City of Hope

Multidisciplinary Approaches to Cancer Symposium

Management of HPV Positive Head and Neck

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City of Hope

Disclosures

- Grant Research Support from Privo Technologies; and Stock/Shareholder (publicly owned company) Bristol Myers Squibb, Milestone Pharmaceuticals, Pacific Biosciences, Pfizer ,Regeneron, & Viking Therapeutics

This presentation and/or comments will be free of any bias toward or promotion of the above referenced companies or their product(s) and/or other business interests.

This presentation and/or comments will provide a balanced, non-promotional, and evidence-based approach to all diagnostic, therapeutic and/or research related content.

This presentation has been peer-reviewed and no conflicts were noted.

Cultural Linguistic Competency (CLC) & Implicit Bias (IB)

STATE LAW:

The California legislature has passed Assembly Bill (AB) 1195, which states that as of July 1, 2006, all Category 1 CME activities that relate to patient care must include a cultural diversity/linguistics component. It has also passed AB 241, which states that as of January 1, 2022, all continuing education courses for a physician and surgeon **must** contain curriculum that includes specified instruction in the understanding of implicit bias in medical treatment.

The cultural and linguistic competency (CLC) and implicit bias (IB) definitions reiterate how patients' diverse backgrounds may impact their access to care.

EXEMPTION:

Business and Professions Code 2190.1 exempts activities which are dedicated solely to research or other issues that do not contain a direct patient care component.

The following CLC & IB components will be addressed in this presentation:

- *Barriers faced by HPV positive patients*

Epidemiology of HPV related OPSCCs

- Human papilloma virus (HPV) cancers have been increasing in incidence
- Oropharynx: Tonsils, Base of tongue, soft palate, posterior pharyngeal wall
- In 2018 OPSCC had surpassed cervical cancer as the most common HPV-associated cancer in the US
- Annual increases in OPSCC incidence rates of 2.7% in men and 0.8% in women from 1999 to 2015.

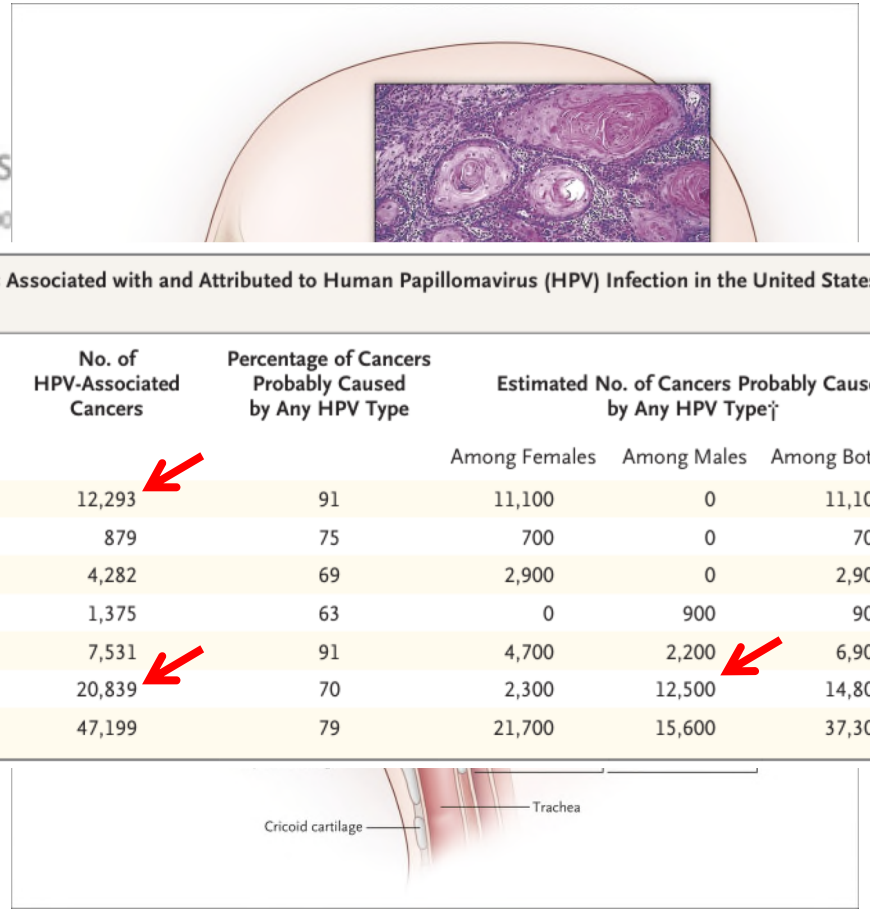


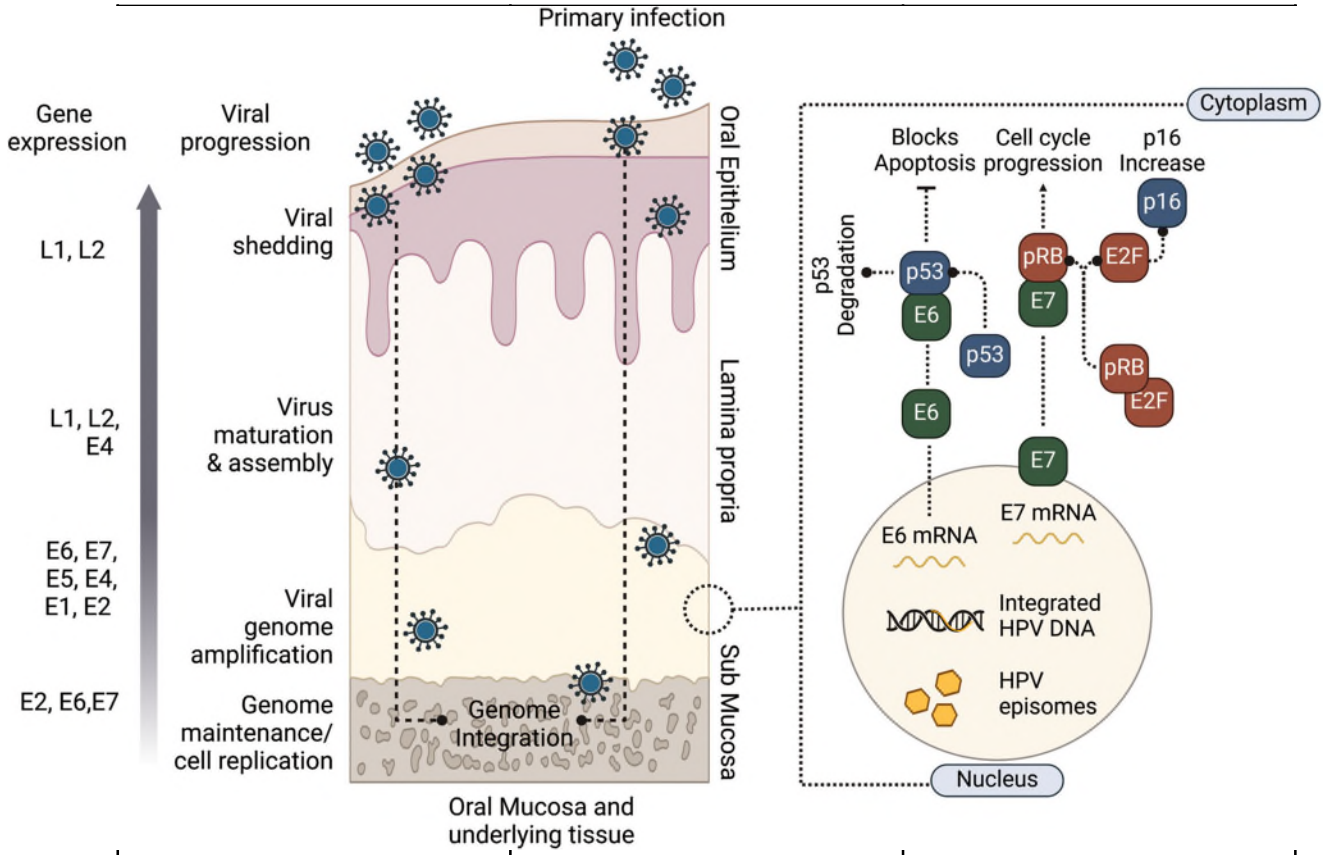
Table 1. Cancers Associated with and Attributed to Human Papillomavirus (HPV) Infection in the United States, 2015–2019.*

