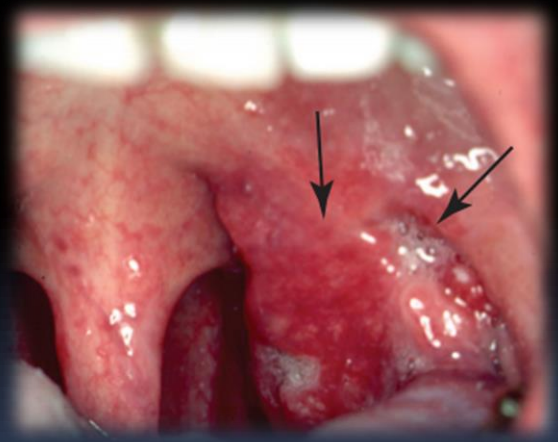
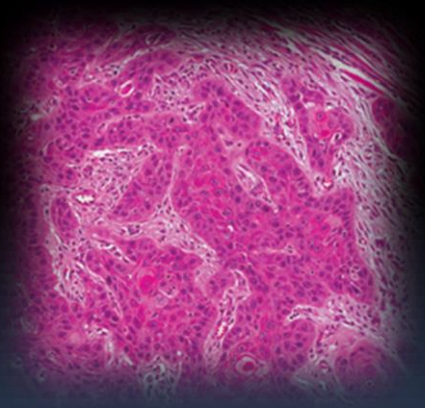
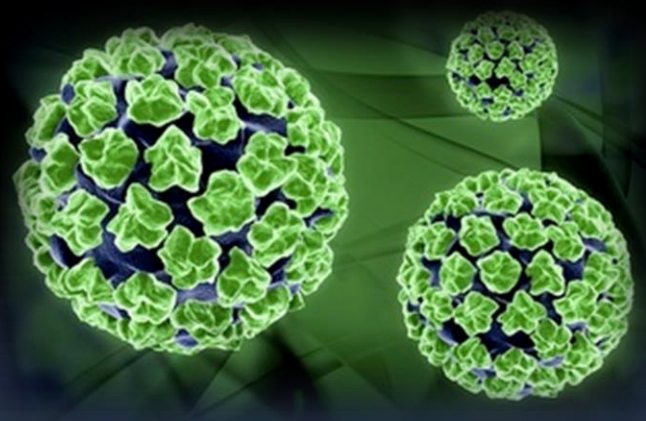
Oropharyngeal Cancer

American Joint Committee on Cancer 8th edition cancer staging manual







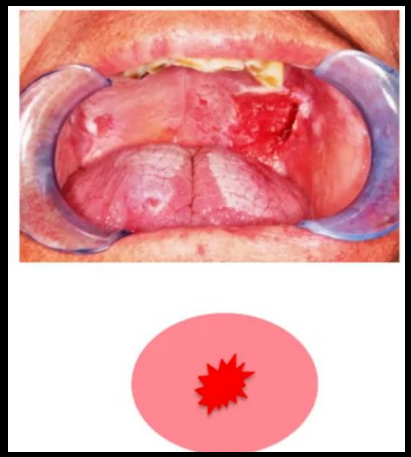
Meritxell Tomas, 3rd year ENT resident

Introduction

- ✓ Head and neck cancer (HNC) represents 5% of oncological cases in adults in Spain
- ✓ More than 90% of these tumours have squamous histology

- ✓ Neoplasm with high possibility of cure if it is diagnosed in early stages
- ✓ 2/3 of the patients are diagnosed at an advanced locoregional stage (stage III and IV)

- ✓ The TNM classification is the internationally accepted system for tumour staging
  - ✓ Predicts survival rates and guides management



