

Head and Neck: A Panel of Thoughts

SCOS/NCOA Joint Conference – Charlotte, NC
February 17th, 2024

Daniel R Carrizosa, MD, MS, FACP
Associate Professor of Medicine, Division of Hematology/Oncology – Wake Forest School of
Medicine
Atrium Health Wake Forest Baptist Comprehensive Cancer Center – Levine Cancer Institute
Charlotte Campus



Agenda

Review current practices for Head and Neck Cancers

- Locally Advanced Oropharyngeal Cancer

- Metastatic Oral Cavity Cancer

Explore the multidisciplinary care of Head and Neck Patients

- Medical Oncology

- Radiation Oncology

- Oral Medicine

- Nutritional Services

Learning Objectives

-Multidisciplinary Head & Neck

- Understand current options and staging differences for oropharyngeal cancer
- Explore radiation sensitizers for definitive chemoradiation in oropharyngeal cancer
- Review therapeutic options for metastatic head and neck cancer
- Discuss vital care from oral medicine in head and neck cancer
- Refine the options for nutritional support in head and neck cancer patients

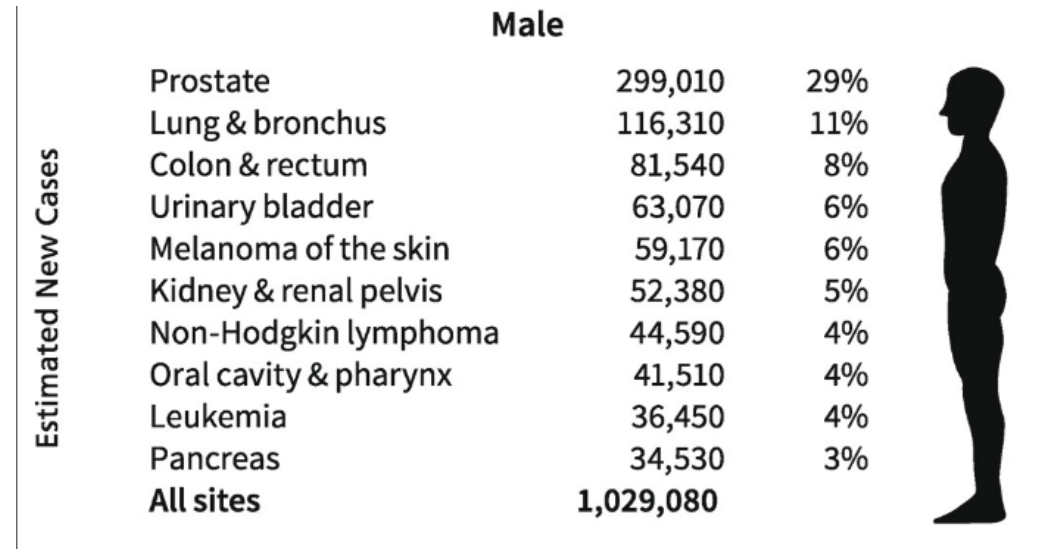
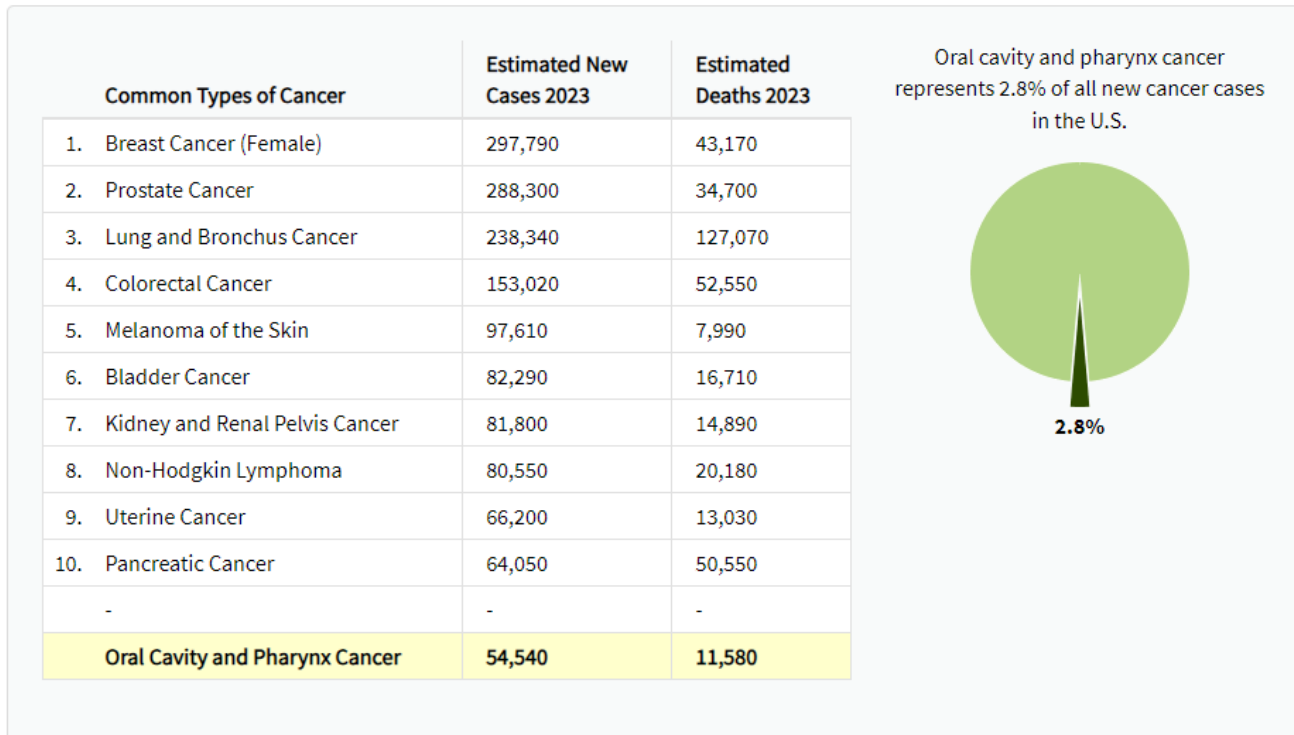
Head and Neck Cancer

Our esteemed panel:

- ❖ Dan Carrizosa, MD, MS, FACP – medical oncology
- ❖ Sid Sheth, DO, MPH – medical oncology
- ❖ Sayyad Zia, MD – radiation oncology
- ❖ Mike Brennan, DDS, MHS – oral medicine
- ❖ Michele Szafranski, MS, RD, CSO, LDN - nutrition

Head and Neck Cancer

How Common Is This Cancer?



©2024, American Cancer Society, Inc., Surveillance and Health Equity Science
<https://acsjournals.onlinelibrary.wiley.com/doi/10.3322/caac.21820>

In 2023, it is estimated that there will be 54,540 new cases of oral cavity and pharynx cancer and an estimated 11,580 people will die of this disease.

2023 NCI SEER Cancer Facts: <https://seer.cancer.gov/statfacts/html/oralcav.html>

Not including larynx, salivary, sinonasal and nasopharynx...