Cancer Site	No. of HPV-Associated Cancers	Percentage of Cancers Probably Caused by Any HPV Type	Estimated No. of Cancers Probably Caused by Any HPV Type†		
			Among Females	Among Males	Among Both Sexes
Cervix	12,293	91	11,100	0	11,100
Vagina	879	75	700	0	700
Vulva	4,282	69	2,900	0	2,900
Penis	1,375	63	0	900	900
Anus‡	7,531	91	4,700	2,200	6,900
Oropharynx	20,839	70	2,300	12,500	14,800
Total	47,199	79	21,700	15,600	37,300

10.1056/NEJMcp2108502
10.1056/NEJMra1715715
10.1002/cncr.34124
Shah J. Jatin Shah's Head and Neck Surgery and Oncology. 5th ed. Elsevier; 2019.

HPV related OPSCCs

- Several different subtypes of HPV
- HPV 16, 18 and 33 most commonly cause cancers
- Patients tend to be younger, fewer comorbidities and less exposure to alcohol and tobacco
- Expression of E6 and E7 oncoproteins, which disrupt cell cycle regulators such as p53 and Rb

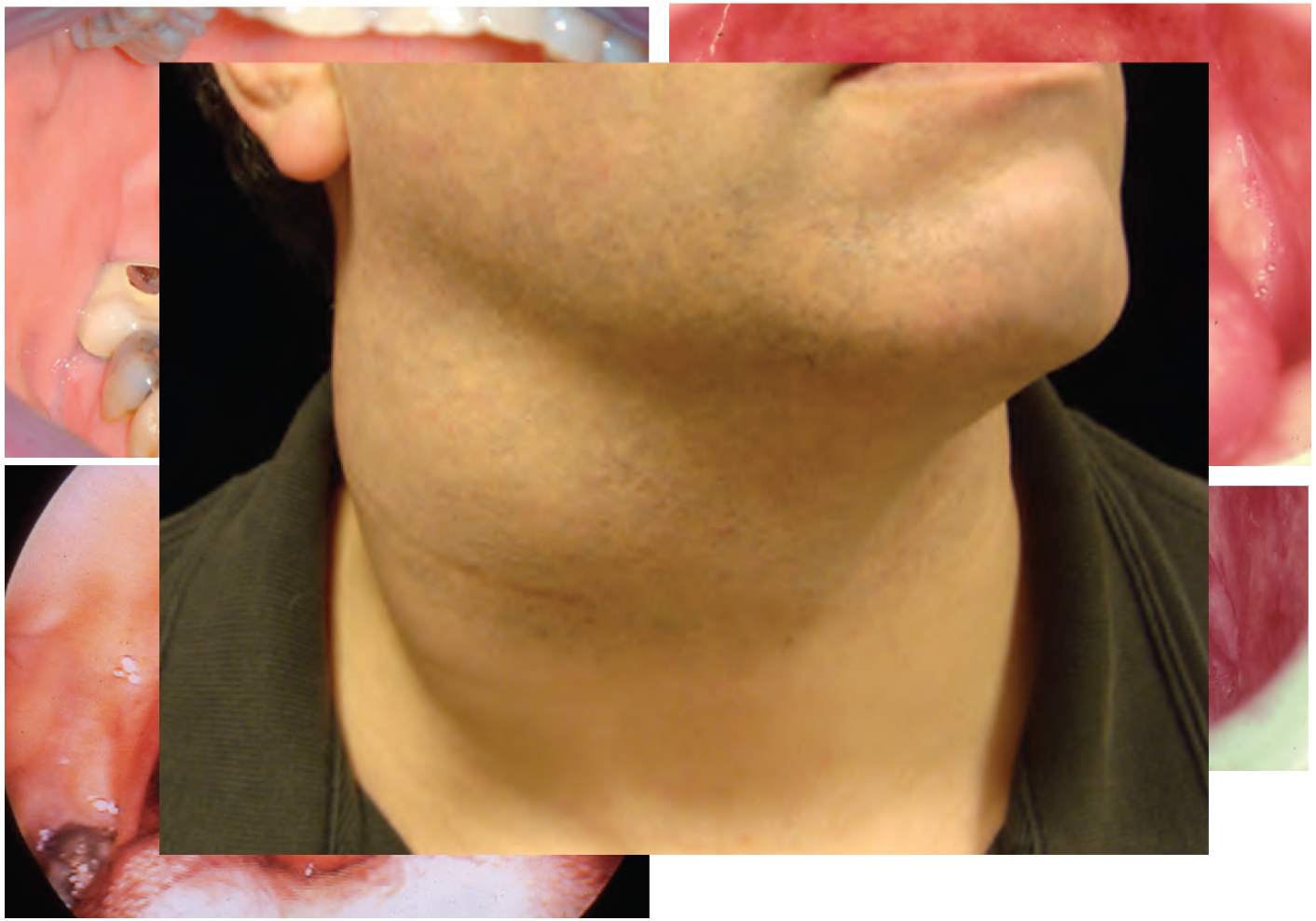


Prognosis	Better than HPV-negative HNSCC	Worse than HPV-positive HNSCC

10.1002/jmv.29746

Clinical Presentation

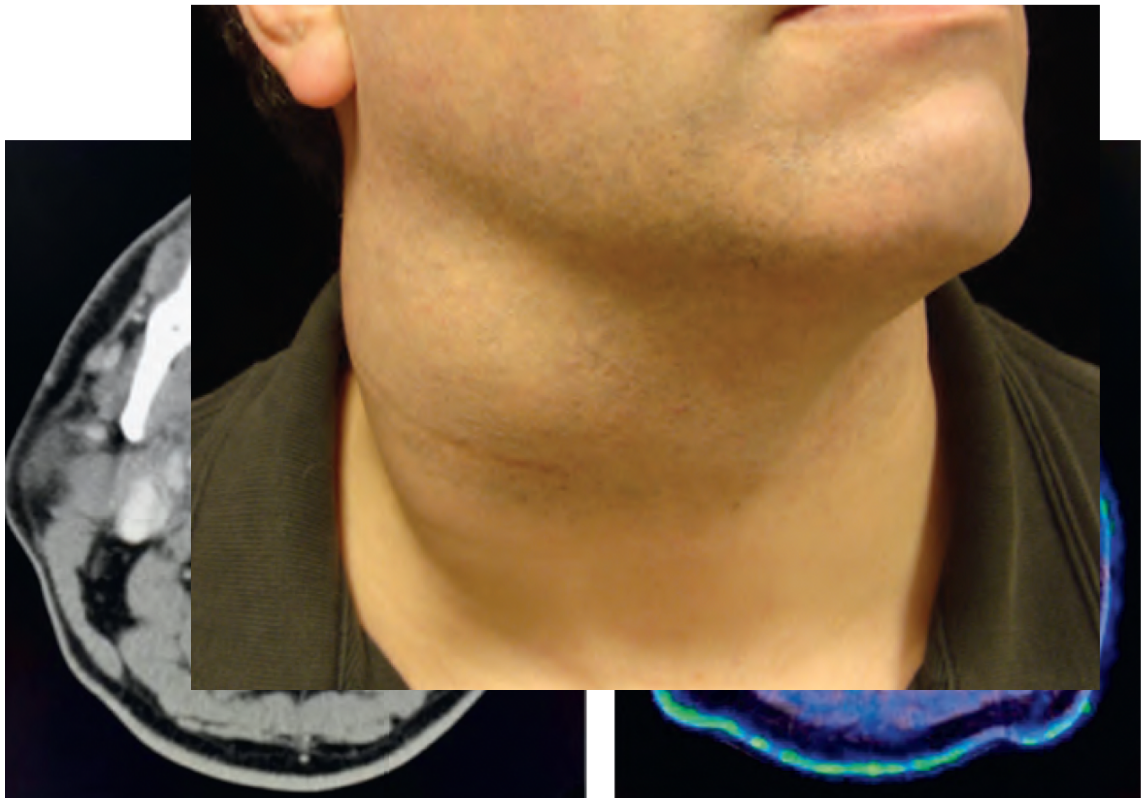
- Neck Mass
- Pain in the back of throat
- Trouble swallowing
- Unilateral ear pain
- Voice change
- Change in diet
- Incidental PET avidity in Oropharynx or Neck



Shah J. Jatin Shah's Head and Neck Surgery and Oncology. 5th ed. Elsevier; 2019.

Diagnostic Workup

- Complete Head and Neck exam including nasopharyngoscopy
- Biopsy of the primary site or FNA of the neck lymph node – excisional biopsies only as last resort
- HPV testing by p16 or in situ hybridization of high risk HPV for oropharyngeal SCCs only
- Imaging:
    - CT neck with contrast or MRI neck w/wo contrast
    - CT chest w/wo contrast
    - PET/CT



10.5858/arpa.2024-0388-CP
Shah J. Jatin Shah's Head and Neck Surgery and Oncology. 5th ed. Elsevier; 2019.

Staging

