MMC Head and Neck Tumor Board

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24th Multidisciplinary Management of Cancers: A Case-based Approach

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- Andrew Birkeland, MD – UC Davis, OHNS
- Saad Khan, MD – Stanford, Medical Oncology
- Fred Baik, MD – Stanford, OHNS
- Sue Yom, MD – UCSF, Radiation Oncology
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Disclosures

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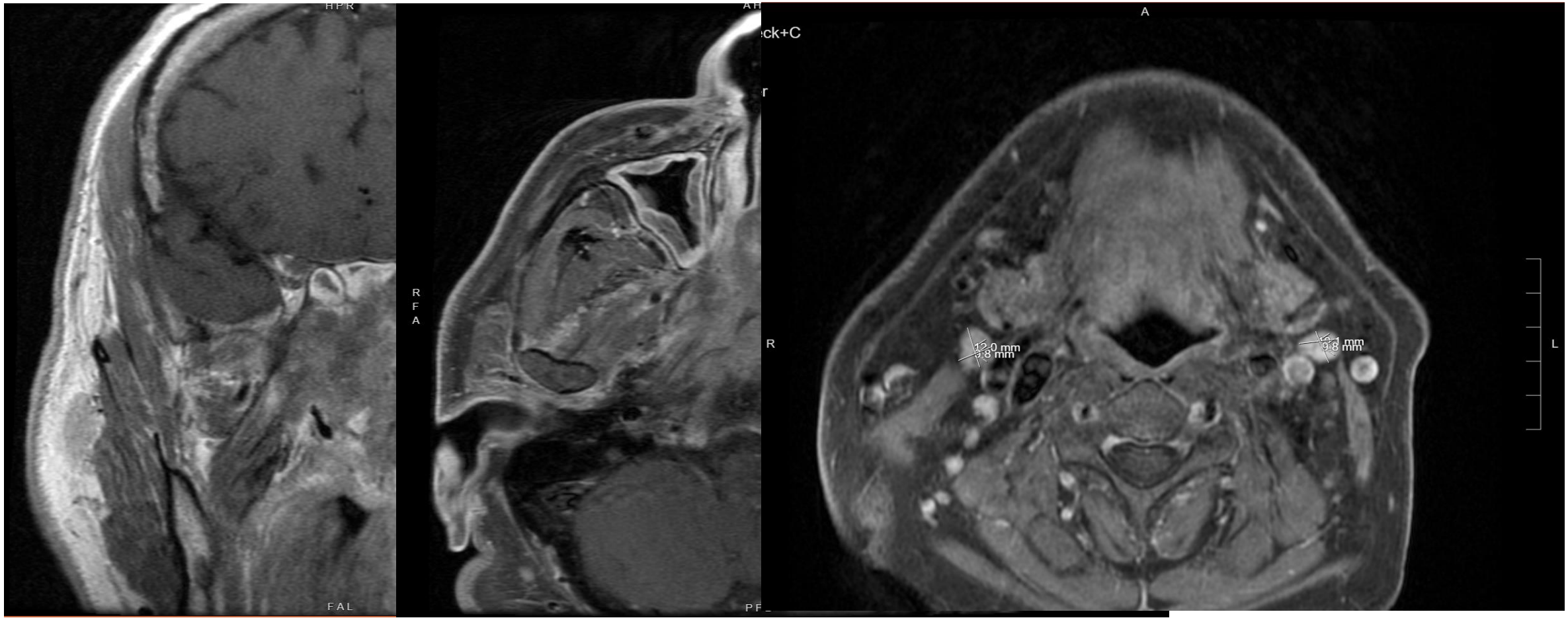
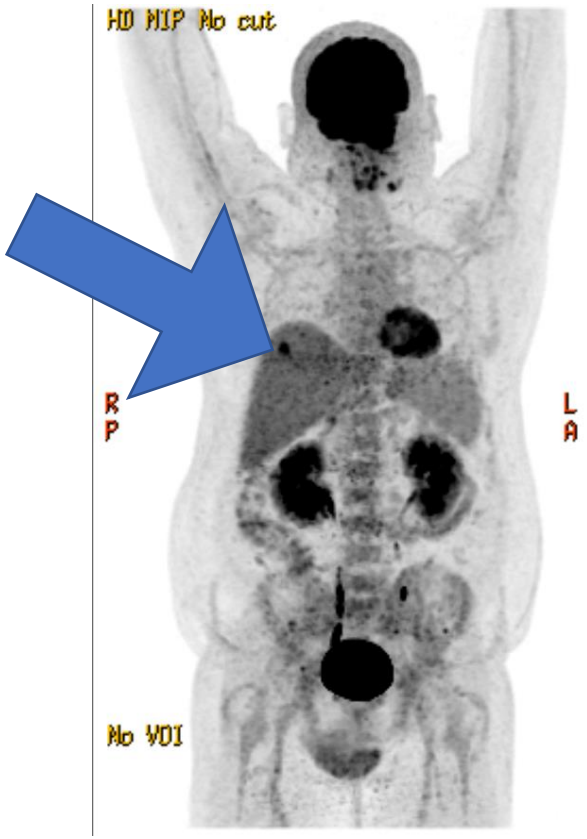
CASE 1
JM – 50 YO M with progressive neurologic complaints

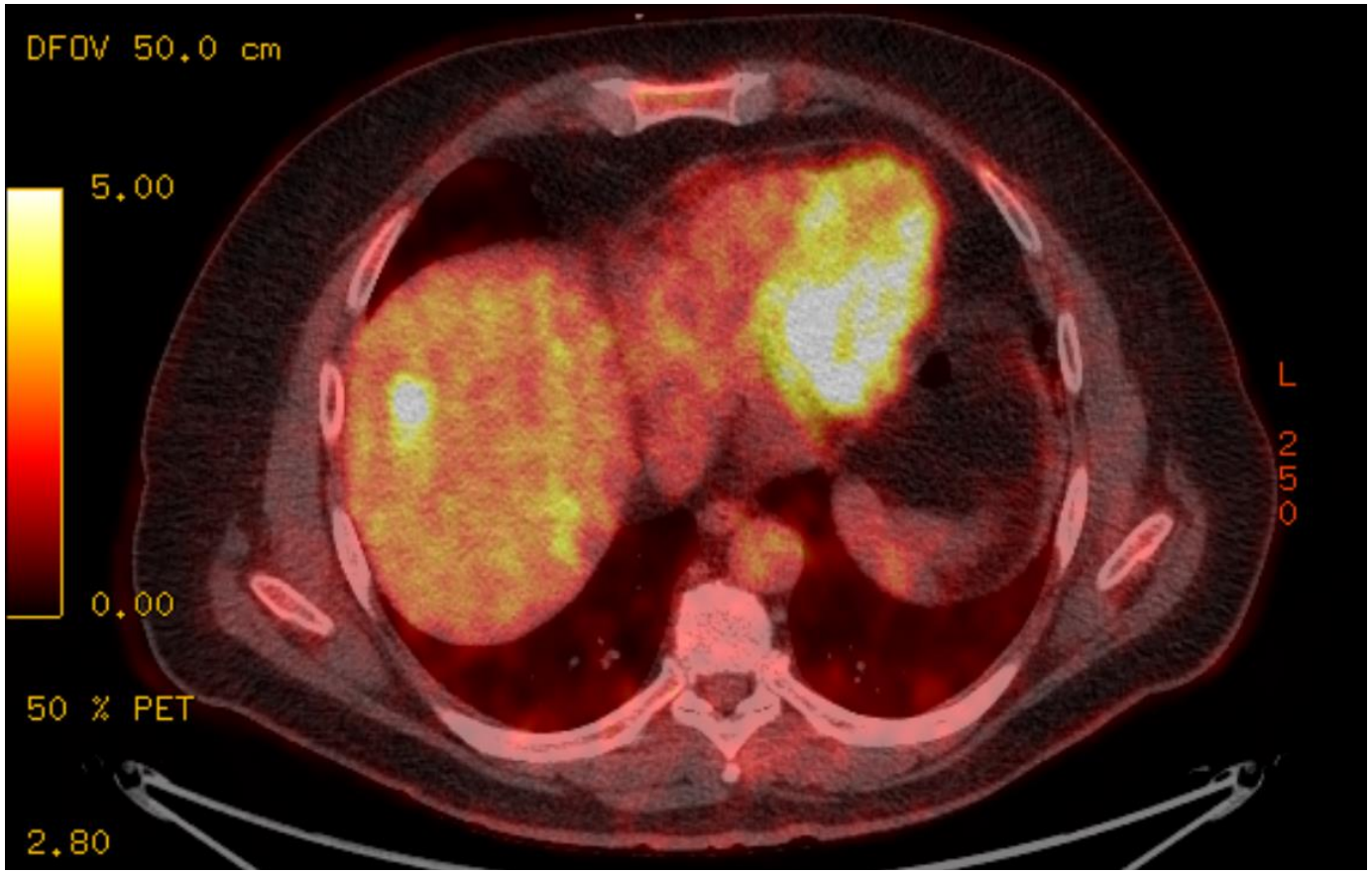
- Admitted for headache, and progressive L facial and LUE weakness
- Exam with left eye deviation, paretic left tongue, whisper voice worsening over the past 2 weeks

MRI Skull Base Neck



PET/CT





Case continued

- NP biopsy c/w non-keratinizing SCC, EBV-positive
- Plasma EBV DNA PCR 39,040 IU/mL

What stage would you call this patient?

A) IVa (i.e. M0)

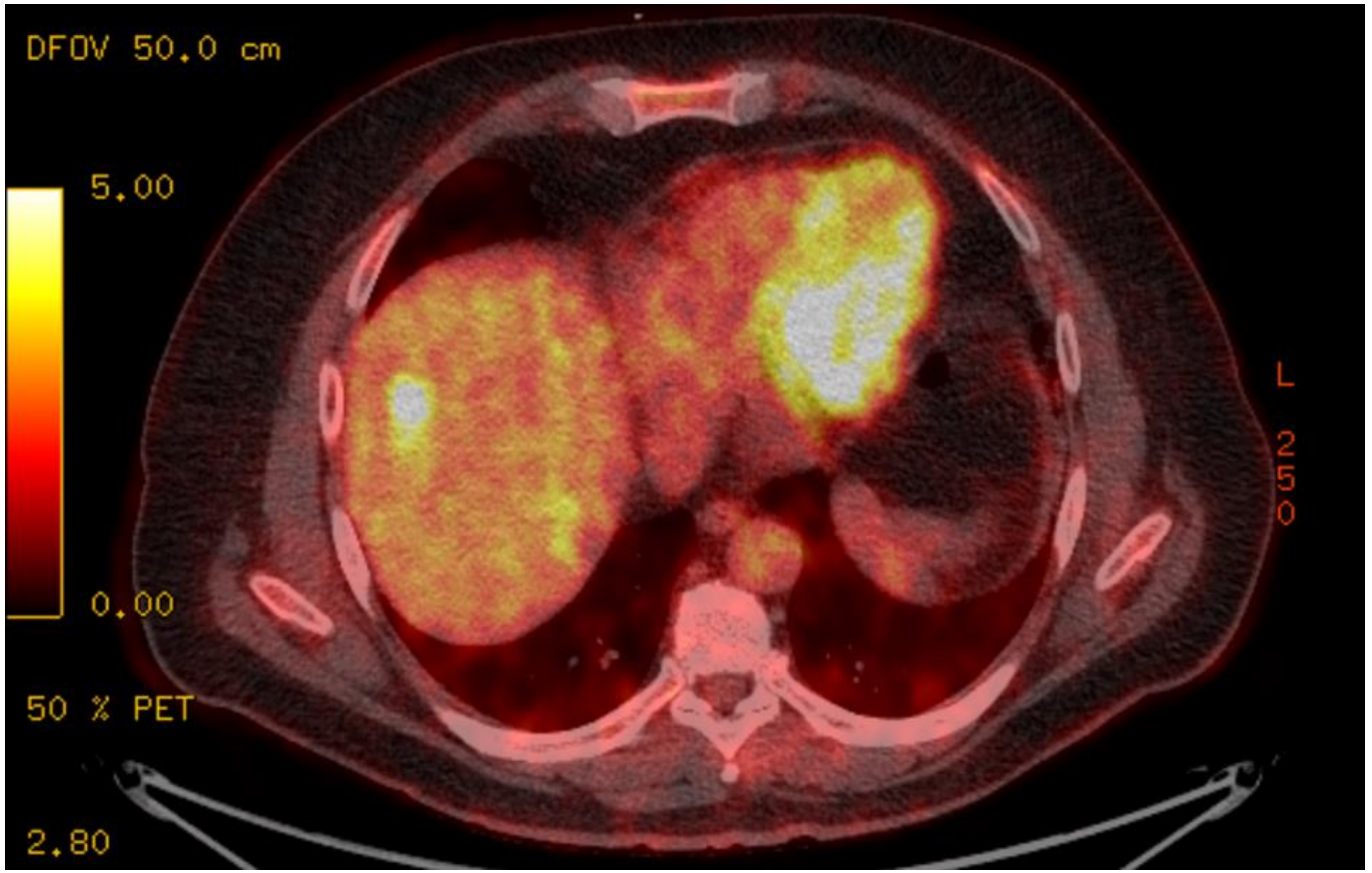
B) IVb (M1)

C) We don't know, we should biopsy

MRI-guided Liver Core Biopsy

Hepatic parenchyma with mild non-specific changes

Who is correct?



