

ONCOLOGY KNOWLEDGE HUB · FOR HEALTH PROFESSIONALS

Oral Cavity Cancer

A mini review for clinicians (from the Head & Neck Cancer module)

For postgraduate residents (medical, radiation and surgical oncology, ENT and head and neck surgery, oral and maxillofacial surgery, dentistry, medicine), practising clinicians and medical students

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Updated 11 October 2026. Educational summary written in our own words from current guidelines and primary trials; no drug doses; not advice for an individual patient. Verify current guidelines and Indian regulatory approvals before treatment decisions. Patients and families: please see the patient guides at drharitha.co.in.

Head & Neck Cancer

Oral cavity · Oropharynx (HPV) · Larynx · Hypopharynx · Nasopharynx (EBV) · PD-L1 CPS · Key points for clinicians · Last updated 11 October 2026

01 At a glance

- Lip and oral cavity cancer is the **commonest cancer in Indian men**: roughly 1.4 lakh new cases and 80,000 deaths a year (GLOBOCAN 2022), about a third of the world total. Worldwide, head and neck cancer causes about 900,000 cases and over 400,000 deaths a year; men outnumber women 2–4 to 1.
- More than 90% are **squamous cell carcinomas**. The site decides the cause, the first symptom and the route of spread: the **oral cavity** (tobacco chewing, areca nut; buccal–gingival cancers in India), the **oropharynx** (tonsil and base of tongue; HPV-driven in 70–80% in the West but a minority in India) and the **larynx and hypopharynx** (smoking and alcohol). The **nasopharynx** is a distinct, EBV-driven disease, rare in India except in the north-east (see section 06).
- **Stage drives cure**: about 70–90% of patients with stage I–II disease are alive at 5 years, usually after a single treatment (surgery or radiotherapy). Two-thirds of Indian patients present with stage III–IV disease, which needs two or three modalities and costs function as well as money.
- Since 2024 the treatment map has moved: **perioperative pembrolizumab** for resectable PD-L1-positive disease ([KEYNOTE-689](#) ^[1]), **nivolumab added to postoperative chemoradiation** for HPV-negative high-risk disease ([NIVOPOSTOP](#) ^[2]) and **immunotherapy first line** for recurrent or metastatic disease ([KEYNOTE-048](#) ^[3]).
- The avoidable harms in Indian practice are **delay before the biopsy** (ulcers treated with ointments, neck nodes treated as tuberculosis, hoarseness treated as a cold), **unplanned radiotherapy gaps**, and **teeth extracted after radiotherapy**.

Figure 1. Three working groups. More than 90% of head and neck cancers are squamous cell carcinomas; the site decides the cause, the first symptom, the route of spread and the first treatment. Proportions are approximate (Indian hospital-based registries).



Figure 2. Where head and neck cancers arise (midsagittal section, schematic). Each subsite has its own staging table, nodal drainage and operation; the oral cavity ends at the circumvallate papillae and the junction of hard and soft palate, where the oropharynx begins.

02 Clinical presentation, common traps & genetic causes

Who is at risk

Factor	Size of risk	Clinical note
Smoked tobacco (cigarettes, bidis, cigars, pipes)	5- to 25-fold in heavy smokers; dose-dependent; excess risk fades over about 20 years after stopping	Larynx, hypopharynx, oropharynx and oral cavity (INHANCE ^[4]).
Smokeless tobacco and areca nut (gutka, khaini, zarda, mawa, pan, pan masala)	Areca nut alone is an independent carcinogen; effect multiplies with tobacco and alcohol	The main cause of buccal mucosa and gingivobuccal cancers in India; also oral submucous fibrosis (Guha 2014 ^[5]).
Alcohol	Five- to sixfold at >50 g/day; multiplies tobacco risk	Spirits carry more risk than wine in some studies; alcohol-containing mouthwash used heavily adds a little.
HPV (mainly type 16)	Causes most tonsil and base-of-tongue cancers in high-income countries	Younger, often non-smoking patients with small primaries and cystic neck nodes; much less common in India.
Epstein-Barr virus	Nasopharyngeal carcinoma	Undifferentiated cancer in a neck node: test EBER and look at the nasopharynx.
Poor oral hygiene, chronic trauma	Modest independent risk (INHANCE ^[6])	Sharp teeth and ill-fitting dentures are not proven causes, but they hide and irritate lesions: examine under them.
Immunosuppression, Fanconi anaemia, prior head and neck RT	Higher and earlier risk	Fanconi anaemia: cancers at a young age and extreme sensitivity to RT and cisplatin.
Oral potentially malignant disorders	Erythroplakia highest risk; leukoplakia and oral submucous fibrosis lower but real	Biopsy the reddest or thickest area; stop tobacco and areca nut; follow up for life.

How head and neck cancers present

Site	Typical first symptom	What to know
Oral cavity	Non-healing ulcer, white or red patch, lump, loose tooth, ill-fitting denture, trismus	Buccal cancers are often treated as infection or trauma and seldom present as T1. Numb lip or chin means mandibular nerve invasion.
Oropharynx	Sore throat, pain on swallowing, referred earache; painless neck lump (HPV)	A cystic neck "branchial cyst" in an adult over 40 is a metastasis until proven otherwise. Palpate the base of tongue.
Larynx (glottis)	Hoarseness	Hoarseness >3 weeks in a smoker needs laryngoscopy, not antibiotics. Glottic cancer is found early and rarely spreads to nodes.
Larynx (supraglottis), hypopharynx	Pain or difficulty swallowing, referred earache, neck mass, late stridor	Usually late and node-positive; weight loss and aspiration common.

Site	Typical first symptom	What to know
Nasopharynx	Neck node (often level II or V, bilateral), unilateral serous otitis media, nasal block or bleeding, double vision or facial numbness	EBV-driven; MRI and nasoendoscopy; treated with radiotherapy and chemotherapy, not surgery (see section O6, nasopharyngeal carcinoma).
Any site	Neck mass without an obvious primary	FNAC first; never excise a neck node before examining the upper aerodigestive tract.

Figure 3. When to examine and biopsy. Most delays in India happen before the first biopsy: ulcers treated with ointments, neck nodes treated as TB, and hoarseness treated as a cold.

- **The two-week rule:** any ulcer, patch or lump in the mouth that persists 2 weeks after removing an obvious irritant needs a biopsy. Repeated courses of antibiotics, antifungals or ointments only buy the tumour time.
- **"Oral TB" and "TB lymphadenitis":** tuberculosis of the tongue and neck exists, but a hard, painless node in a tobacco user is cancer until FNAC says otherwise. Start antituberculous treatment only on microbiological or histological proof.
- **Trismus in an areca nut chewer** may be oral submucous fibrosis, a cancer in the masticator space, or both. Examine carefully and image if mouth opening is falling or one-sided.
- **Second primary cancers:** field cancerisation means up to 1 in 5 survivors develops another tobacco- or alcohol-related tumour (head and neck, oesophagus, lung). Examine the whole upper aerodigestive tract at diagnosis.

03 Screening, workup & staging essentials

Screening

- There is no screening test for pharyngeal or laryngeal cancer. For the mouth, **visual oral examination** works: in the Kerala cluster-randomised trial (over 190,000 people aged 35+, three rounds by trained health workers), screening reduced oral cancer deaths by 27% overall and by 29% in tobacco or alcohol users, despite real-life compliance ([Sankaranarayanan 2005](#) ^[7]). India's NP-NCD programme offers it from age 30.
- Opportunistic screening costs nothing: look in the mouth of every tobacco or areca nut user at every visit, including under dentures, and teach the 2-minute self-check (see the patient handout).
- Oral brush cytology, toluidine blue and autofluorescence devices do not replace a biopsy of a suspicious lesion. No drug prevents oral cancer in people with leukoplakia: retinoids and other agents tried in trials are not recommended outside studies.