- AJCC 8 edition distinguishes between HPV positive and HPV negative due to differences prognosis
- No T4a or T4b in HPV positive OPSCCs
- Only N2 in HPV positive OPSCCs

Table 1. Tumor–Node–Metastasis Classification of Human Papillomavirus (HPV)–Positive and HPV-Negative Oropharyngeal Cancer.*

Classification	HPV-Positive Oropharyngeal Cancer	HPV-Negative Oropharyngeal Cancer
Tumor		
TX	Primary tumor cannot be assessed	Primary tumor cannot be assessed
Tis	Carcinoma in situ	Carcinoma in situ
T0	No tumor identified	No tumor identified
T1	Tumor <2 cm in greatest dimension	Tumor <2 cm in greatest dimension
T2	Tumor >2 cm but <4 cm in greatest dimension	Tumor >2 cm but <4 cm in greatest dimension
T3	Tumor >4 cm in greatest dimension or extension	Tumor >4 cm in greatest dimension or extension to

Table 2. Prognostic Stages According to the TNM Classification.*

Stage	HPV-Positive Oropharyngeal Cancer			HPV-Negative Oropharyngeal Cancer		
	Tumor	Node	Metastasis	Tumor	Node	Metastasis
0	Tis	N0	M0	Tis	N0	M0
I	T0, T1, or T2	N0 or N1	M0	T1	N0	M0
II	T0, T1, or T2	N2	M0	T2	N0	M0
	T3	N0, N1, or N2	M0			
III	T0, T1, T2, T3, or T4	N3	M0	T1, T2, or T3	N1	M0
	T4	N0, N1, N2, or N3	M0			
IV	Any T	Any N	M1			
IVA				T4a	N0 or N1	M0
				T1, T2, T3, or T4a	N2	M0
IVB				Any T	N3	M0
				T4b	Any N	M0
IVC				Any T	Any N	M1

N2b		Metastases to multiple ipsilateral lymph nodes, none >6 cm in greatest dimension, without extranodal extension
N2c		Metastases to bilateral or contralateral lymph nodes, none >6 cm in greatest dimension, without extra-nodal extension
N3	Metastases to one or more lymph nodes, >6 cm in greatest dimension	
N3a		Metastasis to a lymph node, >6 cm in greatest dimension, without extranodal extension
N3b		Metastases to one or more lymph nodes, with clinically overt extranodal extension

