ICRO Pre Conference Workshop

"IMPACT"

Oral Cavity: Adjuvant Treatment

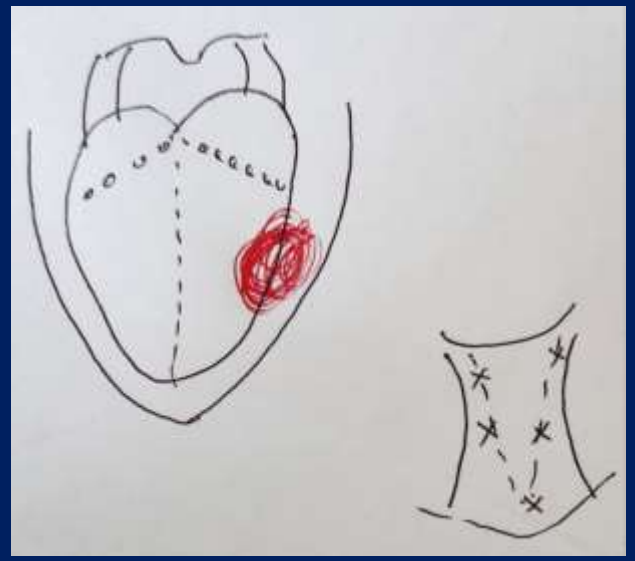
Oral cavity – Adjuvant Treatment				
Faculty				
	Dr Sarbani Ghosh Laskar	TMH, MUMBAI	9820834386	sarbanilaskar@gmail.com
Postgraduates				
1	Dr Rohit Golla	Jawaharlal Nehru Cancer Hospital and Research Center, Bhopal	8555932314	rohitgolla98@gmail.com
2	Dr Kartika sehrawat	Fortis Shalimar Bagh, Delhi	7988380081	kartikasehrawat50@gmail.com
3	Dr Banti Kumar	Indira Gandhi Institute of Medical Sciences, Patna	9798346546	bantikr82@gmail.com
4	Dr Mahak Gupta	KMC Manipal	9861183765	makgupta28@gmail.com
5	Dr Milankumar Mali	HCG Cancer Centre Ahmedabad	7387487090	milankumarmali15@gmail.com
Extra	Dr. Pranjal Maheshwari	JLN Medical College & Hospital, Ajmer	9414149995	pranjal.m95@gmail.com

Mandate for the panel:

Adjuvant RT in

- Intermediate risk oral cancers
- After use of NACT and surgery

Case No 1



70 year/ lady, hypertensive on T Stamlo 2.5mg OD

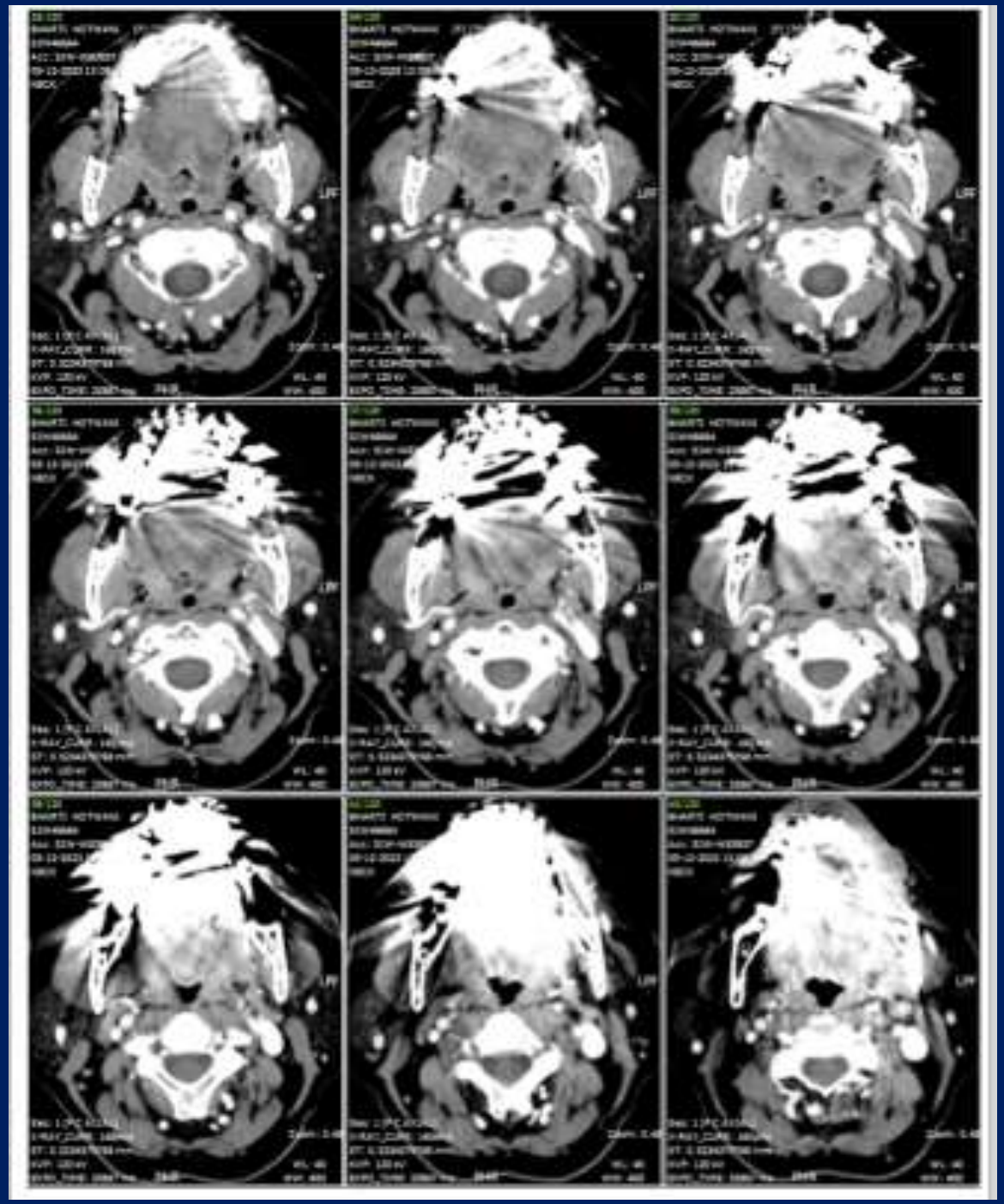
No history of habits/ addiction

H/O proliferative growth on the L side of tongue: 2 months

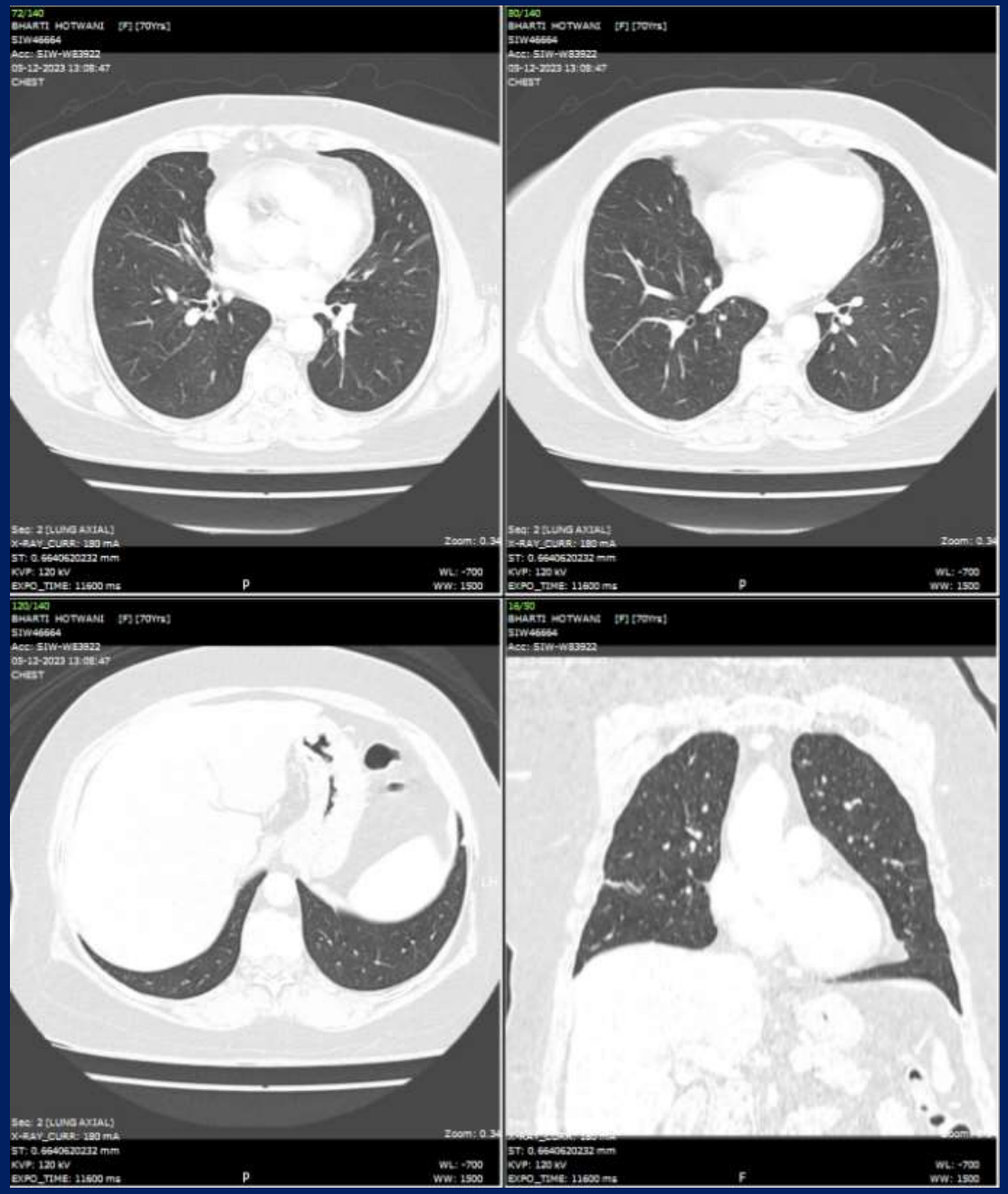
On local examination: 2x2 cm proliferative lesion on the L lateral border of the tongue, not reaching FoM or midline. About a cm behind the tip and well away from the BoT.
No ankyloglossia
No palpable cervical adenopathy

