

# The Contemporary Management of HPV Associated Head & Neck Cancer



## Rush Updates in Otolaryngology 2024

Samer Al-khudari MD FACS

November 8<sup>th</sup> , 2024

Head, Section of Head & Neck Oncologic Surgery  
Rush University Medical Center

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# Rush Multidisciplinary Head and Neck Cancer Symposium | 2025

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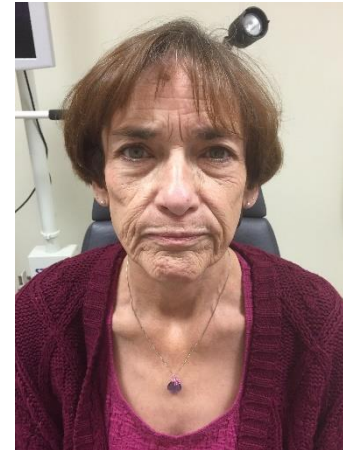
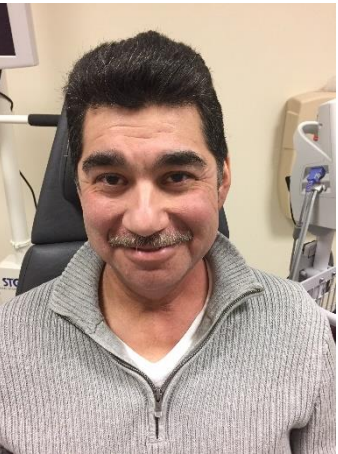
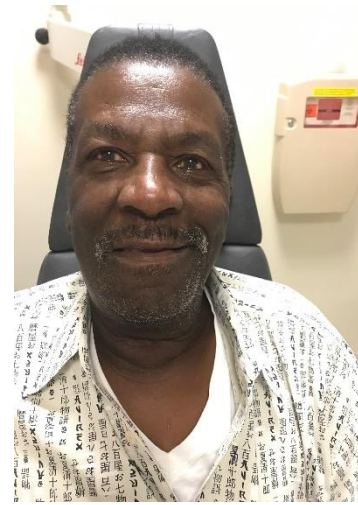
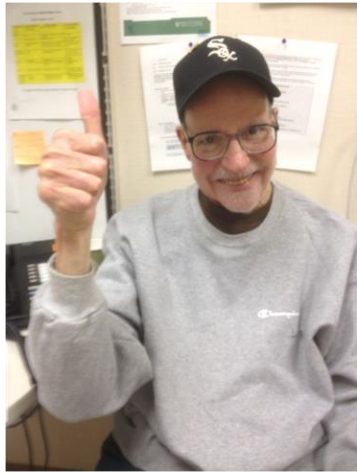
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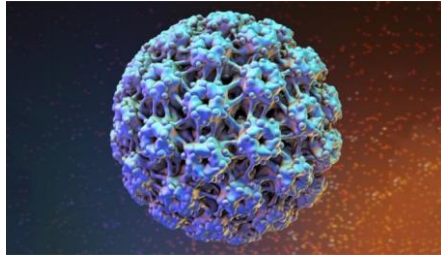




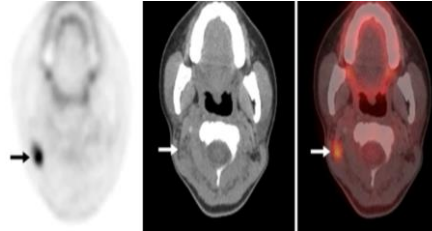
# PAST, CURRENT, FUTURE

## Exciting time in H&N Cancer Treatment

➤ 2007\*



➤ 2010



➤ 2015

➤ 2018

➤ 2022



➤ 2024.....



➤ 2026.....

?



# The Contemporary management of HPV + HNSCC emphasizes a tailored approach due to the biology and prognosis

## 1. **Diagnosis and Staging:**

## 2. **Surgical Options:**

## 3. **Radiation Therapy:**

Radiation is a mainstay, especially in advanced cases.

## 4. **Chemotherapy:**

Chemoradiation remains standard for advanced cases

## 5. **De-intensification Trials:**

Trials focus on reducing treatment intensity for favorable-risk

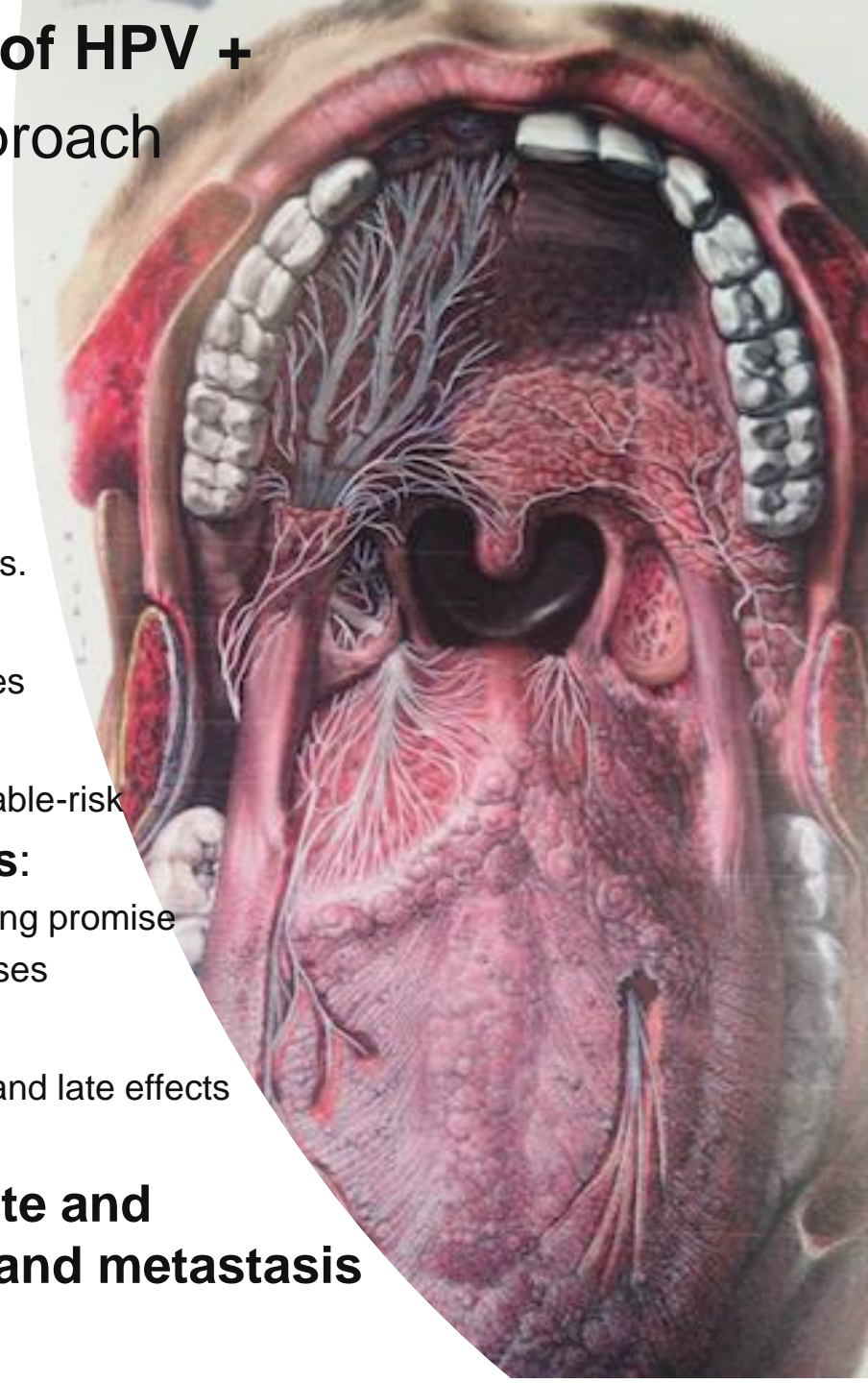
## 6. **Immunotherapy and Targeted Treatments:**

Immunotherapy (e.g., checkpoint inhibitors) is showing promise especially in recurrent or metastatic HPV-positive cases