CT-guided Liver Core Biopsy

Hepatic parenchyma with no significant abnormality. No evidence of malignancy.

Which of the following factors is NOT typically used in the differentiation of stages of nasopharyngeal carcinoma?

A) Tumor Size

B) Lymph Node Involvement

C) Serum Epstein-Barr Virus (EBV) DNR PCR

D) Presence of Distant Metastasis

How do the panelist use EBV?

- Which tests (DNA PCR, other)
- When to order

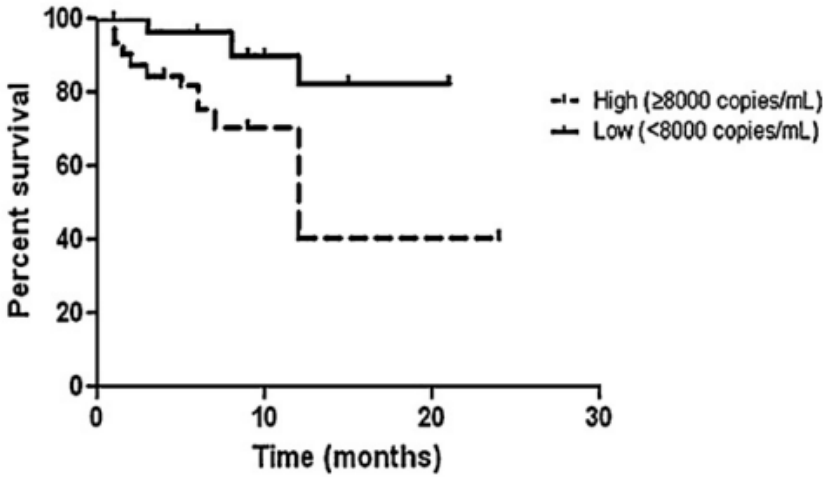
What is the utility of obtaining a serum EBV DNA level?

A) Assessment of infectivity of patient

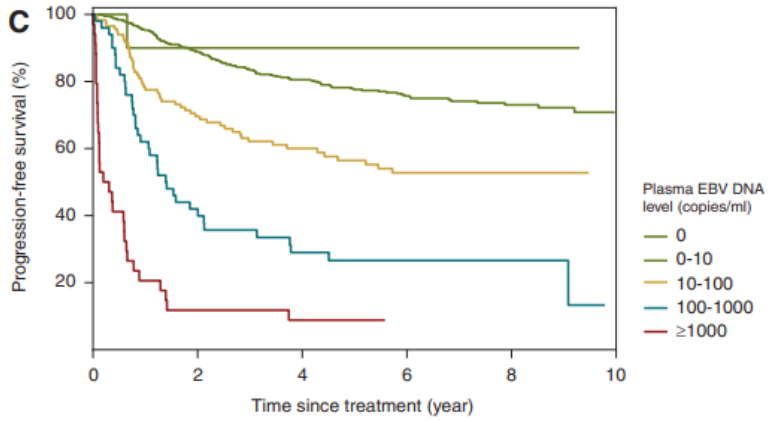
B) Detection of Distant Metastasis

C) Prognostic Indicator and Monitoring Treatment Response

D) Other



Chai, SJ, et. al. J of Clinical Virology. 2012 Sept; 55(1): 34-39



Chan DCT, et. al. Ann Oncol. 2022 Aug;33(8):794-803.

What would be your initial treatment strategy for our patient with T4N1M1 NPC?

A) Gemcitabine/ cisplatin (GC) with pembrolizumab

B) Cisplatin plus XRT with liver SBRT

C) Sequential GC followed by cisplatin + XRT

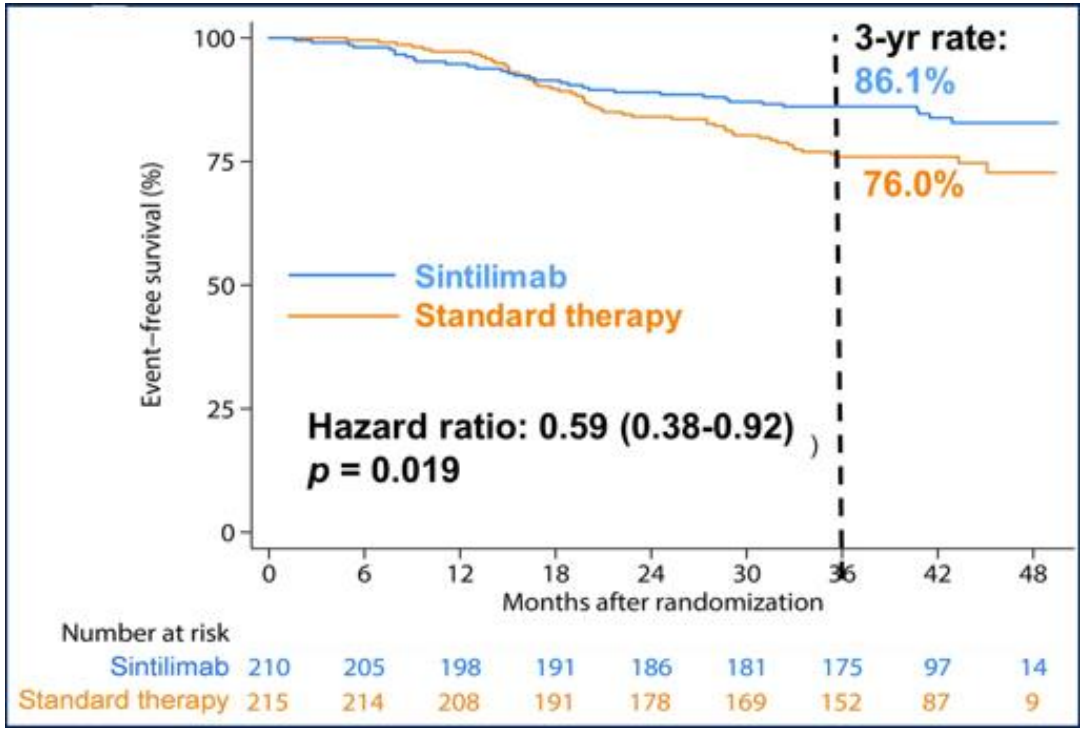
D) Sequential docetaxel, cisplatin and 5FU (TPF) followed by cisplatin + XRT

What we did

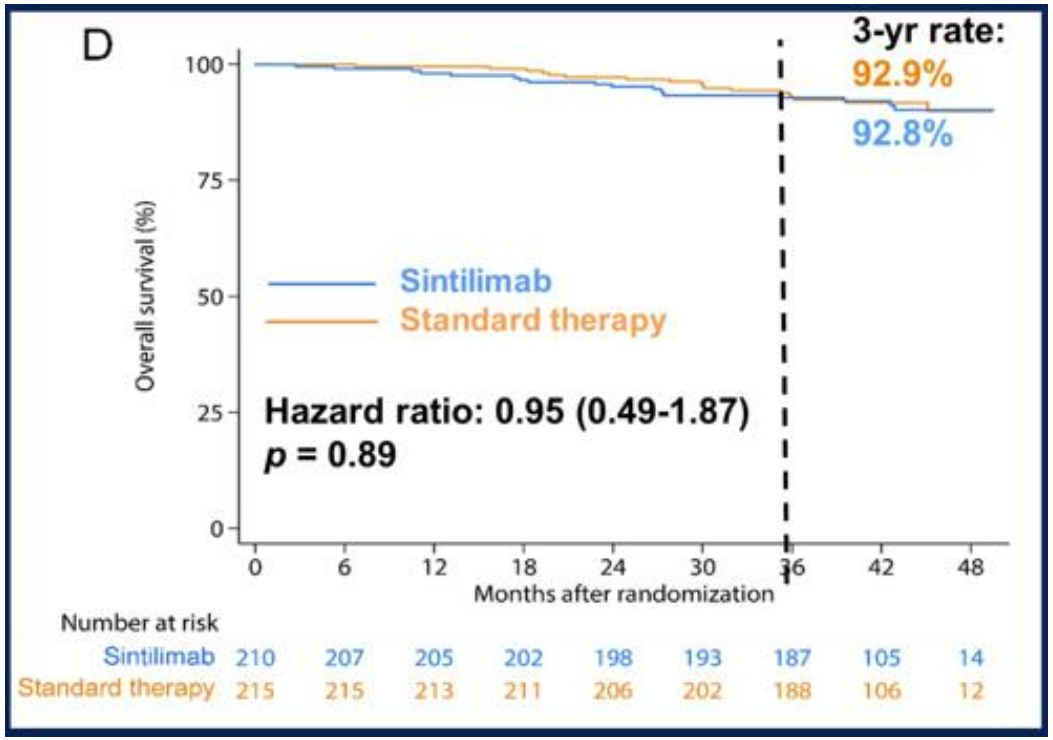
Gemcitabine/Cisplatin + pembrolizumab

What about immunotherapy as part of induction? Sintilimab (ASCO 2023)