CT scan face was noncontributory due to numerous dental artefacts

CT thorax: No abnormality detected



Oral cavity and oropharynx cannot be commented upon due to artefacts. The supraglottic,glottis and subglottic compartment appear normal. Epiglottis, AE folds and pyriform sinuses are normal. Both true and false vocal cords are normal and the pre / paraglottic space fat is intact. Post-cricoid region is normal. Laryngeal cartilages are normal. No erosion / destruction is seen. Carotid sheaths on both sides appear normal. ICAs and IJVs on both sides show normal enhancement. Soft tissues of the neck appear normal. There are multiple bilateral level IB, II, III and V nodes seen with the largest node measuring 11.7 - 13.6mms at left sided level I B and level II stations. The nodes are oval in shape with intact perinodal fat . No obvious signs of extracapsular spread noted. No necrosis / liquefaction seen. No supraclavicular or superior mediastinal lymphadenopathy is seen.


72/140
BHARTI HOTWANI [F] [70Yrs]
SIW46664
Acc: SIW-WE3922
09-12-2023 13:08:47
CHEST
Ser: 2 [LUNG AXIAL]
X-RAY_CURR: 180 mA
ST: 0.6640620232 mm
KVP: 120 kV
EXPO_TIME: 11600 ms
P
WL: -700
WW: 1500
80/140
BHARTI HOTWANI [F] [70Yrs]
SIW46664
Acc: SIW-WE3922
09-12-2023 13:08:47
CHEST
Ser: 2 [LUNG AXIAL]
X-RAY_CURR: 180 mA
ST: 0.6640620232 mm
KVP: 120 kV
EXPO_TIME: 11600 ms
P
WL: -700
WW: 1500
120/140
BHARTI HOTWANI [F] [70Yrs]
SIW46664
Acc: SIW-WE3922
09-12-2023 13:08:47
CHEST
Ser: 2 [LUNG AXIAL]
X-RAY_CURR: 180 mA
ST: 0.6640620232 mm
KVP: 120 kV
EXPO_TIME: 11600 ms
P
WL: -700
WW: 1500
18/50
BHARTI HOTWANI [F] [70Yrs]
SIW46664
Acc: SIW-WE3922
ST: 0.6640620232 mm
KVP: 120 kV
EXPO_TIME: 11600 ms
F
WL: -700
WW: 1500

NED

Need for any other evaluation?

Plan of care:

Treatment:
Surgery
When would you say no to surgery?

Radiation Therapy
When would you want to treat with RT upfront?

09/12/2023: Underwent WL/E of the tongue lesion with L sided ND

Histopathology:
pT: 2x2x0.9cm, proliferative lesion on the L lateral border tongue
Thickness: 0.9 cm, DoI: 0.6cm
WD SCC
All cut margins of excision are free, closest: base and inferior 1 cm away
PPOI/ WPOI: 3/ 3
No LVE/ PNI
L ND: 37/37, uninvolved

Further plan of management?

What factors will you consider to decide on adjuvant RT for patients with early OCSCC?

Patient related	Tumor related
Age Gender Performance status	Grade DoI: C/M status: Dysplasia at the C/M PPOI/ WPOI WPOI vs C/M distance PNI LVE Nodal status: Number, level, adequacy of ND dissection, micro ENE

Tumor depth of invasion and prognosis of early-stage oral squamous cell carcinoma: A meta-analysis

Patrícia Carlos Caldeira[1] | Andrea María López Soto[2] | Maria Cássia Ferreira de Aguiar[1] | Carolina Castro Martins[3]

Results: Twenty-seven studies were included (19 in the meta-analysis) with 2,404 patients with a mean of 60 years of age. High tumor DOI is associated with a greater chance of presenting lymph node metastasis, regardless of the cutoff point for DOI (13 meta-analysis; OR 1.69–53.08), recurrence (five meta-analysis; OR 1.22–3.83), and lower chance of survival (1 meta-analysis; OR 0.49). The certainty of evidence varied from very low to low.

Conclusions: Tumor DOI is a good prognosticator for early-stage OSCC. The findings of the current meta-analysis highlight the clinical relevance of DOI and corroborate its incorporation for staging OSCC.

Depth of invasion alone as an indication for postoperative radiotherapy in small oral squamous cell carcinomas: An International Collaborative Study

Methods: Retrospective analysis of DOI (<5, 5 to <10, ≥10 mm) and disease-specific survival (DSS) in a multi-institutional international cohort of 1409 patients with oral SCC ≤4 cm in size treated between 1990-2011.

Results: In patients without other adverse factors (nodal metastases; close [<5 mm] or involved margins), there was no association between DOI and DSS, with an excellent prognosis irrespective of depth. In the absence of PORT, the 5-year disease-specific mortality was 10% with DOI ≥10 mm, 8% with DOI 5-10 mm, and 6% with DOI <5 mm ($P = .169$), yielding an absolute risk difference of only 4%.

Conclusion: The deterioration in prognosis with increasing DOI largely reflects an association with other adverse features. In the absence of these, depth alone should not be an indication for PORT outside a clinical trial.

ORIGINAL ARTICLE

Oral Squamous Cell Carcinoma

Histologic Risk Assessment, but Not Margin Status, Is Strongly Predictive of Local Disease-free and Overall Survival

Margaret Brandwein-Gensler, MD,† Miriam S. Teixeira, MD,* Carol Ming Lewis, MD, MPH,§ Bryant Lee, MD,* Linda Rolnitzky, MS,‡ Johannes J. Hille, DDS,‖ Eric Genden, MD,* Mark L. Urken, MD,* and Beverly Yiyao Wang, MD†*

- Developed a novel histological risk assessment system based on :
  - PNI
  - WPOI
  - Lymphocytic infiltrate
- Margin status was seen not to have an impact on survival in their cohort

TABLE 9. Proposed Risk Assessment for Oral Squamous Cell Carcinoma

	Point Assignment for Risk Scoring		
Histologic Variable	**0**	**1**	**3**
Perineural invasion	None	Small nerves	Large nerves
Lymphocytic infiltrate at interface	Continuous band	Large patches	Little or none
WPOI at interface	1 or 2 or 3	4	5

Risk Score (sum of all point assignments)	**Risk for local Recurrence**	**Overall Survival Probability**	**Adjuvant Treatment Recommendations**
Score = 0	Low	Good	No local disease-free benefit seen for adjuvant RT
1 or 2	Intermediate	Intermediate	No local disease-free benefit seen for adjuvant RT
3 to 9	High	Poor	RT regardless of 5 mm margins

Depth of invasion, tumor budding, and worst pattern of invasion: Prognostic indicators in early-stage oral tongue cancer

Alhadi Almangush, DDS,[1] Ibrahim O. Bello, BDS, PhD,[1,2] Harri Keski–Säntti, MD, PhD,[3] Laura K. Mäkinen, MD,[3] Joonas H. Kauppila, MD,[4] Matti Pukkila, MD, PhD,[5] Jaana Hagström, DDS, PhD,[1,6] Jussi Laranne, MD,[7] Satu Tommola, MD,[8] Outi Nieminen,[9] Ylermi Soini, MD, PhD,[10] Veli-Matti Kosma, MD, PhD,[10] Petri Koivunen, MD, PhD,[11] Reidar Grénman, MD, PhD,[12] Ilmo Leivo, MD, PhD,[1,9] Tuula Salo, DDS, PhD[13,14*]

233 cases of T1/T2 N0 tongue cancers – following histological parameters assessed

1. Tumour budding
2. Depth of Invasion
3. Histological Risk Assessment (WPOI/ Lymphocytic Response /PNI)
4. Cancer associated Fibroblasts

On Multivariate analysis:
Depth > 4 mm , Tumour budding > 5 cells at the invasive front along with WPOI: significant predictors of Disease Specific Survival: **need Treatment Intensification**

Head Neck 36: 811– 818, 2014

Published literature on impact of adverse histological features in early OSCC.