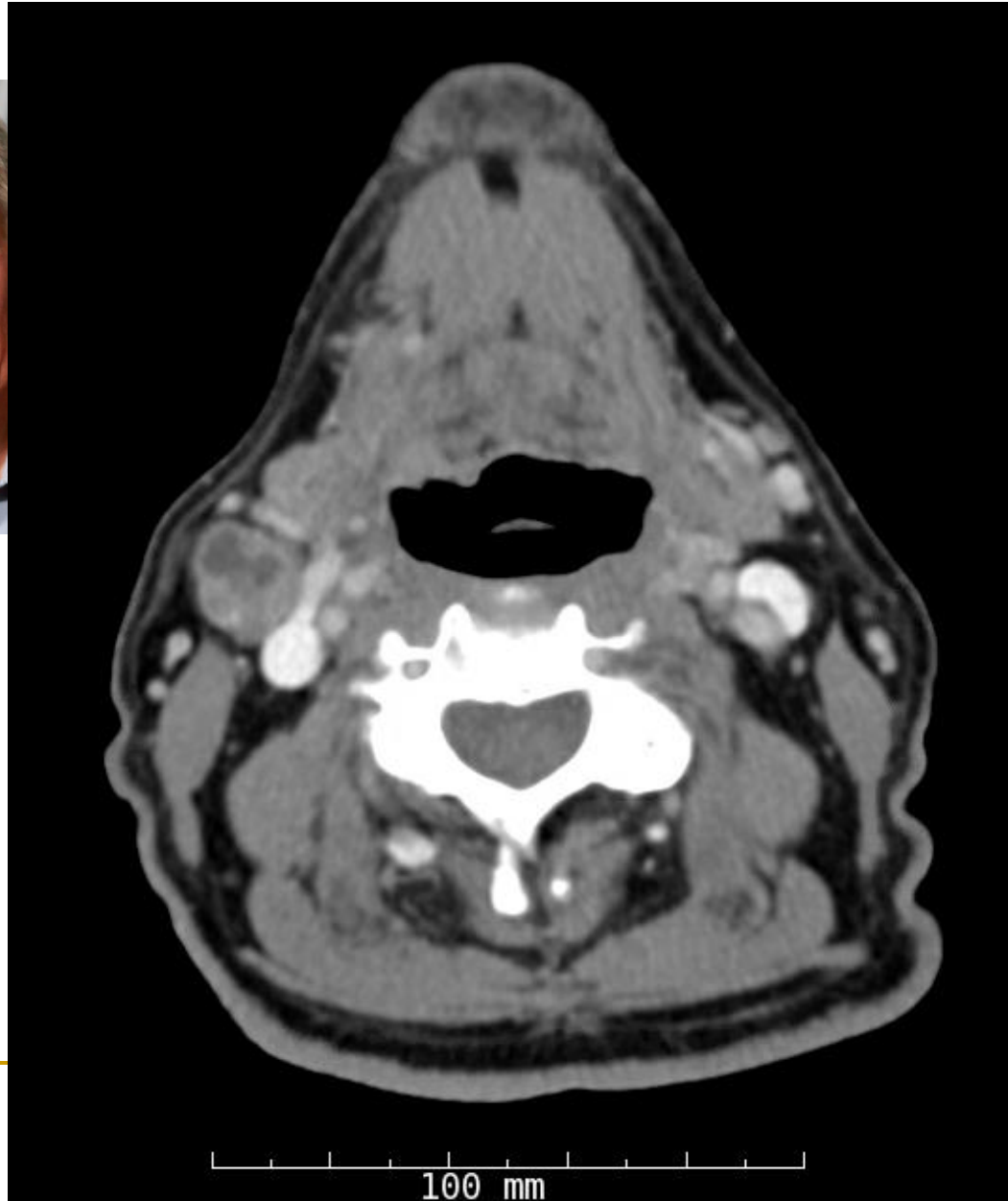
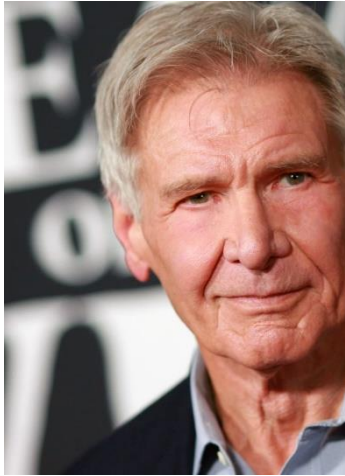
## 7. **Follow-up and Survivorship:**

Long-term follow-up is essential to monitor for recurrence and late effects

**Trend toward de-escalation if appropriate and identifying those at risk for recurrence and metastasis**

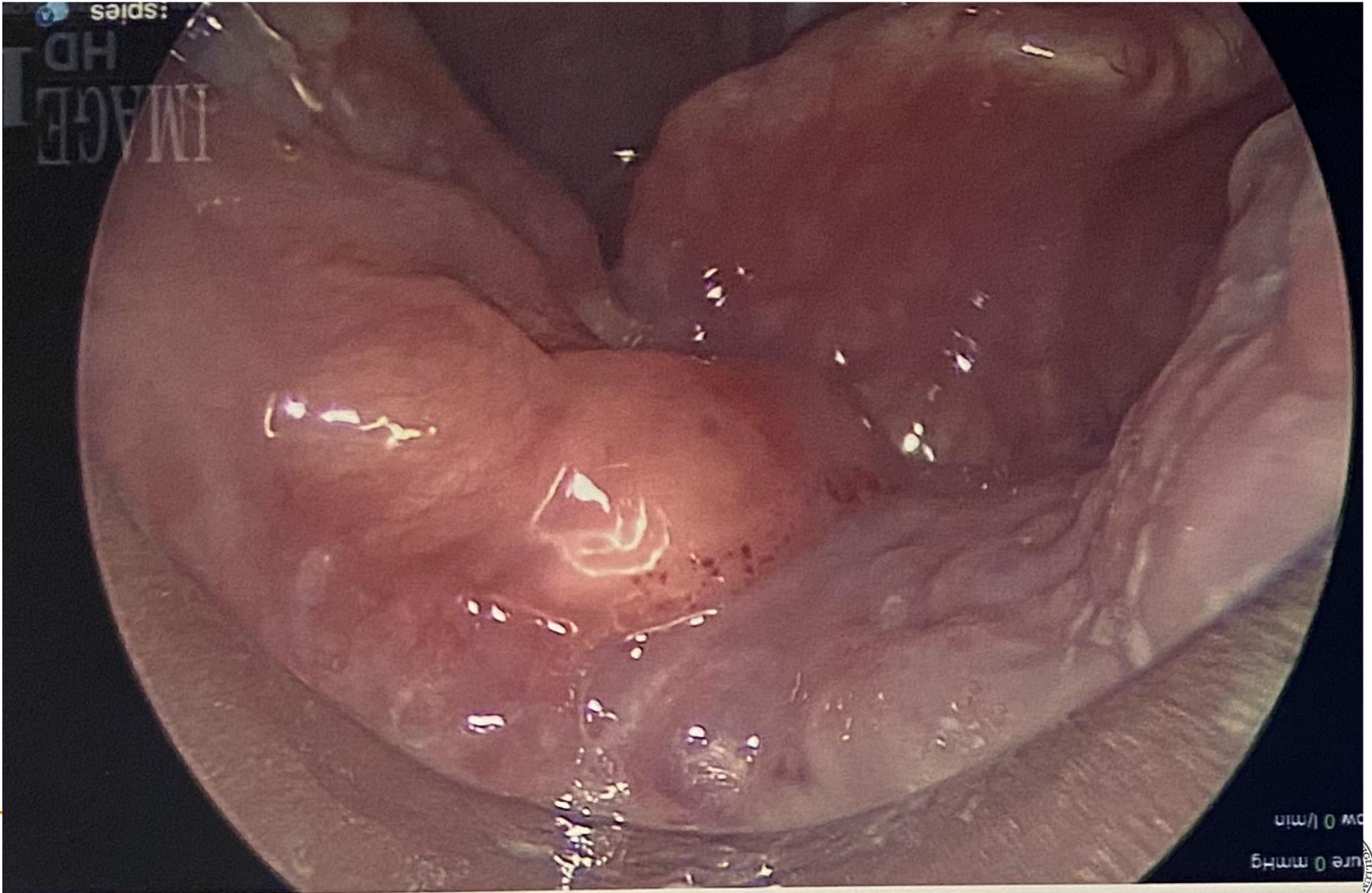


# 69 y/o with a Neck Mass x 3 months





# Small Primary- But Deep



# Robotic Single Port Technology





# General Treatments Principles

HPVOPC is highly sensitive to all modalities

Treatment for OP cancer can impact quality of life

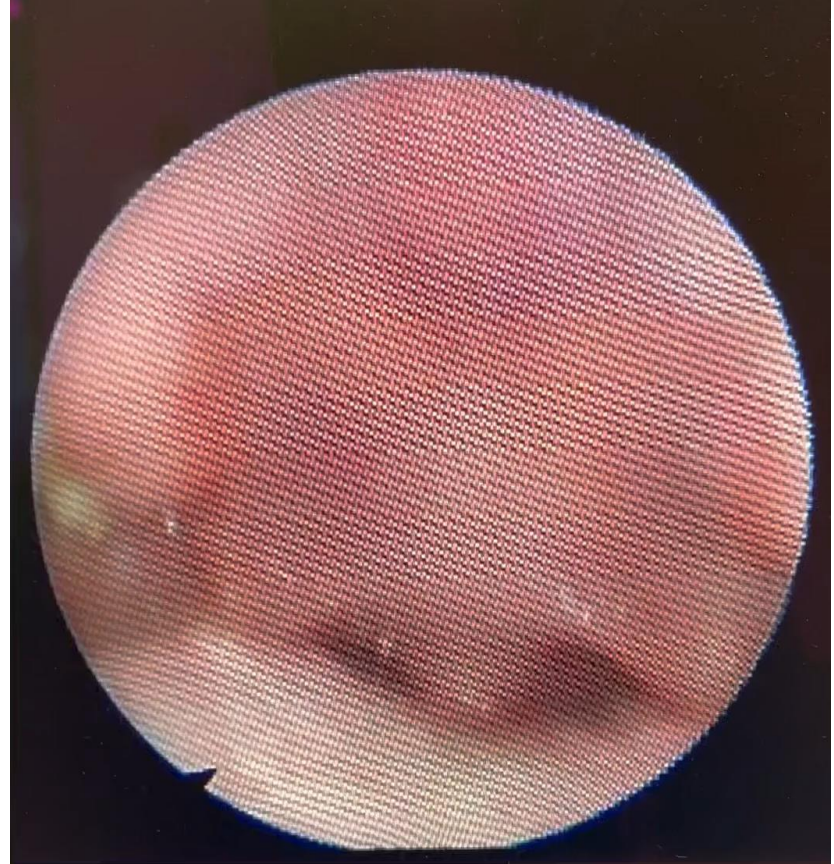
Limit the # of treatment modalities to achieve cure