Event Free Survival



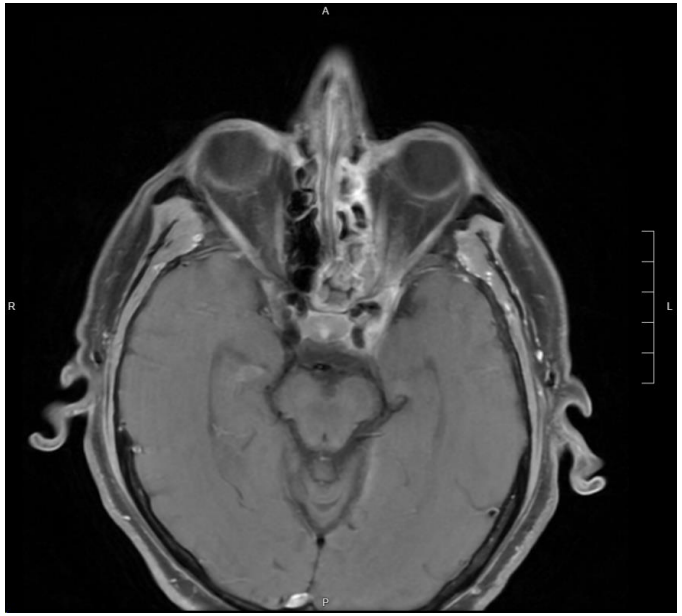
Overall Survival

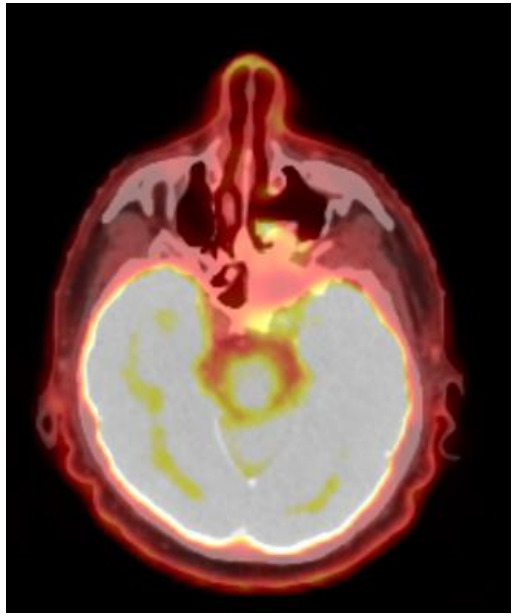


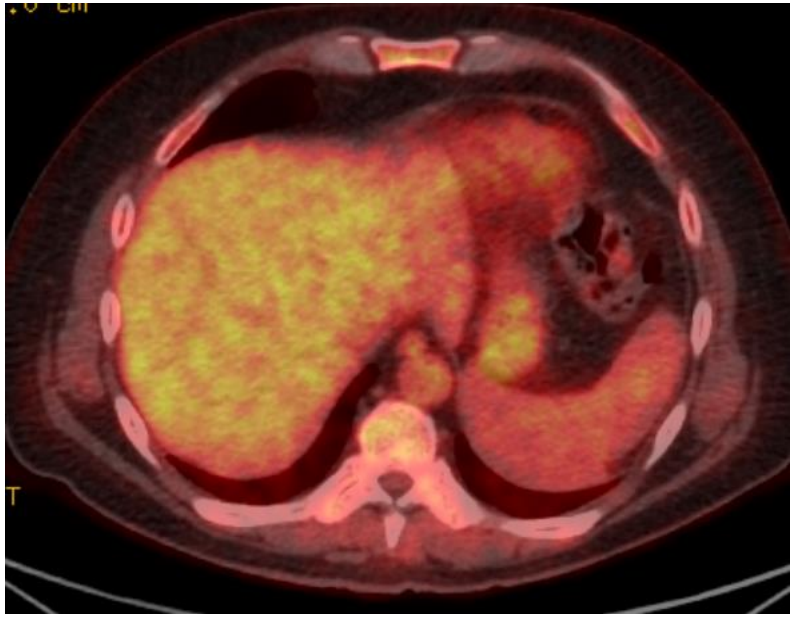
Jun Ma et al. JCO 41, LBA6002-LBA6002(2023).

Case 1 continued

Patient received 2 cycles of gemcitabine/cisplatin + pembrolizumab with very good response







What would you do next?

A) Additional Chemotherapy – how many more cycles?

B) Chemoradiation with full dose XRT

C) Chemoradiation with palliative XRT

D) Palliative XRT alone

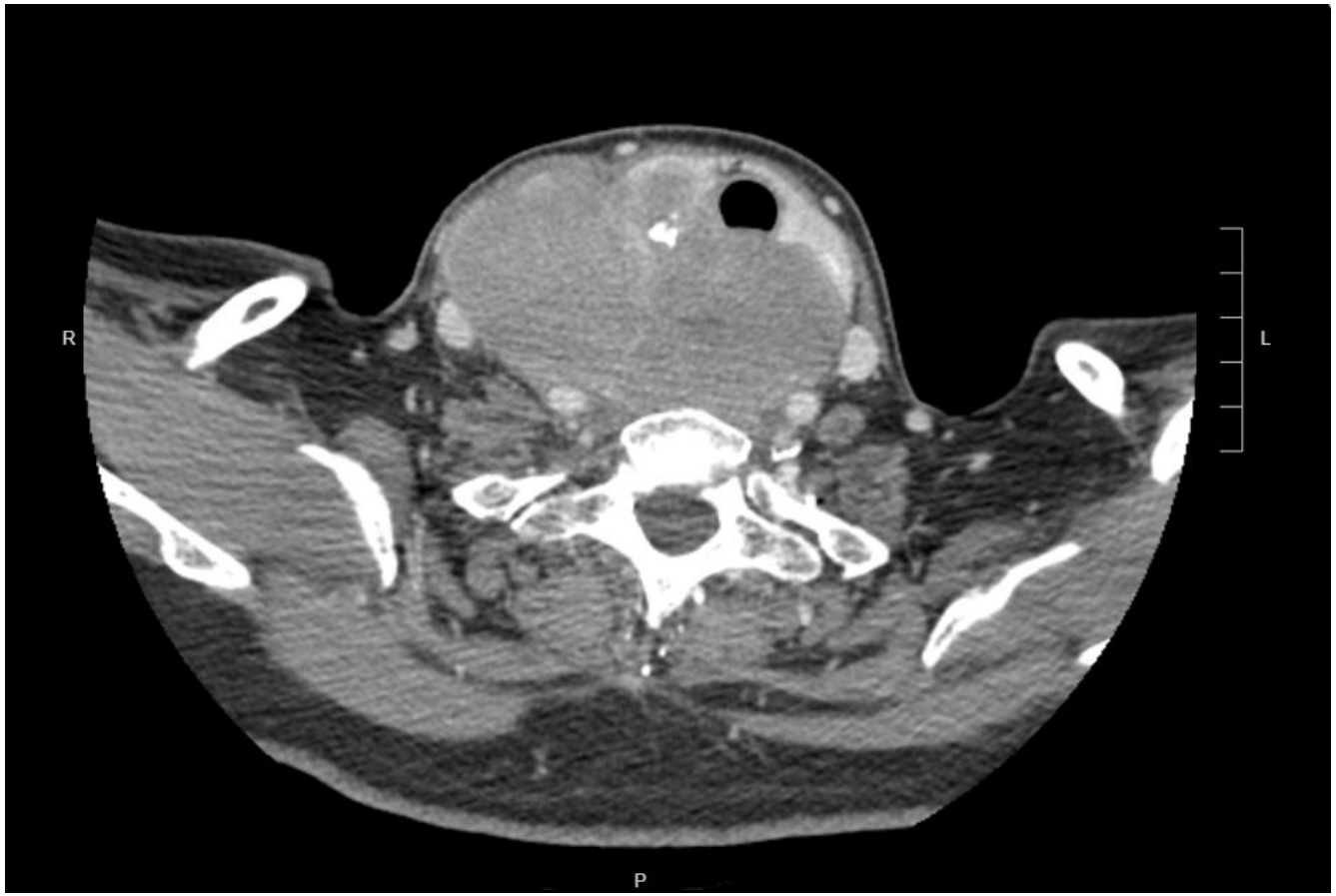
Take Home Points

- EBV DNA PCR can be used as a prognostic indicator and for monitoring treatment response.

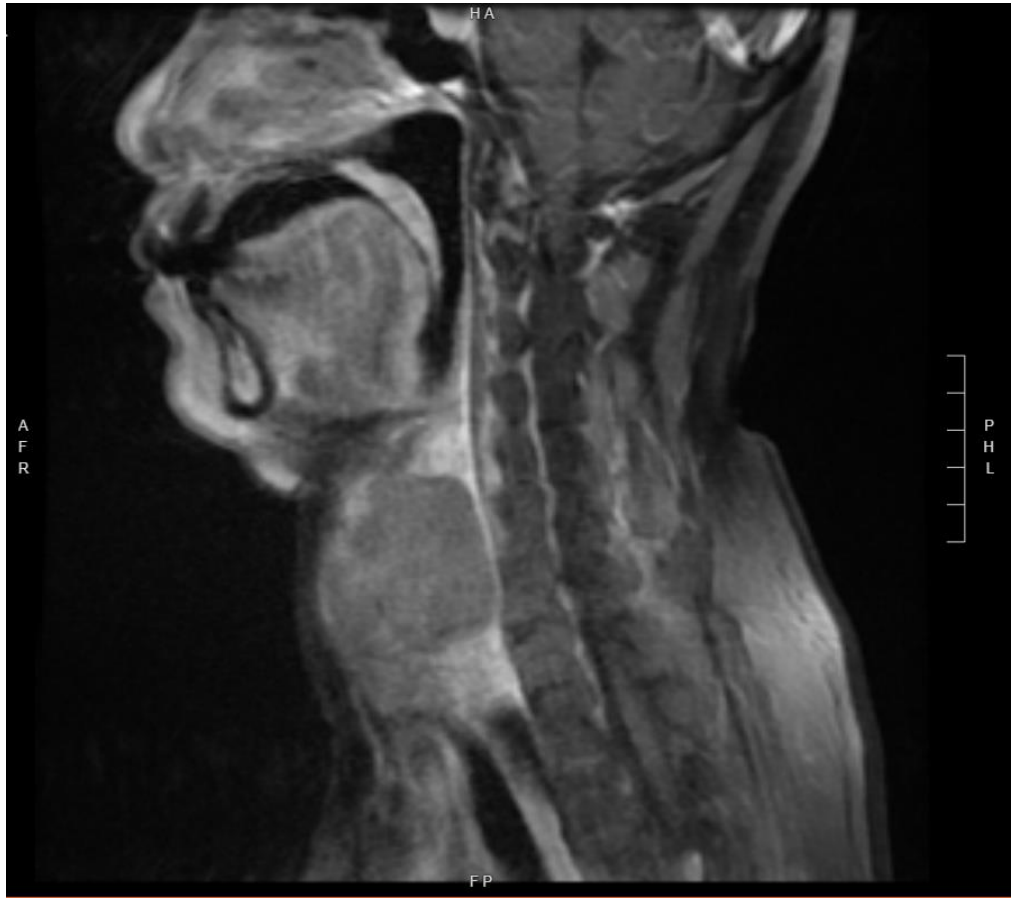
CASE 2
ET – 69F with dysphagia and right sided neck enlargement

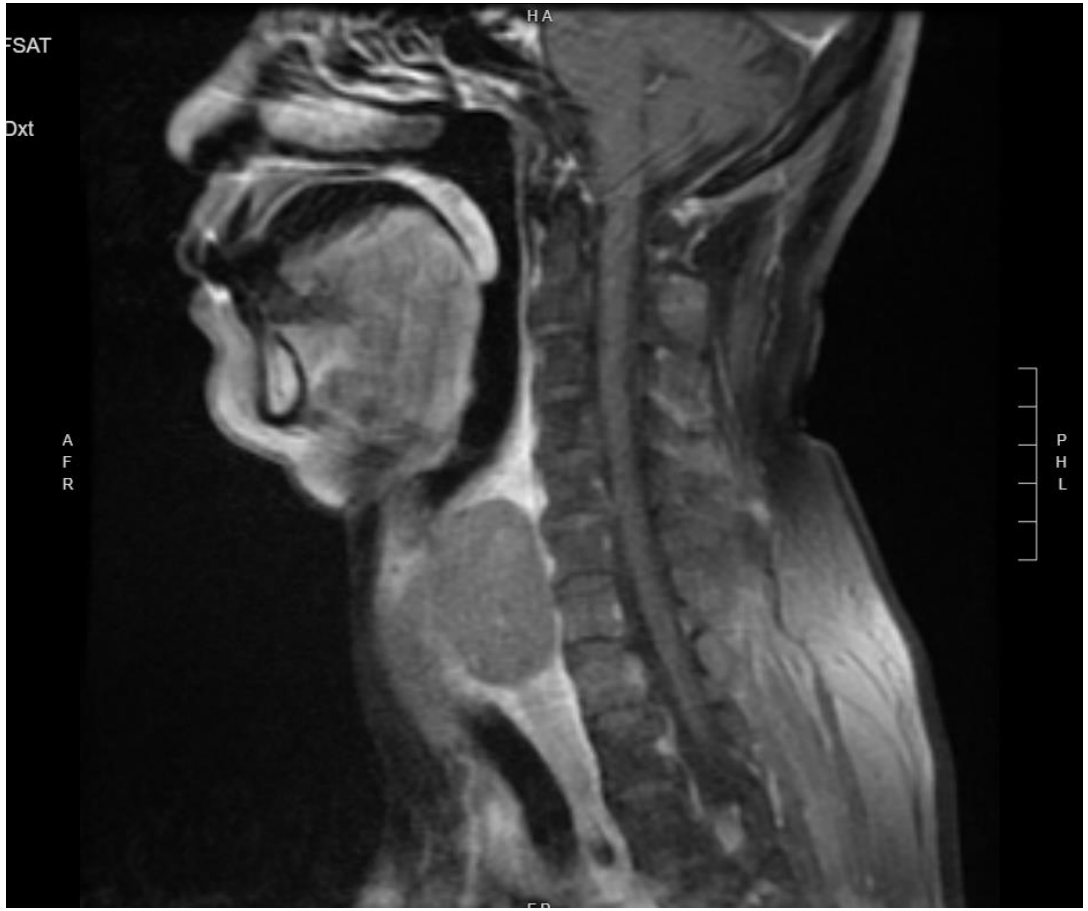
- 8/2019 - CT Neck with a 9.3 x 6.3 cm x 6 cm mass causing leftward displacement of the trachea.
- MRI Neck – 6 cm mass encasing carotid artery. Inseparable from esophagus.
- PET/CT – Only disease was an FDG-avid mass in the right lobe of thyroid.
- US core bx - anaplastic thyroid carcinoma. BRAF V600E+. PD-L1 CPS 90.