Year	Author	No. of patients	Conclusions	Remarks
LVE/LVSI				
2017	Cassidy	180	LVSI associated with worse OS on MVA (HR = 2.20; 95% CI, 1.19–4.06; p = 0.01)	Overall LVSI present in only 20% patients
2013	Chen	442	No significant differences in the .2%, p = 0.51) and OS (90.9 vs 85.2%, p = 0.18) No impact of LVE/PNI on MVA	Only 82 patients had LVE/PNI
PNI				
2018	Nair	1524	PNI higher in tongue cancers The PNI significantly affected both DFS(DFS HR= 1.84) and OS(OS; HR = 1.7). Patients with early p N0 disease and PNI more likely to develop recurrences and have mortality (HR = 2.79 for DFS; H hese patients showed association improvement in surv	-Population predominantly gingivo – buccal cancers(65%) −41% of patients with T3-T4 primaries
2017	Thiagarajan	322	Statistically significant reduction NI (60 months vs 26 months, p = 0.027)	70 patients met criteria for inclusion PNI present in only 6 patients overall
2012	Tai	307	PNI predicted for Neck metastasis (p < 0.001,HR = 3.36,95% CI-1.85–6.1) Neck recurrence (p < 0.001, HR – 4.25,95% CI-2.01–8.98) DSS (p = 0.027,HR −2.08,1.09–3.99) Elective neck dissection contributed to a significantly better 5-year DSS only incN0 patients with PNI-positive tumors (p = 0.0071	PNI Present in 27% patients (84 patients)
Close Margin				
2013	Ch'ng	144	LC with surgery alone-91% DSS with surgery alone 84% (5 years). No pattern of worse LC or DSS with ordered stratification of close margins.	-POI unknown in 10% of patients and pushing in 10% of patients −27% patients WDSCC
2017	Tasche	443	Local recurrence rates (%) by distance from invasive tumor (in mm) < 1–44 2–28 3–17 4–13 5–13 ≥5–14	No history of tobacco usage 41% female patients (likely preponderance of HPV positive disease and lesser relevance of positive margins)
2018	Fridman	1257	5 yr OS Clear margin (995)-80% Close margin (n = 205)- 52% Close margins associated with > 2 fold recurrence (p < 0.0001) Adjuvant therapy significantly improved outcomes for close/positive margins (p = 0.002–0.03)	-No indication of subsites (tongue vs.gingivo- buccal) -Close and positive margins clubbed together

Equivocal

Unequivocal

Unequivocal

Oral Oncology 104 (2020) 104627

What is the definition of adequate margins?
If the C/M < 5 mm, then what?: Revision vs adjuvant RT

Adequacy of Neck dissection:
If < 18 nodes and that is the only adverse feature, then what?
Observation vs Adjuvant RT

Follow-up protocol

Management of the Neck in Squamous Cell Carcinoma of the Oral Cavity and Oropharynx: ASCO Clinical Practice Guideline

Shlomo A. Koyfman, MD[1]; Nofisat Ismaila, MD[2]; Doug Crook, MS[3]; Anil D'Cruz, DNB[4]; Cristina P. Rodriguez, MD[5]; David J. Sher, MD[6]; Damian Silbermins, MD[7]; Erich M. Sturgis, MD[8]; Terance T. Tsue, MD[9]; Jared Weiss, MD[10]; Sue S. Yom, MD, PhD[11]; and F. Christopher Holsinger, MD[12]

Recommendation 1.1a. For patients with SCCOC classified as cT2 to cT4, cN0—that is, no clinical nor radiographic evidence of metastatic spread to the neck—and treated with curative-intent surgery, an ipsilateral elective neck dissection should be performed (Type: evidence based; Evidence quality: high, benefit outweighs harm; Strength of recommendation: strong).

Recommendation 1.1b. For patients with SCCOC classified as cT1, cN0, an ipsilateral elective neck dissection should be performed. Alternatively, for selected highly reliable patients with cT1, cN0, close surveillance may be offered by a surgeon in conjunction with specialized neck ultrasound surveillance techniques (Type: evidence based; Evidence quality: intermediate, benefit outweighs harm; Strength of recommendation: strong).

Recommendation 1.2a. For patients with a cN0 neck, an ipsilateral elective neck dissection should include nodal levels, Ia, Ib, II, and III. An adequate dissection should include at least 18 lymph nodes (Type: evidence based; Evidence quality: high, benefit outweighs harm; Strength of recommendation: strong).

Recommendation 1.2b. An ipsilateral therapeutic selective neck dissection for a clinically node-positive (cN+) neck should include nodal levels Ia, Ib, IIa, IIb, III, and IV. An adequate dissection should include at least 18 lymph nodes. Dissection of level V may be offered in patients with multistation disease (Type: evidence based; Evidence quality: intermediate, benefit outweighs harm; Strength of recommendation: moderate).

Recommendation 2.1a. Adjuvant neck radiotherapy should not be administered to patients with pathologically node-negative (pN0) or a single pathologically positive node (pN1) without extranodal extension after high-quality neck dissection, unless there are indications from the primary tumor characteristics, such as perineural invasion, lymphovascular space invasion, or a T3/4 primary (Type: evidence based; Evidence quality: intermediate, benefit outweighs harm; Strength of recommendation: moderate).

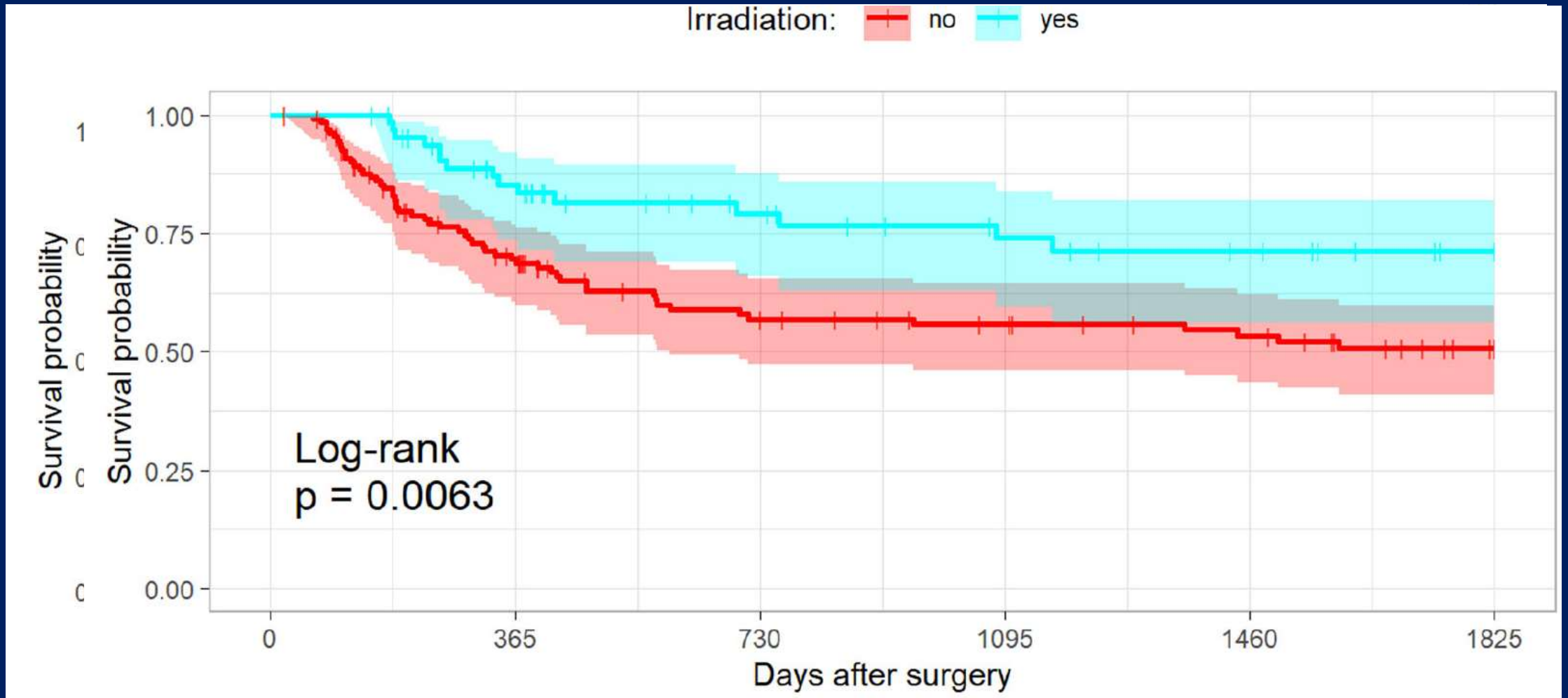
Recommendation 2.1b. Adjuvant neck radiotherapy should be administered to patients with oral cavity cancer and pN1 who did not undergo high-quality neck dissection—as defined in recommendation 1.2b (Type: evidence based; Evidence quality: intermediate, benefit outweighs harm; Strength of recommendation: moderate).

Role of Adj RT in pN1 OCSCCC?

The same patient: pT1pNI vs pT2pN1:
Plan of care?