Head and Neck

Locally Advanced Oropharynx Cancer

69 yo male p/w voice change over 1 month with worsening ear pain and sore throat

- No history of fever or trauma
- No weight loss
- Plays golf on a regular basis
- PSHx:
 - Non-smoker
 - Social ETOH (<1 drink/week)

Head and Neck

Locally Advanced Oropharynx Cancer

Labs: Cr 1.23, LFT and CBCwdiff WNL

Flex Fiberoptic Nasolaryngoscopy:

Endophytic Left Base of tongue mass

Pathology: Base of Tongue Biopsy

HPV-Associated Squamous Cell Carcinoma

p16 positive

PET: midline hypermetabolic mass involving posterior tongue = 3.8*4cm with avid hypermetabolic activity w/ involvement of extrinsic tongue musculature. Bilateral hypermetabolic cervical chain lymph nodes. No distant disease



Head and Neck

Locally Advanced Oropharynx Cancer

Staging:

Stage III: (T4N2M0)

What are our options?

!Need Multidisciplinary Team!



National
Comprehensive
Cancer
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NCCN Guidelines Version 2.2024 Head and Neck Cancers

[NCCN Guidelines Index](#)
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Table 4

**American Joint Committee on Cancer (AJCC)
TNM Staging System for HPV-Mediated (p16+) Oropharyngeal Cancer (8th ed., 2017)**
(Not including: P16-negative (p16-) cancers of the oropharynx)

Primary Tumor (T)

- T0** No primary identified
- T1** Tumor 2 cm or smaller in greatest dimension
- T2** Tumor larger than 2 cm but not larger than 4 cm in greatest dimension
- T3** Tumor larger than 4 cm in greatest dimension or extension to lingual surface of epiglottis
- T4** Moderately advanced local disease
Tumor invades the larynx, extrinsic muscle of tongue, medial pterygoid, hard palate, or mandible or beyond*

Mucosal extension to lingual surface of epiglottis from primary tumors of the base of the tongue and vallecula does not constitute invasion of the larynx.

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

Prognostic Stage Groups

Clinical

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

Pathological

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

Head and Neck

Locally Advanced Oropharynx Cancer

Multidisciplinary Team:

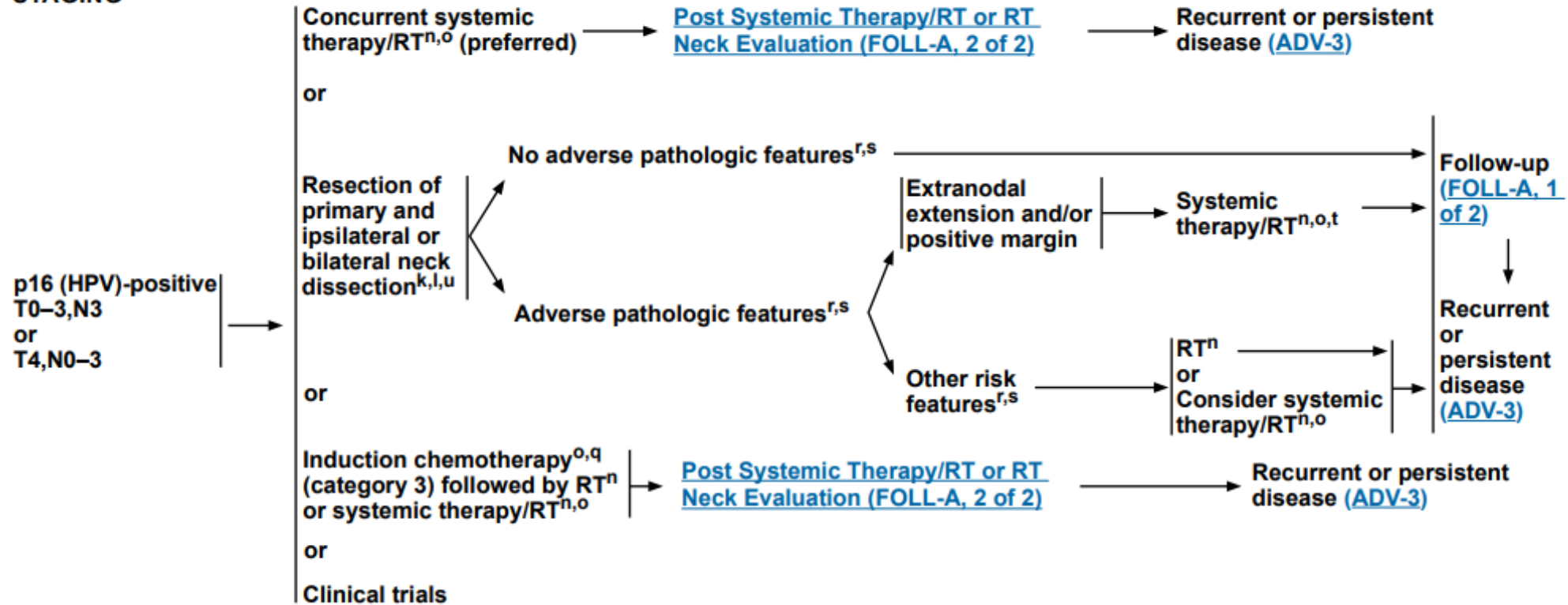
- Surgery
- Radiation
- Medical Oncology
- Oral Medicine
- Nutrition
- Speech Pathology
- Social Work
- Pathology
- Radiologist

Head and Neck

Base of Tongue/Tonsil/Posterior Pharyngeal Wall/Soft Palate
CLINICAL STAGING

TREATMENT OF PRIMARY AND NECK

ADJUVANT TREATMENT



Head and Neck

Locally Advanced Oropharynx Cancer

Chemoradiation:

- 1) High-dose Cisplatin (100mg/m² q3wks * 2-3)
- 2) Weekly Cisplatin (40mg/m² weekly)
- 3) Cetuximab (400mg/m² followed by 250mg/m² weekly)
- 4) Docetaxel (15mg/m² weekly)

Patil VM et al DOI: 10.1200/JCO.22.00980 - Phase II/III compared to Placebo

Improvement in 2yr DFS (30.3 vs 42% HR 0.673) and 2yr OS (41.7 vs 50.8% HR 0.747)

- 5) Carboplatin/Paclitaxel
- 6) Carboplatin/Infusional 5-FU

Head and Neck - Audience Response

Locally Advanced Oropharynx Cancer

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Head and Neck – Audience Response

Locally Advanced Oropharynx Cancer

Chemoradiation but now he is 78 with significant hearing loss.

- 1) High-dose Cisplatin (100mg/m² q3wks * 2-3)
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Locally Advanced Oropharynx Cancer