CT Neck



MRI Neck





What is your initial approach for this patient?

A) Radioactive Iodine (RAI) therapy

B) Checkpoint inhibitor immunotherapy alone

C) BRAF inhibitor monotherapy

D) Combination of BRAF inhibitor and MEK inhibitor

Case 2 Continued

- Patient starts dabrafenib + trametinib
- PET/CT - decreased size of right thyroid mass, new FDG-avid right neck LN
- Had subsequent resection of mass and thyroid
- Pathology: 5 cm unifocal ATA, ETE+, PNI+, no LVI, 1/44 LN involved, pT4a pN1b Mx

What is your next step?

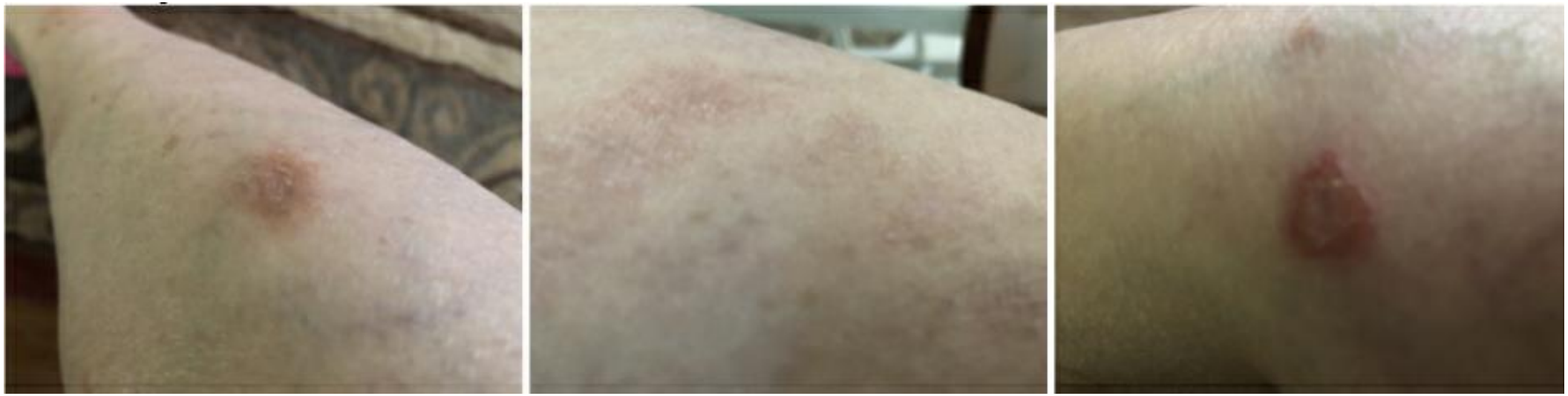
- A) Proceed with adjuvant dabrafinib/trametinib
- B) Add pembro
- C) XRT
- D) Wait and watch

What we did

- 4/2020 - Proceeded with adjuvant dabrafinib/trametinib and added pembrolizumab

Case 2 continued

- Now s/p 4 cycles of pembrolizumab develops a few itchy spots on anterior LLE and R posterior axilla.



How would you manage this skin-related toxicity?

A) Discontinue pembro and give PO steroids

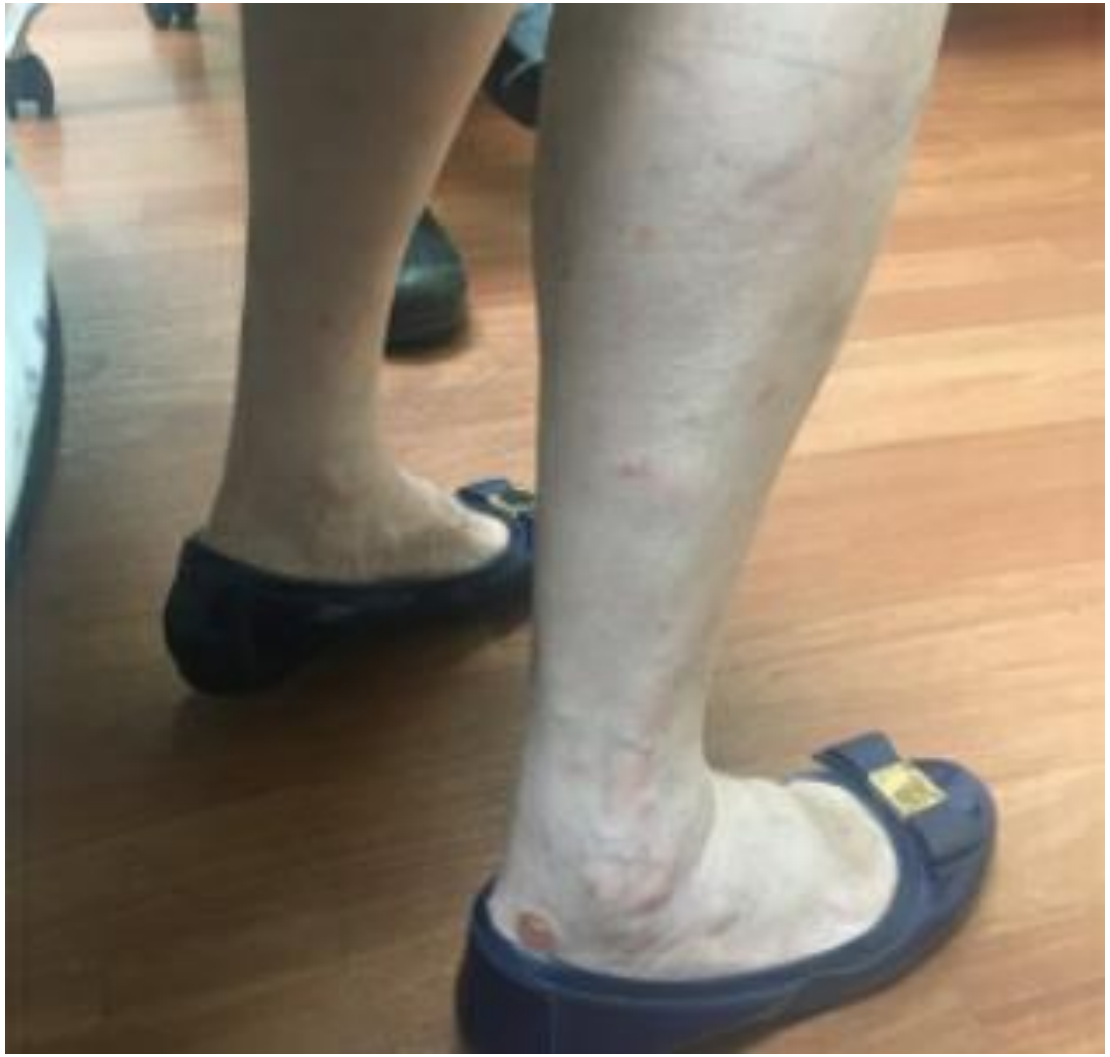
B) Adjust pembro dosing

C) Topical steroids, continue pembro

D) Switch from anti-PD1 to a PDL1

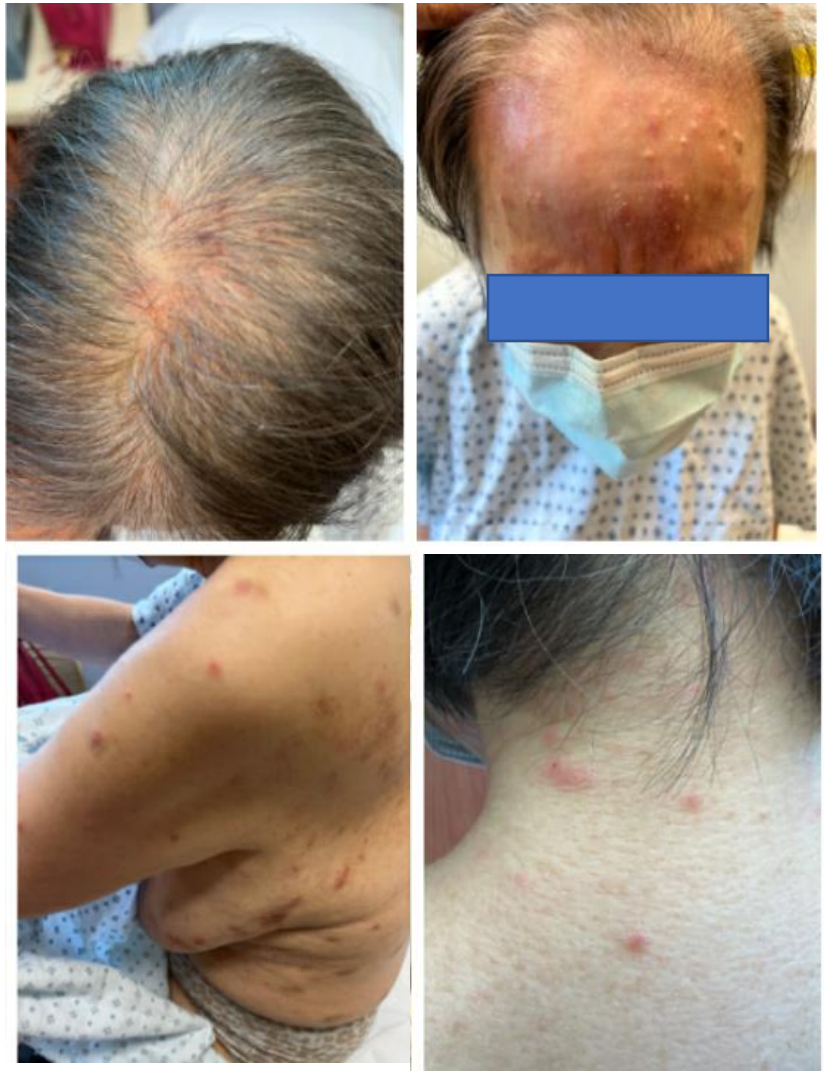
Topical steroids controlled skins AEs

- Exam with new round plaques on legs b/l.
- IgE 1,894 kU/L (H).



Case 2 Continued

- Skin finding worsened to involve 25% TBSA.
- IgE 2,672 kU/L (H).



How would you now manage this skin-related toxicity?

A) Discontinue pembro

B) Increase strength of topical steroids, add oral steroids, continue pembro

C) Increase strength of topical steroids, add oral steroids, start anti-IgE monoclonal antibody, continue pembro.

Case 2 Conclusion

- 10/2021 - Started on omalizumab with pembrolizumab but there was minimal improvement
- 2/2022 - Switched to dupilumab with pembrolizumab with dramatic improvement in skin toxicity.
- 2/8/23 PET/CT No definite findings of local recurrence or metastatic disease.
- 1/2024 continues dabrafinib/trametinib and pembrolizumab

How long should we continue pembro?

A) Indefinitely until POD or unacceptable toxicity

B) Evaluate response after 12 months and consider discontinuation if there is sustained remission.

C) After achieving a CR, regardless of the duration.

D) After 2 years post CR, followed by careful reevaluation.

What about the duration of dabrafinib/ trametinib?

A) Indefinitely

B) After 1-2 years post-CR

C) I don’t know

What is the most appropriate imaging schedule for the first 24 months after treatment?