Workup before treatment

Figure 4. From suspicion to a treatment plan. Biopsy before imaging is fine for an obvious oral lesion, but image before biopsy for deep or laryngeal tumours so the scan is not distorted; never excise a neck node without first looking for a primary.

Step	What to do	Why
Examination	Inspect and palpate the mouth and oropharynx; flexible nasolaryngoscopy; examination under anaesthesia when the extent is unclear	Defines T; looks for synchronous second primaries
Biopsy	Punch or incisional biopsy of the primary; FNAC of a node (core or excision only after the primary search when lymphoma is a question)	Open neck–node biopsy before definitive treatment can worsen control
Imaging of the primary and neck	Contrast CT (bone, larynx cartilage) or MRI (oral tongue, soft tissue, perineural spread, nasopharynx)	Depth, bone invasion, ENE, retropharyngeal nodes
Distant staging	CT chest for all; PET–CT for stage III–IV, heavy smokers and unknown primary	Lung metastases and second lung primaries; PET–CT also finds occult nodes
Pathology	Grade, DOI, PNI, LVI, margins; p16 for every oropharynx cancer; PD–L1 CPS for resectable stage III–IVA and for recurrence	p16 changes staging; CPS opens immunotherapy
Fitness	Performance status, nutrition, creatinine clearance, audiogram, comorbidity, social support	Decides cisplatin versus alternatives and the feasibility of 7 weeks of daily treatment
Dental and swallowing	OPG, extractions, fluoride trays; speech and swallow baseline	Prevents osteoradionecrosis and preserves function

Figure 5. TNM at a glance (simplified from AJCC 8th edition). Depth of invasion, not thickness, now sets the oral cavity T category; ENE moves a neck to N3b; HPV–associated oropharynx cancer has its own, kinder table.

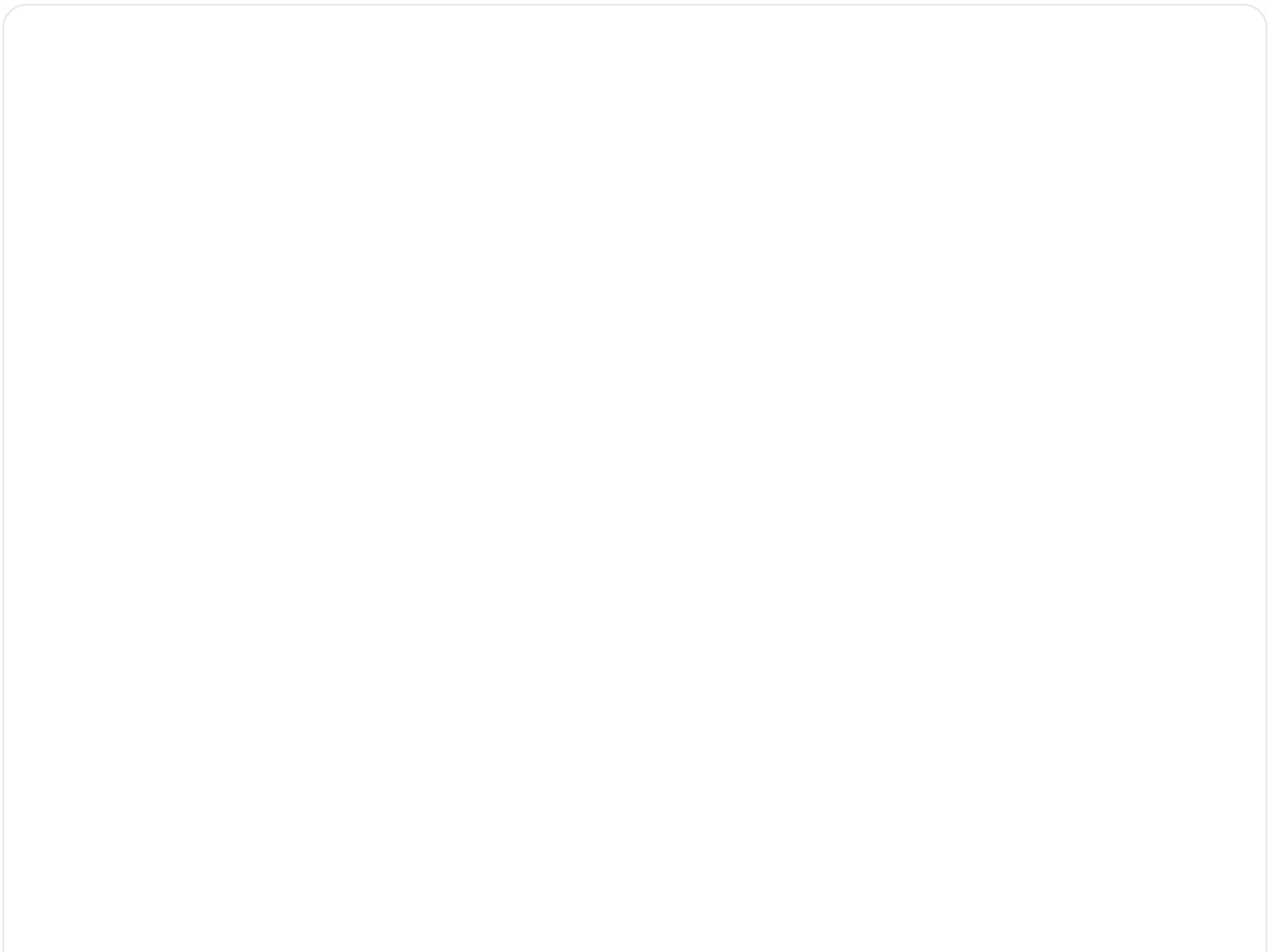


Figure 6. Where each site drains. Levels II–IV carry most nodal disease; midline primaries (base of tongue, soft palate, supraglottis) need both sides of the neck treated.

- **Depth of invasion** is measured from the basement membrane of adjacent normal mucosa, not tumour thickness. It sets the T category (DOI >5 mm = at least T2; >10 mm = T3) and predicts nodal spread: patients with nodal metastases had a mean DOI of 5.6 mm versus 3.8 mm in those without.
- **Mandible:** bone invasion is hard to see before surgery. Edentulous jaws are invaded more easily (no tooth socket barrier); even minimal cortical invasion in an edentulous jaw usually needs a segmental resection.
- **Unknown primary** (squamous cancer in a neck node): p16 and EBER on the node, PET-CT before any biopsy under anaesthesia, then panendoscopy with bilateral tonsillectomy and directed biopsies; transoral lingual tonsillectomy finds many hidden base-of-tongue primaries. N1 without ENE: surgery or RT alone; N2b or more: chemoradiation to both necks and the likely mucosal sites.
- **PET-CT timing:** after chemoradiation, wait 12 weeks; earlier scans give false positives.

04 Biomarkers that change treatment

Biomarkers that change treatment

- **p16/HPV** is the only biomarker that changes staging. In RTOG 0129, 3-year survival was about 82% with HPV-positive and 57% with HPV-negative oropharynx cancer ([Ang 2010](#) ^[8]). Outside trials it does **not** change treatment: replacing cisplatin with cetuximab was worse in [RTOG 1016](#) ^[9] (5-year OS 78 vs 85%) and [De-ESCALaTE HPV](#) ^[10] (2-year OS 89 vs 98%). **p16 outside the oropharynx** is common and does not mean HPV-driven cancer; do not test oral cavity or larynx routinely.
- **PD-L1 combined positive score (CPS)** counts PD-L1-staining tumour cells, lymphocytes and macrophages per 100 tumour cells (22C3 assay). CPS ≥1 opens perioperative pembrolizumab and first-line pembrolizumab; CPS ≥20 identifies those who can have pembrolizumab alone ([KEYNOTE-048](#) ^[3]).
- **Pathological risk features** are the biomarkers that decide adjuvant therapy most often: positive margins and extranodal extension (chemoradiation) versus pT3–T4, multiple nodes, perineural and lymphovascular invasion (RT alone).
- **EGFR** is overexpressed in most head and neck cancers, but its level does not predict benefit from cetuximab and is not tested.
- **Not useful in routine practice:** tumour mutational burden, HRAS, PIK3CA and other NGS findings outside trials; serum markers (SCC antigen, CYFRA 21-1) for diagnosis or follow-up.
- Biology explains radioresistance: tumour hypoxia (well-oxygenated cells are 2.5–3 times more radiosensitive), rapid repopulation during gaps, continued smoking and low haemoglobin. Hypoxic sensitizers such as nimorazole improved locoregional control in a meta-analysis ([Overgaard 2011](#) ^[11]) but are not used widely; erythropoiesis-stimulating agents worsened outcomes ([DAHANCA 10](#) ^[12]).