Radiation Treatment Algorithm and Treatment Timeline

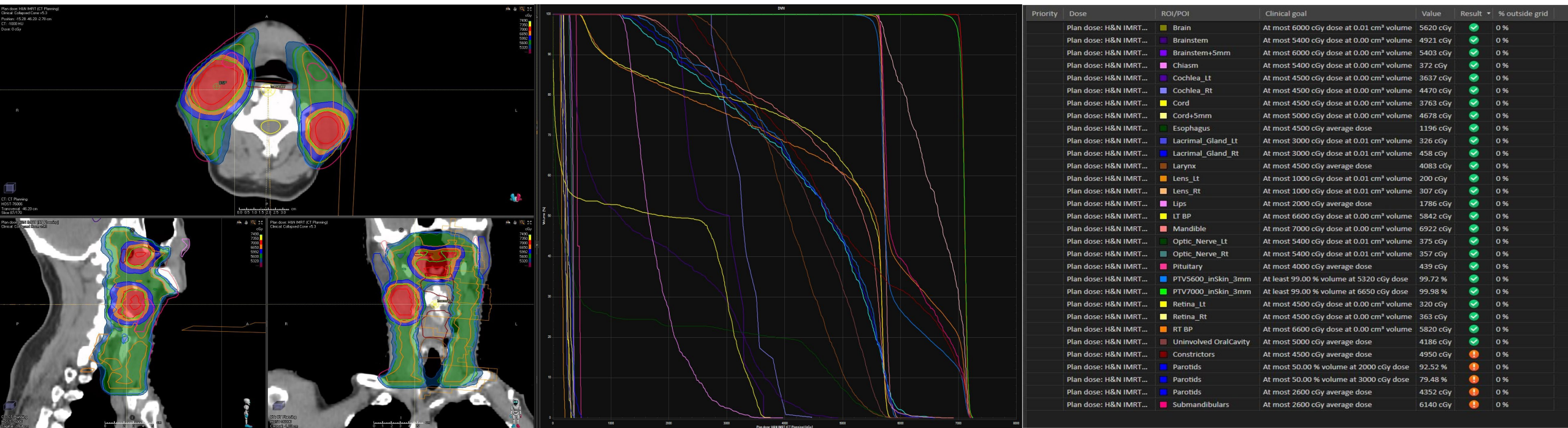
- Consultation with Scope Examination
- Radiation Simulation(CT Scan) in the Treatment Planning Position with Immobilization



https://www.aboutcancer.com/neck_simulation.htm

Locally Advanced Oropharynx Cancer

Radiation Treatment Planning



Locally Advanced Oropharynx Cancer

Radiation Treatment Algorithm and Treatment Timeline

- IMRT plan development takes 1-2 weeks
- Physics Q/A
- Daily Monday-Friday Treatments for 35 fractions to a total delivered dose of 7000cGy to the areas of gross disease and lower dose to at risk areas with concurrent chemotherapy
- Weekly On-Treatment Visits to assess treatment toxicity and management
- Follow q3 months with scope examination alternating with ENT if following
- PET/CT at 3 months and further imaging dictated by clinical findings

Head and Neck

Locally Advanced Oropharynx Cancer

Oral Medicine Considerations

- 1) Timing of RT in relation to invasive dental procedures
- 2) Goal to remove any teeth at risk of post-RT extractions and ORN
- 3) Pre-RT vs. Post-RT extractions

Head and Neck

Locally Advanced Oropharynx Cancer

Nutrition:

- Screening – MST at initial visit to assess risk for malnutrition during therapy
- Assessment
 - Weight History,
 - Current Intake,
 - Nutrition Impact Symptoms,
 - Comorbid Conditions,
 - Treatment Plan and Duration
- Interventions/Plan
 - Pre-treatment Discussion around PEG Placement,
 - Meet with SLP (including EAT-10) provide diet and swallowing recommendations,
 - address any preexisting deficits,
 - management of NIS

Head and Neck

Locally Advanced Oropharynx Cancer

Nutrition:

- Concurrent Chemotherapy/Radiation
 - Discuss Placement of PEG or other alternate means of nutrition
 - Educate on needs/usage/care
 - Engage Home Health or other options
 - Begin adding ONS or tube feeding formula as intake declines
 - PEG Teaching
 - Flush tube 2-3/day until intake declines
 - Titrate tube feeding to reach goal rate
 - PEG Removal
 - Consider removal when eating >75% by mouth and stable weight

Head and Neck

Locally Advanced Oropharynx Cancer

Outcome:

3-month PET post-chemoradiation shows Complete Response

Survivorship:

Watch for Thyroid Dysfunction

Watch for Carotid Atherosclerosis

Watch for recurrence/secondary malignancy



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Perspectives on treatment of HPV associated HNSCC from an Academic H&N Medical Oncologist

Siddharth Sheth

Assistant Professor of Medicine
Division of Oncology
Department of Medicine

Lineberger Comprehensive Cancer Center
UNC School of Medicine
University of North Carolina at Chapel Hill

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Disclosures

- Sheth: Naveris (*honoraria for advisory board*)
- Full COI Disclosure: <https://coi.asco.org/share/F3K-WRFQ/Siddharth%20Sheth>

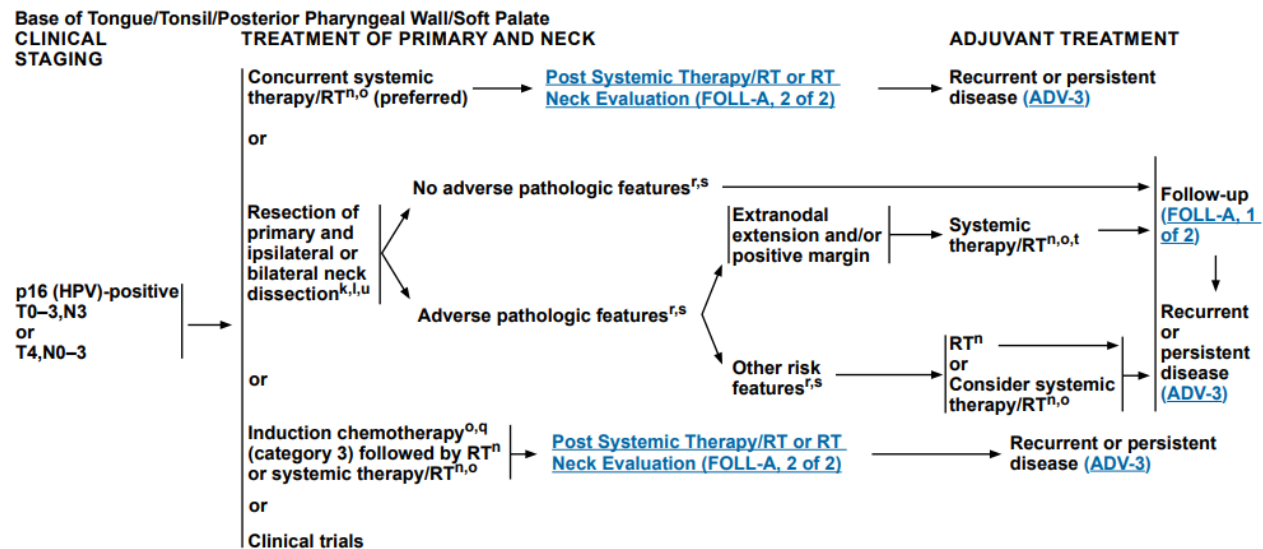
Revisiting our Clinical Case

69 yo M, non-smoker, minimal PMH. Dx with HPV+ T4N2M0 OPSCC

What is the optimal treatment?

 National Comprehensive Cancer Network® **NCCN Guidelines Version 2.2024** [NCCN Guidelines Index](#) [Table of Contents](#) [Discussion](#)

Cancer of the Oropharynx (p16 [HPV]-positive)



Revisiting our Clinical Case

69 yo M, non-smoker, minimal PMH. Dx with HPV+ T4N2M0 OPSCC
What is the optimal treatment?

Concurrent radiation therapy with:

- 1) High-dose Cisplatin (100mg/m² q3wks * 2-3)
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Revisiting our Clinical Case with a Twist

69 yo M, non-smoker, minimal PMH. Dx with HPV+ T4N2M0 OPSCC. However, his Cr is 1.6 and he has severe hearing impairment?

What is the optimal treatment?