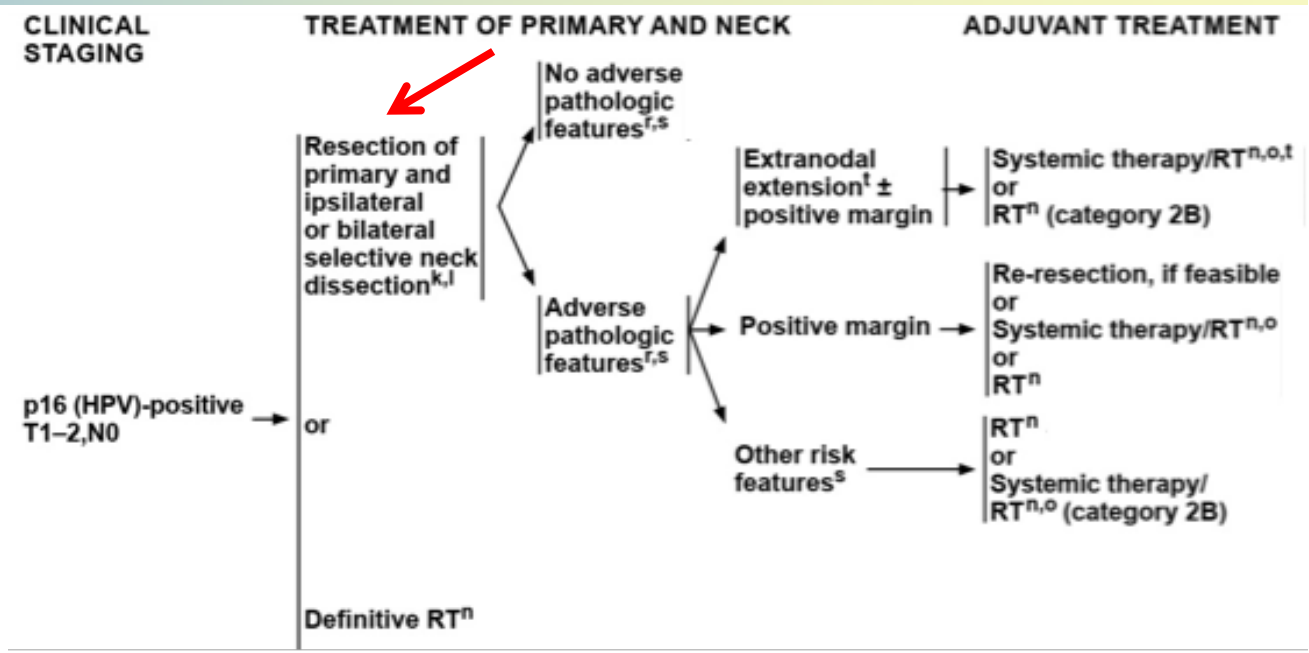
10.1056/NEJMra1715715

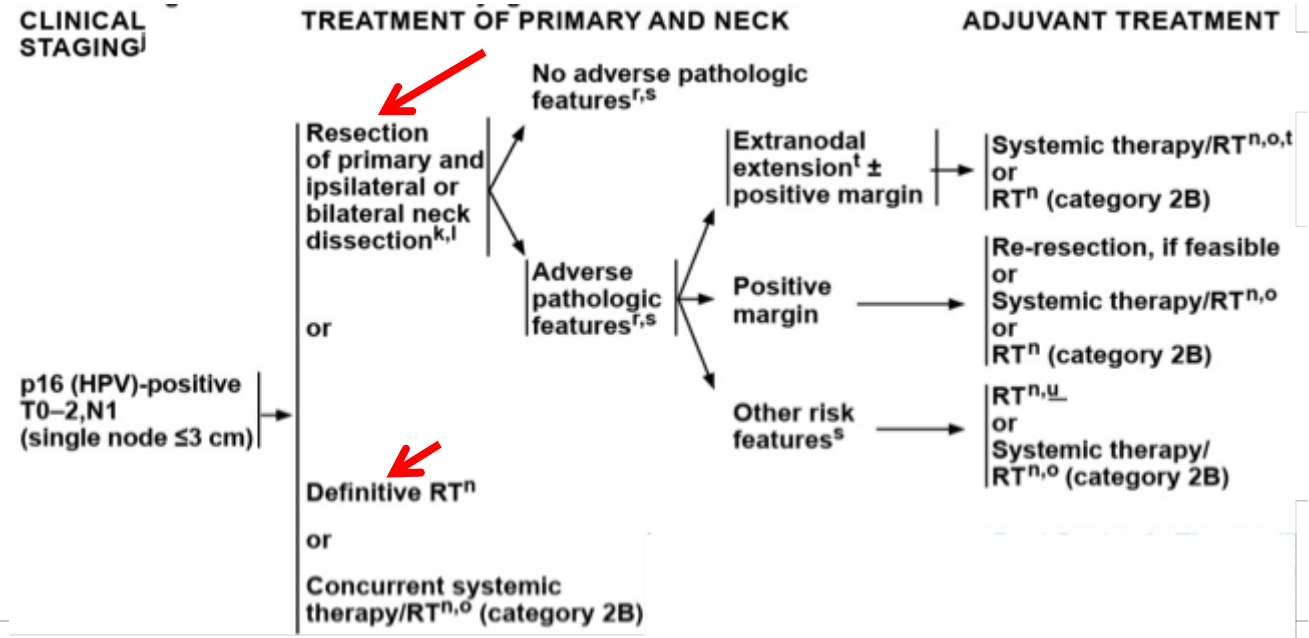
Treatment

- Multidisciplinary team is essential
  - Head and Neck Surgery
  - Radiation Oncology
  - Radiology
  - Dentistry
  - Pathology
  - Nursing
  - Physiotherapy/Occupational therapy
  - Speech pathology
  - Social Work
  - Dietitian
  - Audiology
  - Pain management
  - Tobacco cessation

Treatment

- For **early-stage HPV-positive OPSCC (I or II)**, single-modality therapy—either transoral robotic surgery (TORS) or definitive radiotherapy—is standard
- Treatment choice guided by tumor location, anticipated cure rate, and functional outcomes





NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Head and Neck Cancers

Version 5.2025 — August 12, 2025

Transoral Robotic Surgery

- Goals of Transoral Robotic Surgery
  - Maybe used to provide a pathologically risk-adapted means to determine adjuvant therapy
- Recommended for
  - T1-T2 OPSCC with a high probability of negative margin resection (can consider for select exophytic T3)
  - Lateralized OPSCC
- Not recommended for:
  - if significant soft palate extension
  - Matted nodes or extranodal extension
  - Parapharyngeal fat involvement
  - Abuts the hyoid bone or invades the extrinsic tongue musculature