Adjuvant Radiotherapy in Patients with Squamous Cell Carcinoma of the Oral Cavity or Oropharynx and Solitary Ipsilateral Lymph Node Metastasis (pN1)—A Prospective Multicentric Cohort Study

Peer W. Kämmerer [1,*,†], Silke Tribius [2,†], Lena Cohrs [3], Gabriel Engler [4], Tobias Ettl [5], Kolja Freier [6], Bernhard Frerich [7], Shahram Ghanaati [8], Martin Gosau [9], Dominik Haim [10], Stefan Hartmann [11], Max Heiland [12], Manuel Herbst [13], Sebastian Hoefert [14], Jürgen Hoffmann [15], Frank Hölzle [16], Hans-Peter Howaldt [17], Kilian Kreutzer [12], Henry Leonhardt [10], Rainer Lutz [18], Maximilian Moergel [1], Ali Modabber [16], Andreas Neff [4], Sebastian Pietzka [19], Andrea Rau [20], Torsten E. Reichert [5], Ralf Smeets Christoph Sproll [21], Daniel Steller [3], Jörg Wiltfang [22], Klaus-Dietrich Wolff [23], Kai Kronfeld [24] and Bilal Al-Nawas [1]

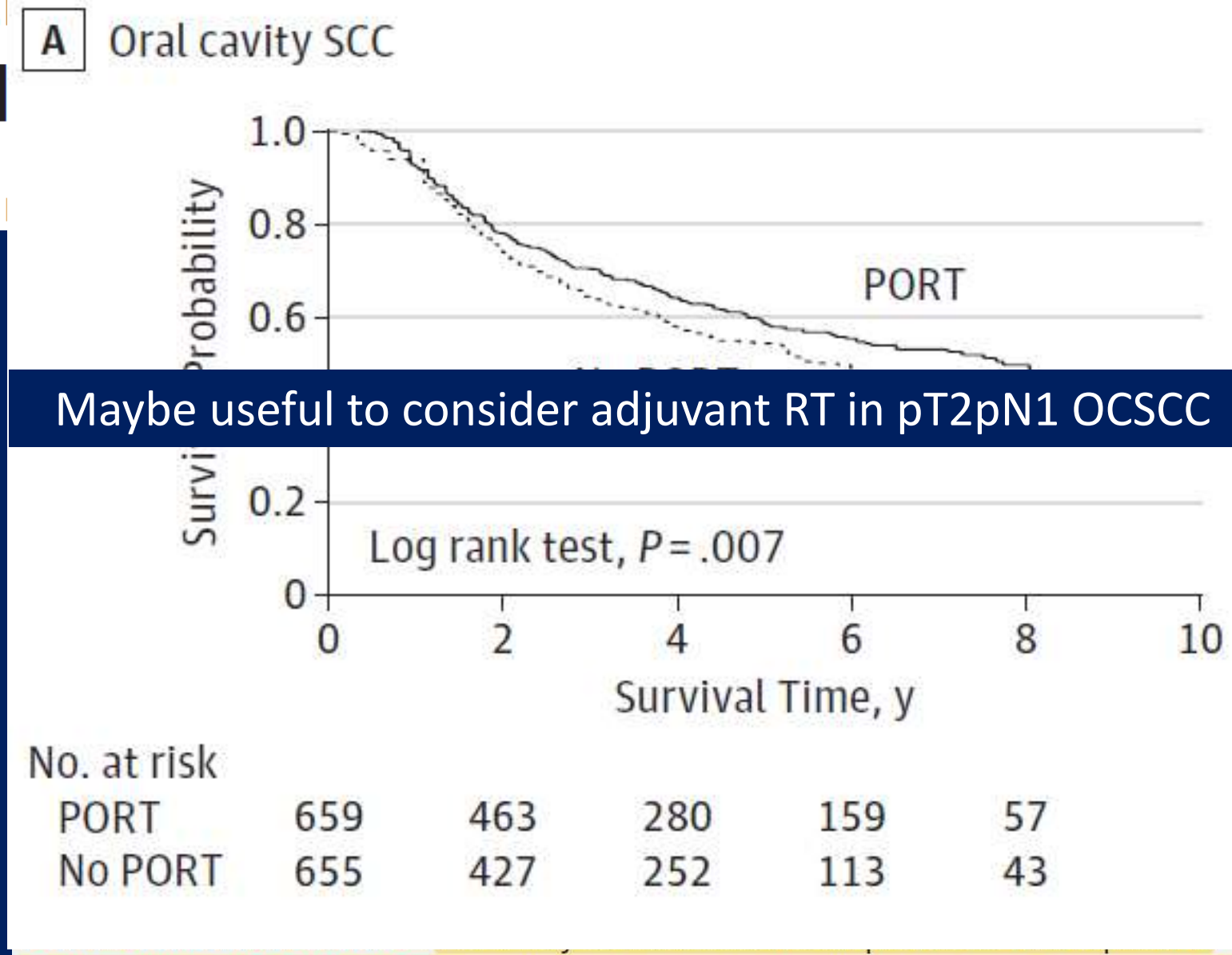


Number at risk

no	134	80	57	50	44	32
yes	66	49	34	27	23	17

three years after therapy compared to the observation group.

DESIGN, SETTING, AND PARTICIPANTS This retrospective cohort study identified 1467 adult patients with OC SCC and 790 patients with OP SCC with pT1N1 or pT2N1 disease in the



Maybe useful to consider adjuvant RT in pT2pN1 OCSCC

with pN1 OC and OP SCC, especially in those younger than 70 years or those with pT2 disease.

? RT volumes: Buccal Mucosa vs Tongue: Primary, Nodes

- Prognosis for the presence of several intermediate risk factors is emerging
- Evidence for use of adjuvant therapy in their presence as the sole factor: Equivocal
- A combination of intermediate risk factors even in early cancers deserve consideration for adjuvant therapy
- Intensification is contentious (RTOG 0920)

Case No 2

44 years old male

Presented in 2014 with complaints of ulcerative lesion on right lateral border of tongue for 4 months.

Baseline examination(2014): Sub centimeter sized erythematous lesion with minimal duration at right lateral border of tongue.

- Biopsy: Squamous cell carcinoma.
- CXR: No abnormality detected.
- USG neck: Indeterminate left level II lymph node.
- FNAC of level II LN: Reactive aspirate.

Accrued in N0 trial

- Underwent wide local excision of tongue lesion followed by primary closure on 8.7.2014
- pT 1.5x0.5x0.4cm,

  Moderately differentiated squamous carcinoma of right lateral border of tongue.

  Maximum thickness 0.4cm, Microscopic thickness 0.6cm

  Closest cut margin: 1cm (lateral margin)

  No lympho vascular emboli/peri neural invasion
- Final diagnosis: **Ca Right lateral border of tongue pT1N0, MDSCC**
- Plan: **Close observation**

Noticed an ulcer adjacent to site of previous lesion since 3 weeks in November 2023 (9 years later).

Baseline examination: 2x2cm ulceroproliferative growth in postero lateral border of tongue. Base of tongue/floor of mouth: free

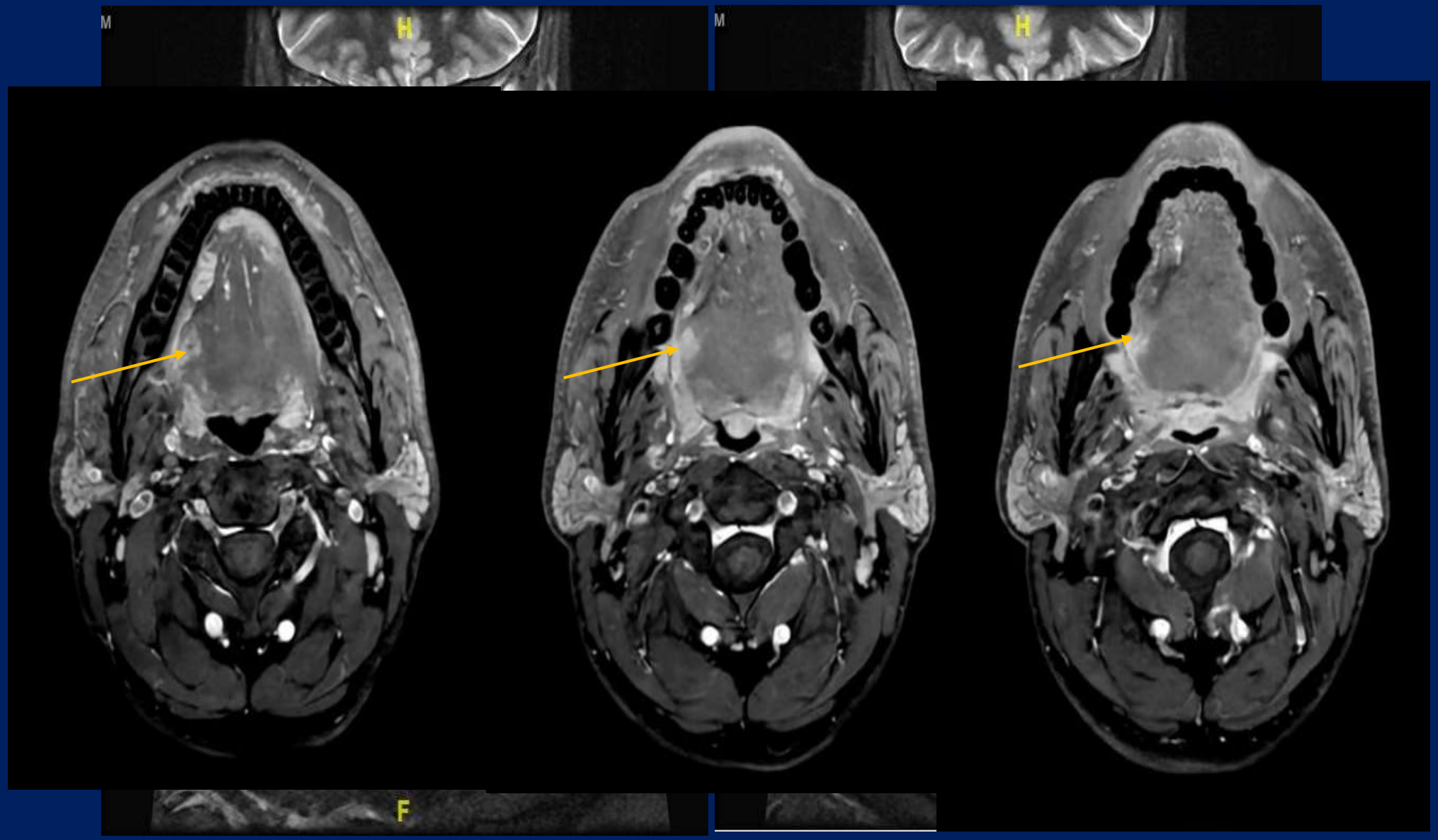
- **Biopsy:** Moderately differentiated squamous cell carcinoma.