05 Local therapy: surgery & radiotherapy

Surgery

Figure 7. What the head and neck surgeon offers. Margin status and extranodal extension on the final pathology decide adjuvant therapy, so the operation and the reconstruction are planned with the radiation oncologist from day one.

- **Oral cavity: surgery first** for almost every resectable tumour; it gives pathological staging (DOI, margins, nodes) and causes less long-term morbidity than radiotherapy to the mouth. Plan a 1 cm mucosal margin to reach a final margin >5 mm; re-excise close (<2 mm) or involved margins in early disease rather than relying on RT.
- **Elective neck dissection in the clinically node-negative neck:** in a Tata Memorial trial of 500 patients with early oral cancer (mostly tongue), elective dissection improved 3-year survival from 67.5% to 80% and disease-free survival from 45.9% to 69.5% compared with watch-and-wait ([D'Cruz 2015](#) ^[13]). The benefit was clearest with DOI >3 mm. Selective dissection of levels I–III (IV for tongue) is standard.
- **Sentinel node biopsy** is an alternative in expert centres for T1–T2 cNO tumours: in [Senti-MERORL](#) ^[14], 5-year neck control and survival matched elective dissection, with less shoulder morbidity. Less reliable for floor of mouth.
- **Neck by site:** tongue and floor of mouth DOI >3 mm → elective neck (bilateral if near the midline); DOI ≤ 1 mm and lateralised → observe; 1–3 mm → SLNB or elective dissection; T1 lower lip → observe; buccal, gingiva, retromolar trigone, hard palate → elective dissection.

- **Buccal mucosa:** deceptively easy-looking but hard to clear; the buccal space allows early deep spread to skin. Reconstruct the cheek lining (free flap for all but the smallest defects) or severe trismus follows; jaw exercises are part of treatment.
- **Mandible:** marginal mandibulectomy keeps continuity when tumour abuts but does not enter medullary bone; segmental resection for invasion, reconstructed with a vascularised fibula (or scapula) and plate. Primary reconstruction is standard; an anterior defect left unreconstructed causes the "Andy Gump" deformity.
- Reconstruction choices: radial forearm (tongue, floor of mouth, soft palate), anterolateral thigh (large soft-tissue defects), fibula or scapula (mandible, maxilla), pectoralis major as a robust regional flap. Free-flap success rates are 93–99% in experienced hands.

Radiotherapy

Figure 8. Radiotherapy schedules (illustrative). Head and neck squamous cancers repopulate fast during treatment gaps, so time matters as much as dose.

- **IMRT is standard:** it spared salivary function compared with conventional RT in randomised trials, including a Tata Memorial trial ([PARSPORT](#) ^[15], [Gupta 2012](#) ^[16]); dysphagia-optimised IMRT improved patient-reported swallowing ([DARS](#) ^[17]). Daily image guidance allows tighter margins.

- **Altered fractionation** without chemotherapy improves survival over standard RT (hyperfractionation most; [MARCH](#) ^[18], [Bourhis 2006](#) ^[19]), but does not replace concurrent chemotherapy; with cisplatin, give once-daily RT.
- **Time matters:** start postoperative RT within 6 weeks and finish within about 100 days of surgery ([Ang](#) ^[20] [2001](#) ^[20]); avoid gaps during definitive RT. Continued smoking during RT lowers response and survival.
- **Definitive RT for oral cancer** is reserved for those who cannot have surgery: it controls the primary less well and carries a higher risk of osteoradionecrosis. Brachytherapy boosts suit small, accessible tumours in experienced centres.
- **After definitive (chemo)RT:** clinical review at 4–6 weeks, PET-CT at 12 weeks; neck dissection only for residual disease or an unequivocally positive PET. In [PET-NECK](#) ^[21] (564 patients with N2–N3 disease), PET-CT surveillance gave the same 2-year survival as planned neck dissection and avoided most operations. Salvage surgery for residual primary disease.
- Protons may spare normal tissue further (lower feeding-tube rates in one trial) but are costly and not standard.
- **Re-irradiation** for recurrence or a second primary in an irradiated field: salvage surgery first if possible; postoperative re-irradiation only for high-risk pathology; re-irradiation with chemotherapy (or SBRT) for selected unresectable recurrences at experienced centres. Treatment deaths approach 10% and severe toxicity up to 50%: select carefully by prior dose, interval, volume and fitness.

o6 Systemic therapy: indications & options

Indications and options only; no doses. Benefits are given in absolute terms where possible. Trial names link to the primary publications.

Chemotherapy with radiotherapy (locally advanced disease)

Figure 9. Three routes for locally advanced disease. Concurrent chemoradiation adds about 6.5% absolute 5-year survival over radiotherapy alone (MACH-NC); the choice of route is about function as much as cure.

- **Concurrent chemoradiation** improved overall survival over RT or surgery alone in 71 trials (10,680 patients): absolute gain 6.5% at 5 years, 3.6% at 10 years, from fewer locoregional failures ([MACH-NC 2021](#) ^[22]). There was **no benefit over age 70** (HR 0.97); RT alone is usual for older or frail patients.
- **Cisplatin is the sensitiser**, weekly or every 3 weeks, aiming at a cumulative dose of at least 200 mg/m². In the Indian ConCERT trial (270 patients, mostly oropharynx), weekly cisplatin had non-inferior locoregional control with less severe mucositis (41 vs 54%) and kidney injury (4 vs 18%). Earlier, a Tata Memorial trial using a lower weekly dose found 3-weekly cisplatin better in the postoperative oral cavity setting ([Noronha 2018](#) ^[23]); weekly dosing must be full-dose to work.
- **Cisplatin-ineligible** (creatinine clearance <50 mL/min, hearing loss, neuropathy, ECOG 2, >10% weight loss): in a Tata Memorial trial of 356 such patients, adding weekly low-dose docetaxel to RT improved 2-year overall survival from 42% to 51% and DFS from 30% to 42%, with more mucositis ([Patil 2023](#) ^[24]). Carboplatin-based regimens are alternatives.

- **Cetuximab** with RT beat RT alone (3-year OS 55 vs 45%; [Bonner 2006](#) ^[25], [5-year update](#) ^[26]) but is inferior to cisplatin ([RTOG 1016](#) ^[9], [De-ESCALaTE HPV](#) ^[10], [ARTSCAN III](#) ^[27]), adds nothing to cisplatin-RT ([RTOG 0522](#) ^[28]) and is not used with RT in older or frail patients.
- **Induction chemotherapy** (TPF) beat PF in [TAX 324](#) ^[29] (5-year OS 52 vs 42%) and [TAX 323](#) ^[30] (median 18.8 vs 14.5 months), but adding induction to chemoradiation did not improve survival in [PARADIGM](#) ^[31] or [DeCIDE](#) ^[32]. Use it selectively: larynx/hypopharynx preservation (response selects patients for RT), bulky N2c–N3 disease, borderline–resectable oral cancer, or when RT will be delayed. Neutropenia is frequent: G-CSF and/or antibiotic prophylaxis.
- **Checkpoint inhibitors added to definitive chemoradiation** have failed: avelumab ([JAVELIN Head and Neck 100](#) ^[33]), pembrolizumab (KEYNOTE–412) and pembrolizumab instead of cetuximab with RT in cisplatin-unfit patients ([PembroRad](#) ^[34]).