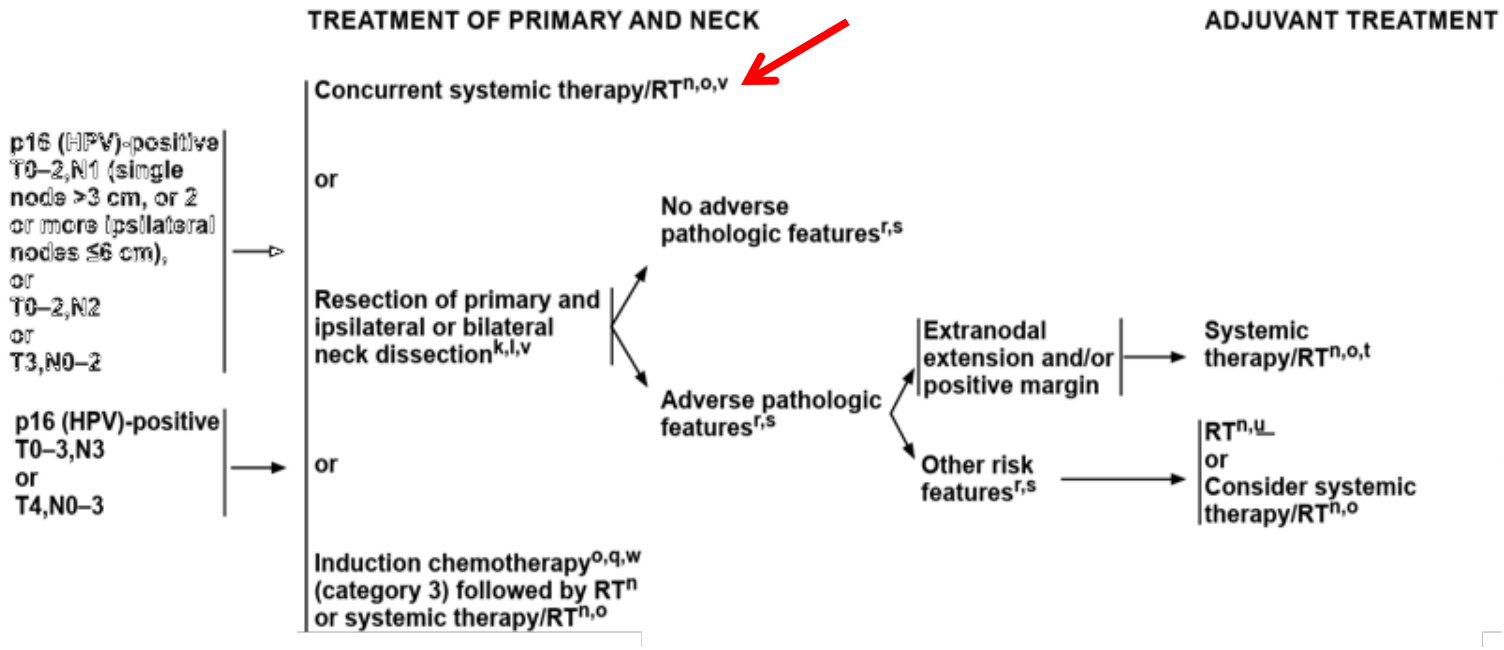
Transoral Robotic Surgery in the Multidisciplinary Care of Patients With Oropharyngeal Squamous Cell Carcinoma: ASCO Guideline

10.1200/JCO-24-02755

- Adjuvant radiation therapy
  - Perineural invasion, lymphovascular invasion
  - 2 – 4 positive nodes and/or < 1 mm extranodal extension
- Adjuvant chemoradiation therapy
  - Positive margins
  - 5 or more positive nodes or > 1 mm ENE

Treatment

- For **advanced-stage disease** (III or higher), concurrent chemoradiation (CCRT)
- Platinum-based chemotherapy (typically cisplatin 100 mg/m² every 3 weeks for 3 cycles, or 40 mg/m² weekly) remains the standard of care



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Head and Neck Cancers

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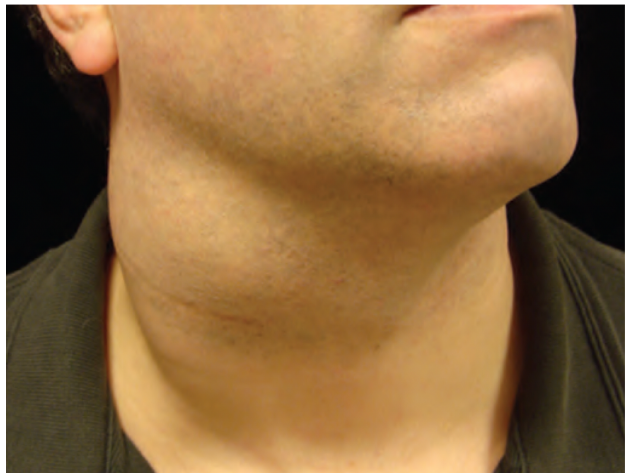
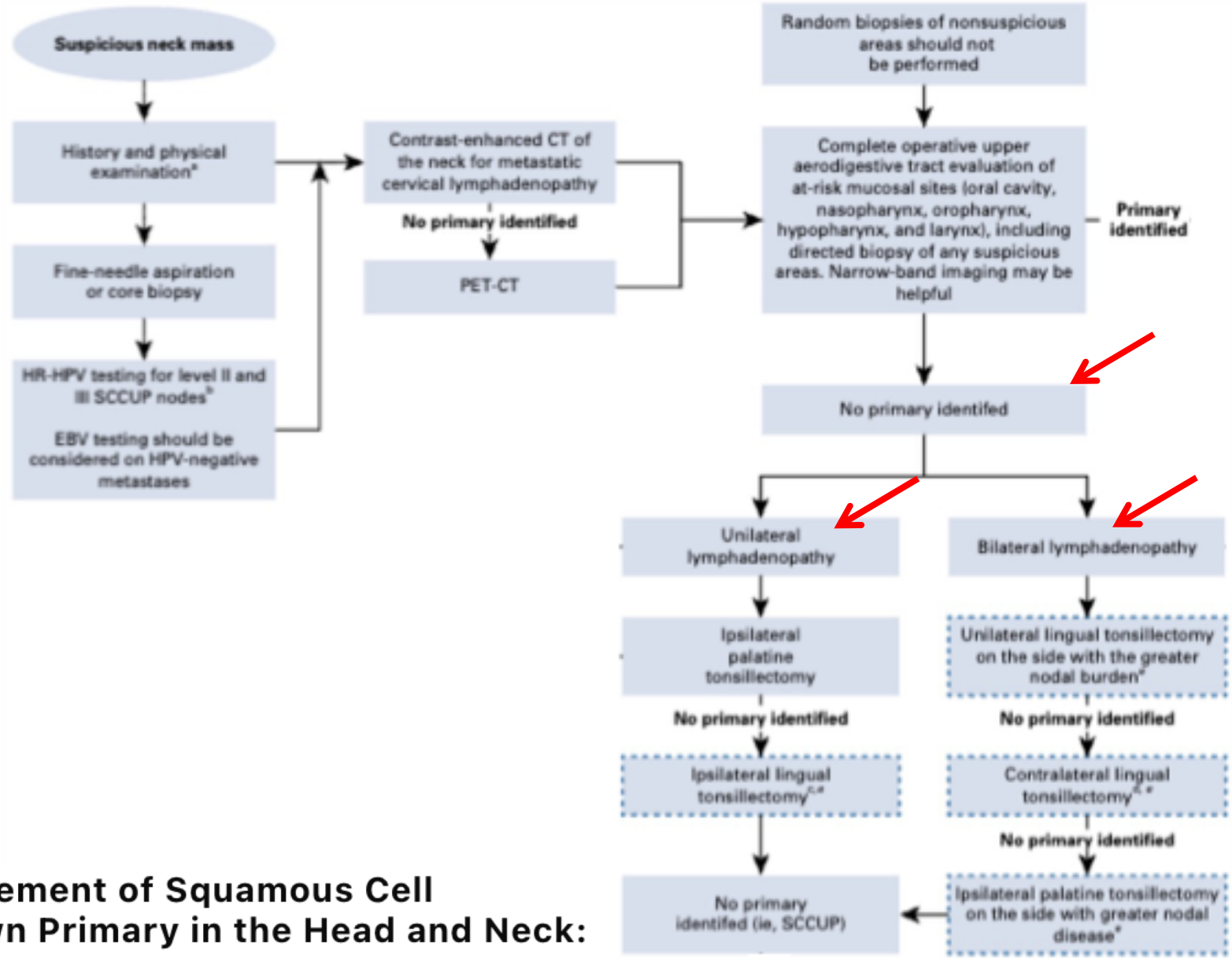
Occult Primary