•**17.11.23 MRI Face and neck:** 2x0.8x1.9cm lesion in right lateral border of tongue

DOI 0.8cm, Not crossing midline, Extrinsic muscles involved. Base of tongue/floor of mouth free.

No suspicious cervical adenopathy.

- **13.11.23 CT Chest:** NED


M
H
M
H
F

- Underwent **Right lateral border of tongue wide local excision** and **right selective neck dissection (level I-IV)** with primary closure and platysmal flap on 14.12.2023
- Moderately differentiated squamous cell carcinoma

  pT 1.3x1x1cm

  Epicentre: Right lateral border of tongue

  DOI 0.9cm, PPOI type 3, WPOI type 4

  LVE/PNI not identified

  All margins free of tumour, Closest margin: lateral mucosal - 0.9cm

  Lymph nodes 0/37

- **Final diagnosis:** Likely second primary in Right lateral border of tongue pT2pN0

Now what?

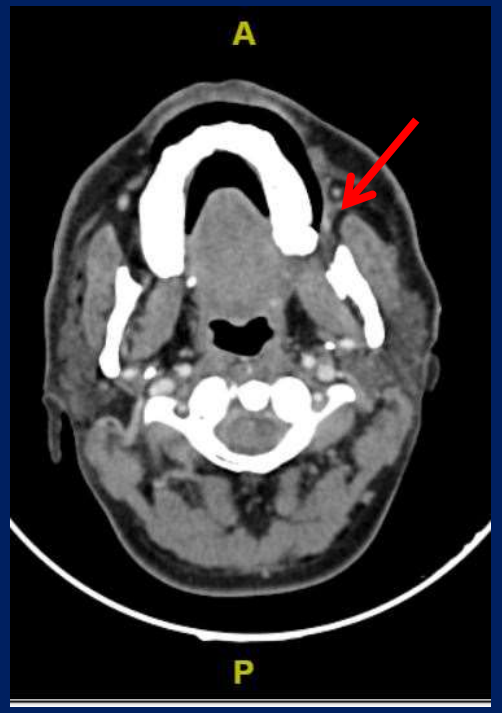
- Opinion?
  - Adjuvant RT
  - Adjuvant CTRT
  - Observe
- Our plan: Adjuvant RT
- RT volumes:

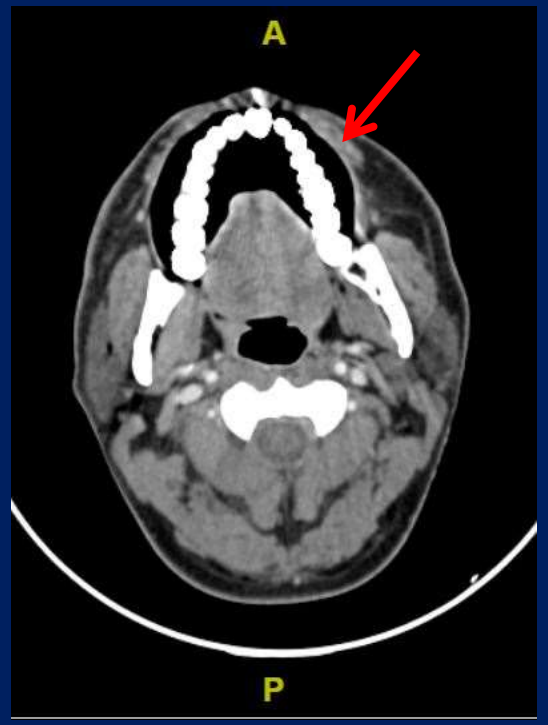
Case No 3

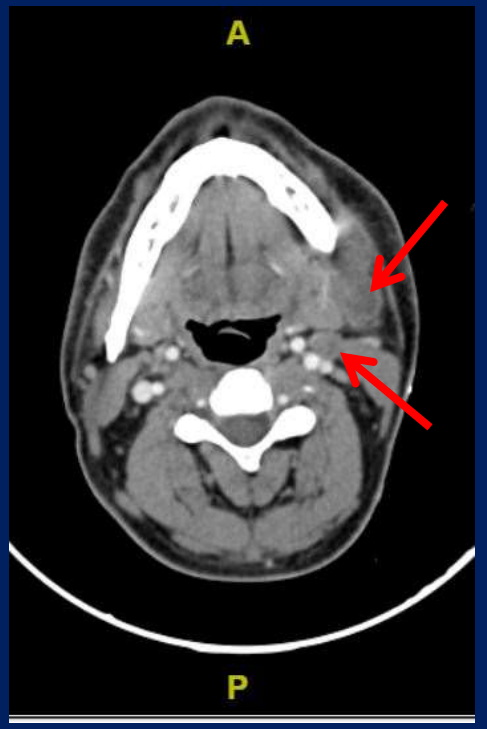
- 34 Y/M, R/o MP. No comorbidities. No F/H/o Malignancy
- H/o Gutka chewing for 15 years , Alcohol consumption for 8 years , reformed 3 months back.
- P/w/c/o Lt sided facial swelling for 6 months
- Evaluated outside for the same
- CT Neck (P+C) 21.5.23 (Images N/A): lesion 12x5mm involving left upper buccal space. Few necrotic cervical Level I and II LN , largest 21x15mm at Level I B.
- Bx done outside- **MDSCC**
- Now came to TMH for further evaluation.
- Lt BM lesion Bx at TMH- **MDSCC**

CECT HN (14.10.23)

- Plaque like enhancing thickening is noted involving the left lower BM and lower GBS adjacent to the left lower alveolus extending into left RMT.
- Metastatic Lt level IB (with ENE) and level II LN.







- U/w Left BCR + B/L ND + Trach +FALT on 20.11.23
- HPR – PDSCC, Left BM , 2.7x2.5x0.3cm. DOI- 1.8 cm
  Skin +, Lt mandible medullary involvement+
  PPOI/WPOI- 4/5
  Extensive extratumoral PNI
  Vascular emboli+
  All margins free, closest 0.7 cm
  Lt ND- 5/37 (Level IIA- 2/8, ENE+; Level IIB- 1/8, ENE+, Level III-2/7). Rt ND- 0/24
  pT4aN3b
- **IMP: PDSCC Lt BM, pT4aN3bM0**

- Started on adjuvant CTRT (28/12/2023)
- Completed 14#RT and C1 cisplatin

- Now c/o **Lt cheek swelling, progressively increasing in size**
- **FNAC (9.1.24)- Recurrent/ residual SCC**

- What could we have done differently in this young man?
  - Treatment: NACT
  - Adjuvant:
  - Timing

- Any imaging with this advanced stage?

Post-operative P… squamous cell c… … early recurrence of

… Oncology 141 (2023) 106400

Background: We evaluate… positron emission tomography with computed tomography (… …arly recurrence (ER) and treatment outcomes in oral squamo…

Methods: We retrospectiv… …t-operative radiation between 2005 and 2019 for OSCC at o… …surgical margins were classified as high risk features; pT3-4, … …l invasion, tumor thickness >5 mm, and close surgical margi… …ts with ER were identified. Inverse probability of treatment … …s between baseline characteristics.

Results: 391 patients wit… …. 237 (60.6%) patients underwent post-operative PET/CT p… …only. Patients screened with post-operative PET/CT were n… …ed with CT only (16.5 vs. 3.3%, p < 0.0001). Among patients … …likely than those high risk features to undergo major treatm… …tion of chemotherapy, or intensification of radiation by ≥ … …/CT was associated with improved disease-free and overall … …(IPTW log-rank p = 0.026 and p = 0.047, respectively) but … …p = 0.96).

Conclusions: Use of post-… …ection of early recurrence. Among patients with intermedia… …ase-free survival.

Logistic Regression Model of Early Recurrence.