Concurrent radiation therapy with:

- 1) High-dose Cisplatin (100mg/m² q3wks * 2-3)
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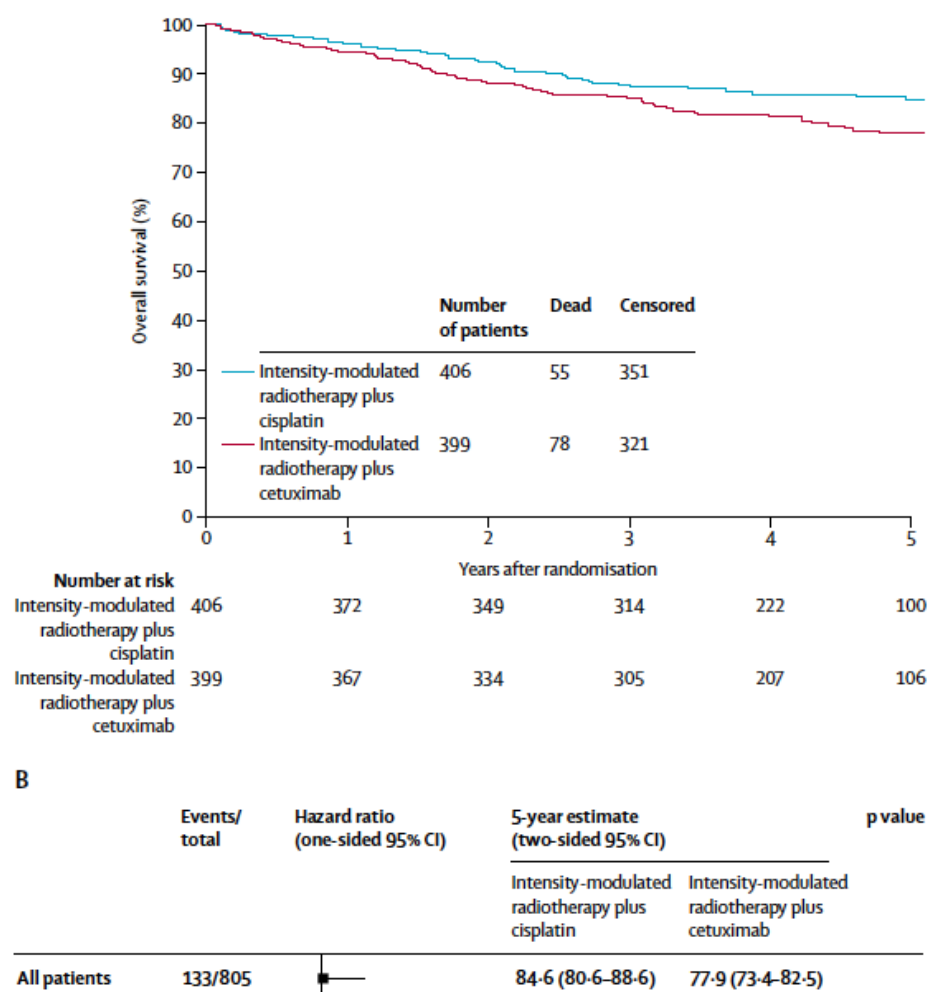
What would I do???



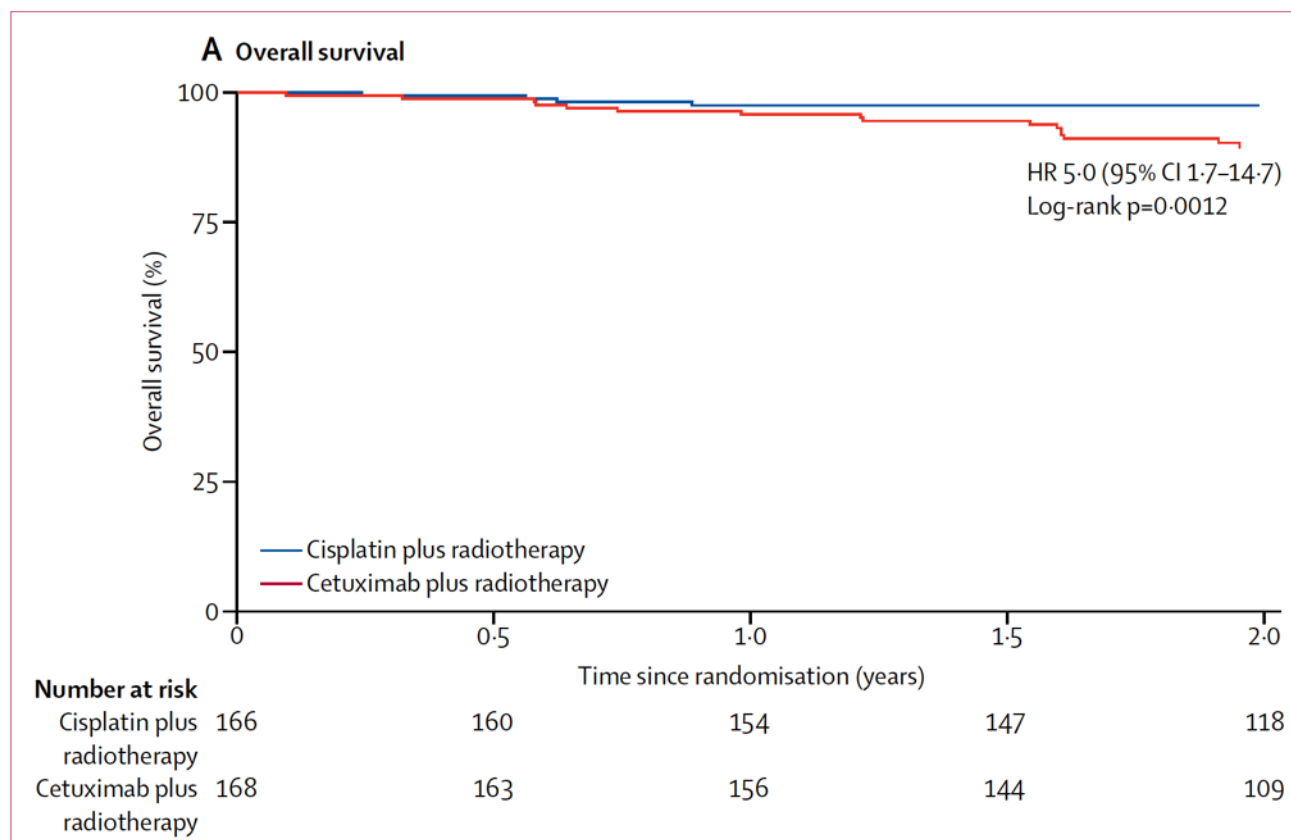
Cisplatin vs. Cetuximab in HPV+ OPSCC

All patients received IMRT 70 Gy

RTOG 1016



De-ESCALaTE:



My conversation with this patient:

Patient: Doc, what is the best treatment?

Me: **Honestly, we really don't know....**

Concurrent radiation therapy with:

- 1) No radiation therapy
- 2) Weekly Cisplatin (**30mg/m²**)
- 3) Weekly Cetuximab (400mg/m² followed by 250mg/m²)
- 4) Clinical trial

What more data can we use to help our patients?