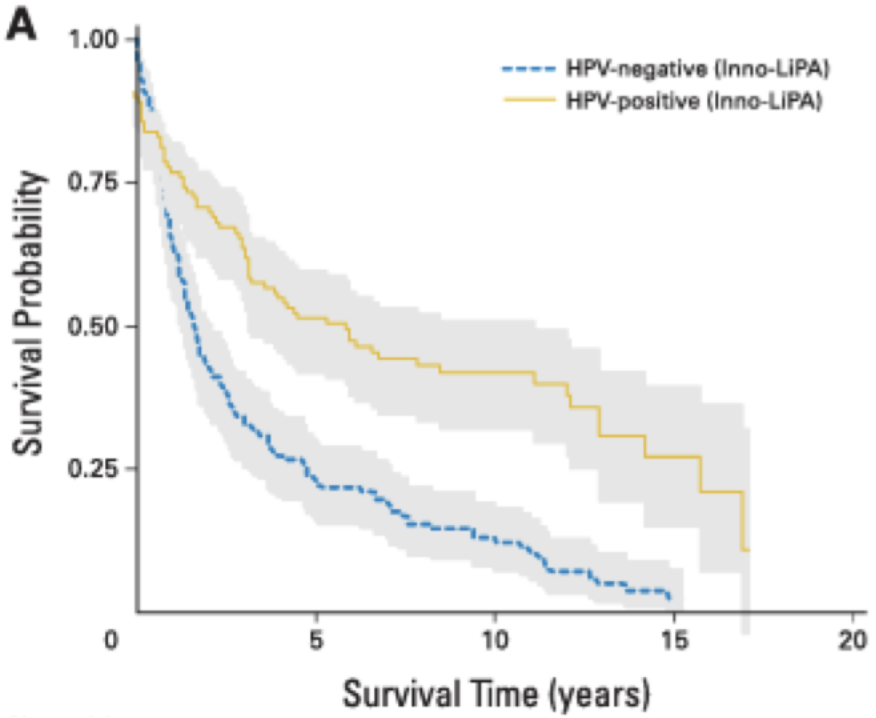
- Adult presents with neck mass
- Cancer until proven otherwise
- Excisional biopsies should not be done until workup has been completed which includes nasopharyngoscopy, palatine and lingual tonsillectomy



Diagnosis and Management of Squamous Cell Carcinoma of Unknown Primary in the Head and Neck: ASCO Guideline 10.1200/JCO.20.00275

Prognosis

- 3-year overall survival rate of **82.4% for HPV-positive OPSCC** versus 57.1% for HPV-negative cases, with a 58% reduction in the risk of death for HPV-positive patients
- Median survival for HPV-positive patients is dramatically longer (**131 months** vs. 20 months for HPV-negative patients)



10.1200/JCO.22.02625

Longterm Outcomes and Quality of Life

TREATMENT TYPE	LONG-TERM EFFECTS	LATE EFFECTS
Surgery (neck dissection, laryngectomy)	Shoulder function • Shoulder mobility, pain Oral health complications • Xerostomia • Dysphagia • Oral infections Musculoskeletal effects • Trismus • Impaired neck motion, pain • Stricture	• Spinal nerve abnormalities • Lymphedema • Neuropathy • Cervical radiculopathy

American Cancer Society Head and Neck Cancer Survivorship Care Guideline

10.3322/caac.21343

Longterm Outcomes and Quality of Life

TREATMENT TYPE	LONG-TERM EFFECTS	LATE EFFECTS
Radiation (IMRT, mediastinal RT)	Oropharyngeal • Xerostomia • Dysphagia Neuromuscular • Cervical dystonia • Trismus Musculoskeletal • Shoulder dysfunction Integumentary • Radiation dermatitis Lymphovascular • Lymphedema Oral health complications • Xerostomia • Oral infections	Vision • Premature cataracts Cardiovascular • Carotid obstruction • Baroreceptor failure Oropharyngeal • Xerostomia • Dysphagia • Dysarthria Pulmonary • Pulmonary fibrosis Neuromuscular • Cervical dystonia • Trismus • Brachial plexopathy • Cervical radiculopathy Musculoskeletal • Osteonecrosis Lymphovascular • Lymphedema • Carotid stenosis Sensory complications • Hearing loss • Ocular issues • Altered or loss of taste

American Cancer Society Head and Neck Cancer Survivorship Care Guideline

10.3322/caac.21343

Longterm Outcomes and Quality of Life

TREATMENT TYPE	LONG-TERM EFFECTS	LATE EFFECTS
Chemotherapy	Neuromuscular • Sensory/motor neuropathy • Sensory ataxia • Gait dysfunction • Vertigo Other effects • Hot flushes/sweats • Weight gain, abdominal obesity • Fatigue/decreased activity • Anemia • Body hair loss • Dry eyes	Neuromuscular • Cardiac abnormality, cardiomyopathy Other • Osteoporosis, fractures • Metabolic syndrome • Cardiovascular disease—possible increased risk of myocardial infarction • Diabetes; decreased sensitivity to insulin and oral glycemic agents • Increased cholesterol • Increased fat mass and decreased lean muscle mass/muscle wasting • Venous thromboembolism • Vertigo • Cognitive dysfunction

American Cancer Society Head and Neck Cancer Survivorship Care Guideline

10.3322/caac.21343

Longterm Outcomes and Quality of Life

GENERAL PSYCHOSOCIAL LONG-TERM AND LATE EFFECTS

- Depression, depressive symptoms
- Distress—multifactorial unpleasant experience of psychological, social, and/or spiritual nature
- Worry, anxiety
- Fear of recurrence
- Pain-related concerns
- End-of-life concerns: Death and dying
- Changes in sexual function and/or desire
- Challenges with body image (secondary to surgery, laryngectomy, radiation)
- Challenges with self-image
- Relationship and other social role difficulties
- Return to work concerns and financial challenges

American Cancer Society Head and Neck Cancer Survivorship Care Guideline

10.3322/caac.21343

Surveillance

- Clinical follow-up every 1 to 3 months during the first year after treatment, every 2 to 6 months in the second year, every 4 to 8 months in years 3 to 5, and annually thereafter
    - Practically, every 3 months during first 2 years, every 6 months in years 3 – 5, yearly after 5 years if patient prefers
- Imaging is recommended once at 3 to 6 months post-treatment to establish a new baseline, with further imaging at the discretion of the treating team, typically guided by symptoms or clinical suspicion of recurrence