A) Neck/Chest CT every 3 months

B) Neck/Chest/Abdomen CT with contrast every 1 to 3 months

C) Neck/Chest/Abdomen CT with contrast every 4 to 12 months

D) PET/CT scan every 3 months

Up to date recommends Neck/Chest/Abdomen CT with contrast every 1 to 3 months

NCCN does not provide surveillance recommendations

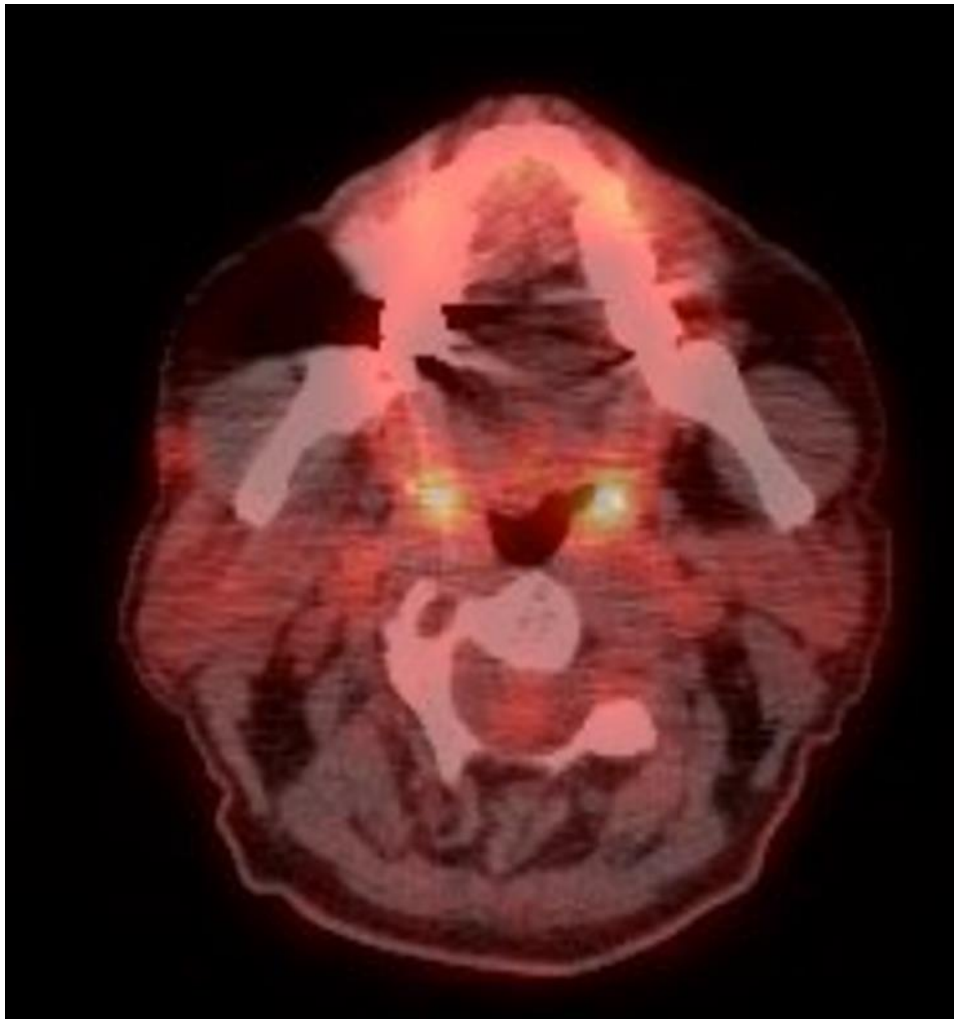
Take Home Points

- Consider expedited IHC/FISH testing for BRAF/MEK at diagnosis of anaplastic thyroid cancer
- Further studies are needed to assess the benefits of immunotherapy for anaplastic thyroid carcinoma.
- Consider a multi-disciplinary team for the management of AEs.

CASE 3
SP – 69 M with R neck lump noted while shaving. Former 10 pack-year smoker.

- R Neck LN excisional biopsy – metastatic 2.3 cm SCC in one of two lymph nodes. ENE+. P16+. HPV+
- Exam without any palpable mass or adenopathy. Fiberoptic exam with irregular bumps on midline base of tongue
- 10/12/23 PET after excisional bx – no distant disease found

PET/CT



Any additional workup needed?

A) ctHPV DNA
B) Endoscopy
C) Biopsy of mucosa

Case 3 Continued

- MR naso/oro: Status post excisional lymph node biopsy. Otherwise, negative.
- TORS oropharynx Biopsy with two separate OP SCC, p16+, HPV+.
    - 1. cm R GP sulcus
    - 0.6 cm R medial tongue base

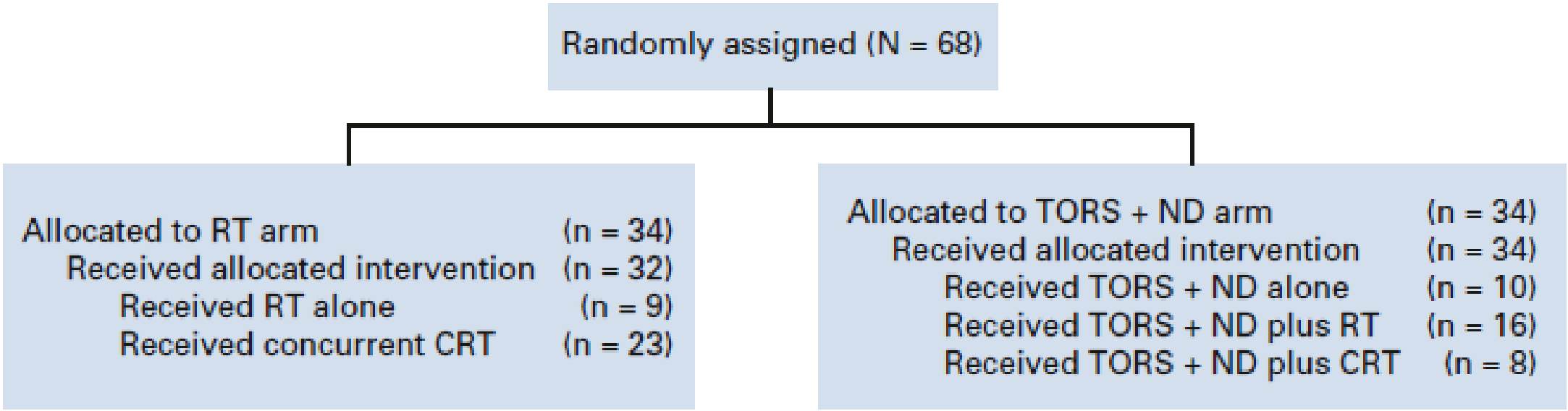
What would you recommend next?

A) XRT

B) XRT + chemo

C) Definitive tongue base resection and lymph node dissection

ORATOR I Trial



Anthony C. Nichols, et al. Journal of Clinical Oncology 2022 40:8, 866-875

Primary end point: Swallowing QOL Assessment at 1 year. (secondary endpoint OS: no difference)

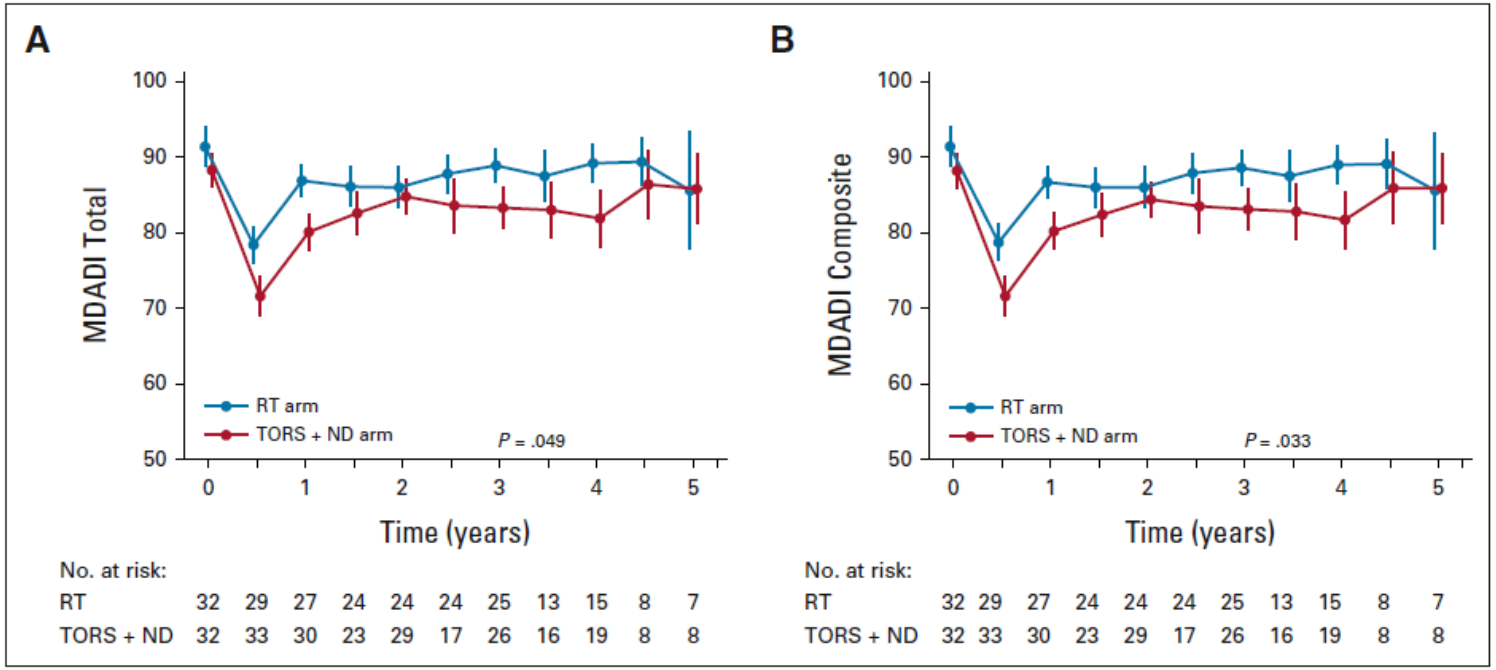
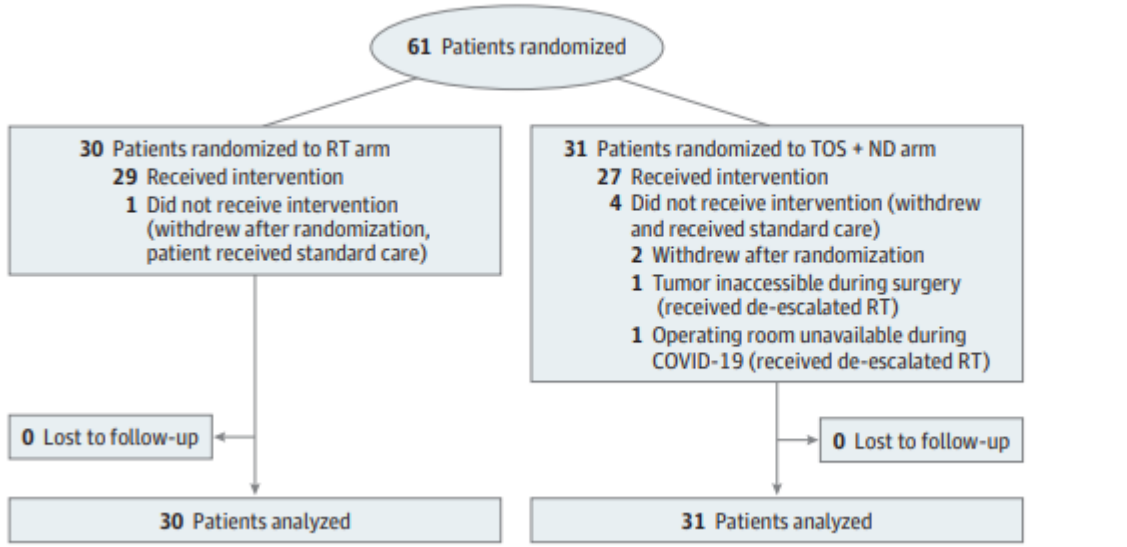


FIG 2. Changes in MDADI (A) total and (B) composite quality-of-life scores over time by treatment arm. Error bars represent standard errors. MDADI, MD Anderson Dysphagia Inventory; RT, radiotherapy; TORS + ND, transoral robotic surgery plus neck dissection.