Immunotherapy around surgery

- **Perioperative pembrolizumab** ([KEYNOTE–689](#) ^[1]): in resectable stage III–IVA oral cavity, larynx, hypopharynx or HPV-negative oropharynx cancer, two neoadjuvant doses before surgery and pembrolizumab with and after postoperative RT ($\pm$ cisplatin) improved 3-year event-free survival (about 60 vs 46% in CPS ≥ 1 ; HR 0.73 overall). Overall survival is immature and pathological complete response was only about 3%. About 60% had oral cavity cancer. Benefit was confined to CPS ≥ 1 .
- **Nivolumab with postoperative chemoradiation** ([NIVOPOSTOP](#) ^[2]): after resection with high-risk features (ENE, involved margin, ≥ 4 nodes or multiple PNI), adding nivolumab to cisplatin-RT and then 6 months of nivolumab improved 3-year DFS (63 vs 53%; HR 0.76) through better locoregional control, regardless of PD-L1. Grade ≥ 3 toxicity 74 vs 68%. Very few HPV-positive patients: use only for HPV-negative disease. OS immature.
- These two strategies have not been compared; choose one per patient (pembrolizumab started before surgery continues after it). Cost limits access in India: discuss trial and assistance programmes openly.

Adjuvant therapy after surgery

Figure 10. Adjuvant treatment follows the pathology report. Only positive margins and extranodal extension benefited from adding cisplatin in both EORTC 22931 and RTOG 9501.

- In [EORTC 22931](#) ^[35], adding cisplatin to postoperative RT improved 5-year overall survival from 40% to 53%; in [RTOG 9501](#) ^[36] locoregional control improved but survival did not. A pooled analysis showed the benefit was confined to **positive margins and extranodal extension** ([Bernier 2005](#) ^[37]; [RTOG 9501 at 10](#) ^[38] **years** ^[38]).
- Weekly cisplatin with postoperative RT was non-inferior to 3-weekly and less toxic in [JCOG1008](#) ^[39] (3-year OS 72 vs 59%; less neutropenia, hearing loss and kidney injury).
- Intermediate-risk features (pT3–T4, ≥2 nodes without ENE, PNI, LVI, levels IV–V, close margins) → RT alone; cetuximab with RT improved DFS but not OS and doubled late severe toxicity.
- **Early oral cancer:** re-excision for close or involved margins rather than RT; RT for pN+ disease, bone invasion and DOI >4 mm with other risk features.

Recurrent or metastatic disease

Figure 11. First-line choices by PD-L1 combined positive score (CPS). Immunotherapy prolongs overall survival and gives a small group durable control; response rates alone underestimate its value.

- **First, ask whether the recurrence is curable:** resectable local or isolated neck recurrence without distant spread → salvage surgery (elective bilateral neck dissection for recurrent larynx and pharynx cancers), with postoperative re-irradiation only for high-risk pathology; unresectable → re-irradiation with chemotherapy in selected patients at experienced centres. Distinguish a second primary from a recurrence (biopsy; especially a new lung lesion). Palliative systemic therapy is for the rest.
- **Pembrolizumab first line** ([KEYNOTE-048](#) ^[3], [4-year update](#) ^[40]): pembrolizumab with platinum–5FU beat cetuximab–platinum–5FU in all patients (median OS 13 vs 11 months; 4-year OS 19 vs 5%). Pembrolizumab alone was better in CPS ≥1 (4-year OS 17 vs 6%), driven by CPS ≥20 (median 15 vs 11 months), with a lower response rate (17 vs 36%), early progression in some, and far less grade ≥3 toxicity (17 vs 69%).
- **EXTREME** (platinum–5FU–cetuximab, then cetuximab maintenance) improved median OS from 7.4 to 10.1 months ([EXTREME](#) ^[41]) and remains the choice when immunotherapy is unsuitable. Nivolumab–ipilimumab did not beat it ([CheckMate 651](#) ^[42]).
- **Platinum-refractory disease** (progression within 6 months of platinum): nivolumab (median OS 7.7 vs 5.1 months; 1-year OS 34 vs 20%; [CheckMate 141](#) ^[43]) or pembrolizumab (median 8.4 vs 6.9 months; [KEYNOTE-^{\[44\]} 040](#) ^[44]) over methotrexate, docetaxel or cetuximab.
- **Indian evidence for low-cost care:** oral metronomic methotrexate–celecoxib (± erlotinib) is active and well tolerated ([Patil 2019](#) ^[45]); adding **low-dose nivolumab** to metronomic chemotherapy improved overall survival in a randomised Tata Memorial trial ([Patil 2023](#) ^[46]), a pragmatic option where full-dose immunotherapy is unaffordable.

- Later lines: taxanes, cetuximab, methotrexate, platinum rechallenge after a long interval. Offer palliative care early; many patients need help with pain, bleeding, airway, feeding and wound care.



Quick-reference tables

Quick-reference tables (also printable as one PDF from the Printable Teaching Resources page). No chemotherapy doses; check current approvals and product information.

Table A. Pathology and biomarker tests that change management

Test	Where it matters	How tested	What it changes	Key evidence
p16 (surrogate for HPV)	Every oropharyngeal squamous cancer; neck node of unknown primary	IHC: strong, diffuse nuclear and cytoplasmic staining in ≥70% of cells; confirm with HPV DNA/RNA (ISH or PCR) when decisions hinge on it; FNA cell blocks under-call p16	Selects the HPV staging table; better prognosis; points the unknown-primary search to tonsil and base of tongue	Ang 2010 ^[8] , EPIC-OPC 2023 ^[47]
p16/HPV discordance	Oropharynx cancers tested both ways	p16 IHC plus HPV DNA/RNA	p16+/HPV- or p16-/HPV+ behaves close to HPV-negative disease (5-year OS about 55% vs 81% when both positive): do not de-escalate	EPIC-OPC 2023 ^[47]
Depth of invasion (DOI)	Oral cavity, above all oral tongue	Measured from the basement membrane of adjacent normal mucosa (not tumour thickness)	Sets T category (>5 mm = at least T2, >10 mm = T3); DOI >3 mm → elective neck treatment; >4 mm favours adjuvant RT	AJCC 8th; D'Cruz ^[13] 2015 ^[13]
Margins	Every resection	Clear >5 mm; close 1–5 mm (oral cavity <2 mm in some guidance); involved = tumour at ink	Involved: re-excise or postoperative chemoradiation; close: re-excise (early oral) or RT	Bernier 2005 ^[37]
Extranodal extension (ENE)	Every neck dissection	Pathology: tumour through the node capsule (record major vs minor if possible)	Adds cisplatin to postoperative RT (± nivolumab in HPV-negative disease); upstages to pN3b in non-HPV sites	EORTC 22931 ^[35] , RTOG 9501 ^[36] , NIVOPOSTOP ^[2]
PNI, LVI, grade, nodal number	Resected specimens	Pathology synoptic report	Intermediate risk → postoperative RT alone; ≥2 nodes is a weaker reason for chemotherapy	Bernier 2005 ^[37]
PD-L1 combined positive score (CPS)	Resectable stage III–IVA (perioperative pembrolizumab) and recurrent/metastatic disease	22C3 assay; CPS = PD-L1+ positive tumour cells and immune cells ÷ tumour cells × 100	CPS ≥1: pembrolizumab-based first line; CPS ≥20: pembrolizumab alone is an option; CPS ≥1 needed for KEYNOTE-689 benefit	KEYNOTE-048 ^[3] , KEYNOTE-689 ^[1]
EBV DNA / EBER	Nasopharynx; neck node of unknown primary with undifferentiated histology	EBER ISH on tissue; plasma EBV DNA	Points to nasopharynx; plasma EBV DNA for prognosis and follow-up (see Nasopharyngeal carcinoma , section O6)	—
Cisplatin fitness	Before chemoradiation	Creatinine clearance, audiogram, neuropathy, performance status, age, weight loss	Ineligible: RT alone (older/unfit) or RT + weekly docetaxel / carboplatin; avoid cetuximab in HPV-positive disease	Patil 2023 ^[24] , RTOG 1016 ^[9]