Primary site and neck need to be addressed

**Balance cure rates with  
treatment toxicity**

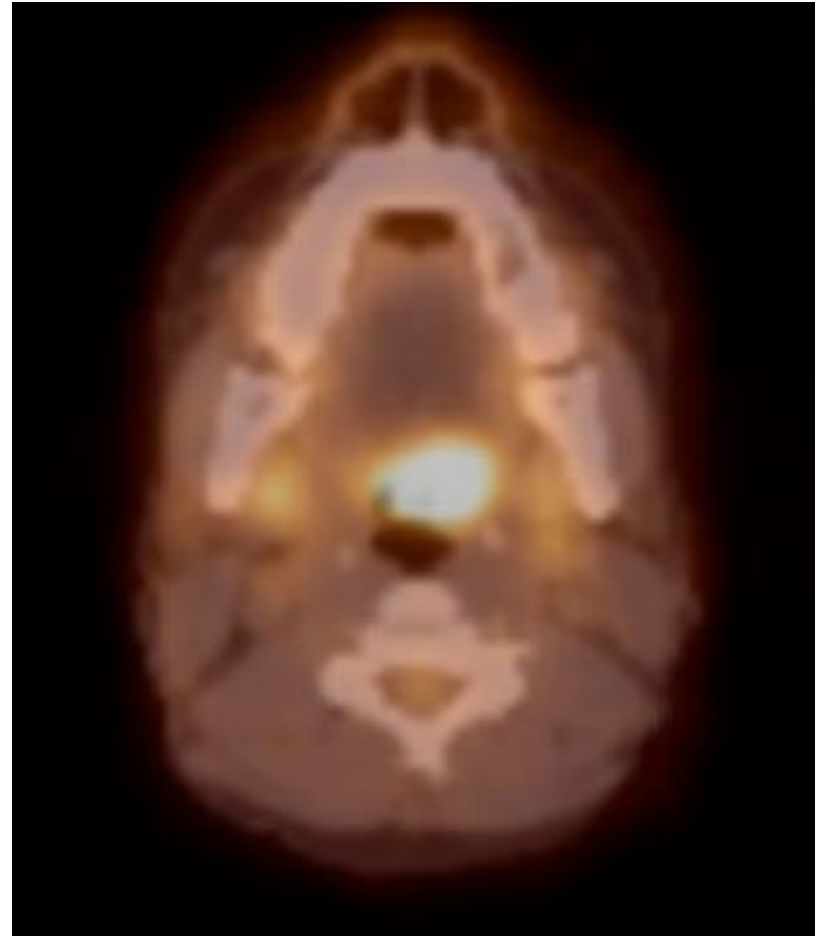
Risk of recurrence and metastasis

# 41 y/o Throat Discomfort and Nasal Blockage





# T2N1 P16+ Stage 1



# Contemporary in 2022 Provocative in 2018

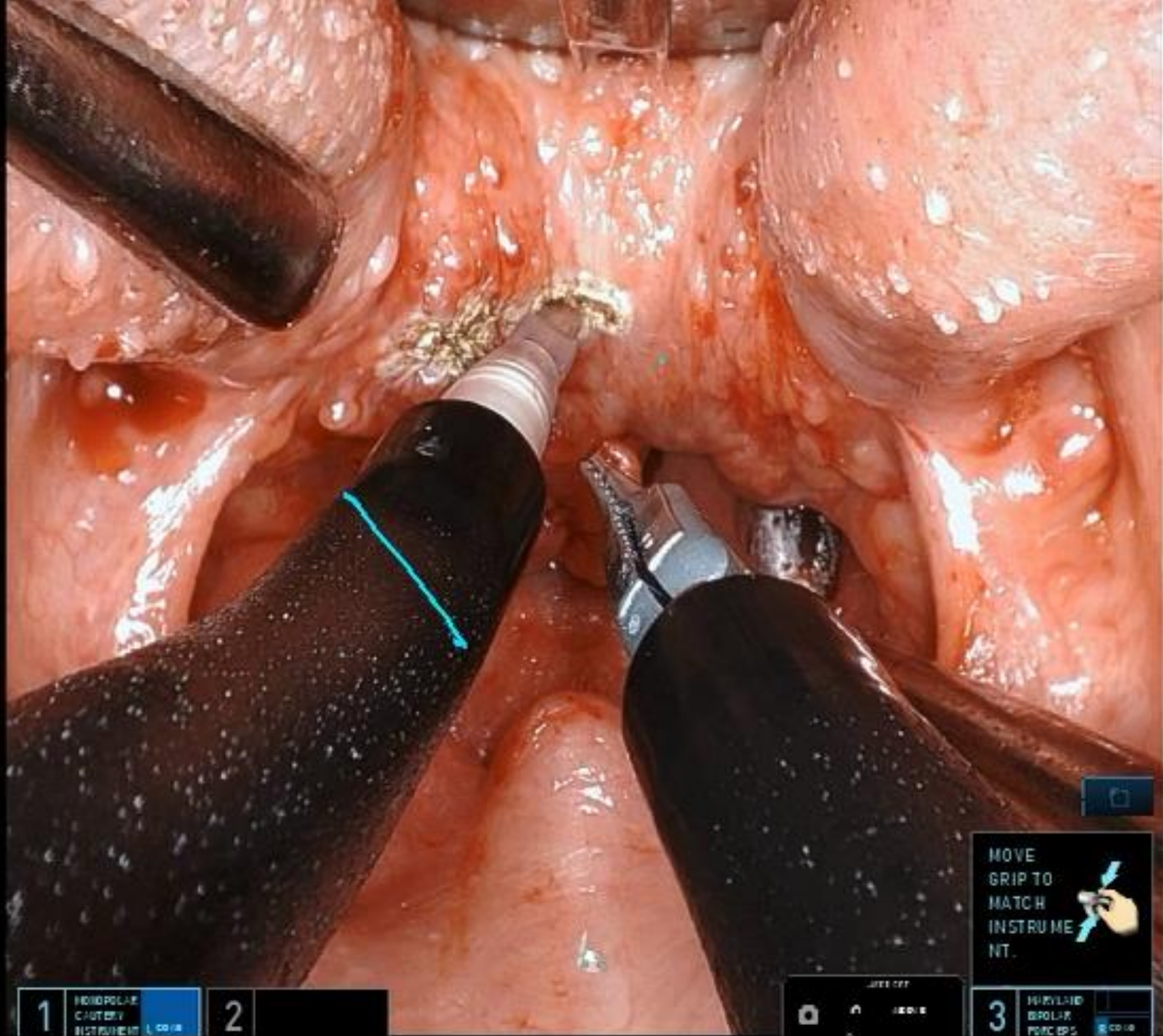
- Favoring Surgery
- TORS with neck dissection
- SP system
- Circulating HPV DNA (+)



**100 TTMV-HPV16-Frag / ml plasma**







MOVE GRIP TO MATCH INSTRUMENT.