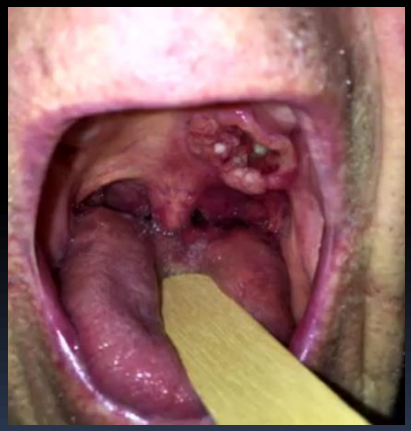
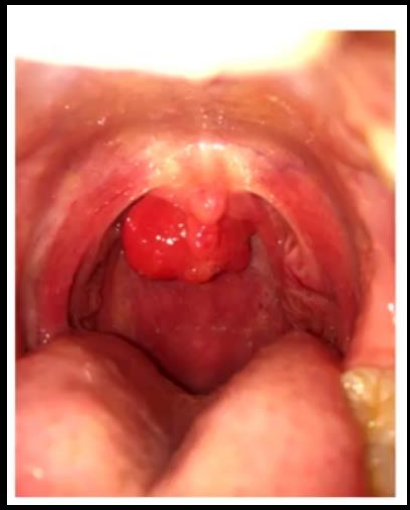
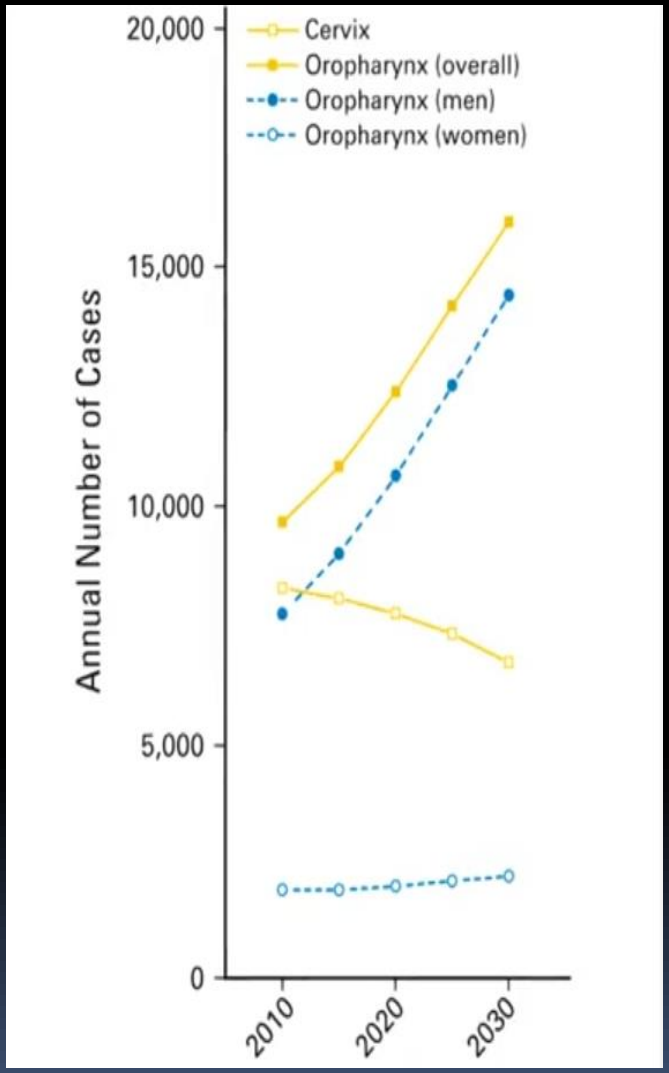


TABLE 97-3. **Traditional vs. HPV–Associated Oropharyngeal SCC: Demographics, Clinical Presentation, and Prognosis**

Variables	Traditional Oropharyngeal SCC	HPV-Associated Oropharyngeal SCC
Demographics	≥60 yr, M:F = 3:2	40-60 yr, M:F = 3:1
Risk profile	Tobacco, alcohol	Reduced/no addiction habit Epidemiologic sexual history correlation
Molecular biology	p16 inactivation	p16 overexpression
Pathology	Keratinizing SCC, well to moderate to poorly differentiated	Nonkeratinizing SCC, poorly differentiated
Clinical presentation	Less bulky nodes	Small/unknown primary with bulky, cystic, or multiple nodes
Prognosis	Guarded, 5-year survivals ~40% to 60%	Good, 5-year survivals ~80% to 90%
Prognostic variables	T, N, and AJCC stage, margin, ECS, smoking	T stage, margins, three or more nodes
Local recurrence	Higher	Infrequent
Distant metastasis	~20%	~5% to 6% (surgical ± adjuvant therapy), ~7% to 12% (nonsurgical therapy)





2011 publication --- WORLD WIDE EPIDEMIC

HPV-Infection is now the Leading Cause of Oropharyngeal Cancer

Nation	1985	2004
USA[1]	40%	80%
UK[2]	22%	67%
Australia[3]	19%	60%
Sweden[4]	29%	93%

Head and Neck Cancers—Major Changes in the American Joint Committee on Cancer Eighth Edition Cancer Staging Manual

William M. Lydiatt, MD[1]; Snehal G. Patel, MD[2]; Brian O'Sullivan, MD[3]; Margaret S. Brandwein, MD[4]; John A. Ridge, MD, PhD[5]; Jocelyn C. Migliacci, MA[6]; Ashley M. Loomis, MPH[7]; Jatin P. Shah, MD[8]