Anthony C. Nichols, et al. Journal of Clinical Oncology 2022 40:8, 866-875

ORATOR2 Phase 2 Randomized Clinical Trial

Figure 1. CONSORT Diagram

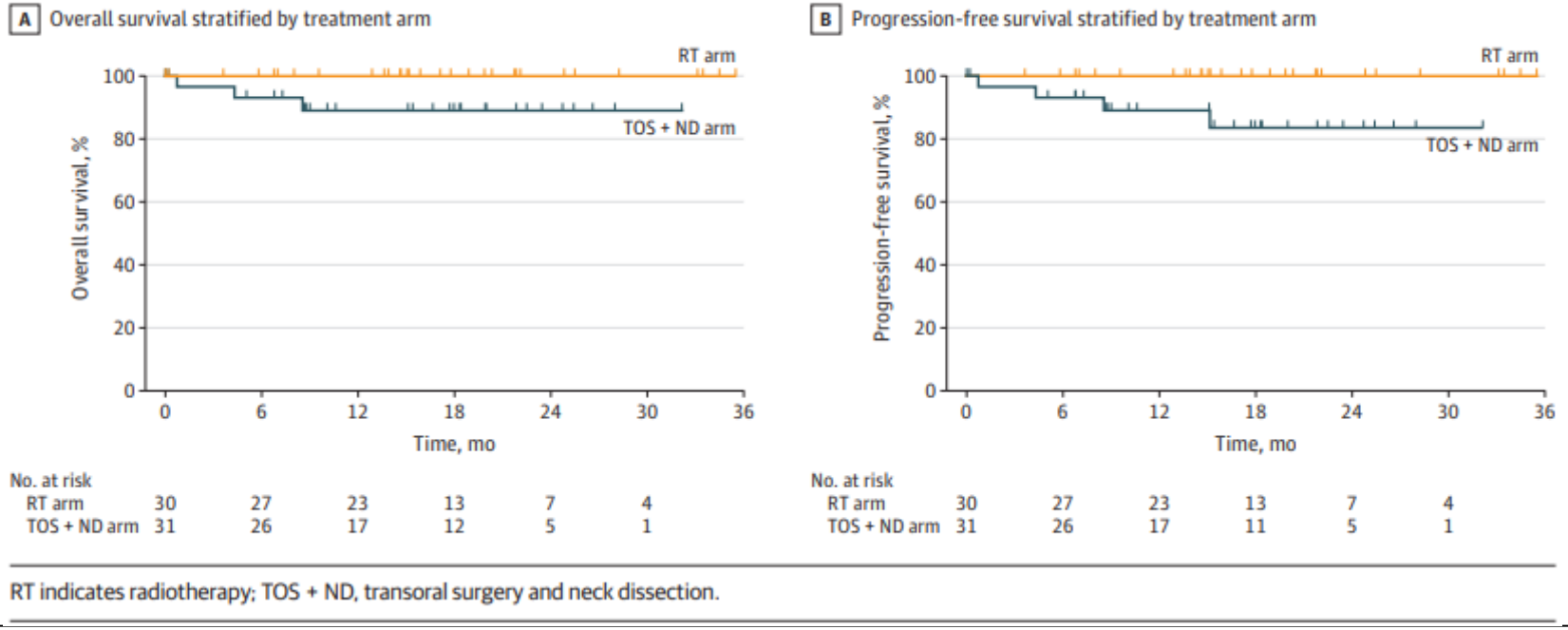


RT indicates radiotherapy; TOS + ND, transoral surgery and neck dissection.

Palma DA, et al. JAMA Oncol. 2022 Jun 1;8(6):1-7.

Primary end point was overall survival (OS), compared separately for each arm against a historical control (NRG-HN002 trial)

Figure 2. Preliminary Analyses of Time-to-Event Outcomes for Overall Survival and Progression-Free Survival Stratified by Treatment Arm



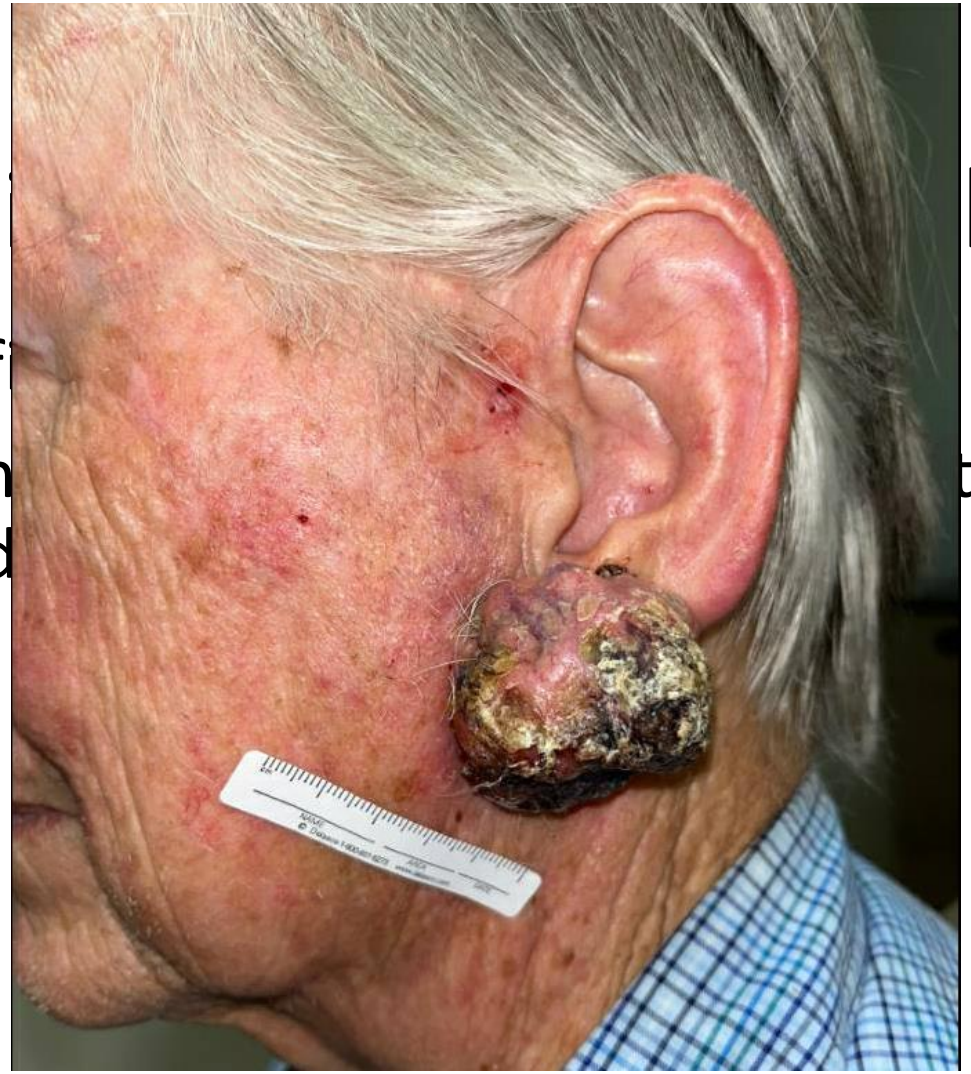
RT indicates radiotherapy; TOS + ND, transoral surgery and neck dissection.

Palma DA, et al. JAMA Oncol. 2022 Jun 1;8(6):1-7.

Take Home Points. Who agrees with this?

- There are no overall survival differences between XRT vs primary transoral surgery (TOS)
- Primary TOS is associated with an up-front risk of treatment-related mortality, and caution is warranted with this approach.
- Both XRT and TOS achieve good swallowing outcomes at 1 year.