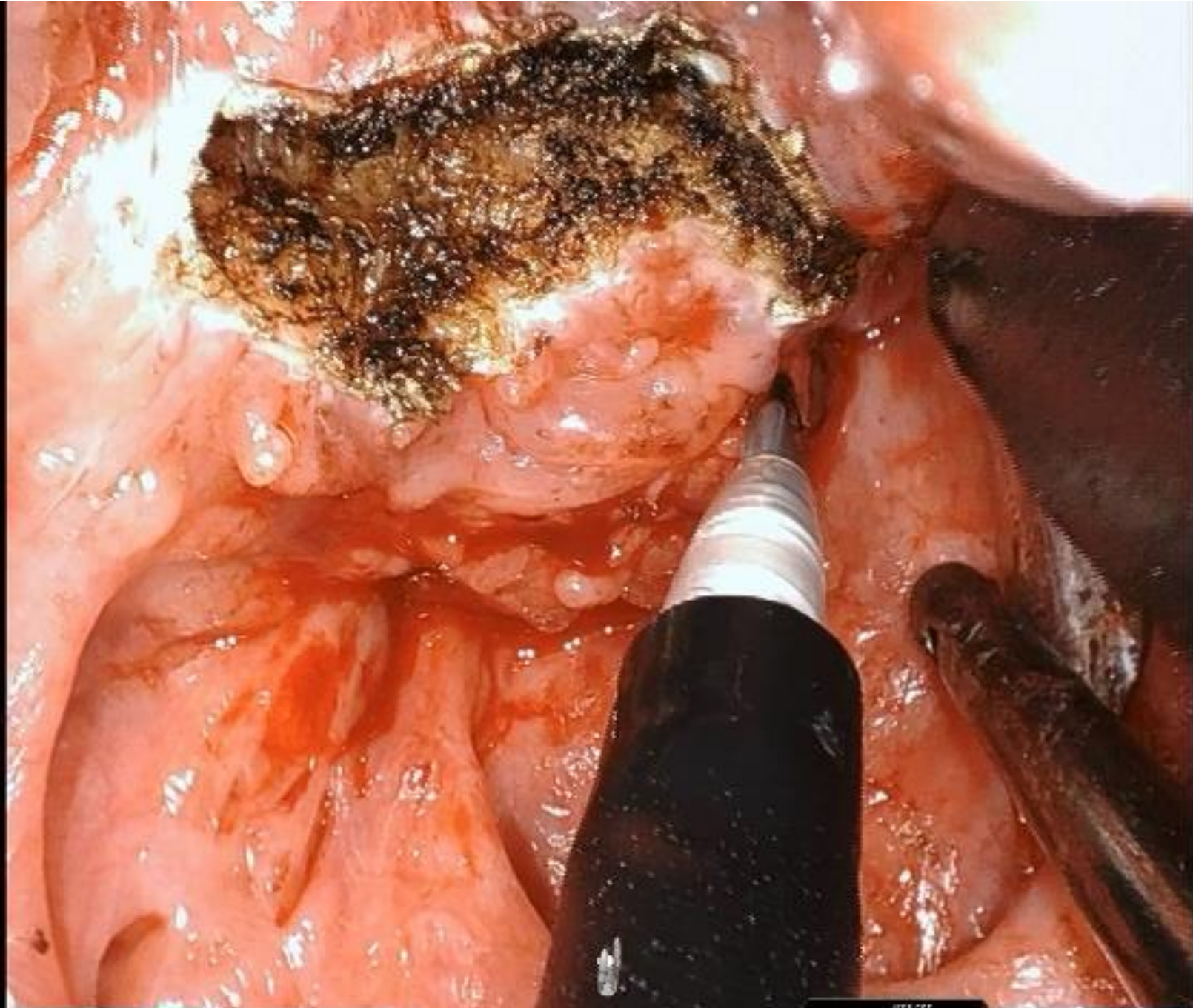
1 BIPOLAR CAUTERY INSTRUMENT CO. US

2

VIEW OFF  
VIEW

3 HANDED BIPOLAR FORCEPS CO. US





1

BIPOLAR  
CAUTERY  
INSTRUMENT



2

STOP OFF



ABOVE

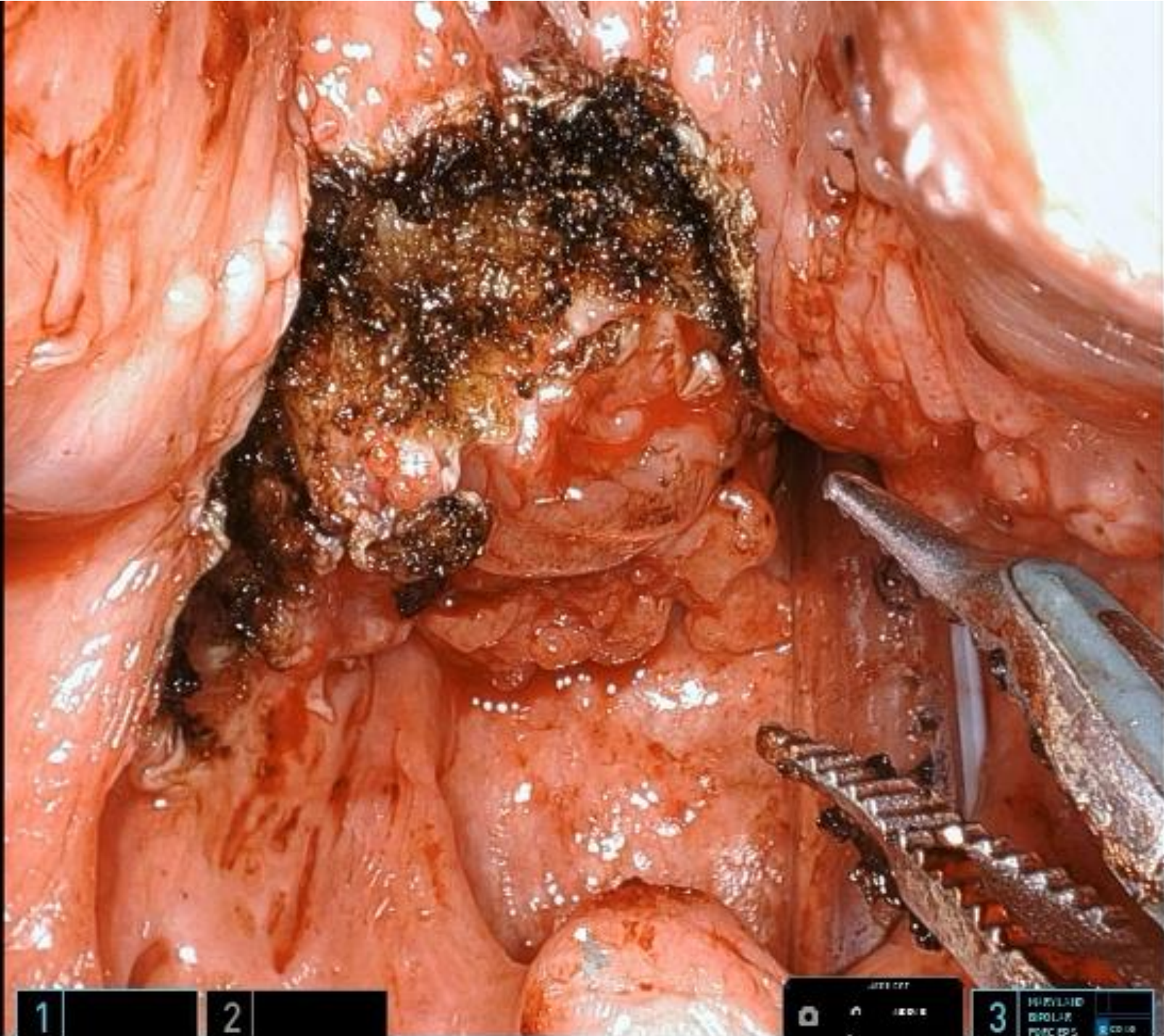
3

BIPOLAR  
CAUTERY  
INSTRUMENT



CD 18





1

2

UNIT OFF

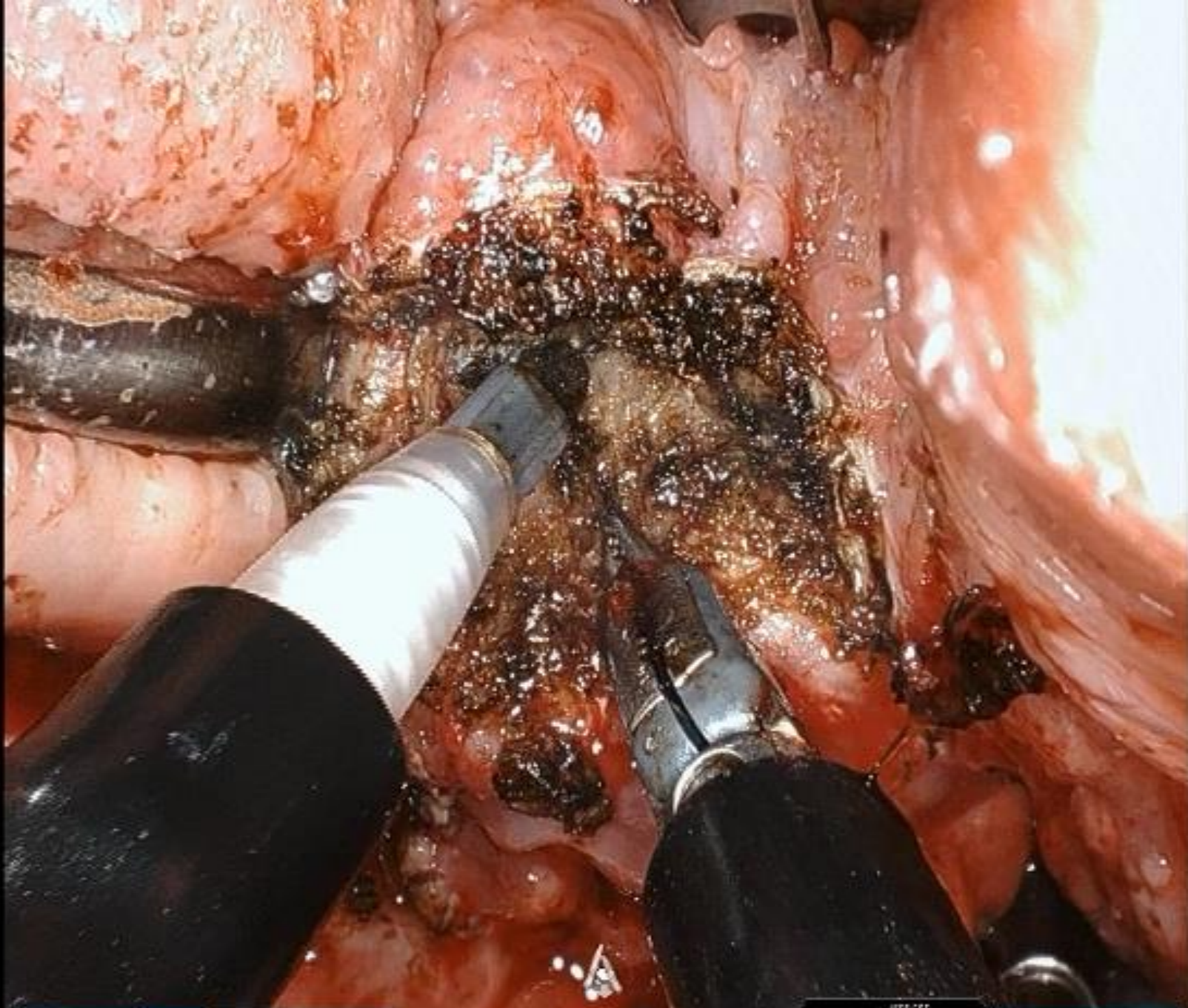
MODE

3

HUYLAID  
BIPOLAR  
PMIC EP5

CD 18





1	BIPOLAR CAUTERY INSTRUMENT CO. US	2	JES OFF JES ON	3	HYFLAD BIPOLAR PWR EPS CO US
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1 BIPOLAR  
CAUTERY  
INSTRUMENT CO.®