Changes in staging in HR-HPV-Associated OPCs

- ✓ With the increased incidence of HPV + OPC, the 7th edition staging algorithm lost the ability to differentiate between stages (hazard discrimination)
  - ✓ NEED for an HR-HPV OPC staging system

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MAJOR CHANGES IN OPC

I. PHARYNX CLASSIFICATION
   I. 7th edition -- Together naso/oro/hypopharynx
   II. 8th edition -- chapters: 1) nasopharynx,2) HR-HPV associated OPC and 3) non HR-HPV associated OPC/hypopharynx

I. T categories both for p16 + and – were equally valid from a prognostic standpoint
   I. Exception: T4b has been removed from HR-HPV+ OPC
      I. T4a and T4b curves proved indistinguishable

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MAJOR CHANGES IN OPC

III. CLINICAL LYMPH NODES FOR HR-HPV + OPC

III. C lymph nodes, whether 1 or multiple, ipsilateral, < 6 cm had similar impact on survival (hazard consistency) --- N1

IV. C/R bilateral or contralateral lymph nodes had a worse outcome --- N2

V. > 6 cm had the worst survival --- N3

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MAJOR CHANGES IN OPC

III. PATHOLOGY LYMPH NODES FOR HR-HPV + OPC

- III. Applicable to PTs managed by surgery
- IV. SIZE OR PRESENCE OF CONTRALATERAL NECK --- NOT PREDICTIVE OF SURVIVAL
- V. FUNDAMENTAL DIFFERENCE IN OUTCOME SEEN WITH Nº OF + LYMPH NODES
  - III. 1-4 : N1
  - IV. >5: N2

SEOM clinical guidelines for the treatment of head and neck cancer (2017)

B. Oropharynx p16-negative[a]

T1	Tumour 2 cm or less in greatest dimension
T2	Tumour more than 2 cm but not more than 4 cm in greatest dimension
T3	Tumour more than 4 cm in greatest dimension extension to lingual surface of epiglottis
T4a	Tumour invades any of the following: larynx, deep/extrinsic muscle or tongue, medial pterygoid, hard palate, or mandible
T4b	Tumour invades any of the following: lateral pterygoid muscle, pterygoid plates, lateral nasopharynx, skull base; or encase carotid artery

Oropharynx p-16 + tumours T4a and T4b categories are classified as T4

TABLE 4. Clinical N Category for Non-Human Papillomavirus-Associated (p16-Negative) Oropharyngeal Cancer, 8th Edition Staging Manual[a]

N CATEGORY	N CRITERIA
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in a single ipsilateral lymph node, 3 cm or smaller in greatest dimension and ENE-negative
N2	Metastasis in a single ipsilateral lymph node larger than 3 cm but not larger than 6 cm in greatest dimension and ENE-negative; or metastases in multiple ipsilateral lymph nodes, none larger than 6 cm in greatest dimension and ENE-negative; or metastasis in bilateral or contralateral lymph nodes, none larger than 6 cm in greatest dimension and ENE-negative
N2a	Metastasis in a single ipsilateral lymph node larger than 3 cm but not larger than 6 cm in greatest dimension and ENE-negative
N2b	Metastasis in multiple ipsilateral lymph nodes, none larger than 6 cm in greatest dimension and ENE-negative
N2c	Metastasis in bilateral or contralateral lymph nodes, none larger than 6 cm in greatest dimension and ENE-negative
N3	Metastasis in a lymph node larger than 6 cm in greatest dimension and ENE-negative; or metastasis in any lymph node(s) and clinically overt ENE-positive
N3a	Metastasis in a lymph node larger than 6 cm in greatest dimension and ENE-negative
N3b	Metastasis in any node(s) and clinically overt ENE-positive

American Joint Committee on Cancer (AJCC)
TNM Staging System for HPV-Mediated (p16+) Oropharyngeal Cancer (8th ed., 2017)

Regional Lymph Nodes (N)
Clinical N (cN)

NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	One or more ipsilateral lymph nodes, none larger than 6 cm
N2	Contralateral or bilateral lymph nodes, none larger than 6 cm
N3	Lymph node(s) larger than 6 cm

Pathological N (pN)

NX	Regional lymph nodes cannot be assessed
pN0	No regional lymph node metastasis
pN1	Metastasis in 4 or fewer lymph nodes
pN2	Metastasis in more than 4 lymph nodes