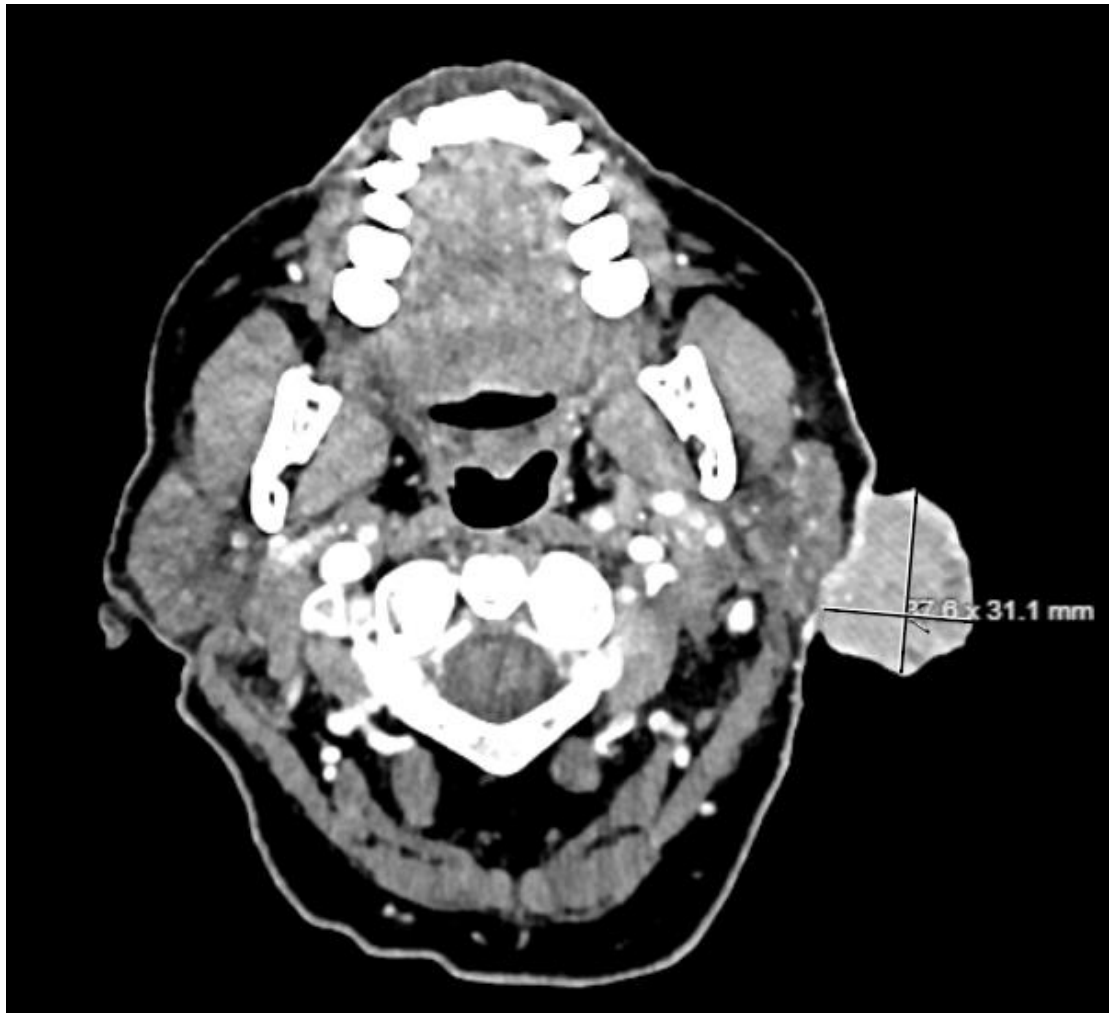
CASE 4
JP - 79M wi heek lesion



- Had years of diff
- 3 months prior h th well-differentiated SCC and planned

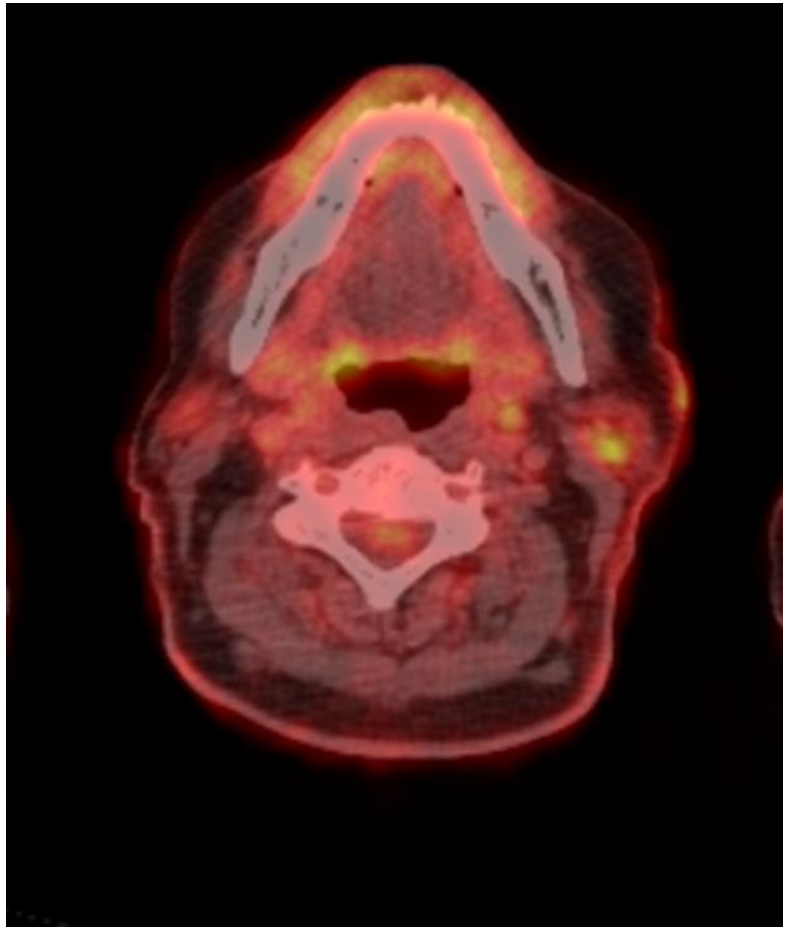
CT Neck

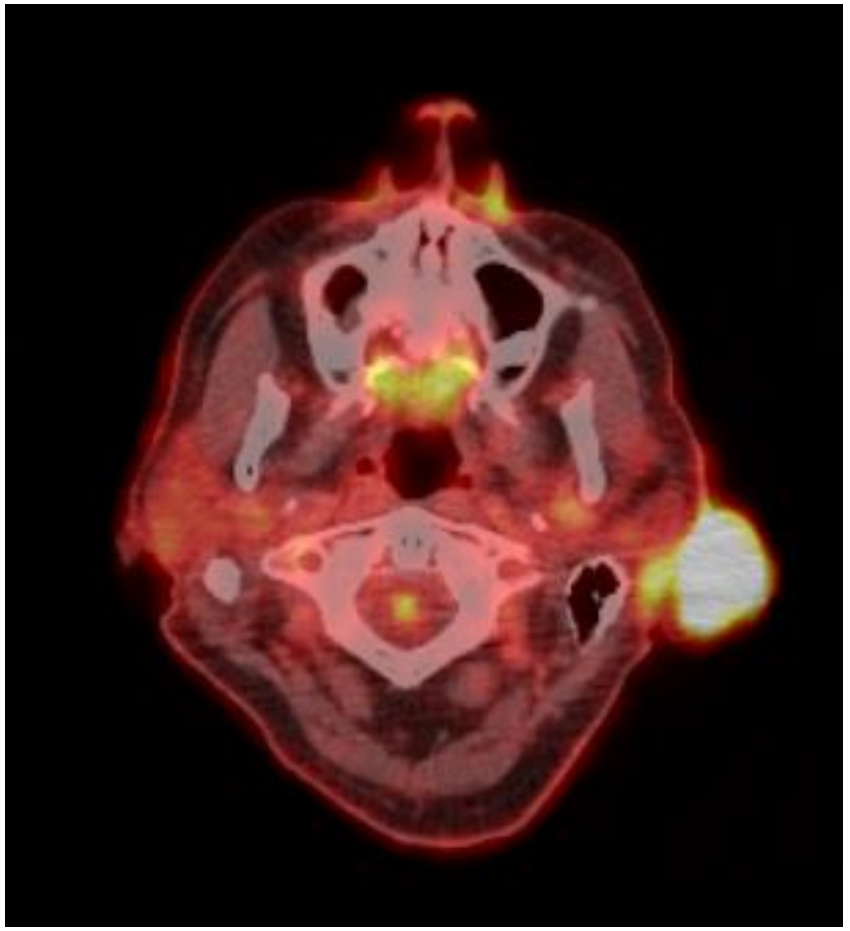
- Due to concern for lymphadenopathy, CT Neck was obtained and notable for a large exophytic mass. Asymmetric left parotid and infraparotid LN.



PET/CT

- Several mildly FDG-avid adjacent LNs within the parotid and upper cervical stations





What is your treatment recommendation?

A) Surgery

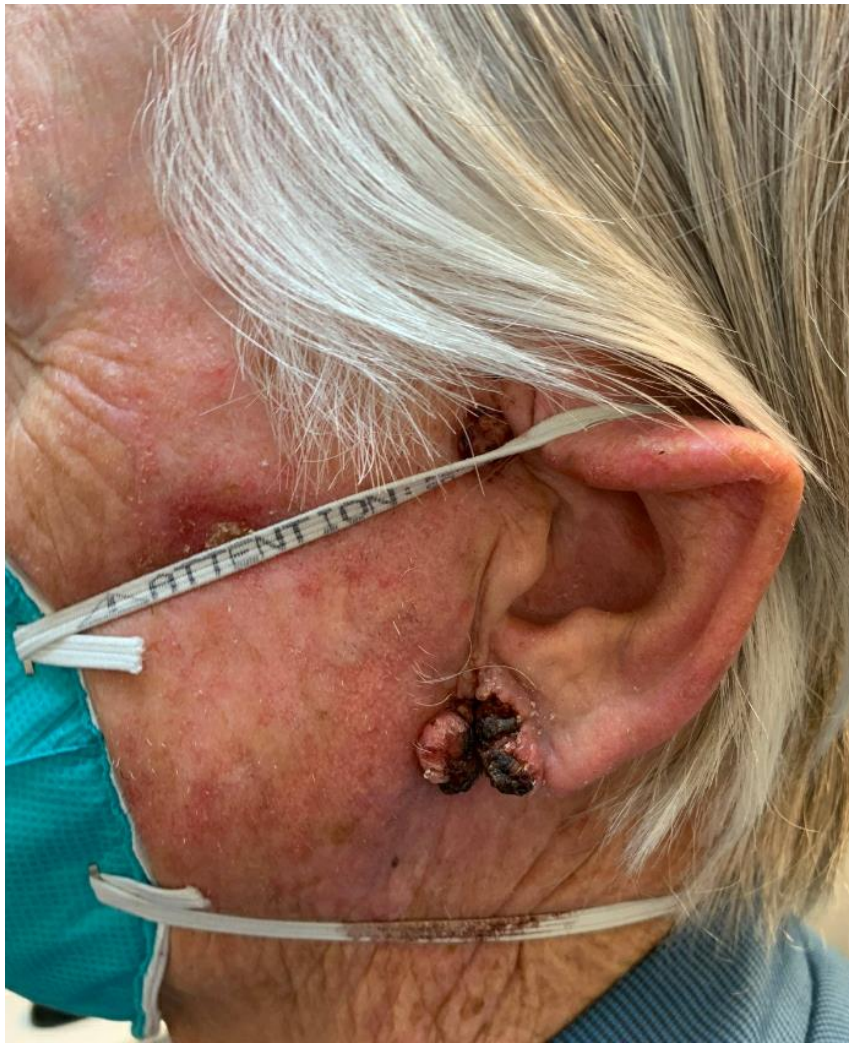
B) Surgery followed by XRT

C) Chemotherapy

D) Neoadjuvant immunotherapy followed by surgery

Case 4 Continued

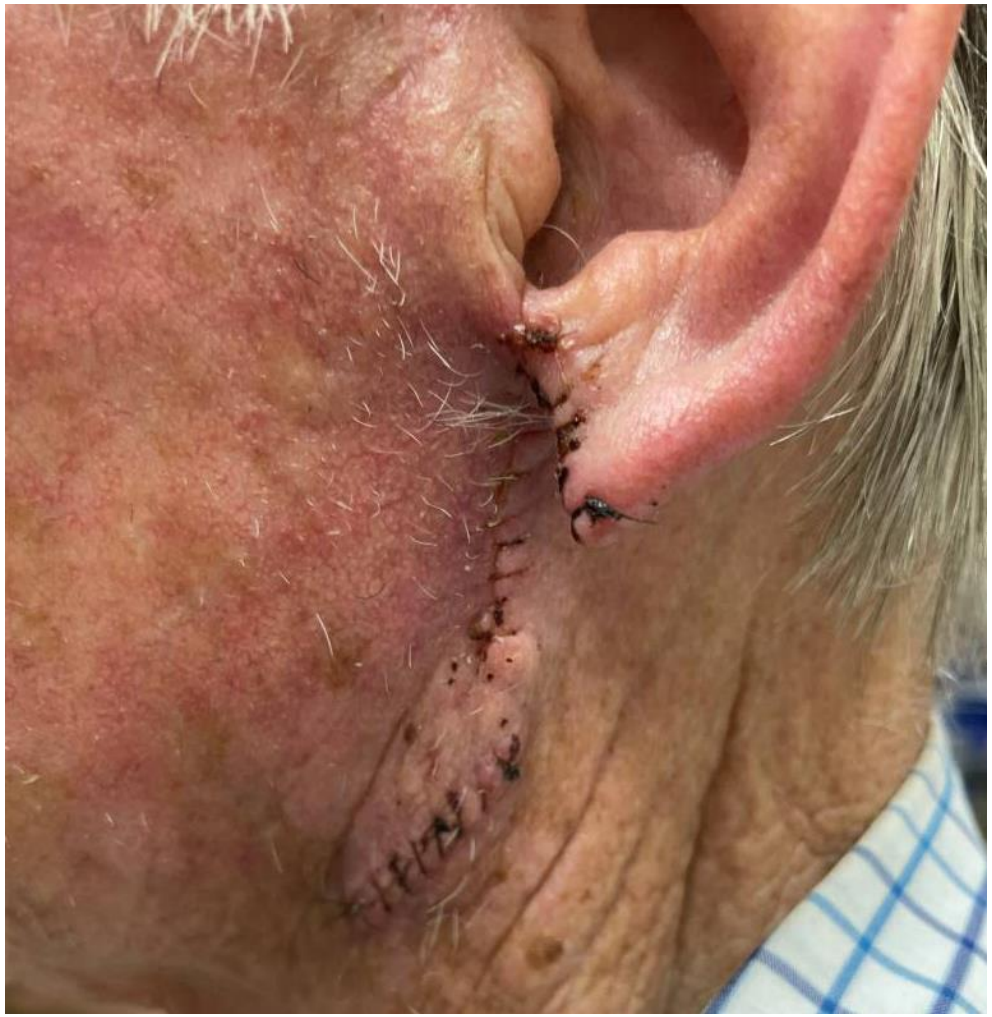
- Patient received 3 cycles of neoadjuvant atezolizumab.