2

STOP OFF  
AERO®

3 HARVEY  
BIPOLAR  
FORCEPS CO.®





1" **MINI POLAR CATTERY INSTRUMENT** 1.00 1.00 1.00

2

3" **MINI POLAR BIPOLAR FORCEPS** 1.00 1.00 1.00

3" **MINI POLAR BIPOLAR FORCEPS** 1.00 1.00 1.00

# Final Pathology- T2 N1 SCC P16+

- 2.2 cm mass , negative margins
- Left Neck : 1/ 12 nodes +, 9mm
- Right Neck: 0/12 nodes
  
- 6 weeks later did have a tonsillectomy to verify negative given no adjuvant treatment recommendation from Tumor Board





# Thoughts—Post treatment

- No Adjuvant Treatment
- Stage 1
- T2N1
  
- Surgery Alone

Gender: Female | DOB: 05 Dec 1979

<b>Tumor Tissue-Modified Virus (TTMV)<sup>™</sup></b> <b>Not Detected</b>  TTMV-HPV-16 fragments/ mL plasma	<b>Report Details</b> Issued: 18 Nov 2021 Sample: Blood Collection: 12 Nov 2021  Receipt: 16 Nov 2021	<b>Contact Details</b> Physician: Samer Al-Khudari Facility: RUSH University Medical Center Address: 1611 W. Harrison Street Chicago, IL 60612, USA Additional Recipients:
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**Clinical Details**  

ICD 10 Code:	C10.9, Oropharynx cancer
Tumor p16 Status:	Positive
Pre-Treatment TTMV-HPV Status:	Positive, TTMV-HPV-16
FFPE NavDx Test Result:	N/A

SURVEILLANCE

Time Point	TTMV-HPV-16 fragments/mL plasma
P1 (12/07/20)	~100
S1 (11/22/21)	1
S2-S12	1

**TEST RESULT:** Negative for TTMV-HPV-16.

**INTERPRETATION:**  
 Patients negative for NavDx were reported to have a <1% chance of having a recurrence at the time of sample collection.<sup>1</sup>

TTMV-HPV-16 fragments/mL	TTMV-HPV-18, -31, -33, -35 fragments/mL	Interpretation
<5	<5	Negative
5-7	5-12	Indeterminate
>7	>12	Positive

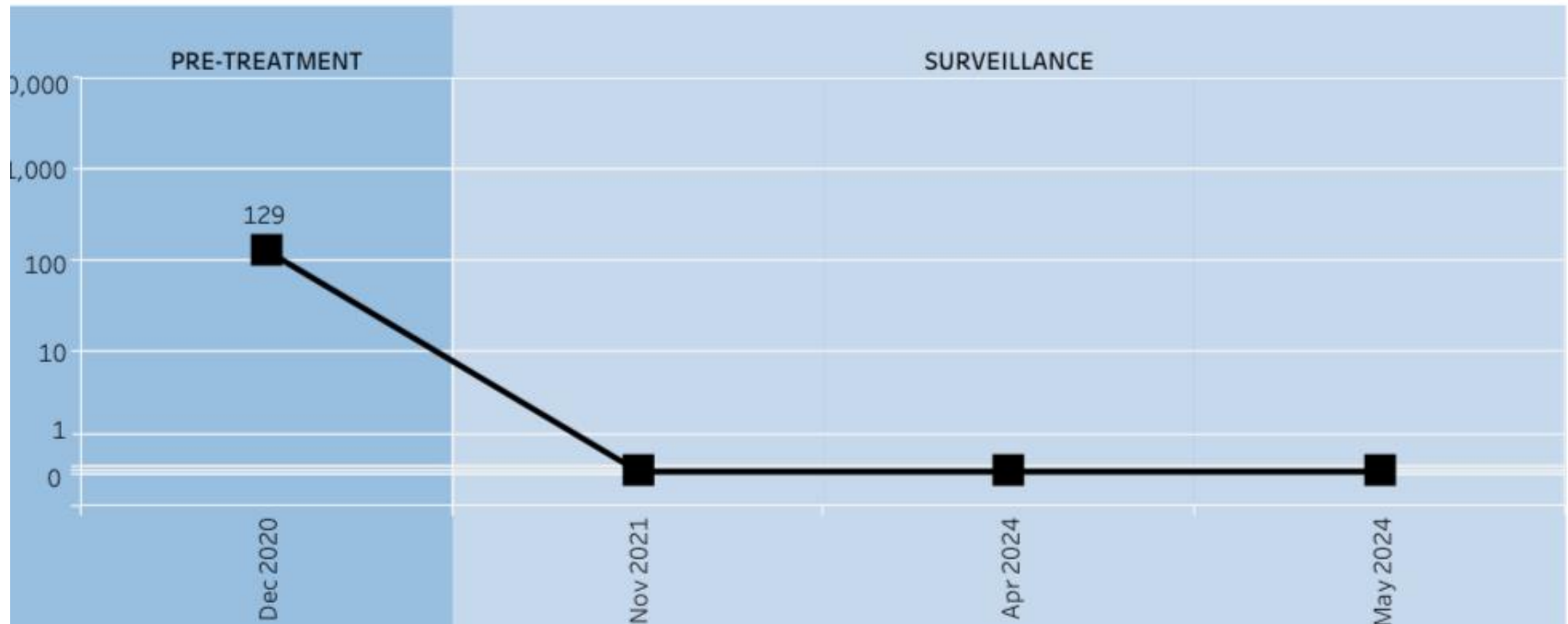
Values <5 are below the Limit of Detection. The NavDx Indeterminate range is determined by the sensitivity of each assay.

# Negative Imaging and Circulating Fragments @ 48 months

## Case Details

Diagnosis (ICD 10 Code): Z85.819, C10.9  
Immunization Status: Positive  
Pathologic Status: Unknown  
-HPV DNA Status (at First Detection): Positive, TTMV-HPV16 DNA  
-HPV DNA Status (FFPE): Not Determined

## SURVEILLANCE







## Healing Post TORS - Tonsil



# Strategies to “De-escalate”

## In the properly selected patient

- Less invasive surgery
- No Adjuvant treatment
- Alternative systemic therapy ?
  - Dosing of cisplatin to weekly
- Dose-reductions of radiation and chemotherapy
- Induction therapy response-adapted de-escalation



# 57 y/o with a Right Neck Mass

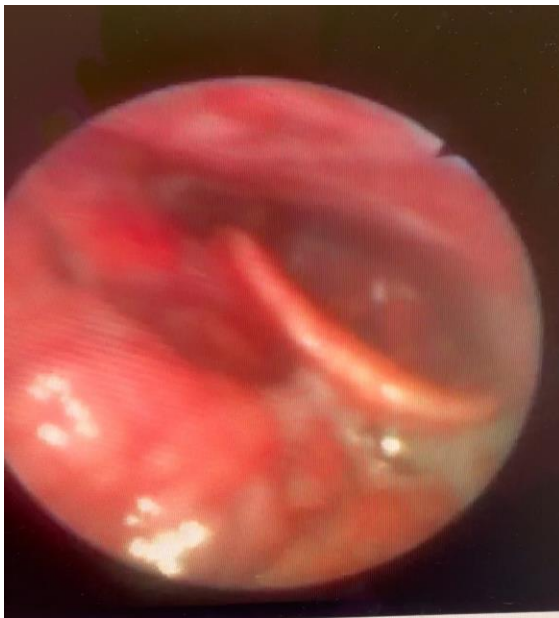


## Past History:

- <10 pack years, current non-smoker
- ◀ Moderate Alcohol
- ◀ No throat symptoms

## Exam:

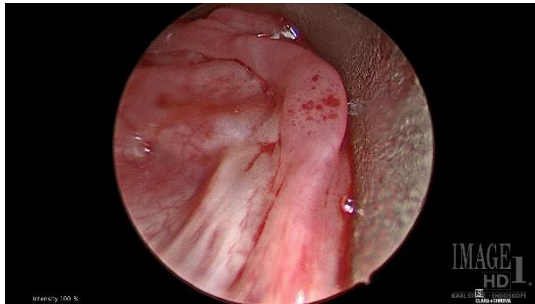
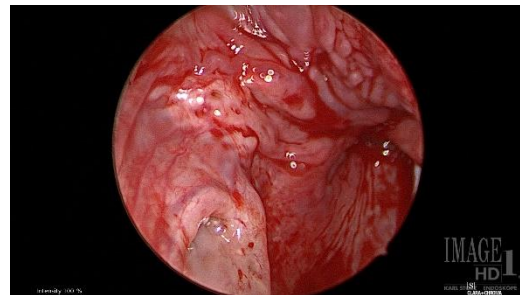
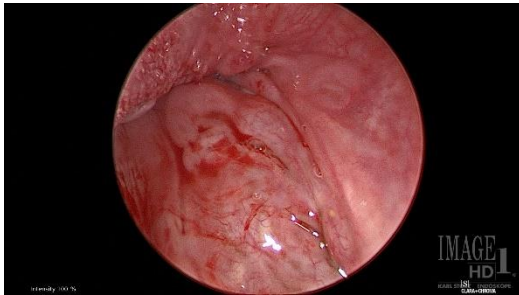
- Right neck non-tender level II lymph node
- FL - Diffuse Lingual Tonsil Prominence