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Head and Neck Cancers

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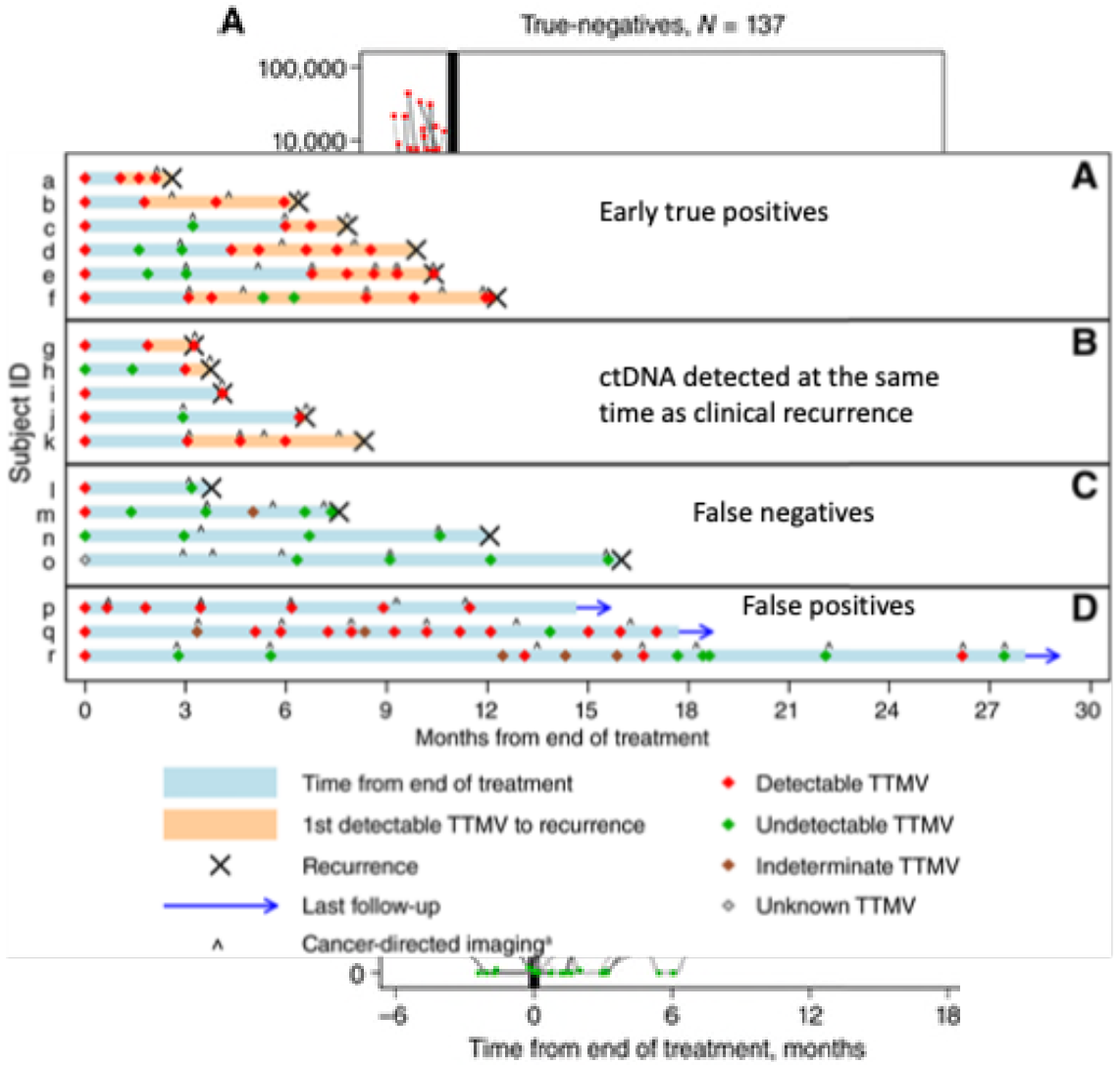
Circulating Tumor DNA

- Disease recurrence was diagnosed in 9% of patients, with 1- and 2-year RFS of 91% (95% CI = 86%–95%) and 89% (95% CI = 84%–94%), respectively. Detectable TTMV during surveillance was strongly associated with decreased RFS
- Patients with either undetectable TTMV in all surveillance tests or with a single indeterminate TTMV result that returned to undetectable upon subsequent testing remained disease-free and were thus considered true-negatives
- The trajectory of surveillance TTMV values was uptrending just prior to diagnosis of recurrence for most true-positive subjects



10.1158/1078-0432.CCR-24-3053

HPV Vaccines

- CDC Advisory Committee on Immunization Practices (ACIP) recommends routine HPV vaccination for all children at 11 or 12 years of age, with the option to initiate as early as 9 years. Catch-up vaccination is recommended for all previously unvaccinated individuals up to age 26, and for adults aged 27 to 45 years, vaccination may be considered based on shared clinical decision making.

- The only HPV vaccine currently marketed in the United States is the 9-valent vaccine (Gardasil-9), which covers HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58

- For patients already diagnosed with HPV-positive head and neck cancer, prophylactic HPV vaccination does not treat existing infection or established malignancy, but may provide protection against new infections at other mucosal sites

Morbidity and Mortality Weekly Report

Human Papillomavirus Vaccination for Adults: Updated Recommendations of the Advisory Committee on Immunization Practices

Table 2. Recommendations for HPV Vaccination in the United States.*

Variable	Recommendation
Age group	
11 or 12 yr; can be initiated starting at 9 yr	Routine-vaccination age group
13–26 yr	Catch-up vaccination for previously unvaccinated persons
27–45 yr	Shared clinical decision making for previously unvaccinated persons
No. of doses	
Among persons 9–14 yr of age at vaccine initiation	2 doses, with the second dose administered 6–12 mo after the first dose†
Among persons ≥15 yr of age at vaccine initiation or those with an immunocompromising condition	3 doses, with the second dose administered 1–2 mo after the first dose and with the third dose administered 6 mo after the first dose‡