Surgery

Pathology:
L ear: negative for residual malignancy

Left Neck LN: 6 LN negative for carcinoma



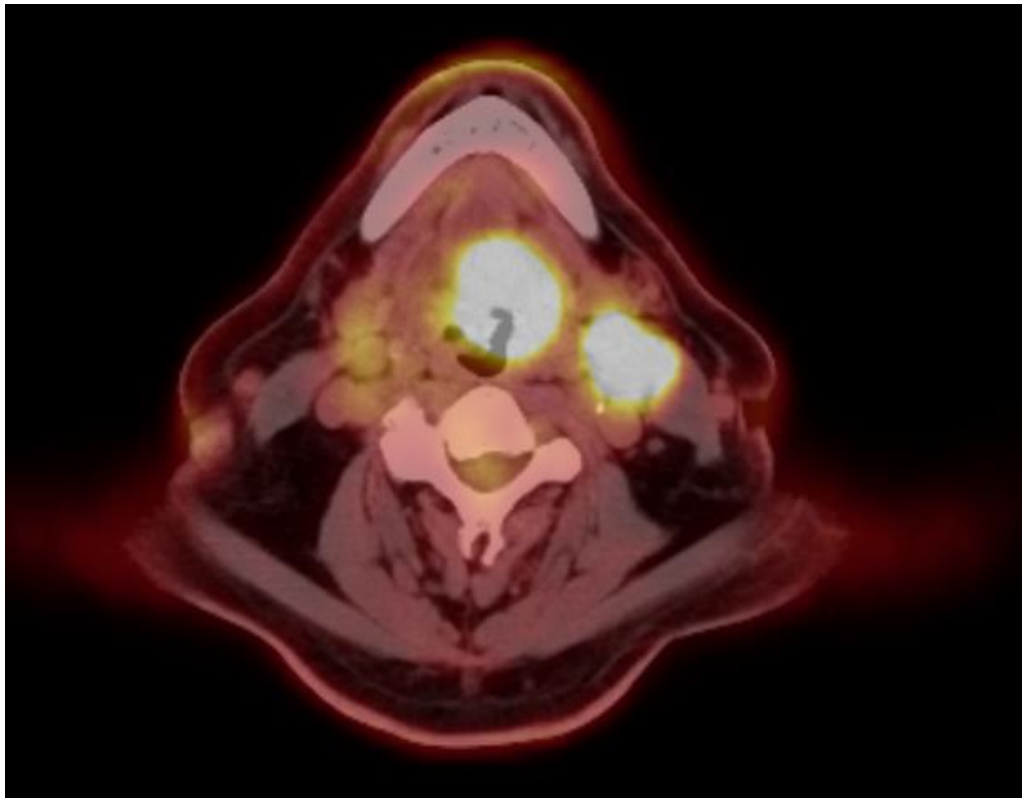
Take Home Points

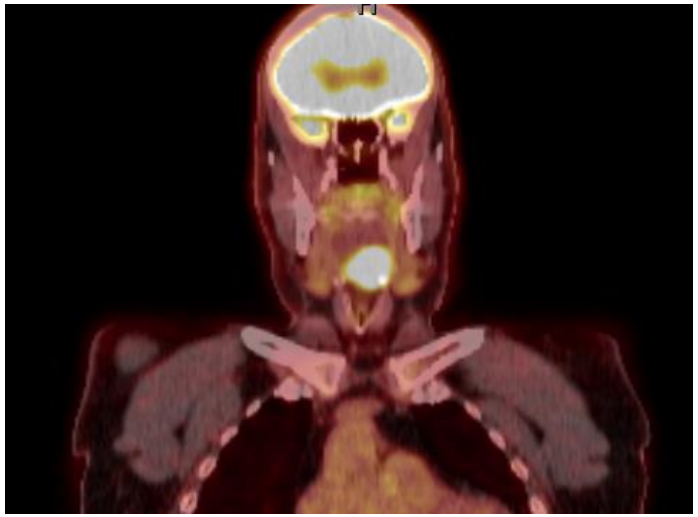
- Consider neoadjuvant atezolizumab for SCC to reduce morbidity of surgical resection

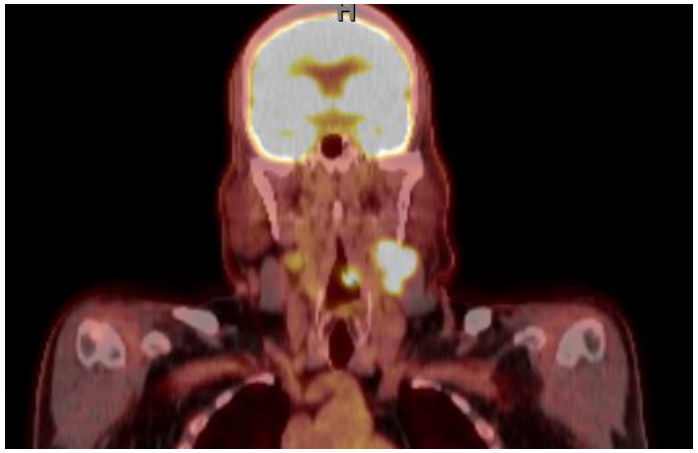
CASE 5 – courtesy of Dr. Ghatge @ KP

- 67-year-old man, nonsmoker, 4 ETOH/ wk with sore throat for ~ 3 months
- CT Neck with contrast: 6 x 3.5cm necrotic mass at the left base of tongue extending inferiorly into the epiglottic space, anteriorly to the oral floor, crossing the midline, with bilateral necrotic lymph nodes
- Biopsy : Poorly differentiated SCC. p16(+)

PET/CT







How would you treat this patient with T4 disease?

A. Concurrent chemotherapy and RT
B. Surgery followed by RT
C. Chemo+RT followed by surgery
D. Sequential chemoRT
E. Immunotherapy with RT

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2024
Cancer of the Oropharynx (p16 [HPV]-positive)

NCCN Guidelines Index
Table of Contents
Discussion

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

CLINICAL STAGING

p16 (HPV)-positive
T0–3,N3
or
T4,N0–3

TREATMENT OF PRIMARY AND NECK

- Concurrent systemic therapy/RT[n,o] (preferred) → Post Systemic Therapy/RT or RT Neck Evaluation (FOLL-A, 2 of 2)
- or
- Resection of primary and ipsilateral or bilateral neck dissection[k,l,u]
  - No adverse pathologic features[r,s] → Follow-up (FOLL-A, 1 of 2)
  - Adverse pathologic features[r,s]
    - Extranodal extension and/or positive margin → Systemic therapy/RT[n,o,t] → Follow-up (FOLL-A, 1 of 2)
    - Other risk features[r,s] → RT[n] or Consider systemic therapy/RT[n,o] → Follow-up (FOLL-A, 1 of 2)
- or
- Induction chemotherapy[o,q] (category 3) followed by RT[n] or systemic therapy/RT[n,o] → Post Systemic Therapy/RT or RT Neck Evaluation (FOLL-A, 2 of 2)
- or
- Clinical trials

ADJUVANT TREATMENT

- Recurrent or persistent disease (ADV-3)
- Follow-up (FOLL-A, 1 of 2) → Recurrent or persistent disease (ADV-3)
- Recurrent or persistent disease (ADV-3)

Case 5 Continued

- Case was presented to a Regional Head & Neck Multi-Disciplinary Tumor Board: Consensus was for Concurrent chemoradiation therapy
- Patient enrolled in NRG- HN009
- Randomized to Cisplatin 100mg/m2 q3 weeks with RT
- Planning for treatment: Dental extractions, Speech and Swallow PT for swallowing exercises, Audiology for audiogram, Dietician consultation

NRG-HN009 Randomized Phase II/III Trial of Radiation with Cisplatin at 100 mg/m^2 Every Three Weeks versus Radiation with Weekly Cisplatin at 40 mg/m^2 for Patients with Locoregionally Advanced Squamous Cell Carcinoma of the Head and Neck (SCCHN)

PI/Rad Onc Study Chair: Paul Harari, MD
Rad Onc Co-Chairs: Quynh-Thu Le, MD; Matthew Witek, MD
Med Onc Co-Chairs: Christine Chung, MD; Jed Katzel, MD
QOL Co-Chair: Farzan Siddiqui, MD, PhD
Translational Research Co-Chair: Scott Bratman, MD, PhD
Pathology Co-Chair: Brittany Holmes, MD

How do you prescribe cisplatin in this setting?

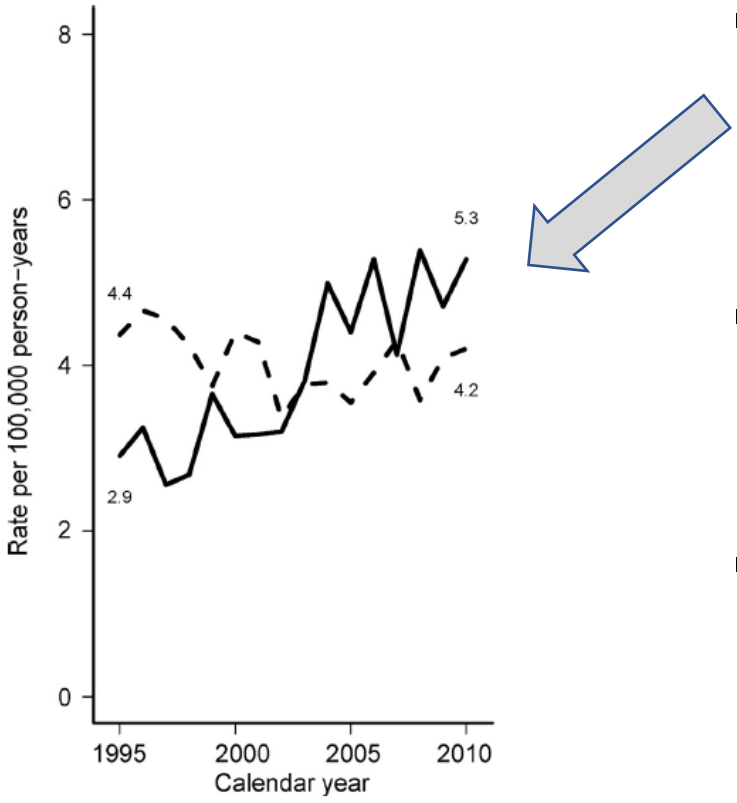
A) 40 mg/m2 weekly

B) 100 mg/m2 every 3 weeks

As of March 2024, what is your approach to testing for circulating HPV DNA (TTMV-HPV DNA) in HPV+ HNC?

A. No role for testing
B. Should be tested in all patients at the time of diagnosis
C. Should be used for monitoring after CR to therapy
D. Only ordered per patient request

HPV Circulating DNA Testing



- Incidence rate for HPV+ HNC is increasing in KP NCAL population (3.8% per year when adjusted for age/sex)
- Approximately 80% of patients in KP with Oropharynx cancer are HPV related
- 15-25% of patients with HPV+ HNC will have recurrence within 5 years

Katzel JA et al. *Cancer Epidemiol Biomarkers Prev* 2015

HPV Circulating DNA Testing

- Circulating tumor tissue-modified viral HPV DNA (TTMV-HPV DNA) commercially available in USA 2020
- Sample are sent to Naveris Lab, digital droplet PCR to detect circulating tumor HPV DNA

- Testing is not recommended by NCCN
- NavDx (Naveris, Inc) advertised as an alternative to biopsy ($1800)
- Results in 7-10 days
- Economic impact analysis 2022 estimated cumulative cost of routine surveillance $11,674 vs. $20,756 for ctHPV DNA strategy[1]

Ward M, Miller J, Walker G, Moeller B, Koyfman S, Chah C. *Oral Oncology.* 2022.

Framing the Discussion

ctDNA Testing in HPV+ Oropharyngeal Ca Patients

Advantages	Disadvantages
▪ Few recurrences are identified on routine surveillance ▪ Recurrences often clinically undetectable, found on imaging or patient symptoms ▪ Detects recurrence sooner	▪ No data to support improved outcomes ▪ Not clear how long to continue testing ▪ Added cost ▪ Positive test may detect disease sooner by that leads to patient and provider anxiety
▪ Sensitivity 80-93% ▪ High positive predictive values of testing 95-100% ▪ Specificity 99.4% and NPV 98.4%	▪ Commercial payers that do NOT cover testing: Cigna, Aetna, Anthem BlueCross, United Healthcare, Blue California, Humana

Take Home Points

- Incidence rate of HPV+ OPC is increasing despite rates of tobacco use declining
- Concurrent chemo-RT with Cisplatin remains a standard of care
- Clinical Trial NRG-HN009 is enrolling patients, comparing weekly vs. every 3 week cisplatin and RT for patient with HNC
- Circulating HPV DNA is emerging as a biomarker with extensive potential in the management of HPV-driven HNC. Currently, not recommended by NCCN

Thank you!