# DL and TORS & Neck Dissection



Initial frozen biopsies- Negative  
Right Palatine Tonsil - Negative  
Left Palatine Tonsil - Negative  
Right lingual tonsil- Negative  
Left lingual tonsil- Negative

# Pathology

All Mucosal Tissue Negative for Cancer

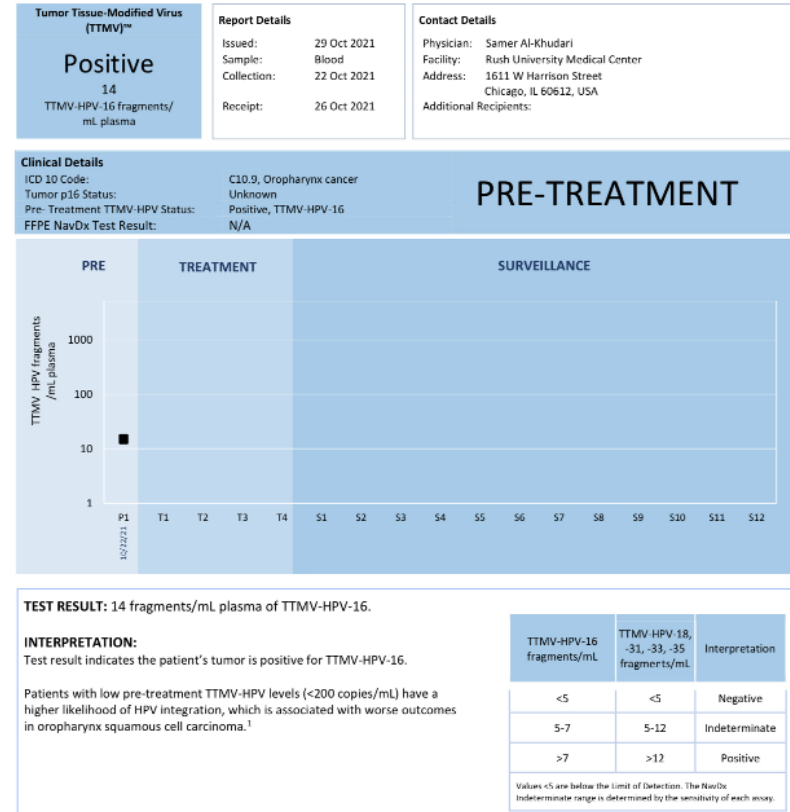
Right Neck:

- 1/18 Nodes Positive SCC
- 2cm size, no ENE

Moderate to focally strong staining for p16 in 50% residual viable tumor cells

P16 expression: NEGATIVE

- HPV (E6/E7) RNA ISH is negative
- Tested 16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, 82





# Unknown Primary, 2cm node , P16 staining Indeterminate , Circulating TTMV +

What are we calling this?

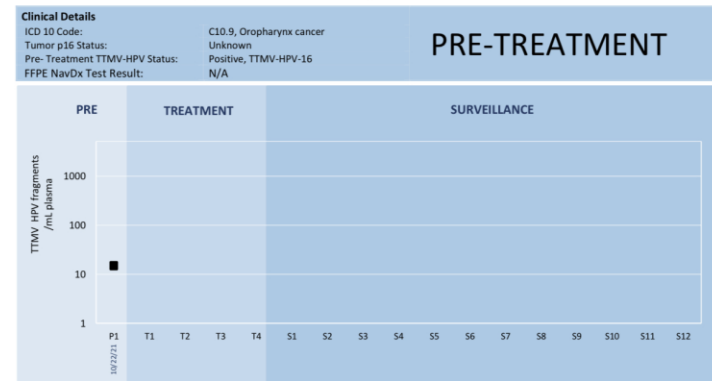
A. P16+ unknown Primary ? (Early Stage)

B. P16- unknown primary ? (Advance stage)

## Overall Clinical Staging HPV + OPC

T CATEGORY	N CATEGORY			
	N0	N1	N2	N3
T0	NA			
T1				
T2				
T3				
T4				

<b>Tumor Tissue-Modified Virus (TTMV)<sup>TM</sup></b>  <b>Positive</b>  14 TTMV-HPV-16 fragments/ mL plasma	<b>Report Details</b>  Issued: 29 Oct 2021 Sample: Blood Collection: 22 Oct 2021 Receipt: 26 Oct 2021	<b>Contact Details</b>  Physician: Samer Al-Khudari Facility: Rush University Medical Center Address: 1611 W Harrison Street Chicago, IL 60612, USA Additional Recipients:
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**TEST RESULT:** 14 fragments/mL plasma of TTMV-HPV-16.

**INTERPRETATION:**  
 Test result indicates the patient's tumor is positive for TTMV-HPV-16.

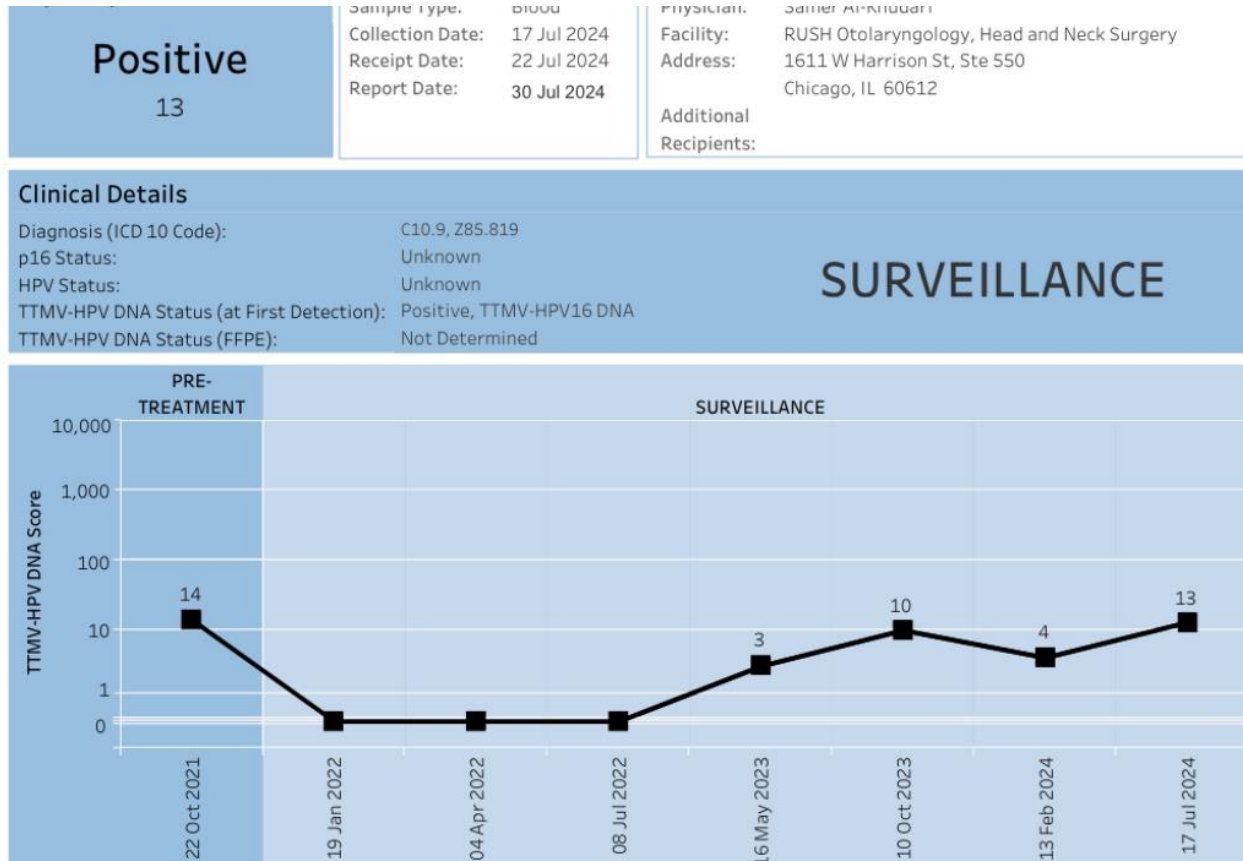
Patients with low pre-treatment TTMV-HPV levels (<200 copies/mL) have a higher likelihood of HPV integration, which is associated with worse outcomes in oropharynx squamous cell carcinoma.<sup>1</sup>

TTMV-HPV-16 fragments/mL	TTMV-HPV-18, -31, -33, -35 fragments/mL	Interpretation
<5	<5	Negative
5-7	5-12	Indeterminate
>7	>12	Positive

Values <5 are below the Limit of Detection. The NavDx indeterminate range is determined by the sensitivity of each assay.