PRACTICE GUIDELINES

WILEY

AHNS Series: Do you know your guidelines? Principles of treatment for locally advanced or unresectable head and neck squamous cell carcinoma

Cory D. Fulcher[1] | Missak Haigentz Jr MD[2,3,4] | Thomas J. Ow MD, MS[5]; The Education Committee of the American Head and Neck Society (AHNS)

- ✓ 2/3 of patients with head and neck squamous cell carcinoma (HNSCC) present with advanced-stage disease

- ✓ HPV-associated oropharyngeal cancers have a more favorable prognosis
  - ✓ Staged differently from HPV –
  - ✓ TREATMENT STRATEGIES REMAIN THE SAME despite HPV status

Early disease (clinical stage I–II) treatment

- ✓ Surgery and radiotherapy (RT) provide similar locoregional control and survival outcomes
  - ✓ Not compared in randomized clinical trials

- ✓ Treatment choice will depend on
  I. Functional outcome
  II. General condition
  III. Possibility of adequate follow-up
  IV. Likelihood of developing a 2nd primary tumour

Early disease (clinical stage I–II) treatment

American Joint Committee on Cancer (AJCC)
TNM Staging System for the Oropharynx (p16-) and Hypopharynx (8th ed., 2017)

Prognostic Stage Groups			
Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
	T1	N1	M0
	T2	N1	M0
	T3	N1	M0
Stage IVA	T1	N2	M0
	T2	N2	M0
	T3	N2	M0
	T4a	N0, N1,N2	M0
Stage IVB	T4b	Any N	M0
	Any T	N3	M0
Stage IVC	Any T	Any N	M1

Early disease (clinical stage I–II) treatment

American Joint Committee on Cancer (AJCC)
TNM Staging System for HPV-Mediated (p16+) Oropharyngeal Cancer (8th ed., 2017)

Prognostic Stage Groups

Clinical

Stage I	T0, T1, T2	N0,N1	M0
Stage II	T0, T1, T2	N2	M0
	T3	N0, N1, N2	M0
Stage III	T0, T1, T2, T3	N3	M0
	T4	N0, N1, N2, N3	M0
Stage IV	Any T	Any N	M1

Pathological

Stage I	T0, T1, T2	N0, N1	M0
Stage II	T0, T1, T2	N2	M0
	T3, T4	N0, N1	M0
Stage III	T3, T4	N2	M0
Stage IV	Any T	Any N	M1

STAGING CLASSIFICATION CHANGES FROM 7TH TO 8TH EDITION (AN EXAMPLE)

T --- 2 CM

N --- 2 positive lymph nodes ipsilateral

P16 +

7th edition

T1N2b
PROGNOSTIC STAGE: IVa

8th edition

T1N1
PROGNOSTIC STAGE: I

Early disease (clinical stage I–II) treatment

Oropharyngeal carcinoma

- ✓ Ideally treated with single modality therapy
  - ✓ Primary surgery or RT

Surgery →

I. Transoral approach
   I. Transoral laser microsurgery
   II. Transoral robotic surgery

II. Open surgery
   I. Lateral pharyngotomy
   II. Suprahyoid resection

+ ipsilateral selective neck dissection vs. bilateral neck dissection (midline tumour)

Early disease (clinical stage I–II) treatment

Oropharyngeal carcinoma

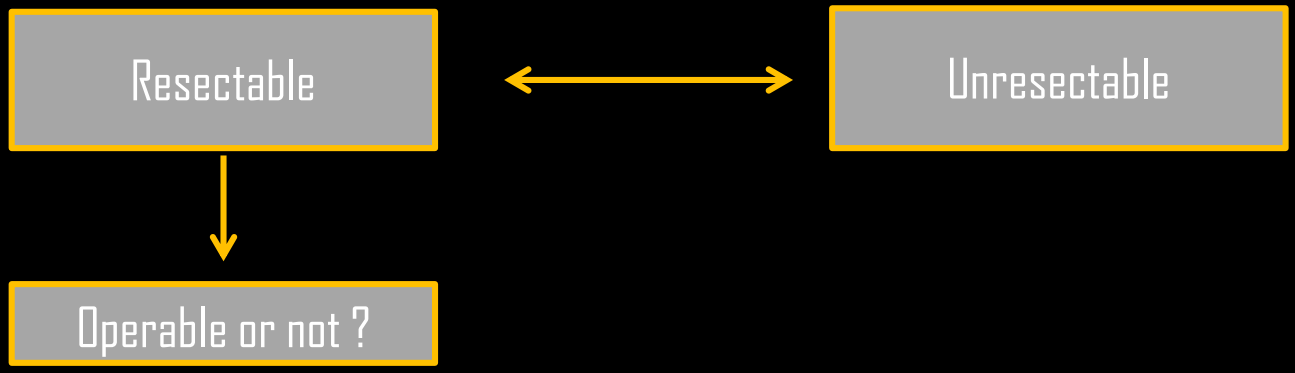
- ✓ Ideally treated with single modality therapy
  - ✓ Primary surgery or RT