Circulating tumor DNA (ctDNA)

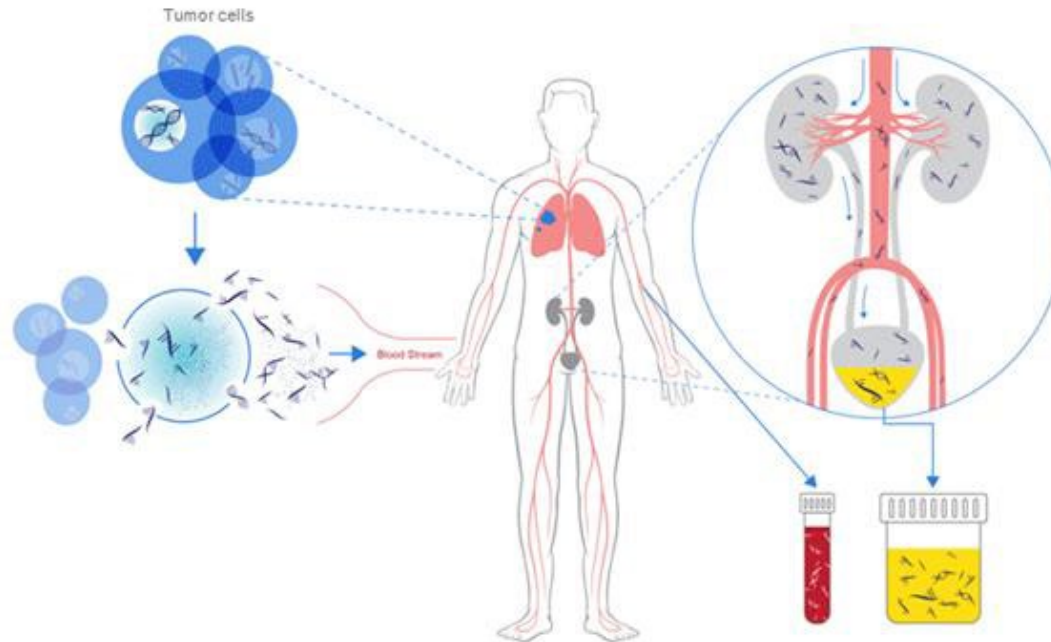
What is ctDNA?

- Cancer cell DNA fragments can enter the bloodstream. This is circulating tumor DNA (ctDNA)
- ctDNA is measurable in blood plasma

When should ctDNA be ordered?

- Not standard of care
- Growing consensus for monitoring virus-driven HNSCC
- My advice: do not order unless part of a study or clinical trial unless for HPV associated cancers

Circulating Tumor DNA (ctDNA)



Main Advantages of ctDNA

- Captures intratumor heterogeneity
- Systemic overview of cancer
- Frequent sampling options for monitoring applications
- Different analyte options depending on clinical context

ctHPVDNA is measurable, quantifiable, and prognostic

What assay is used to measure ctHPVDNA?

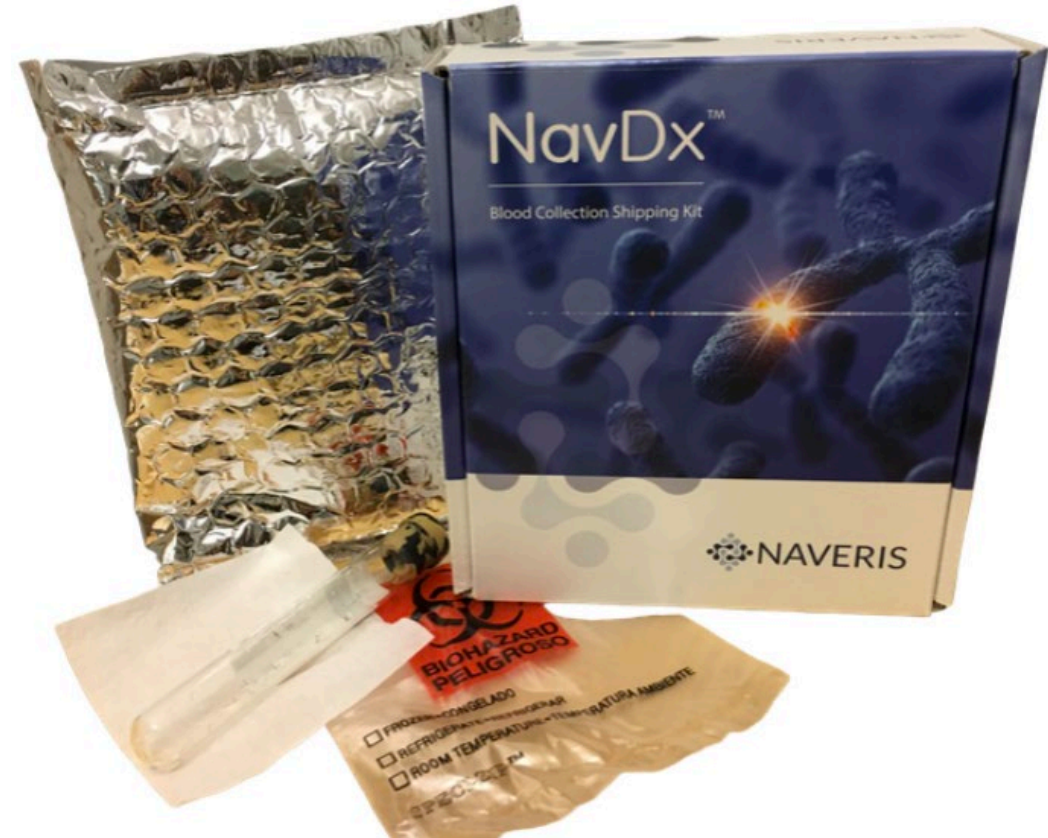
- Two most common: PCR and NGS
- Research grade and commercial based

Naveris (NavDx)

