (Optimal)
- Total Laryngectomy +/- TEP\* OR Near-total laryngectomy; with partial/total pharyngectomy + appropriate neck dissection+ appropriate reconstruction. Post op RT/CTRT as appropriate*
  - (Optional)

Laryngeal function intact & cisplatin unfit

- Total laryngectomy +/- TEP\* OR Near-total laryngectomy with partial/total pharyngectomy + appropriate neck dissection+ appropriate reconstruction and Adjuvant RT/CTRT as appropriate*
  - (Optimal)
- Radical Radiation (Essential)
- Concurrent RT with Biologicals # (Optional) or other regimes@ (Optimal)

Laryngeal Function Compromised

- Total laryngectomy +/- TEP\* OR Near-total laryngectomy with partial/total pharyngectomy + appropriate neck dissection+ appropriate reconstruction. Post op RT/CTRT as appropriate*
  - (Optimal)
For patients undergoing Total Laryngectomy, a Tracheo-Esophageal Prosthesis (TEP) for speech rehabilitation is appropriate and optimal

* Indication for adjuvant post-op radiotherapy are T3-T4 primary, Node positivity, perineural invasion, lympho-vascular invasion, and poorly differentiated disease. Adjuvant post-op concurrent chemoradiation is indicated for positive margin, and presence of extra nodal extension/extracapsular spread.

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#- Either Cetuximab or Nimotuzumab can be used in this setting, Optimal if affordable (employer insurance scheme, personal insurance schemes) and available. However, these options were tested in platinum fit patients and hence while administering them in cisplatin unfit patients caution is mandated. Expertise in delivering chemotherapy is required for these regimens.
Hypopharynx T4 Any N
CT Scan show Gross Cartilage Destruction/ Exolaryngeal Spread
Operable Neck Nodes.

Intact Laryngeal function and framework
(Exolaryngeal without cartilage destruction)

- Near – Total Laryngectomy/Total Laryngectomy (+/- TEP) with partial pharyngectomy/ total pharyngectomy with appropriate neck dissection + appropriate pharyngeal reconstruction with adjuvant therapy (RT/CT-RT) (Optimal)
- NACT FOLLOWED BY Response Evaluation^^ (Optional)
  - If CR/PR – CTRT
  - If <PR / stable disease – Surgery followed by RT/CTRT
- Concurrent CHEMORADIATION (Optional)
  1. CISPLATIN 100 MG/M2 3 WEEKLY + RADIATION
  2. CISPLATIN 40 MG/M2 WEEKLY + RADIATION
  3. CISPLATIN 30-40 MG/M2 + NIMOTUZUMAB 200 MG WEEKLY + RADIATION
  4. OTHER REGIMENS$

- Radical Radiation (Cisplatin unfit) +Salvage Surgery if appropriate ( cure likely to be significantly compromised) (Optional)
- Concurrent RT with Biologicals # or other regimens (Cisplatin unfit patient)@ (Optional)

Laryngeal function and framework compromised

Near – Total Laryngectomy/Total Laryngectomy (+/- TEP) with partial pharyngectomy/ total pharyngectomy with appropriate neck dissection + appropriate pharyngeal reconstruction with adjuvant therapy (RT/CT-RT) (Optimal)
Surgery remains the preferred option. Non-surgical options are likely to compromise cure rates especially in the setting of cartilage erosion. Patients may however choose for a laryngeal preserving non-surgical option despite the risks towards cure.

For patients undergoing Total Laryngectomy, a Tracheo-Esophageal Prosthesis (TEP) for speech rehabilitation is appropriate and optimal.

The options in non-cisplatin fit are carboplatin -5FU or 5FU-Hydroxyurea. These options were tested in platinum fit patients and hence while administering them in cisplatin unfit patients caution is mandated. Expertise in delivering chemotherapy is required for these regimens.

Either Cetuximab or Nimotuzumab can be used in this setting, Optimal if affordable (employer insurance scheme, personal insurance schemes) and available. However, these options were tested in platinum fit patients and hence while administering them in cisplatin unfit patients caution is mandated. Expertise in delivering chemotherapy is required for these regimens.
Larynx and Hypopharynx
Any T Inoperable Neck Nodes

ECOG performance 0-1

- Cisplatin fit
- NACT FOLLOWED BY Response Assessment\(^\wedge\wedge\) (Optimal)
  - Re-evaluate for Curative treatment

- Concurrent CHEMORADIATION
  - CISPLATIN 100 MG/M2 3 WEEKLY + RADIATION (optimal)
  - CISPLATIN 40 MG/M2 WEEKLY + RADIATION (essential)
  - CISPLATIN 30-40 MG/M2 + NIMOTUZUMAB 200 MG WEEKLY + RADIATION (optimal)