RT →

- ✓ Radical RT is a good option – total dose equivalent of 70 Gy (35 fractions)
- ✓ Prophylactic RT
  - ✓ Ipsilateral lymph nodes
  - ✓ Contralateral if midline tumours

Locally advanced disease (clinical stages III, IV-A, IV-B) treatment

Oropharyngeal carcinoma

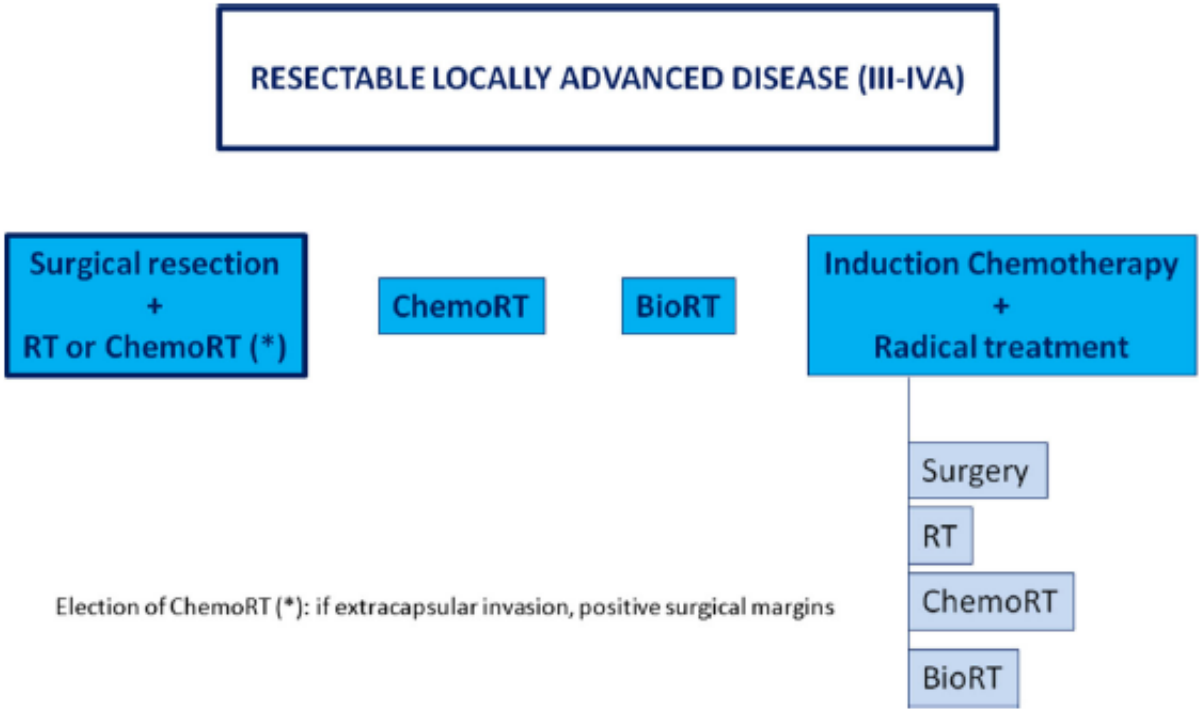


Unequivocal anatomical criteria

- ✓ Involvement of skull base
- ✓ Cervical vertebrae/prevertebral muscles
- ✓ Carotid artery
- ✓ Brachial plexus
- ✓ Mediastinal spread

Locally advanced disease (clinical stages III, IV-A, IV-B) treatment

Fig. 1 Treatment algorithm for resectable locally advanced disease (III–IVA)