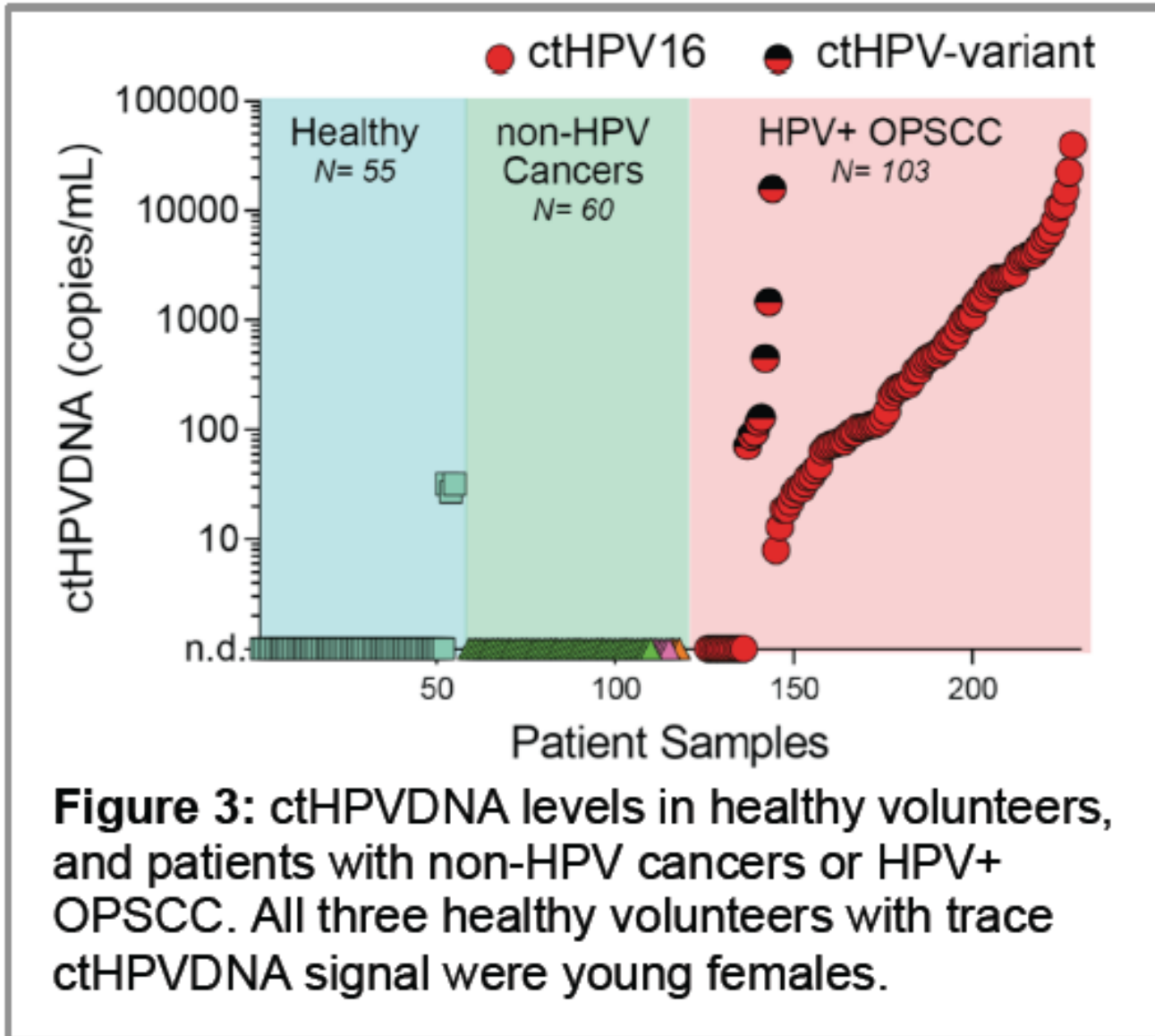
- ddPCR
- Circulating, cell free, tumor tissue modified viral (TTMV) HPV DNA
- Detects and scores the normalized fragment of high risk-HPV (16, 18, 31, 33, 35)

Sysmex (HPV Safe-SEQ)

- NGS
- Only HPV 16/18



Clinical validation of ctHPV measurement



Cohort of 218 patients

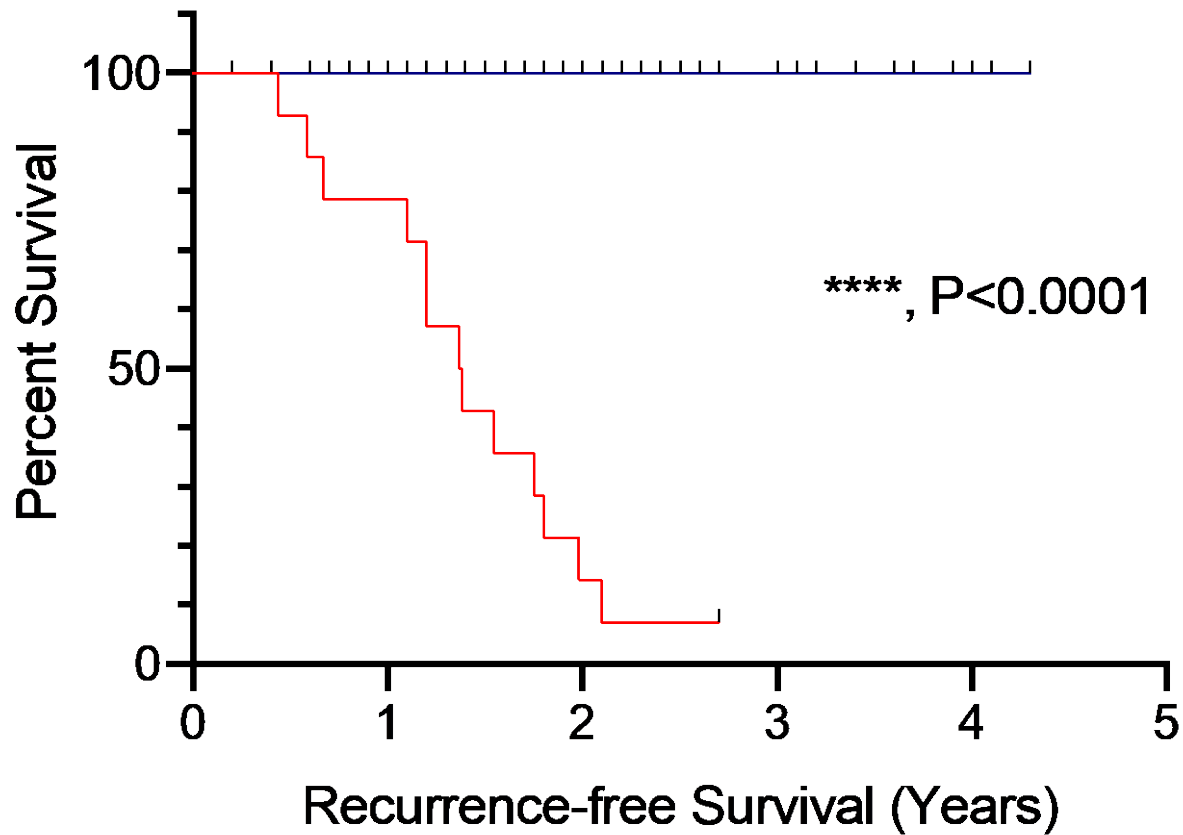
- 55 healthy pts (without cancer)
- 60 non-HPV cancer pts
- 103 non-metastatic HPV- OPSCC pts (p16+ IHC)

Results

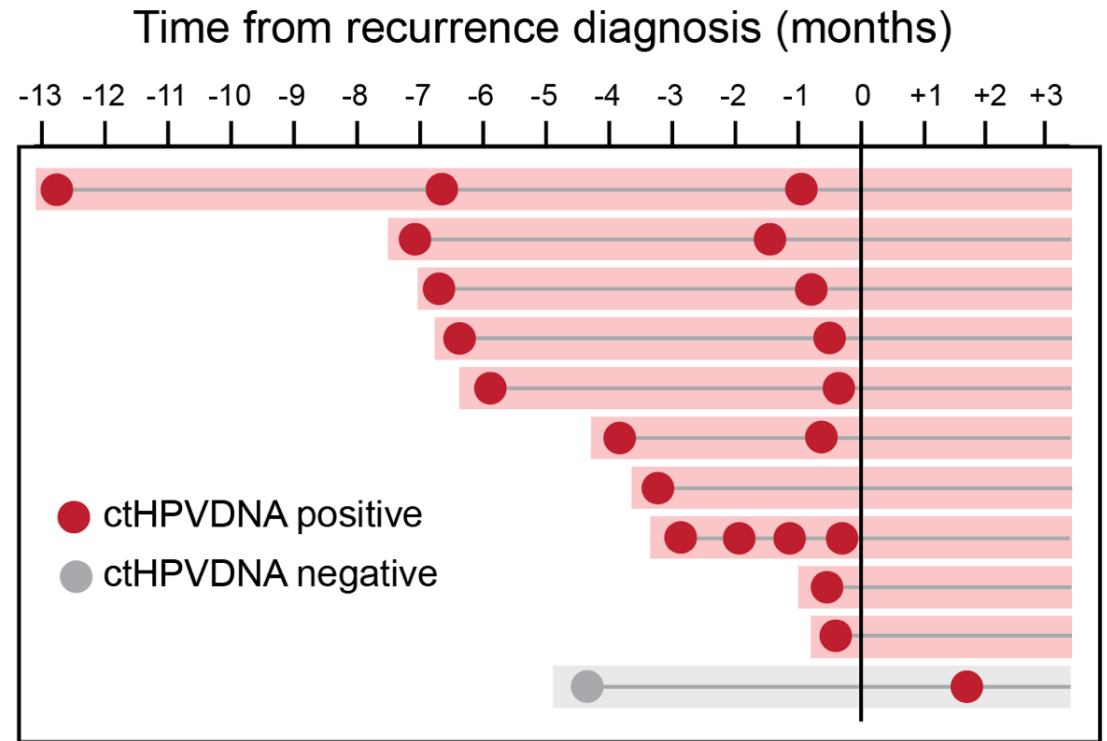
- 98% Specificity, 89% Sensitivity
- 11 ctHPVDNA-negative pts