Table B. Treatment by setting (no doses)

Setting	Standard	Alternatives / notes	Evidence
Oral cavity T1–T2 NO	Wide excision (margin >5 mm) + elective neck dissection if DOI >3 mm (SLNB in expert centres)	DOI ≤1 mm lateralised: observe neck; close margin: re-excise; RT only if surgery not possible	D'Cruz 2015 ^[13] , Senti- ^[14] MERORL ^[14]
Oral cavity T3–T4a or N+	Resection + neck dissection + reconstruction → adjuvant RT ± cisplatin	CPS ≥1: perioperative pembrolizumab option; borderline resectable: TPF induction then reassess	KEYNOTE-689 ^[1] , EORTC 22931 ^[35]
Oropharynx T1–T2 NO–N1	Definitive RT or transoral surgery + neck dissection	Choose the route that is least likely to need a second or third modality	ORATOR ^[48]
Oropharynx stage III–IV (HPV+ or –)	Cisplatin chemoradiation (weekly or 3-weekly)	Cisplatin-ineligible: carboplatin-based or weekly docetaxel; never cetuximab in HPV+; TORS for selected small primaries	RTOG 1016 ^[9] , De- ^[10] ESCALaTE HPV ^[10] , Noronha 2018 ^[23]
Glottic T1–T2	RT (small field, slightly hypofractionated) or transoral laser surgery	No elective neck treatment; voice outcomes similar	NCCN; EHNS–ESMO–ESTRO guideline
Supraglottic T1–T2	RT or transoral surgery with bilateral elective neck (II–IV)	Open supraglottic laryngectomy for selected cases	NCCN
Larynx/hypopharynx stage III–IVA, larynx preservation wanted	Cisplatin chemoradiation, or TPF induction → RT in responders	T4a with cartilage destruction or a non-functional larynx: total laryngectomy + adjuvant RT	RTOG 91-11 ^[49] , VA ^[50] Larynx ^[50] , TAX ^[29] 324 ^[29]
Postoperative: positive margin or ENE	RT + cisplatin (weekly preferred)	HPV-negative: add nivolumab (NIVOPOSTOP); cisplatin-ineligible: RT ± weekly docetaxel	JCOG1008 ^[39] , NIVOPOSTOP ^[2] , Patil ^[24] 2023 ^[24]
Postoperative: intermediate risk	RT alone, within 6 weeks of surgery	Cetuximab with RT improved DFS but not OS and doubled severe toxicity	Ang 2001 ^[20]
Unfit, ≥70 years or comorbid	RT alone (accelerated or hyperfractionated if feasible)	Hypofractionated palliative RT for symptoms	MACH-NC 2021 ^[22] , MARCH meta-analysis ^[18]
Recurrent/metastatic, first line, CPS ≥1	Pembrolizumab alone (CPS ≥20) or with platinum–5FU	Rapid progression: add chemotherapy regardless of CPS	KEYNOTE-048 ^[3] , KEYNOTE-048 update ^[40]
Recurrent/metastatic, CPS <1 or IO not possible	Platinum + 5FU or taxane ± cetuximab (EXTREME) ± pembrolizumab	Frail: single-agent taxane, methotrexate or oral metronomic regimens	EXTREME ^[41] , Patil ^[45] 2019 ^[45]
Platinum-refractory (<6 months)	Nivolumab or pembrolizumab	Low-dose nivolumab with metronomic chemotherapy improved survival in an Indian trial	CheckMate 141 ^[43] , KEYNOTE-040 ^[44] , Patil 2023 ^[46]
Nasopharyngeal carcinoma (stage III–IVA)	Induction gemcitabine–cisplatin (or TPF) → cisplatin–IMRT; metronomic capecitabine if high risk	Stage I: IMRT alone; metastatic: gemcitabine–cisplatin + PD-1 inhibitor; local recurrence: endoscopic surgery or hyperfractionated re-IMRT	Zhang 2019 ^[51] , Chen ^[52] 2021 ^[52] , JUPITER- ^[53] Q2 ^[53]

Setting	Standard	Alternatives / notes	Evidence
Isolated local recurrence	Salvage surgery if resectable	Re-irradiation (IMRT or SBRT) in selected patients at experienced centres	NCCN

Table C. Before, during and after treatment: supportive care checklist

When	What	Why
Before	Dental assessment and OPG; extract unsalvageable teeth ≥10–14 days before RT; fluoride trays	Extractions in irradiated bone are the main trigger for osteoradionecrosis
Before	Dietitian: baseline weight, BMI, swallowing; plan feeding route (prophylactic tube in selected high-risk patients)	Weight loss >10% predicts toxicity and treatment breaks
Before	Speech and swallowing assessment; start swallow and jaw exercises	Preventive exercises improve swallowing outcomes whatever the timing (PRO-ACTIVE)
Before	Stop tobacco and areca nut; alcohol counselling; quitline 1800- 11-2356	Continued smoking lowers response and survival and raises toxicity
Before	Audiogram, creatinine clearance, hepatitis B screen, TSH baseline	Cisplatin eligibility; baseline for late hypothyroidism
During	Weekly review: mucositis, pain (step up to opioids early), weight, hydration, skin	Avoid unplanned RT breaks: every lost day lowers local control
During	Salt-and-soda rinses several times a day; soft, non-spicy food; treat oral candida	Mucositis is unavoidable; good care limits it
During	Fever on cisplatin/TPF: same-day neutropenia check; G-CSF ± antibiotic prophylaxis with TPF	Febrile neutropenia in about 1 in 8 on TPF
After	Clinic + scope per schedule; PET-CT at 12 weeks after CRT for node-positive disease	Earlier PET gives false positives
After	TSH every 6–12 months; dental review 6-monthly; fluoride for life	Hypothyroidism and radiation caries are common and silent
After	Swallow, jaw (trismus) and shoulder physiotherapy; lymphoedema care	Late dysphagia and trismus can appear years later
After	Screen for depression and suicide risk; return-to-work and family support	Head and neck survivors carry a high psychological burden

Table D. Managing common side effects

Problem	Usual cause	Prevent	Act when
Oral mucositis	RT ± chemotherapy	Oral hygiene, salt-soda rinses, IMRT, stop tobacco	Cannot swallow liquids or pain uncontrolled: admit, IV fluids, opioids, feeding tube
Xerostomia	RT to parotid/submandibular glands	Parotid-sparing IMRT (PARSPORT)	Saliva substitutes, sips of water, sugar- free gum; pilocarpine in selected patients