	Univariable Analysis			Multivariable Analysis		
Risk Factor	ORR	95% CI	p-value	ORR	95% CI	p-value
Post-op PET vs CT	8.06	4.09 – 18.02	<0.0001	7.91	2.88 – 26.8	0.00023
ECE	5.30	3.17 – 9.04	<0.0001	5.21	2.14 – 13.4	0.00038
Margins						
Negative	Ref	–	–	Ref	–	–
Close	0.75	0.41 – 1.40	0.35	0.79	0.33 – 1.99	0.61
Positive	2.32	1.18 – 4.59	0.015	2.06	0.69 – 6.19	0.19
T3-4 vs. T1-2	2.87	1.71 – 4.96	<0.0001	1.98	0.87 – 4.58	0.11
N2-3 vs. N0-1	2.86	1.72 – 4.84	<0.0001	1.00	0.37 – 2.61	1.00
Tumor Thickness (mm)	1.04	1.01 – 1.07	0.0045	1.01	0.96 – 1.06	0.77
Num Nodes (per node)	1.09	1.04 – 1.14	0.00011	1.07	0.99 – 1.18	0.14
PNI	1.89	1.12 – 3.27	0.019	1.67	0.73 – 3.98	0.23
LVI	2.11	1.22 – 3.56	0.0060	1.44	0.59 – 3.43	0.41
Time to sim (per day)	1.02	1.01 – 1.03	0.0015	0.36	0.14 – 0.92	0.029
Referral pattern (internal referral vs. tertiary referral)	0.46	0.26 – 0.84	0.0086	0.36	0.14 – 0.92	0.029
Free Flap	1.24	0.75 – 2.07	0.41	–	–	–
Oral Tongue vs other	0.76	0.45 – 1.25	0.29	–	–	–

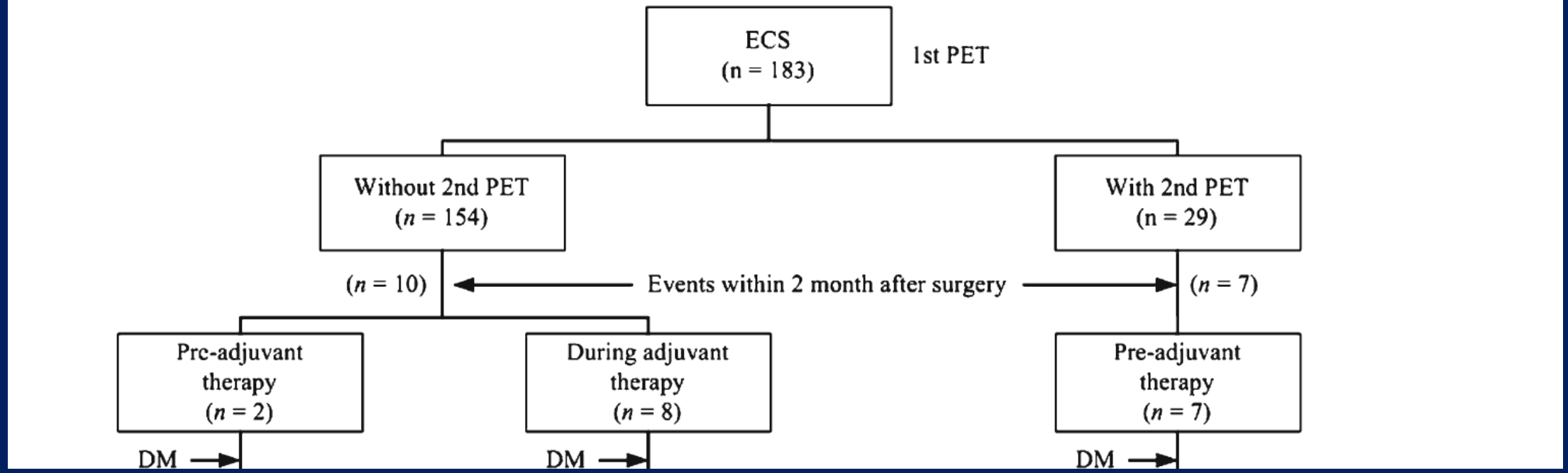
- Patients with ER after surgery and prior to postoperative radiation (RT) for SCC of the OC have aggressive biology and poor prognosis.
- With introduction of PET/CT simulator in the department, post-operative PET/CT as part of RT planning was done

- Hypothesis: PET/CT would improve detection of macroscopic disease before postoperative RT.

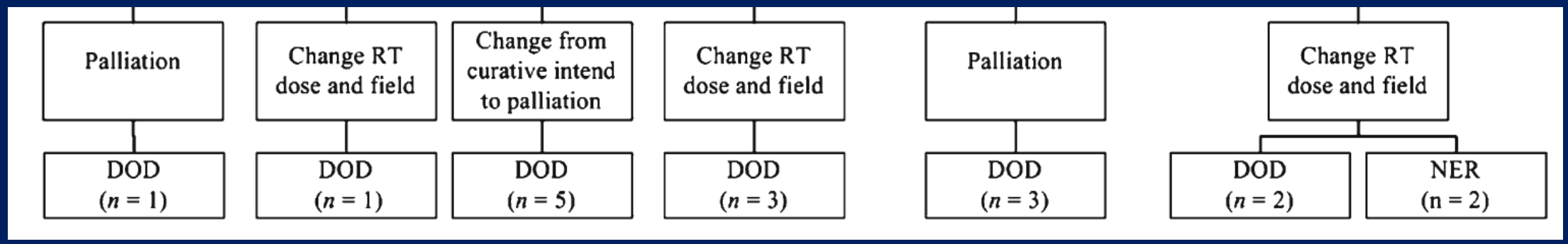
- **Methods:** Retrospective review of medical records of patients treated with postoperative radiotherapy between 2005 and 2019 for OC SCC.
- Clinicopathologic risk factors were recorded:
- Intermediate risk factors (IRFs) included pT3-4 disease, nodal disease, perineural invasion (PNI), lymphovascular invasion (LVI), and close (< 5mm) surgical margins (SM);
- High-risk factors (HRF)extranodal extension (ENE) and positive SM
- Patients were stratified into risk groups based upon the number and type of risk factors: 0-1 IRFs, 2 IRFs, ≥3 IRFs, and any HRF.
- Patients were considered to have ER if they had biopsy confirmed recurrence, or if the imaging or exam was sufficiently suspicious, after discussion with the head and neck team, to warrant treatment to definitive doses of RT (70 Gy).

Results: N= 391 patients
35% had pT3-4 disease,
36% had pN2a-3 disease,
53% had PNI, 20% had LVI,
30% had ENE, and
14% had positive SM.
The most common sites were oral tongue (46%), alveolar ridge (18%), and buccal mucosa (13%).
237 (61%) patients underwent postoperative PET/CT planning, and 165 patients (41%) were planned with CT only.
Patients screened with post-operative PET/CT were more likely to be diagnosed with ER (46/237, 19.4%) than those simulated with CT only (6/154, 3.9%, $p < 0.0001$).
Among patients simulated with PET/CT, 7%, 9%, 14%, and 35% of patients were diagnosed with ER for patients with 0-1 IRFs, 2 IRFs, ≥3 IRFs, and any HRF, respectively.
Median follow-up was 4.1 years (95% CI 3.6 – 4.5). Among 52 patients with ER, 24 (49.0%) had local, 41 (83.7%) had regional, and 5 (10.2%) had distant recurrence. 17 (33%) of ER were biopsy proven. For patients with ER, 3-year freedom from locoregional recurrence, distant-metastasis free survival, and overall survival were 45.2% (95% CI 32% - 64%), 55% (95% CI 42% – 72%), and 43% (95% CI 30% - 61%), respectively. For patients without ER, use of postoperative PET/CT was associated with improved disease-free survival (HR 0.68, 95% CI 0.46 – 0.98, $p = 0.041$) and overall survival (HR 0.59, 95% CI 0.38 – 0.91, $p = 0.019$). **Conclusions:** Postoperative PET/CT may increase detection ER compared to CT simulation alone and improve risk stratification. Patients with ER are at high risk of locoregional failure, distant metastases, and mortality, despite salvage therapy. A prospective

Impact of a second FDG PET scan before adjuvant



The present findings support the clinical value of pre-RT/CCRT FDG PET for defining treatment strategy in OSCC patients with both ECS and high nodal SUV, even when FDG PET had already been performed during the initial staging work-up.



- Plan: In view of early recurrence, to plan for palliative Chemotherapy
- Continue RT till 50Gy/25# equivalent

- ? Systemic Therapy: OMCT/ Chemotherapy/ Immunotherapy

Indications for the use of Induction Chemotherapy

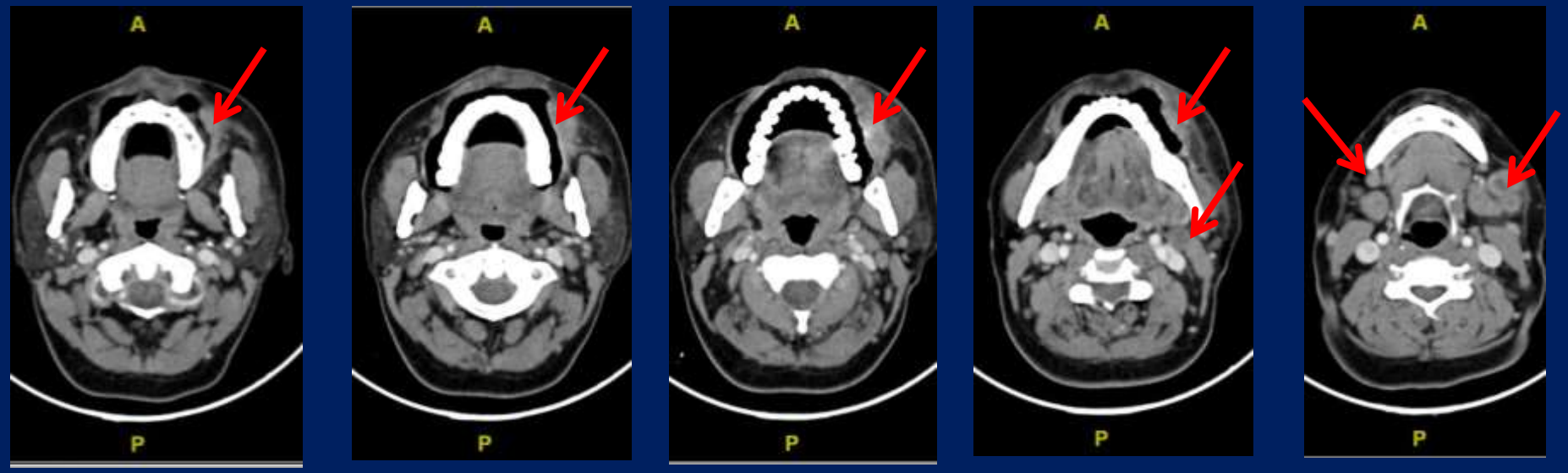
- Organ preservation/ Induction CT in resectable Advanced OCSCC:
  - Preserve the mandible/ organ without compromising the disease related outcomes
- Tiding over time/ beating the waiting list:
  - Prevent disease progression
  - Prevention metastases
- Borderline resectable/ Technically unresectable:
  - Improve the resectability, achieve R0 resections
  - Improve disease related outcomes