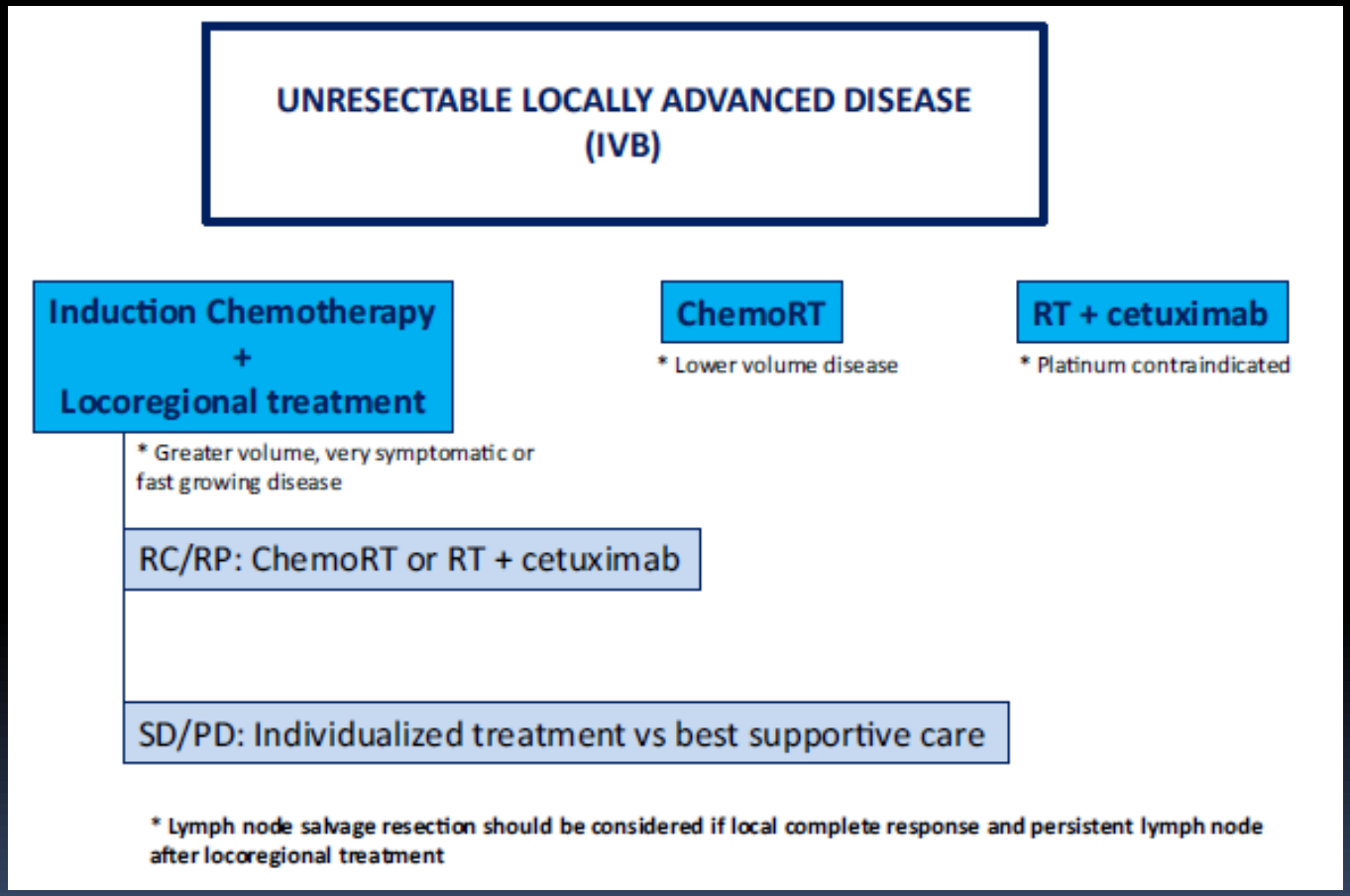
Locally advanced disease (clinical stages III, IV-A, IV-B) treatment

I. **Surgical resection + RT or CRT**
    I. Adjuvant CRT (3-weekly cisplatin 1, 22, 43) if high risk pathological features

II. CRT treatment if PT not candidate or refuses surgery
    I. Standard schedule: cisplatin
    II. Cetuximab is an alternative treatment (if neuropathy, nephropathy, heart disease or hearing loss)

III. Induction CT in TPF schedule (3-weekly cisplatin + docetaxel + 5-FU)
    I. NOT AN STANDARD LOCOREGIONAL TREATMENT FOR RESPONDERS

Locally advanced disease (clinical stages III, IV-A, IV-B) treatment



Unresectable locally advanced disease (IV-B)

NCCN guidelines base treatment options on an individual's ECOG performance status

3 options

I. INDUCTION CT + LOCOREGIONAL TREATMENT
    I. ICT: TPF x 3 cycles if ECOG 0-1 + good renal/liver function
    II. Recommended in greater volume, very symptomatic and fast-growing disease
        I. If CR/PR: RT + cisplatin or RT + cetuximab
        II. If SD/PD: individualized treatment