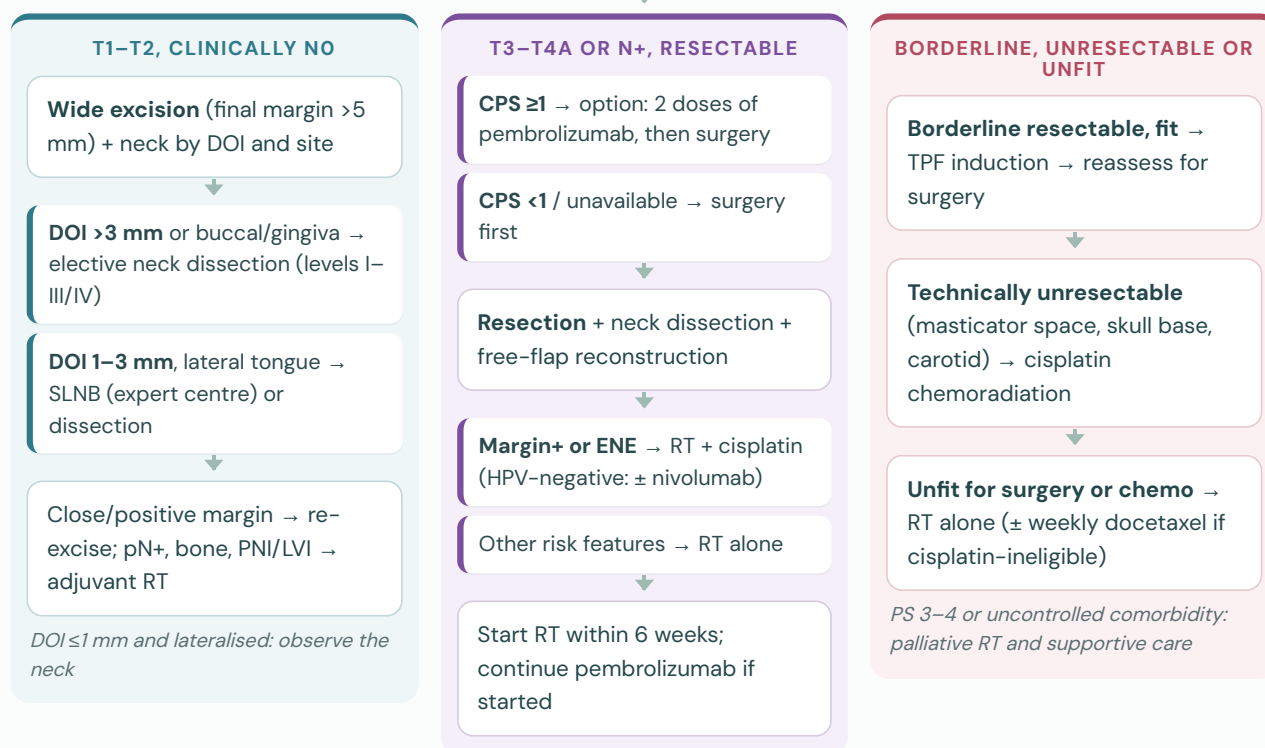
Problem	Usual cause	Prevent	Act when
Radiation caries, osteoradionecrosis	Xerostomia; extractions after RT	Fluoride trays for life; extractions before RT; atraumatic dentistry later	Exposed bone >3 months: oral surgery referral; pentoxifylline–tocopherol or surgery for advanced cases
Dysphagia, aspiration	RT to pharyngeal constrictors, surgery	Swallow exercises; keep eating by mouth when safe; DO-IMRT (DARS)	Cough with meals, chest infections: video–fluoroscopy or FEES; dilatation for stricture
Trismus	RT to masticator muscles, surgery	Jaw–stretch exercises from day one	Mouth opening <35 mm: structured therapy (stacked spatulas, devices)
Hearing loss, tinnitus	Cisplatin, RT near the ear	Baseline audiogram; switch agent if hearing falls	Hearing aids; consider weekly schedule or alternative sensitiser
Kidney injury, hypomagnesaemia	Cisplatin	Hydration, magnesium, avoid nephrotoxins	Creatinine rise: hold and reassess eligibility
Acneiform rash, infusion reaction	Cetuximab	Skin care, sun protection, premedication	Grade 3 rash: hold and treat; anaphylaxis: stop permanently
Immune–related effects	Pembrolizumab, nivolumab	Baseline TSH, LFT, glucose; patient alert card	Diarrhoea, breathlessness, rash, fatigue: grade and treat early (steroids as per guidelines)
Hypothyroidism	Neck RT, immunotherapy	TSH every 6–12 months	Raised TSH: thyroxine replacement
Neck fibrosis, lymphoedema, shoulder drop	Neck dissection (nerve XI), RT	Nerve–sparing dissection; early physiotherapy	Manual lymph drainage, shoulder rehabilitation
Weight loss	All of the above	Weekly weights; early dietitian; tube before >10% loss	Rapid loss or dehydration: feeding tube, admission

07 Management algorithms

ALGORITHM 1

Oral cavity cancer

Biopsy-proven oral SCC: CT or MRI of the primary and neck · CT chest (PET-CT if stage III–IV) · DOI estimate · dental OPG · nutrition · tobacco cessation · PD-L1 CPS if stage III–IVA · tumour board

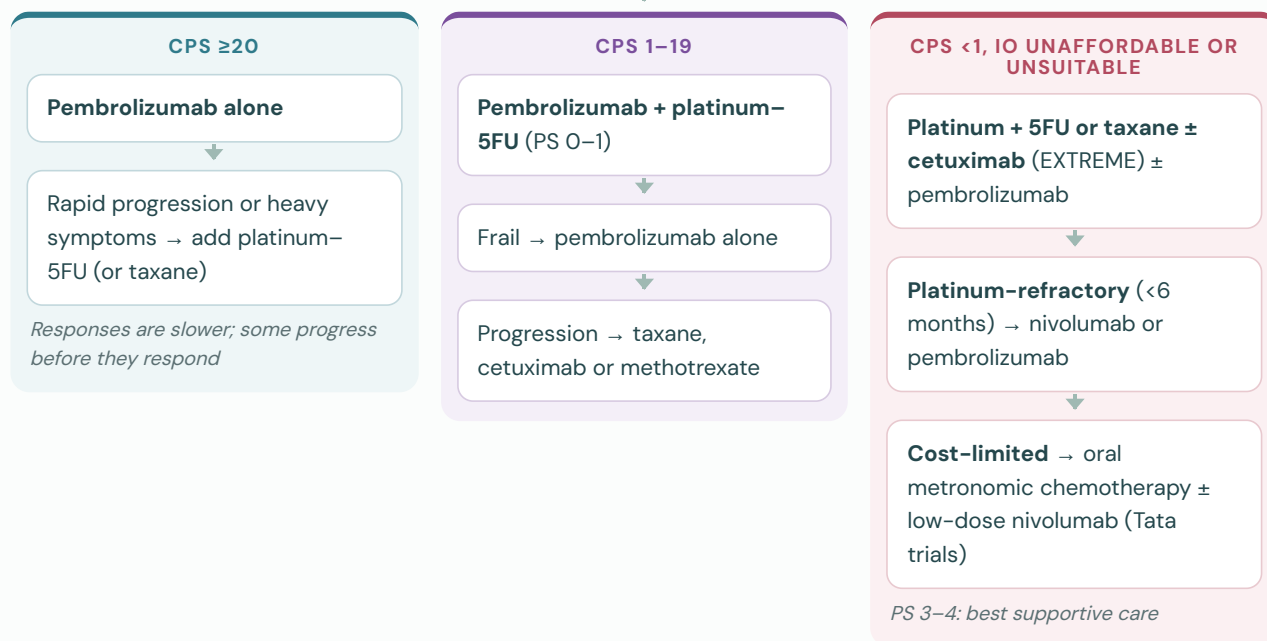


All patients: dental clearance before RT · swallow and jaw exercises · weight weekly · PET-CT at 12 weeks only after definitive (chemo)RT · TSH every 6–12 months after neck RT · stop tobacco and areca nut for life.

ALGORITHM 5

Recurrent or metastatic disease

Recurrence suspected: biopsy · PET-CT · is it curable? (isolated local/neck → salvage surgery or re-irradiation at an experienced centre) · PD-L1 CPS · performance status · goals of care



All patients: early palliative care · pain, bleeding and airway plans · nutrition and feeding route decisions with the family · trials where available · carboplatin rather than cisplatin after previous cisplatin.

o8 Survivorship, follow-up & reducing recurrence

Figure 13. When relapses happen (illustrative shapes, not to scale). About 80–90% of recurrences appear within 2–3 years, so follow-up is most intensive then; second primary cancers continue for life.