Case No 4

- 43 year old lady from Bangladesh. No comorbidities
- Pan chewer for 20 yrs reformed 6 months back.
- H/o hip replacement surgery in 2017 (Details N/A)
- P/w/c/o **non healing ulcer in Lt BM** since July 2023
- Bx at Bangladesh: **MD SCC**
- Came to TMH for further evaluation
- Baseline exam: MO: 2cm. **UPG on Lt BM, 3x3 cm, from AOM till 1cm Short of RMT, involving Lt lower GBS. Overlying skin not pinchable.** Clinically edema reaching upto zygoma
- **Lt level IB LN, hard, fixed 2.5x2 cm**
- Block review at TMH**: MD SCC**

CECT HN + thorax (31.8.23)

- 5.2 x 1.4 x 3.7 cm growth seen in the Lt BM, involving upper and lower GBS. Overlying skin involved. No bony erosion.
- Metastatic left level IB/II LN with ENE. Rt IB LN is suspicious.
- No distant mets.



Clinicoradiologic impression: **MD SCC Lt BM, cT4a cN2b cM0**

Any other evaluation?

Plan of care:
Surgeons

Medical Oncologist

Radiation Oncologist

If Induction: Reasons, schedule, drugs

Assessment post Induction

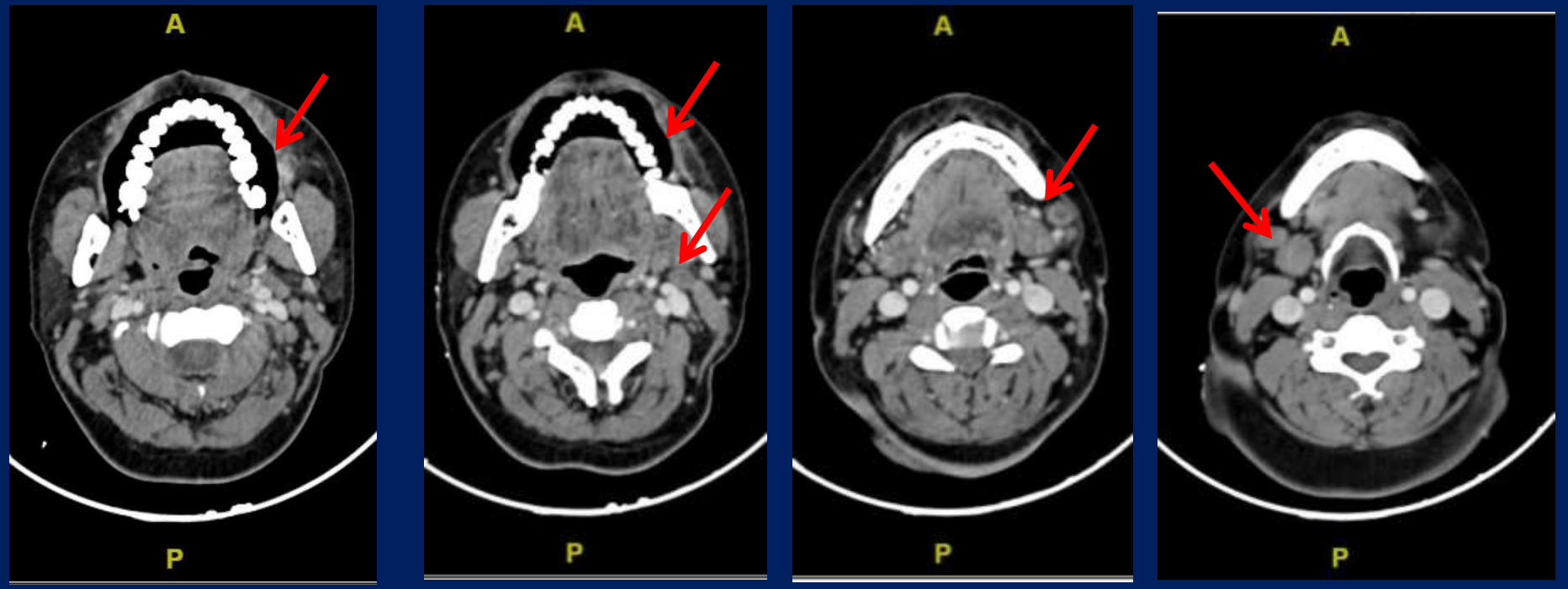
- Plan: NACT f/b reassessment for local treatment
- Received **3 cycles of 3 weekly Paclitaxel + Carboplatin + OMCT** from 11.9.23 to 26.10.23.

Response assessment?

Intent?

Response assessment CECT post C2 (19.10.23)

- Decrease in size of Lt BM lesion and metastatic neck nodes.



Surgery: Volumes, Margins?

- U/w Lt BCR + WLE of tongue lesion + B/L MRND I-V + Free flap (Lt parascapular flap with scapular bone) reconstruction on **5.12.23.**
- Intraop- Rt lateral border tongue 1 x 1 cm indurated lesion present.

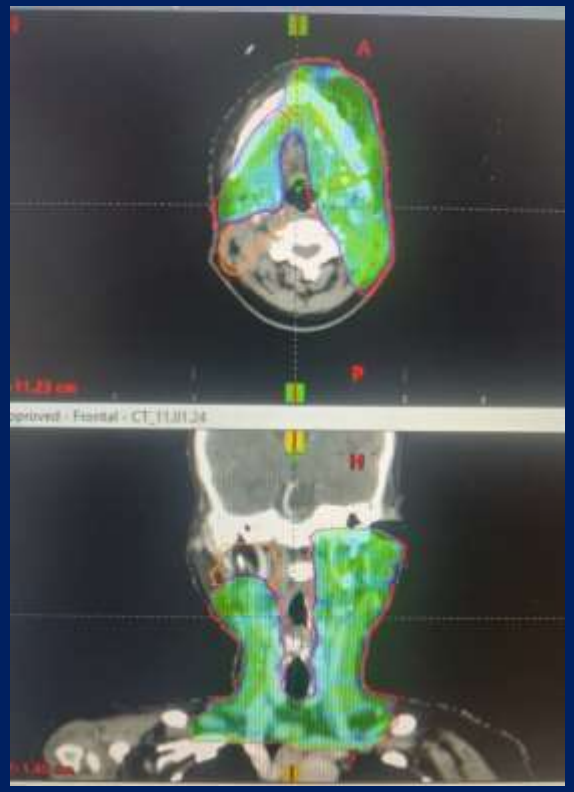
- HPR: Lt BCR- No residual viable tumor; tongue- hyperplastic squamous mucosa
- Lt ND- 6/32 (IB- 3/4, ENE+; IIA- 2/6, ENE+; III-1/5, No ENE)
- Rt ND- 2/29, No ENE (IB- 1/3, IV-1/4)
- IMP: **MDSCC Lt BM, ypT0 ypN3b**

- **What next?:**

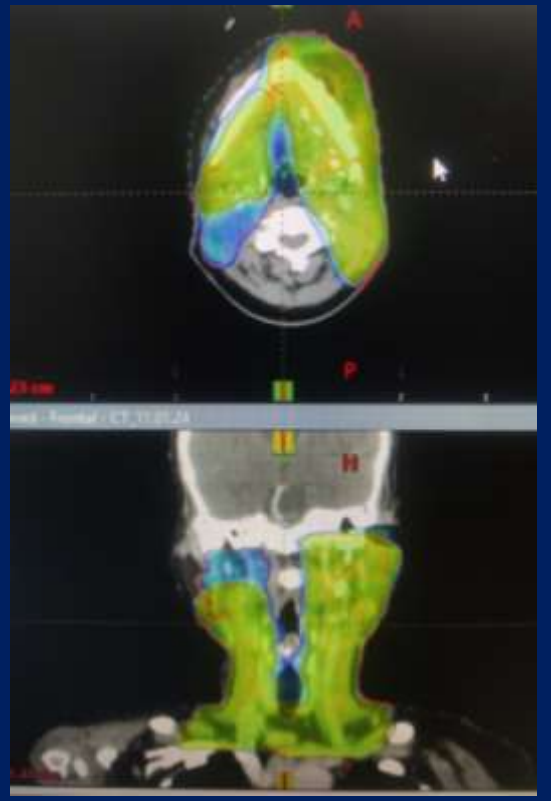
- Plan: **Adjuvant CTRT i/v/o residual disease in multiple neck nodes; ENE+**

RT planning: Volumes, doses?