10.15585/mmwr.mm6832a3
10.1056/NEJMcp2108502

Clinical Trials at City of Hope – NCT05451004

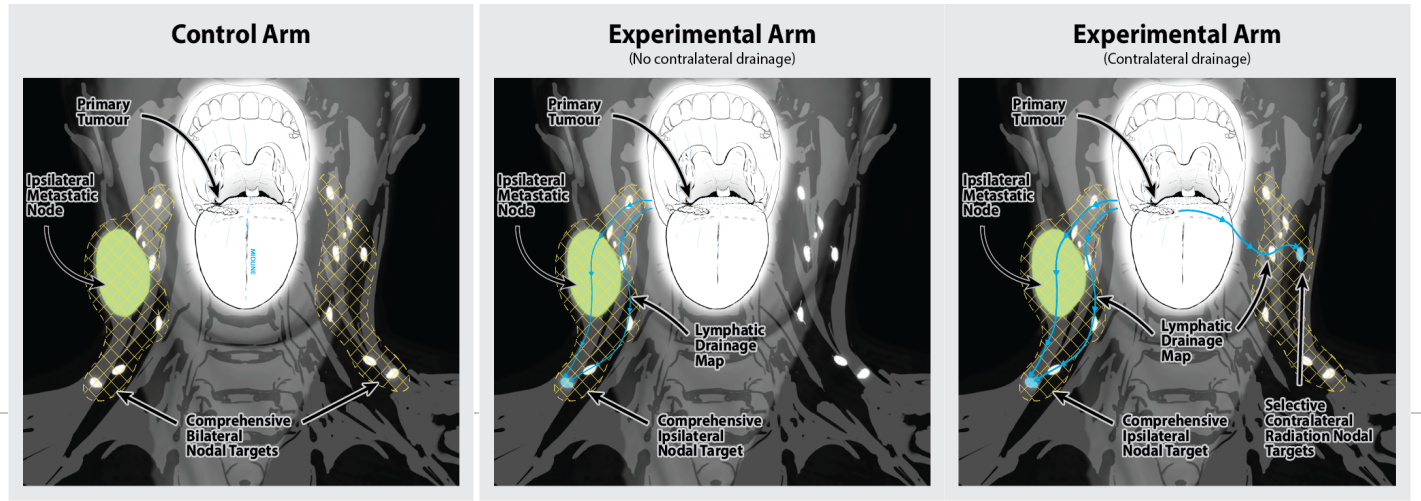
SPECT-CT Guided Elective Contralateral Neck Treatment (SELECT) for Patients with Localized Oropharyngeal Cancer: A Phase III Randomized Controlled Trial

- T1-T3 lateralized OPC not involving or crossing midline
- No contralateral involved nodes or nodes >6 cm on CT, MRI, PET-CT (if available).*
- P16 positive or negative
- Planned for Bilateral neck RT

→ REGISTER and RANDOMIZE*

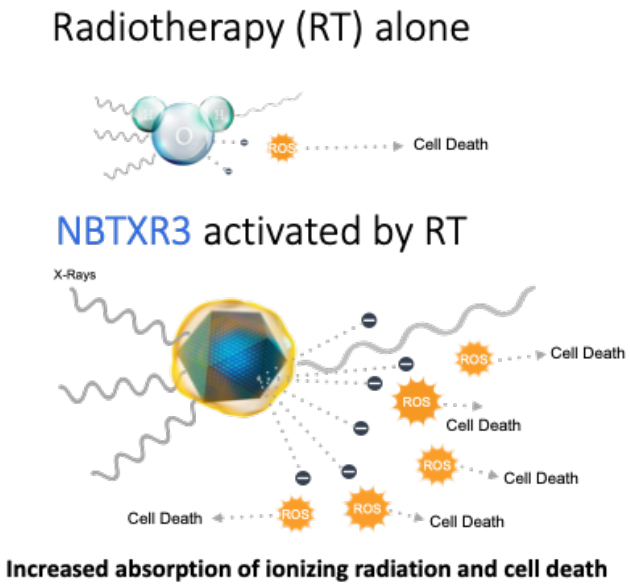
→ Arm A: Experimental Arm → Lymphatic Mapping with SPECT-CT → Ipsilateral Neck Radiotherapy and SPECT-CT Guided Contralateral Neck Radiotherapy

→ Arm B: Control Arm → Bilateral Neck Radiotherapy



Clinical Trials at City of Hope – NCT04892173

A Phase III Study of NBTXR3 Activated by Investigator's Choice of Radiotherapy Alone or Radiotherapy in Combination With Cetuximab for Platinum-based Chemotherapy-ineligible Elderly Patients With LA-HNSCC



Target population

Treatment-naïve, elderly adult subjects (≥60 years) with T3–T4 any N or T2, if ≥ N2, LA-HNSCC who are ineligible for platinum-based chemotherapy

n = 500

Investigator's choice

- Radiotherapy alone
- Radiotherapy + cetuximab

R 1:1

A NBTXR3 + Investigator's choice

B Investigator's choice

Endpoints

- **Primary**: PFS
- **Key Secondary**: OS

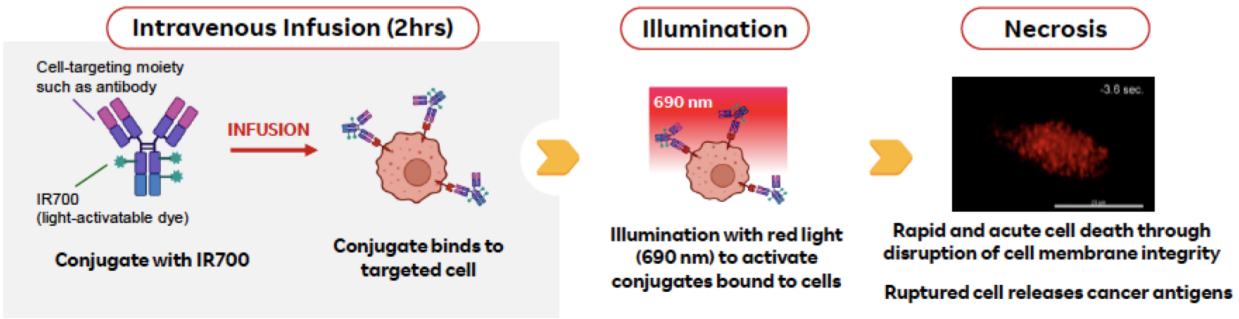
Stratification Factors

- Investigator's choice
- HPV status
- ACCI score at screening (2–3 vs ≥ 4)
- Region (North America & Western Europe vs Rest of World)

ACCI, Age-adjusted Charlson Comorbidity Index.

Clinical Trials at City of Hope – NCT06699212

A Phase III Multicenter, Randomized, Open-label Study of ASP-1929 Photoimmunotherapy in Combination with Pembrolizumab Versus Standard of Care in the First Line Treatment of Patients with Locoregional Recurrences of HNSCC with no Distant Metastases



Patient Population:

- Evidence of HNSCC (no nasopharynx, cuSCC)
- No distant metastases
- Anti-PD-1- and anti-PD-L1-treatment naïve
- CPS≥1
- Eligible for treatment with pembrolizumab plus chemotherapy in first line setting

2:2:1

Experimental Arm

ASP-1929 PIT (320 mg/m²) + Pembrolizumab

Dose Selection

ASP-1929 PIT (640 mg/m²) + Pembrolizumab

IA1

Standard of Care Arm

Pembrolizumab
OR
Pembrolizumab + Chemotherapy
Physician's Choice

2:1

Survival follow-up (Q3M)

Questions