Figure 14. A simple follow-up rhythm (NCCN, American Cancer Society survivorship guideline). Imaging is a baseline at about 12 weeks; afterwards the examination and the patient's symptoms drive tests.

Follow-up protocol (NCCN, American Cancer Society)

Interval	What	Also
Year 1	Clinic with examination and flexible scope every 1–3 months	Baseline imaging of primary and neck about 12 weeks after treatment (PET-CT after chemoradiation)
Year 2	Every 2–4 months	Imaging only for symptoms or a hard-to-examine site
Years 3–5	Every 4–6 months	TSH every 6–12 months after neck RT; dental review 6-monthly
After 5 years	Yearly, for life	Late effects, second primaries; low-dose chest CT yearly if ≥20 pack-years and fit

- **Second primaries and lifestyle:** up to 20% of survivors develop a second tobacco- or alcohol-related cancer. Stopping tobacco and areca nut is the most effective step after treatment; offer cessation support at every visit (quitline 1800-11-2356).
- **Teeth and jaw:** lifelong fluoride, 6-monthly dental review, atraumatic dentistry; osteoradionecrosis affects about 5–7% after IMRT and most cases follow extractions in irradiated bone. Trismus affects up to a third: jaw exercises.
- **Swallowing:** keep eating by mouth when safe; start or continue swallow exercises; late radiation-associated dysphagia can appear years later ([Hutcheson 2012](#) ^[54]). 10–25% of survivors depend on tube feeding in some series.
- **Thyroid:** TSH every 6–12 months after neck RT; hypothyroidism is common and silent.
- **Neck and shoulder:** lymphoedema (face and neck), fibrosis and shoulder dysfunction after neck dissection: physiotherapy and manual lymph drainage.

- **Mind and family:** survivors face high rates of depression, anxiety and suicide; disfigurement, speech and eating changes affect work and marriage. Screen at every visit; involve counsellors and support groups ([ACS^{\[55\]} guideline^{\[55\]}](#)).
- **Shared care with the family doctor and dentist:** give them the follow-up plan, red flags (new ulcer, lump, pain, bleeding, hoarseness, swallowing change, breathlessness) and the TSH schedule.

Figure 15. A four-week target from first visit to treatment. Longer intervals from diagnosis to treatment are linked with worse survival in large observational studies; in India most of the delay happens before the biopsy.

09 Landmark trials

Figure 16. How to read a survival curve (illustrative). Use the absolute gap at a fixed time and overall survival, not the median or PFS alone, when weighing benefit against toxicity and cost.

- **MACH-NC (2021)** ^[22]: 107 trials, 19,805 patients → concurrent chemoradiation +6.5% absolute 5-year survival; no gain over 70; induction or adjuvant chemotherapy alone does not improve survival → concurrent cisplatin-RT is the backbone.
- **EORTC 22931** ^[35] / **RTOG 9501** ^[36]: postoperative RT ± cisplatin → benefit confined to positive margins and ENE → defines high-risk adjuvant therapy.
- **D'Cruz (2015)** ^[13]: elective vs therapeutic neck dissection in early oral cancer (Tata Memorial, 500 patients) → 3-year OS 80 vs 67.5% → elective neck dissection when DOI >3 mm.
- **Senti-MERORL** ^[14]: sentinel node biopsy vs elective dissection (cT1–T2N0 oral/oropharynx) → equal 5-year survival, less shoulder morbidity → SLNB in expert centres.
- **KEYNOTE-689** ^[1]: perioperative pembrolizumab in resectable stage III–IVA disease → 3-year EFS about 60 vs 46% in CPS ≥1; OS immature → new option for PD-L1-positive resectable disease.

- **NIVOPOSTOP** ^[2]: nivolumab + postoperative cisplatin-RT in high-risk resected disease → 3-year DFS 63 vs 53% → option for HPV-negative high-risk disease.
- **PET-NECK** ^[21]: PET-CT surveillance vs planned neck dissection after chemoradiation for N2–N3 → same survival, far fewer operations → PET-CT at 12 weeks decides.
- **TAX 324** ^[29]: TPF vs PF induction → 5-year OS 52 vs 42% → if induction is used, use TPF; **PARADIGM** ^[31] and **DeCIDE** ^[32] found no survival gain from adding it to chemoradiation.
- **Tata docetaxel trial (2023)** ^[24]: RT ± weekly docetaxel in cisplatin-ineligible patients → 2-year OS 51 vs 42% → an affordable sensitiser.
- **KEYNOTE-048** ^[3]: pembrolizumab ± chemotherapy vs EXTREME first line → longer survival (4-year OS 19 vs 5% with chemotherapy) → immunotherapy first line by CPS.
- **CheckMate 141** ^[43]: nivolumab after platinum → 1-year OS 34 vs 20% → PD-1 inhibitors for platinum-refractory disease.
- **Tata low-dose nivolumab trial (2023)** ^[46]: low-dose nivolumab + metronomic chemotherapy vs metronomic chemotherapy → better overall survival → an access-driven option for Indian practice.
- **PARSPORT** ^[15] and **DARS** ^[17]: parotid-sparing and dysphagia-optimised IMRT → less dry mouth and better swallowing → function is an endpoint too.

10 Practice pearls & pitfalls

- A non-healing ulcer or patch for more than 2 weeks after removing an irritant needs a biopsy, not another ointment.
- A painless, hard or cystic neck node in an adult is metastatic cancer until proven otherwise: FNAC, then look for the primary; do not excise it first.
- Hoarseness for more than 3 weeks in a smoker means laryngoscopy.
- Measure DOI and treat the neck: elective neck dissection saves lives in early oral cancer when DOI exceeds 3 mm (D'Cruz).
- Re-excite close margins in early oral cancer; radiotherapy is a poor substitute for a clear margin.
- In edentulous patients the mandible is invaded more easily; plan segmental resection and fibula reconstruction early.
- Weekly cisplatin works only at full dose; count the cumulative dose (aim ≥ 200 mg/m²).
- Over 70 or frail: radiotherapy alone; chemotherapy added no survival in MACH-NC.
- Extract hopeless teeth before radiotherapy, not after; prescribe fluoride for life.
- Every day of unplanned RT break costs control: solve pain, nutrition and transport problems before they cause a gap.
- PET-CT after chemoradiation at 12 weeks, not earlier.
- Check PD-L1 CPS early: it decides perioperative pembrolizumab and first-line therapy at recurrence.
- Where full-dose immunotherapy is unaffordable, low-dose nivolumab with metronomic chemotherapy is evidence-based (Tata Memorial).
- Ask about tobacco, areca nut and alcohol at every visit for life; cessation is treatment.

11 Case vignettes: lines of management

Eight cases, written for postgraduates and practising clinicians. Read the presentation, decide on diagnosis, workup and plan, then open the line of management. No doses are given.

CASE 1 Oral tongue · early · DOI

A tongue ulcer treated with gels for three months

46 years, man

Lateral tongue, 1.8 cm

cNO, DOI ~4 mm on MRI

A 46-year-old shopkeeper who chews gutka has a painful ulcer on the left lateral tongue next to a sharp molar. Two dentists prescribed gels and smoothed the tooth; it persisted for 3 months. Examination: 1.8 cm indurated ulcer, no palpable nodes. Punch biopsy: moderately differentiated SCC.

Before you open the answer: what is the likely diagnosis, what must be done before treatment, and what is the plan?

1

STAGING

MRI of the oral cavity and neck: DOI about 4 mm, no suspicious nodes; CT chest clear. Dental review; tobacco cessation.

2

SURGERY

Partial glossectomy with a 1 cm planned margin and an ipsilateral selective neck dissection (levels I–IV), because DOI is above 3 mm.