Unresectable locally advanced disease (IV-B)

3 options

II. CRT with cisplatin 100mg/m2 (1,22, 43)

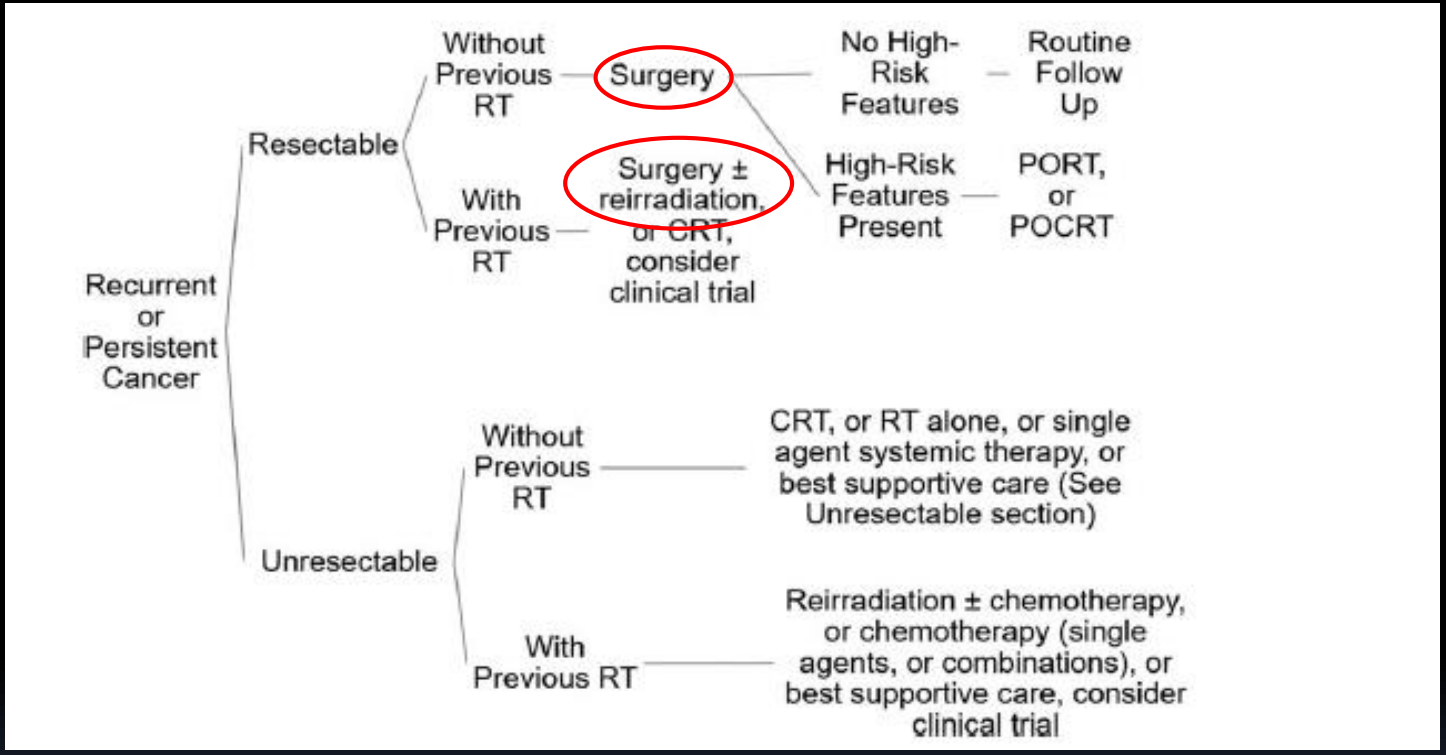
    II. Low volume locally advanced disease

III. Concomitant bioradiotherapy and cetuximab

    II. PTs no eligible for platinum chemoradioherapy

* LOCAL COMPLETE RESPONSE + PERSISTENT LYMPH NODE AFTER TREATMENT --- LYMPH NODE SALVAGE RESECTION

Treatment scheme for recurrent/persistent disease



- ✓ First option, if RESECTABLE --- SURGERY

Treatment scheme for recurrent/persistent disease

- ✓ The rationale to support salvage surgery is a complex topic
  - ✓ May offer a high chance of long-term disease control + possible cure in selected PTs
  - ✓ High morbidity from surgery

- ✓ Improved outcome after salvage surgery in…
  - ✓ Lower stage disease
  - ✓ Disease free interval > 6 months
  - ✓ Initial treatment RT vs. CRT
  - ✓ Laryngeal recurrence subsite

Next topics talk…

I. Treatment de-escalation for HPV-driven oropharyngeal cancer: where do we stand?

II. Transoral robotic surgery techniques for oropharyngeal cancer

References

I. Myers J, Hanna E, Myers E. Cancer of the head and neck. Philadelphia: Wolters Kluwer; 2017.Chapter 14, Cancer of the Orophaynx.