Chera. CCR. 2019

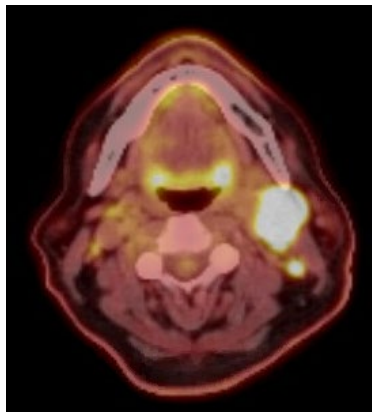
ctHPVDNA Clinical Trial Data



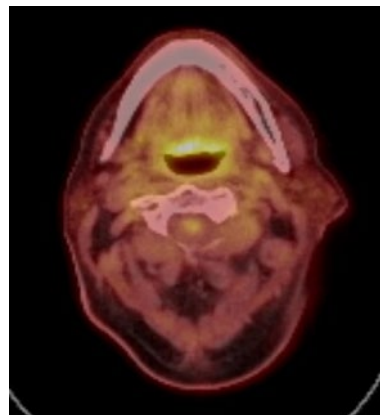
- ctHPVDNA positive, 2x (n = 16)
- ctHPVDNA negative (n = 99)



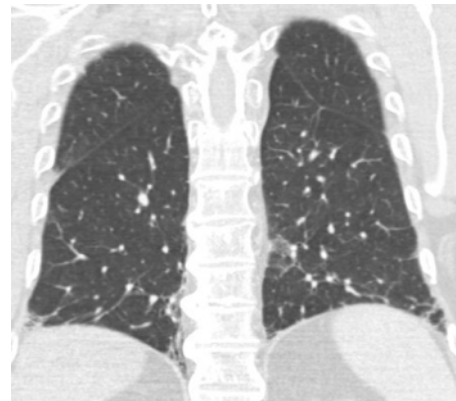
Our Case Revisited Again



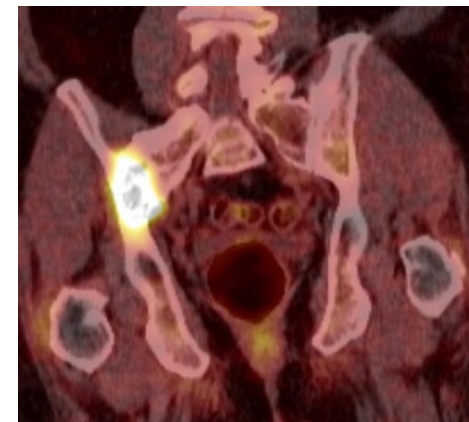
T4N2 OPSCC (p16+)



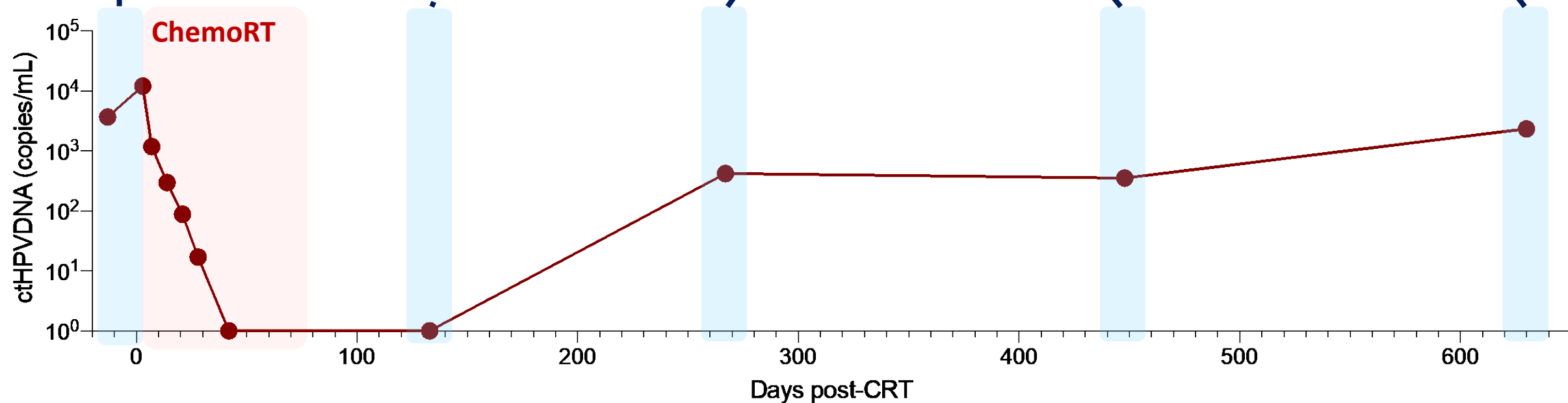
3 month PET →
Complete Response



Neck/Chest CT → NED

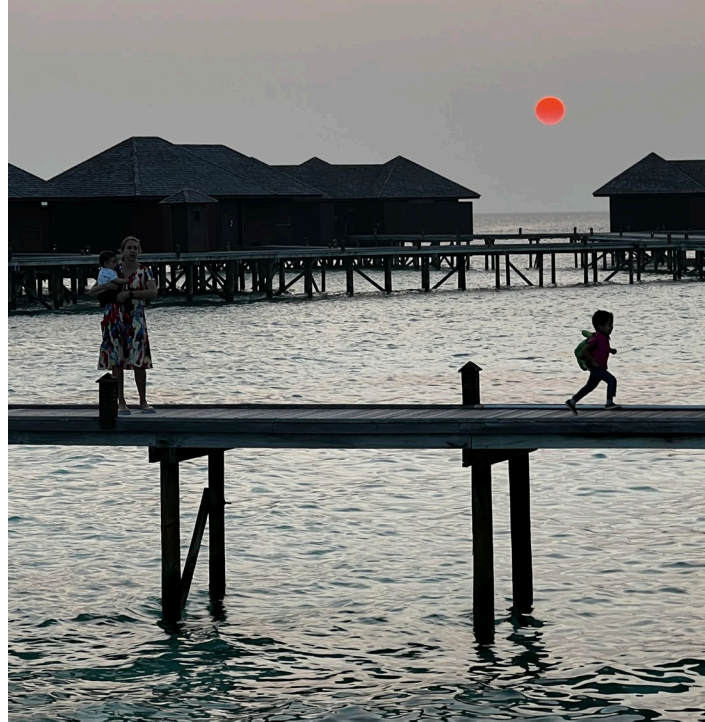


PET → biopsy
bone metastasis



Conclusions/Questions?