3

PATHOLOGY

pT2 (DOI 6 mm), margins clear at 7 mm, 0 of 28 nodes, no PNI or LVI: stage II.

4

AFTER SURGERY

No adjuvant therapy. Follow-up 1–3-monthly in year 1; stop gutka permanently (the field is at risk).

TEACHING POINTS

- Two weeks is the limit for an unexplained mouth ulcer: biopsy.
- DOI, not size alone, drives T stage and elective neck treatment.
- Elective neck dissection improved survival in early oral cancer (D'Cruz).

See: Sections 02, 03, 05 · Algorithm 1 · [D'Cruz 2015](#) ^[13], [Senti-MERORL](#) ^[14]

CASE 2 Buccal mucosa · pN1 · adjuvant RT

A cheek ulcer in a long-time khaini user

52 years, woman

Buccal mucosa, 3.5 cm

Oral submucous fibrosis

A 52-year-old agricultural worker who has used khaini and pan for 30 years has a 3.5 cm ulceroproliferative lesion of the right buccal mucosa. Mouth opening is two fingers (submucous fibrosis). A 1.5 cm mobile level IB node is palpable. Biopsy: SCC.

Before you open the answer: what is the likely diagnosis, what must be done before treatment, and what is the plan?

1

STAGING

Contrast CT face and neck: no bone invasion, no masticator space involvement; one 1.6 cm level IB node without ENE. CT chest clear. Dental clearance; dietitian.

2

SURGERY

Wide excision with a margin of the buccal pad and skin preserved, modified neck dissection, radial forearm free flap to reline the cheek.

3 PATHOLOGY

pT3 (DOI 11 mm), margins clear (6 mm), 1 of 32 nodes positive (2 cm, ENE negative), PNI present.

4 ADJUVANT

Postoperative RT (about 60 Gy) to the primary and neck, starting within 6 weeks; no chemotherapy (no positive margin or ENE). Jaw-stretch exercises during and after RT to prevent trismus.

TEACHING POINTS

- Buccal cancers spread deep early; reconstruct the lining or trismus follows.
- Adjuvant RT alone for intermediate-risk features; cisplatin only for margins or ENE.
- Submucous fibrosis makes examination and follow-up harder: train the patient in self-examination.

See: Sections 02, 05, 06 · Algorithm 1 · [Bernier 2005](#) ^[37], [Ang 2001](#) ^[20]

CASE 3 Gingivobuccal T4a · CPS ≥1 · ENE**A loose tooth that was extracted**

58 years, man

Lower gum, bone invasion

cN2b, CPS 15

A 58-year-old man had a loose lower molar extracted; the socket never healed and a growth appeared. Examination: 4 cm lesion of the lower gingivobuccal sulcus with chin numbness and two palpable ipsilateral nodes. Biopsy: SCC; PD-L1 CPS 15.

Before you open the answer: what is the likely diagnosis, what must be done before treatment, and what is the plan?

1 STAGING

CT: erosion into the medullary mandible (T4a), two nodes (N2b). PET-CT: no distant spread. Stage IVA. Fit, PS 1.

2 OPTIONS AT THE TUMOUR BOARD

Surgery first, or two doses of neoadjuvant pembrolizumab followed by surgery and pembrolizumab with and after adjuvant RT (KEYNOTE-689, CPS ≥1). Cost and access discussed; he chooses the pembrolizumab route through an assistance programme.

3 SURGERY

Composite resection with segmental mandibulectomy, comprehensive ipsilateral neck dissection, fibula free flap with plate.

4 PATHOLOGY

pT4a, margins clear, 3 nodes positive, one with extranodal extension.

5 ADJUVANT

RT with cisplatin (ENE) plus pembrolizumab, then maintenance pembrolizumab. (Had he not received neoadjuvant pembrolizumab, nivolumab with cisplatin-RT would be the NIVOPOSTOP option for this HPV-negative, ENE-positive disease.)

TEACHING POINTS

- A non-healing extraction socket is a classic presentation of gingival cancer.
- Bone invasion → segmental resection and free-flap reconstruction.
- ENE → chemoradiation; checkpoint inhibitors now extend the options before or after surgery.

See: Sections 04–06 · Algorithm 1 · [KEYNOTE-689](#) ^[1], [NIVOPOSTOP](#) ^[2], [EORTC 22931](#) ^[35]

CASE 4 Recurrent/metastatic · CPS ≥20 · access

Lung nodules eight months after chemoradiation

60 years, man

Oral cavity cancer

CPS 25

Eight months after surgery and adjuvant cisplatin-RT for an oral tongue cancer, a 60-year-old man has cough. CT: multiple lung nodules; biopsy confirms metastatic SCC (rather than a new lung primary). PD-L1 CPS 25. PS 1. Family income is limited.

Before you open the answer: what is the likely diagnosis, what must be done before treatment, and what is the plan?

1

IS IT CURABLE?

Multiple lung metastases: no; aim for longer life with good quality.

2

BEST EVIDENCE

Pembrolizumab alone (CPS ≥20: median OS 15 vs 11 months over EXTREME, with far less toxicity); add chemotherapy if symptoms progress fast.

3

IF FULL-DOSE IMMUNOTHERAPY IS UNAFFORDABLE

Low-dose nivolumab with oral metronomic chemotherapy (Tata Memorial trial, improved survival), or metronomic chemotherapy alone; EXTREME-type chemotherapy if fit.

4

PALLIATIVE CARE

Introduced at the same visit: symptom control, home care, and discussion of goals with the family.

TEACHING POINTS

- Biopsy a new lung lesion: second primary or metastasis changes treatment.
- CPS decides first-line immunotherapy.
- Evidence-based, lower-cost options exist and should be offered openly.

See: Sections 06, 07 · Algorithm 5 · [KEYNOTE-048](#) ^[3], [Patil 2023](#) ^[46], [Patil 2019](#) ^[45]

12 References & guidelines

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- American Cancer Society head and neck cancer survivorship care guideline; MASCC/ISOO mucositis guidance.
- Indian context: National Programme for Prevention and Control of Non-Communicable Diseases (NP-NCD) oral cancer screening; GLOBOCAN 2022 (India); Tata Memorial Centre randomised trials cited above.
- Cross-checked in October 2026 against 39 UpToDate topic reviews (epidemiology and risk factors; HPV-associated cancer; diagnosis and staging; overview of treatment; early oral cavity, oropharynx and larynx; locoregionally advanced oral cavity and oropharynx; chemoradiation approaches; adjuvant RT/chemoradiation; general principles of RT; radiation resistance; complications during treatment; mandibular and palatal reconstruction; speech and swallowing rehabilitation; quality of life; long-term survivors; recurrent and metastatic disease; plus, in a second batch, larynx and hypopharynx (early and advanced), unknown primary, management of the neck after RT, surveillance, re-irradiation, local recurrence, second primaries, chemoprevention and screening, late complications, dose and fractionation, pathology, HPV virology, epidemiology and treatment, treatment protocols, HIV and malignancy, sarcomas, alcohol, and sexual health). Facts only, in our own words; primary sources cited.
- Not covered by the supplied topics and written from guidelines or memory, flagged for Dr. Haritha's review: India incidence figures and stage distribution; ConCERT (abstract, no PubMed record yet); KEYNOTE-412 (abstract); NP-NCD screening age; extraction timing before RT.
- Nasopharyngeal carcinoma: no UpToDate nasopharynx topics were supplied; the 16 NPC citations were checked on 11 October 2026 against UpToDate reference lists (4) and PubMed, ClinicalTrials.gov or journal records (12). Citation audit (11 October 2026): every reference is numbered in order of first citation, each in-text trial link carries its number, and every printed journal, year, volume and first page matches its PubMed link.

Core trials cited on this page (55)

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Educational summary for health professionals, written in our own words from current guidelines and primary trials. No chemotherapy doses

are given. Verify current guidelines, Indian regulatory approvals and individual patient factors before treatment decisions.