# 60 y/o TxN1 HPV related SCC

## 3 Years S/P Neck Dissection Palatine and Lingual Tonsillectomy





# Treatment Specific Considerations

## Surgery

Therapeutic for early-stage disease

Allows for pathologic Staging

Identifies the primary site in unknown primary scenario

Patient selection is critical

## Non-Surgical

Radiation delivered over 4-6 weeks

Must lay flat with mask daily

Systemic therapy for advanced stage disease or metastatic



# General Treatments Principles

HPVOPC is highly sensitive to all modalities

Treatment for OP cancer can impact quality of life

Limit the # of treatment modalities to achieve cure

Primary site and neck need to be addressed

**Balance cure rates with  
treatment toxicity**

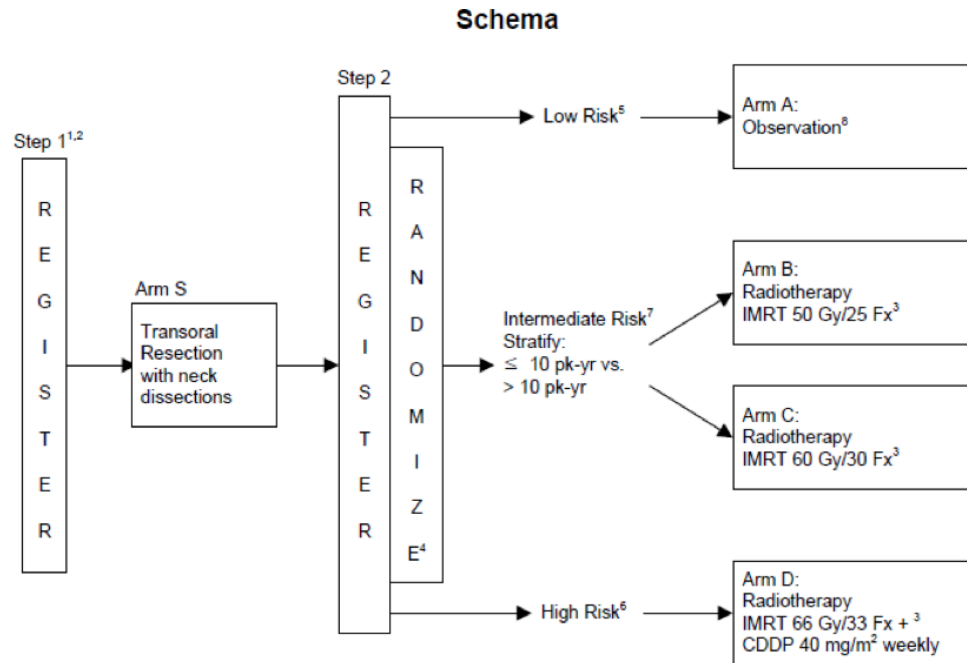
## 78 y/o post CRT for p16 + right Tonsil 2014

- Considered for TORS in 2014
- Developed Tongue P16(-) SCC s/p parital glossectomy 2020
- Right mandible ORN
- NED despite 2 H&N Cancers
- Chronic aspiration, Rec'd G-tube





# ECOG 3311- Phase II Trial 2013-2017- Not So Contemporary Now



Accrual: 377

1. Resectable oropharynx carcinoma, p16<sup>+</sup> by IHC, PS 0-1
2. Credentialing of surgeon required as part of site participation, neck levels dissected and nodal yield (> nodes/neck)
3. Radiotherapy will be given with an intensity modulated radiotherapy (IMRT) technique. Standard ECOG credentialing through QARC will be required.
4. Stratify by current/former smoking history(<10pk-yr vs. >10pk-yr)
5. Low risk: T1-T2, N0-N1, 0-1 metastatic lymph nodes, negative margins
6. High risk: > 1mm ECS or > 5 metastatic lymph nodes, positive margins
7. Intermediate risk: Close (< 3mm) margins, < 1mm ECS, 2-4 metastatic lymph nodes.
8. If ≥ 2 events are observed among the first ten patients registered on Arm A within one year, currently enrolled and subsequently enrolled low risk patients who have not progressed will be treated with IMRT 50 Gy

# Recurrence Risks

- The risk of locoregional recurrence is 10-15% and its best to identify these patients early
- The risk of distant metastasis of HPVOC is approximately 10% with the Lung being most common but rare sites well reported
- Post treatment monitoring recommendations include serial examination with laryngoscopy and serial imaging
- The clinical applications of blood circulating HPV related DNA is currently being studied as a tool for post treatment surveillance

# Strategies to “De-escalate”

## In the properly selected patient

- Less invasive surgery
- Alternative adjuvant therapy regimens
- **No Adjuvant treatment**
- Alternative systemic therapy-- Immunotherapy
- Dose-reductions of radiation and chemotherapy
- Induction therapy response-adapted de-escalation



# Case - 76 y/o s/p TORS and Adjuvant RT

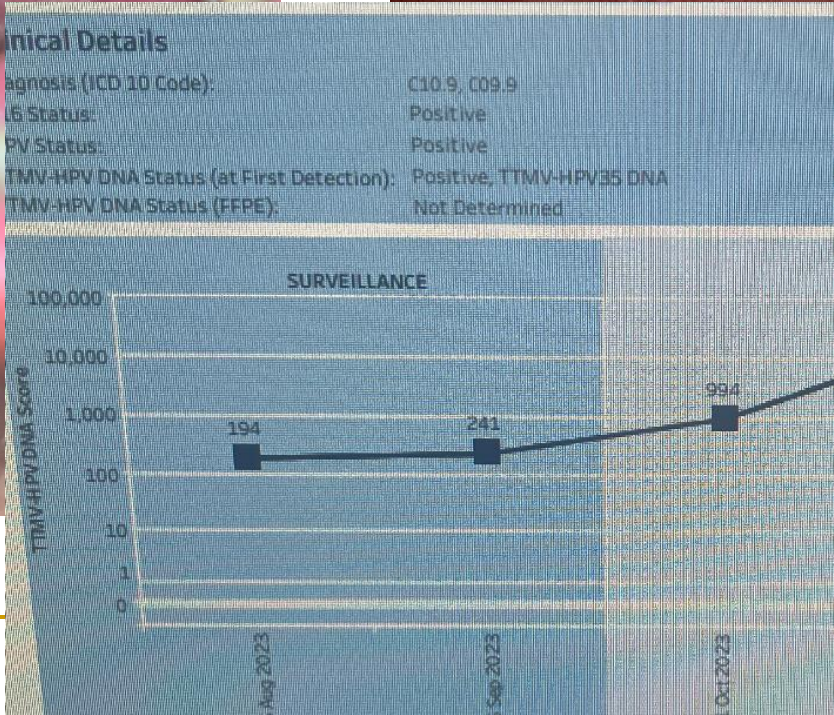
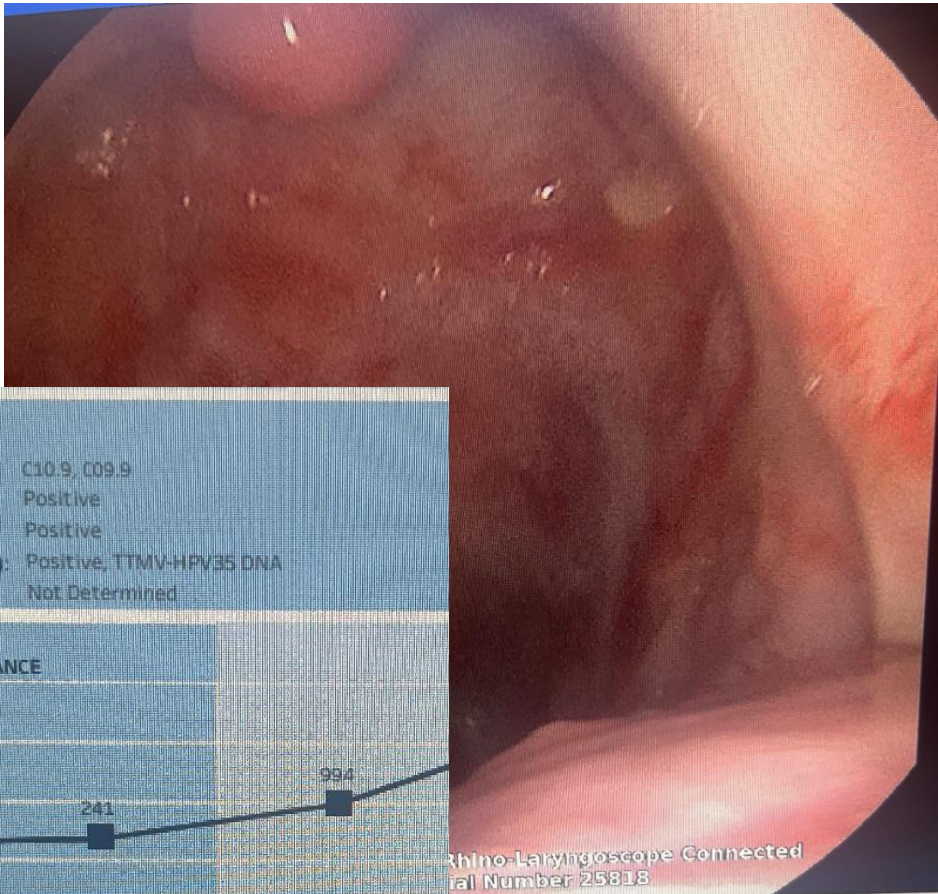


- 1.5 years post treatment a new lung nodule
- S/p VATS

Right Lower Lobe-  
SCC P16 + 1.1 cm  
margins free

Role of systemic therapy  
to prevent Metastasis?