- Cisplatin unfit+
  - Concurrent RT with Biologicals # (Optional) or other regimens@ (Optimal)
  - Radical Radiation (Essential)

ECOG performance >2

Palliative RT/Chemotherapy / RT+CT (Optimal) OR Best Supportive Care (Essential)
PARANASAL SINUS AND NASAL CAVITY MANAGEMENT ALGORITHM

Symptomatology

Nasal Symptoms
- Nasal Obstruction
- Nasal Discharge
- Epistaxis
- Anosmia

Orbital Symptoms
- Epiphora
- Blurring of vision
- Diplopia
- Visual Loss

Other Symptoms
- Headache, Vomiting (raised ICP)
- Midfacial Hyperesthesia / Anesthesia
- Loosening of teeth
- Neck lymph node Symptoms
- Distant Metastasis Symptoms

Work up on patients
- Diagnostic nasal endoscopy (Essential)
  - Map disease
  - Biopsy (Appropriate IHC is Near-Essential for making a correct diagnosis of the type of tumour)
- CT Scan (Primary/Neck) (Essential) or
  - Bone erosion (Posterolateral wall / cribiform /floor of orbit)
- MRI Scan (Primary/Neck) (Optimal)
  - Soft tissue involvement / ITF/Dura/Brain/orbit
  - Post treatment setting (Surgery / RT)

Distant Metastasis Workup: CXR (Essential), CT Thorax (Optimal), PET-CT (optional)
Ophthalmic Evaluation (Optimal)
Endocrine Work up (Optimal)

PRIMARY IN PARANASAL SINUSES
REFER TO ALGORITHM FOR PARANASAL SINUSES

PRIMARY IN NASOPHARYNX
REFER TO ALGORITHM FOR NASOPHARYNX
Paranasal Sinus Cancers
Early disease (T₁₂ N₀)

- Surgical resection (preferred)
- Radical radiotherapy (unfit/unwilling for surgery)

Paranasal Sinus Cancers
Advanced Disease (T₃-₄ N₀-N₁/ T₁-₂N₁+)

- Surgical resection**
- NACT# +followed SX

- Margin Negative
  - RT alone

- Margin Positive/ECS
  - Chemo RT

- Perineural Invasion
  - Revision surgery (If Possible)

- Margin Positive
  - Adjuvant RT*

- Perineural Invasion

Paranasal Sinus Cancers
Early disease (T₁₂ N₀)

- Surgical resection (preferred)
- Radical radiotherapy (unfit/unwilling for surgery)

- Margin Negative
  - Observe

- Margin Positive
  - Adjuvant RT*

- Perineural Invasion
  - Revision surgery (If Possible)

- Margin Positive
  - Adjuvant RT*

- Perineural Invasion

- Margin Positive
  - Adjuvant RT*

- Perineural Invasion

**Surgical resection**

#NACT

*Adjuvant RT*

**Chemo radiation/RT (Unfit/Unwilling for surgery)**

NACT# followed by CTRT

Revision surgery (If Possible)

Adjuvant RT*

Chemo RT
*Radiation in the PNS is optimally delivered with IMRT due to the vicinity of cranial nerves, intracranial contents and orbit. (IMRT Optimal). For advanced tumors and posteriorly positioned tumors radiation therapy should include coverage for the retropharyngeal node.

**- Surgery should achieve a R0 Resection. The appropriate surgical technique may be accordingly selected (endoscopic, partial, total or extended maxillectomy, orbital Exentration, craniofacial resection). Neck Dissection is undertaken for a N+ neck. Prognosis is however very guarded for N+ disease except in the situation of Level I nodes related to anterior PNS Tumour/Skin involvement.

#NACT indication- should be considered optimal for advanced tumors with non-squamous high-grade histology {ENB (Gr3,4)/SNUC/SNEC/NUT/Small cell/Others}.

NACT can be considered for SCC (Optional) in situations wherein surgical resection may not yield a R0 Resection or lead to unacceptable morbidity (Intracranial extension; High ITF involvement; orbital preservation in intraocular extension)
Orbit in Sino nasal malignancy

- Lamina papyracea intact
- Extraconal disease
  - Orbital periosteum
    - Free
    - Involved
      - Orbital fat FS
        - Free
        - Involved
          - Unresectable
            - RT or CTRT

- Intracanal disease
  - Apex of orbit
    - Involved
      - Unresectable
        - RT or CTRT

Orbital Preservation

Orbital Exentration
NASOPHARYNX

**Staging Workup**
- Endoscopic examination & biopsy
- CT Scan/ MRI face, neck including PNS
- Chest X-Ray / HRCT Chest
- PET-CT