1. Cisplatin remains the preferred radiation sensitizer in HNSCC, especially in HPV+ disease
2. Still a lot we are learning about optimal management of HPV+ HNSCC. Our pool of patients is finite so placement in clinical trial is essential
3. ctHPVDNA is a power tool. It's reliable and likely will make guidelines



Siddharth Sheth

Siddharth.sheth@med.unc.edu

Head and Neck

Metastatic Oral Cavity Cancer

58 yo with history of a Stage IVa (T4aN0M0) tongue cancer presents with several month history of cough.

Treated with Antibiotics * 2 without improvement

Past Hx:

5 years prior to presentation, partial glossectomy with neck dissection and radial forearm free flap (T1N0M0)

2 years prior to presentation, hemimandibulectomy and partial glossectomy w/ left tonsil/soft palate resection and partial pharyngectomy with fibular free flap (T4aN0M0)

Adjuvant XRT alone (60 Gy)

PSHx:

45 Pack-Year Tobacco History

Moderate ETOH (6-12 pack/week)

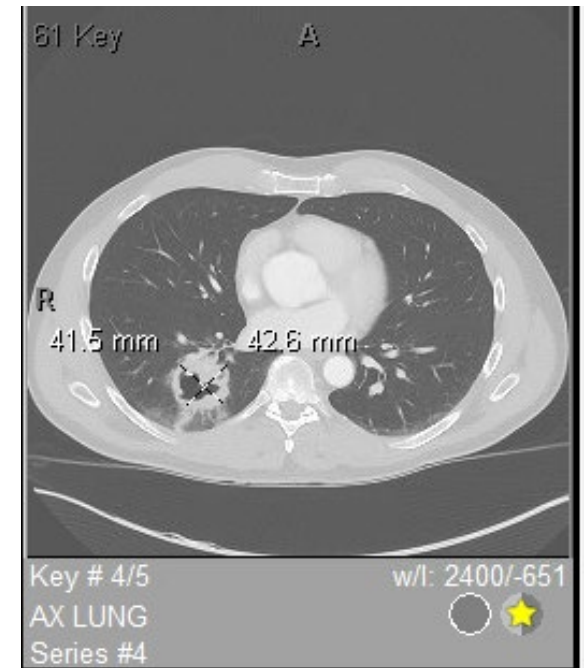
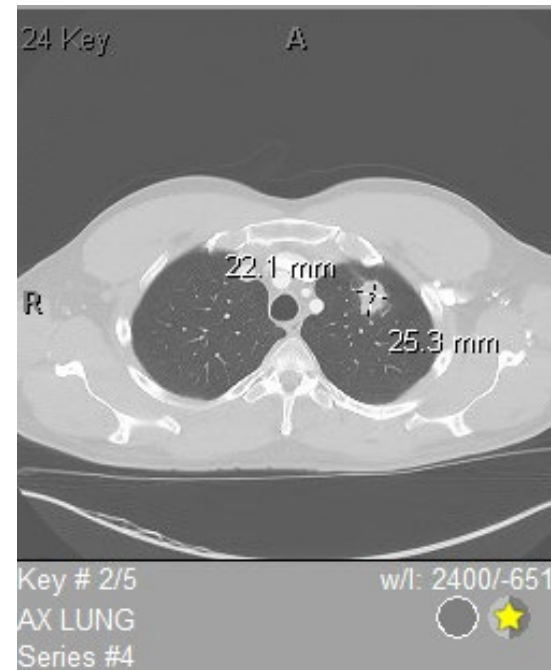
Works Full-time in Sales

Head and Neck

Metastatic Oral Cavity Cancer

CT: No evidence of recurrence in Neck;
numerous bilateral pulmonary nodules with
largest measuring 4.3cm

Pathology: Robotic bronchoscopy – positive for
keratinizing squamous cell carcinoma. CPS 7



Head and Neck

Metastatic Oral Cavity Cancer

Staging: Stage IVc (T0N0M1)

What are our options?

Head and Neck

Metastatic Oral Cavity Cancer

Immunotherapy:

Pembrolizumab 200mg IV q3wks or 400mg IV q6wks

Chemoimmunotherapy:

Platinum (Cis or Carbo)/Infusional 5-FU/pembrolizumab

Clinical Trial:

?

Head and Neck – Audience Response

Metastatic Oral Cavity Cancer

1) Immunotherapy:

Pembrolizumab 200mg IV q3wks or 400mg IV q6wks

2) Chemoimmunotherapy:

Platinum (Cis or Carbo)/Infusional 5-FU/Pembrolizumab

3) Chemoimmunotherapy (not approved):

Platinum/Pembrolizumab

4) Chemoimmunotherapy (not approved):

Platinum/Paclitaxel/Pembrolizumab

Head and Neck

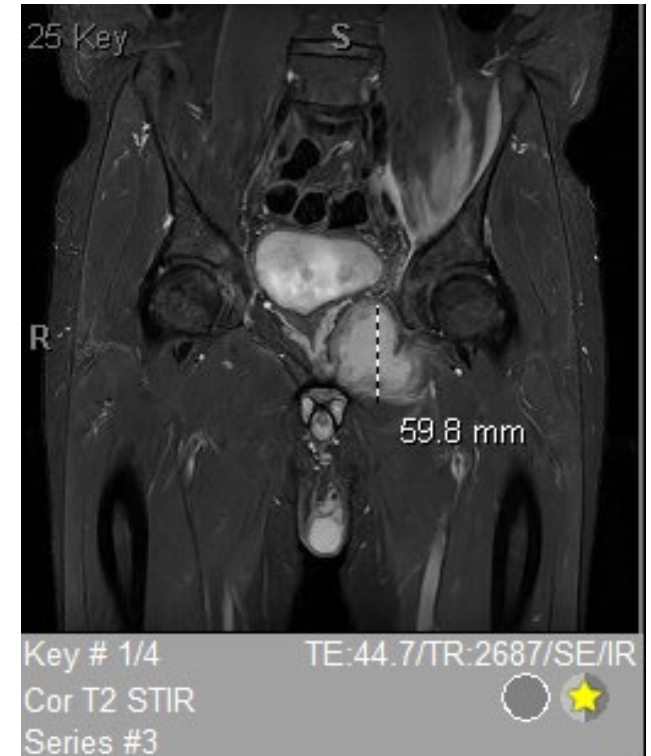
Metastatic Oral Cavity Cancer

He was able to join a clinical trial but came off trial due to travel
Trial had used pembrolizumab as a backbone so continued
Pembro.

6 months later, developed back/leg pain = sciatica

MRI: 6.2cm lytic lesion in left pubic ramus/pubis with
large soft tissue necrotic mass.

Declines chemotherapy – continue pembrolizumab and started
on Denosumab therapy



Head and Neck

Metastatic Oral Cavity Cancer

Risks of Osteoradionecrosis?

Other Supportive Care options (c/o anorexia)

Head and Neck

Metastatic Oral Cavity Cancer

He completed radiation therapy to hip but slowly had a diminishing performance status and went on hospice.

Head and Neck

-Panel Pearls and Questions