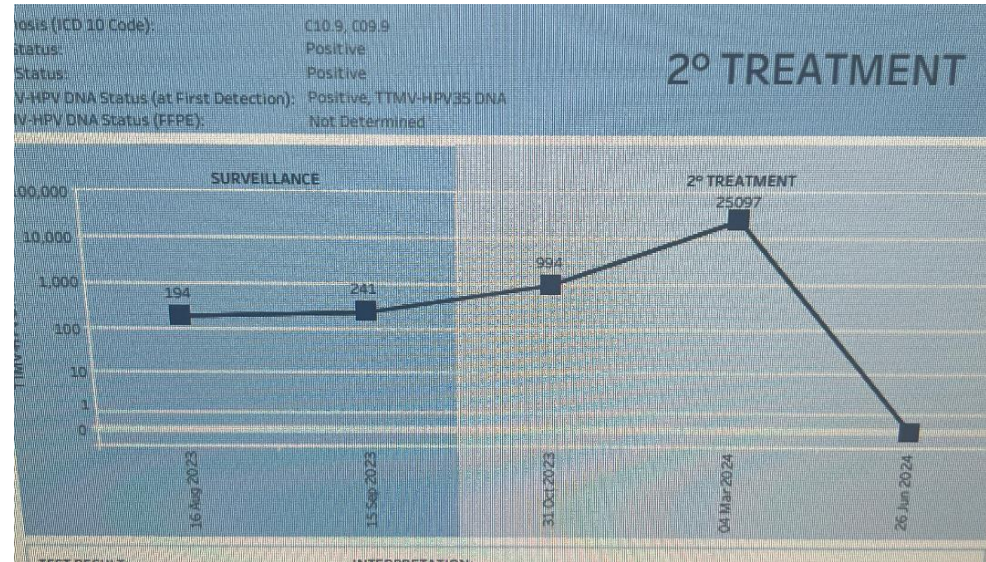
# cT4N2M0 s/p CRT





# cT4N2M0 s/p CRT

- Attempt Clinical Trial
- Identified with lung nodules
- On Immunotherapy
- 50 Gy in 5 Fractions to Left upper lobe



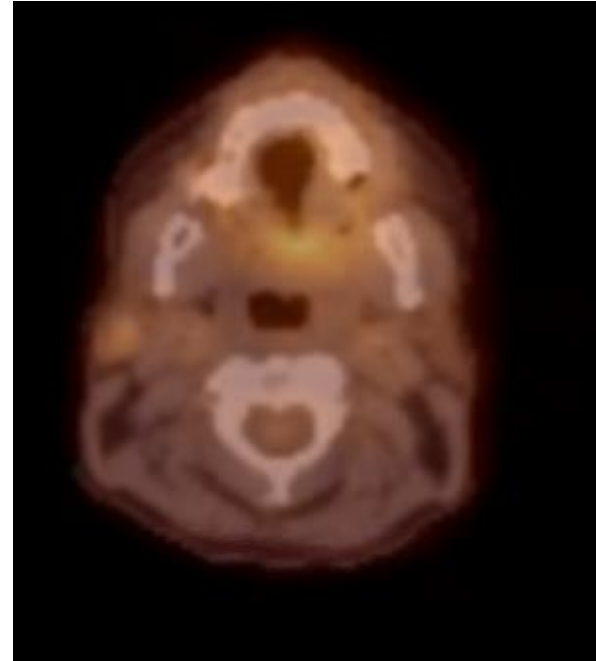
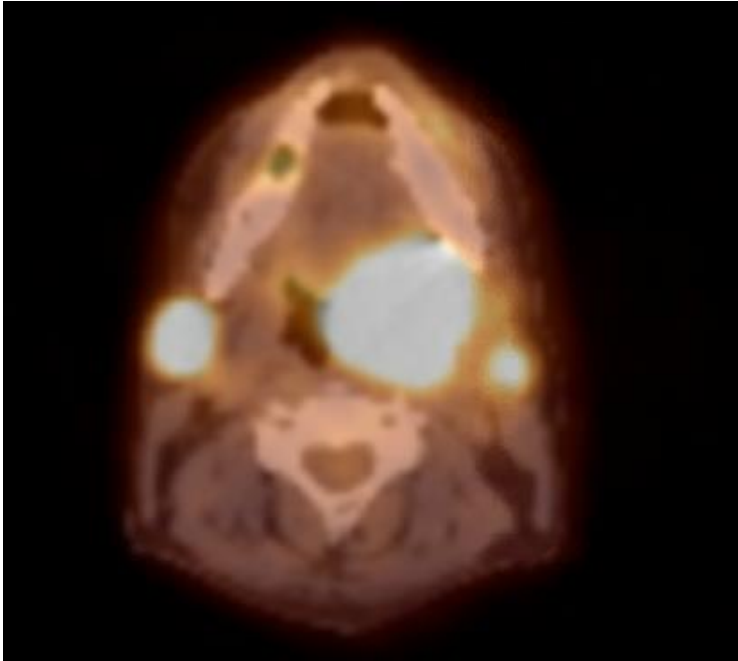


# Metastasis at Presentation – P16 +

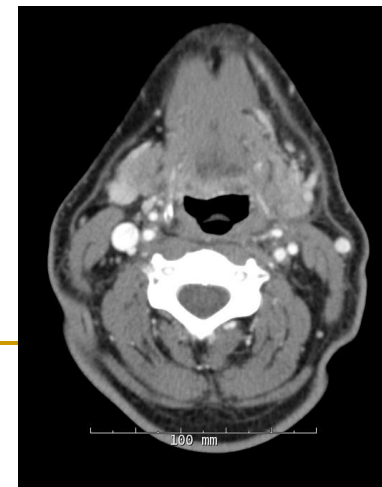
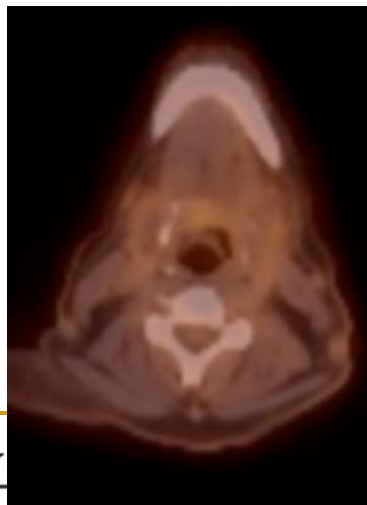
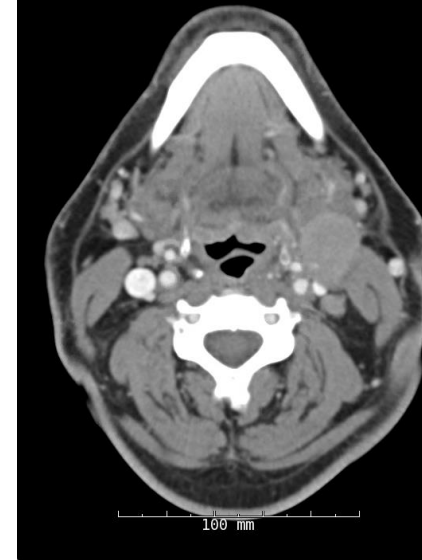
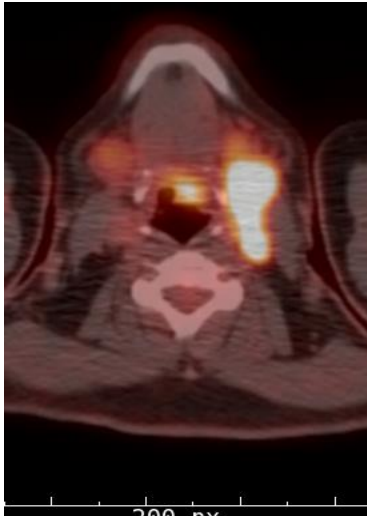


Approach in this Scenario?

# 54 y/o T4 N2- Standard - CRT



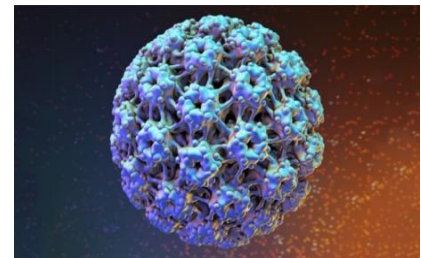
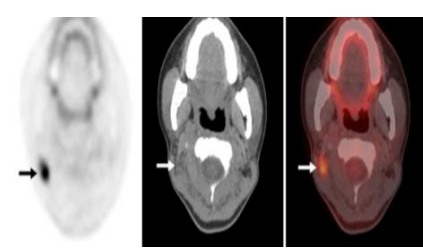
# 56 y/o male – T3N2 – CRT





# Conclusion

- Exciting time to be treating Oropharyngeal Cancer
- HPV Related Oropharynx cancer Is a different disease
- Individualized multidisciplinary approach and evaluation
- Focus on quality of life and functional outcomes after treatment



# Thanks!

*Save the date!*

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# Questions?