**Other workup**
- EBV Titres
- Dental Prophylaxis
- Audiometry & visual field testing
- Nutritional counselling
- Endocrine workup including Thyroid function

<table>
<thead>
<tr>
<th>T1 N0 M0</th>
<th>T2 N0 M0</th>
<th>T3-4 N0-3 M0</th>
<th>Any T Any N M1</th>
</tr>
</thead>
</table>
| 1. Radical RT alone (Optimal)  
2. Lesions classified as T2a by previous staging - CTRT (Optional) |
| 1. CTRT + adjuvant CT (Optimal)  
2. Neo Adjuvant CT x 2 cycles + CTRT (Optimal)  
3. CTRT (Optional) |
| 1. Neo Adjuvant CT x 2 cycles + CTRT (Optimal)  
2. CTRT + Adjuvant CT (Optional) |
| 1. Palliative Chemotherapy (platinum based) (Essential)  
2. Palliative radiotherapy (Symptomatic bone metastasis) (Essential)  
3. RT/RT+CT (as indicated) (optional)  
OR  
4. Best Supportive Care (Essential) |

**FOLLOW-UP**
- PET-CT/MRI for response evaluation
- Examination of the nasopharynx and neck, cranial nerve function
- For T3 and T4 tumours, PET-CT/MRI might be done annually for 5 years
- Thyroid function at 1 year, annually thereafter
- Audiometry
- EBV titres
- IMRT or 3DCRT are preferred modalities for radiotherapy for Nasopharyngeal Cancer (Optimal)
- All treatments to be titrated as per patient’s general condition and tolerability
Major Salivary Gland

Long Standing mobile, Tail parotid → Nodule/mass in salivary glands (parotid/ submandibular) → Features of malignancy: fast growing, painful, fixed, nerve involvement, neck node

Through clinical assessment including Fine Needle Aspiration Cytology (Optimal)

Benign: MRI imaging (Preferred)

Superficial lobe parotid only

Superficial parotidectomy. Adequate parotidectomy only if small lesion in superficial lobe

Consider PORT only for multiply recurrent tumors

Malignant: Consider MRI for soft tissue/ deep lobe and facial nerve imaging. Consider CT for bone involvement

Superficial + deep lobe parotid

Total parotidectomy. Nerve sacrifice only if involved pre/intraoperatively

Assess Resectability

Resectable

Inoperable/Unresectable (Inoperable: intradural, extensive skull base, ICA)

Consider Radical RT OR Palliative RT

- Superficial/ Total parotidectomy depending on lob involved
- Facial nerve sacrifice only if pre-operatively involved or adherent to tumour as assessed intraoperatively.
- Neck dissection if node positive

Adjuvant RT if:
1. T3/T4 cancers
2. Close or Positive margins
3. Lymph node metastasis
4. High or intermediate grade tumours
5. Recurrent cancers
Cervical nodes with an unknown primary

- FNAC

  - Poorly Differentiated/Undifferentiated neoplasm
    i. If lymphoma suspected, consider lymph node biopsy and H-E section for further characterization
    ii. *IHC (HMWCK, p63, CK7, CK20, LCA, CD30, p16, HMB-45, EBV-EBERISH, S100), Chromogranin, Synaptophysin)

  - Squamous Cell Carcinoma
    i. $PET CT Scan
    ii. IHC-p16, EBERISH
    iii. EUA, NP Scopy, Direct laryngoscopy, PET Directed biopsy, consider tonsillectomy & biopsy

  - Adenocarcinoma
    i. $PET CT Scan
    ii. Tumour marker
    iii. Lymph node bx-
* IHC (Ck7, Ck20, CDx2, PSA, TTF-1 Thyroglobulin, Mammoglobin, ER, PR, WT1

- Management

  - Treat as per guidelines of site

  - Appropriate neck% dissection + Adjuvant RT+/-Conc. CT
    RT Alone/CTRT

  - Followed by Salvage neck dissection SOS

  - Primary tumour site detected → treat as per guidelines for primary site

*Preferred
$ PET-CT where not available → CECT of the Face & Neck
CECT thorax
USG (Abdomen)

%Depending on nodal stage and institutional policy
**Consider early palliative care.**

**Options for first line palliative chemotherapy include-**

- Cytotoxic chemotherapy (single agent or combination)- metronomic chemotherapy consisting of weekly methotrexate-celecoxib; or combination Chemotherapy (Platinum, 5-FU, Taxane)
- 5FU– Platinum–Cetuximab - or Paclitaxel -Platinum-Cetuximab - (Optional);
- Pembrolizumab (if deemed appropriate with genetic testing for PDL1 and mutation load ) – Optional