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V. Mirghani H, Blanchard P. Treatment de-escalation for HPV-driven oropharyngeal cancer: Where do we stand?. 2018.

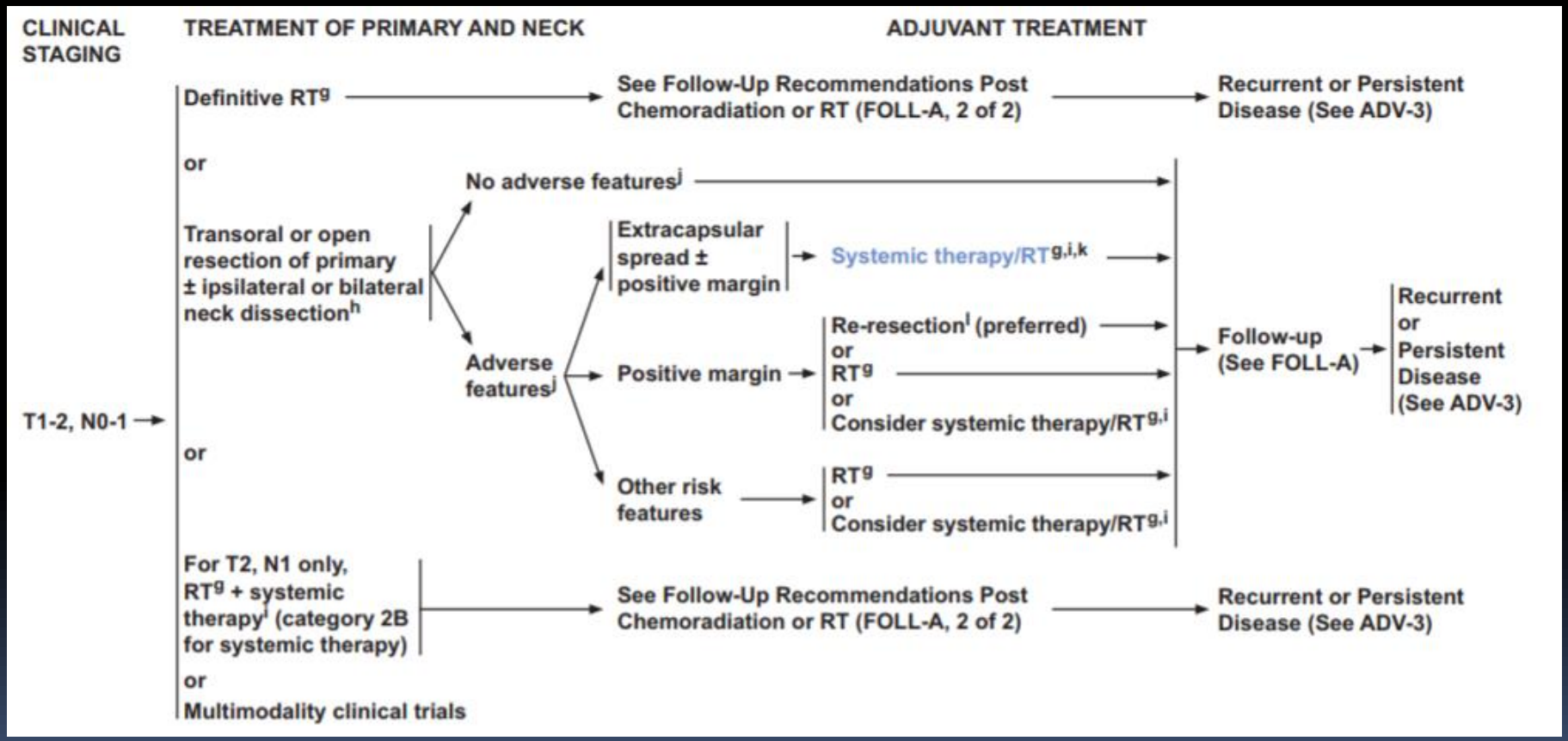
Thank you!

NCCN Guidelines® Insights

Head and Neck Cancers, Version 2.2017

Featured Updates to the NCCN Guidelines

P16 negative



P16 positive