HR-CTV	Tumor bed + Lt IB-IV, Lt VIIB,Rt IB, Rt III-IV	60Gy/30#
LR-CTV	Rt level II	54Gy/30#



95% dose wash of 60Gy



95% dose wash of 54Gy

Primary Chemotherapy in Resectable Oral Cavity Squamous Cell Cancer: A Randomized Controlled Trial

2003

By Lisa Licitra, Cesare Grandi, Marco Guzzo, Luigi Mariani, Salvatore Lo Vullo, Francesca Valvo, Pasquale Quattrone, Pinuccia Valagussa, Gianni Bonadonna, Roberto Molinari, and Giulio Cantù

VOLUME 31 · NUMBER 6 · FEBRUARY 20 2013

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Randomized Phase III Trial of Induction Chemotherapy With Docetaxel, Cisplatin, and Fluorouracil Followed by Surgery Versus Up-Front Surgery in Locally Advanced Resectable Oral Squamous Cell Carcinoma

Lai-ping Zhong, Chen-ping Zhang, Guo-xin Ren, Wei Guo, William N. William Jr, Jian Sun, Han-guang Zhu, Wen-yong Tu, Jiang Li, Yi-li Cai, Li-zhen Wang, Xin-dong Fan, Zhong-he Wang, Yong-jie Hu, Tong Ji, Wen-jun Yang, Wei-min Ye, Jun Li, Yue He, Yan-an Wang, Li-qun Xu, Bo-song Wang, Merrill S. Kies, J. Jack Lee, Jeffrey N. Myers, and Zhi-yuan Zhang

Prospective Phase II Open-Label Randomized Controlled Trial to Compare Mandibular Preservation in Upfront Surgery With Neoadjuvant Chemotherapy Followed by Surgery in Operable Oral Cavity Cancer

2021

Devendra Chaukar, MBBS, MS[1]; Kumar Prabash, MD, DM[2]; Pawan Rane, MS[3]; Vijay Maruti Patil, MD, DM[2]; Shivakumar Thiagarajan, MS[1]; Sarbani Ghosh-Laskar, MD[4,5]; Shilpi Sharma, MS, MCh[6]; Prathamesh S. Pai, MS[1]; Pankaj Chaturvedi, MS[1]; Gouri Pantvaidya, MS[1]; Anuja Deshmukh, MS, MCh[1]; Deepa Nair, MS[1]; Sudhir Nair, MS, MCh[1]; Richa Vaish, MS, MCh[1]; Vanita Noronha, MD[2]; Asawari Patil, MD[5]; Supreeta Arya, MD[7]; and Anil D'Cruz, MS[8]

- Of the 3 studies: the indications for adjuvant RT were different:
- Only for high risk features, warranting Adj RT only
- For traditional adverse features (not specified whether based on pre-op features or post-op HPR) No concurrent CTRT
- All received adjuvant CTRT except those with pCR
- Timing: Same
- Dose: Different
- Volumes: Similar

Tiding over time/ beating the waiting list

ecancermedicalscience

Oral metronomic chemotherapy as a feasible preoperative therapy in advanced resectable oral cavity squamous cell carcinomas—a preliminary experience

V P Praveen Kumar Shenoy[1], Avaronnan Manuprasad[1], Sajith Babu[2,3], Sithara Aravind[4], Vinin N Narayanan[5], Sangeetha Nayanar[4] and Satheesan Balasubramanian[2]

Preoperative Chemotherapy and Metronomic Scheduling of Chemotherapy in Locally Advanced Oral Cancers

Vijay M Patil [1], Vanita Noronha, Amit Joshi, Sripad D Banavali, Vamshi Muddu, Kumar Prabhash

Describe the safety and feasibility of OMCT in the waiting period to surgery

The indications for adjuvant therapy are ‘standard’

Randomised Controlled Trial Oral Metronomic Chemotherapy to Standard Surgery and Adjuvant Therapy in Stage III/IV Operable Oral Cancers

CTRI/2015/01/005405

Head & Neck DMG. TMH

Design: Prospective, Open Labelled, Two Arm, Randomised Controlled Trial

Standard Arm	Interventional Arm
Surgery followed by Appropriate adjuvant radiation / chemoradiation	Oral Metronomic chemotherapy Induction phase- 4 weeks prior to surgery Intermediate phase- 2 weeks after surgery till adjuvant RT begins Maintenance phase- 2 weeks after completion of RT for 12 months

Primary end point

Disease Free Survival

Sample Size = 400

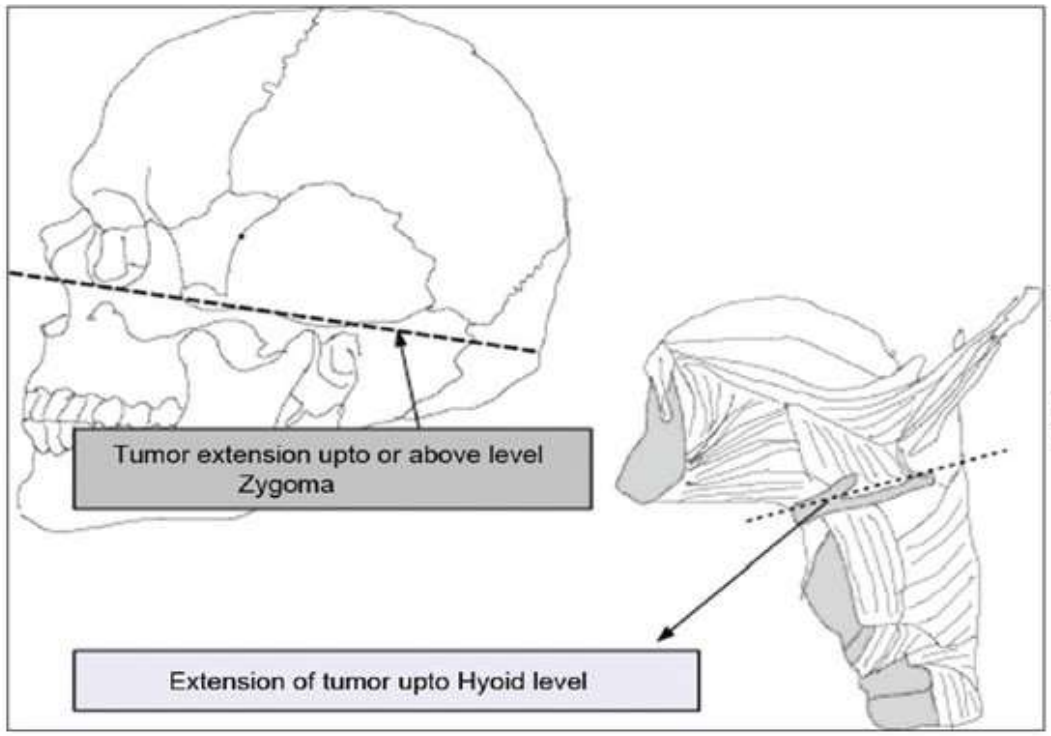
Secondary endpoints

- Toxicity – Acute & Late
- Quality of life

Aug 2013 – Accrual Completed, FU Ongoing

Courtesy: PS Pai, PI

Borderline Resectable/ Technically Unresectable



Tongue tumor involving Vallecula

BM tumor involving high ITF

Patil et al.Indian J Cancer. 2014 Apr-Jun;51(2):100-3.
Patil et al .Oral Oncology 50 (2014) 1000–1004

Neoadjuvant chemotherapy followed by surgery in very locally advanced technically unresectable oral cavity cancers

V.M. Patil [a], K. Prabhash [a,*], V. Noronha [a], A. Joshi [a], V. Muddu [a], S. Dhumal [a], S. Arya [b], S. Juvekar [b], P. Chaturvedi [d], D. Chaukar [d], P. Pai [d], S. Kane [e], A. Patil [e], J.P. Agarwal [c], S. Ghosh-Lashkar [c], A. Dcruz [d]

All patients with technically unresectable oral cancers were assessed in a multidisciplinary clinic and received 2 cycles of NACT.

After 2 cycles, patients were reassessed and planned for either surgery with subsequent CTRT or nonsurgical therapy including CT-RT, RT or palliation.

Results: 721 patients with stage IV oral-cavity cancer received NACT. 310 patients (43%) had sufficient reduction in tumour size and underwent surgical resection.
Adjuvant Chemoradiation was planned for most patients who underwent surgery, only 66.3% could complete the same.

Long-term outcomes of neo-adjuvant chemotherapy on borderline resectable oral cavity cancers: Real-world data of 3266 patients and implications for clinical practice

Oral Oncology 148 (2024) 106633

Vanita Noronha [a,1], Aditya Dhanawat [a,1], Vijay Maruti Patil [a,1], Nandini Menon [a], Ajay Kumar Singh [a], Pankaj Chaturvedi [b], Prathamesh Pai [b], Devendra Chaukar [b], Sarbani Ghosh Laskar [c], Kumar Prabhash [a,*]

Most patients who underwent surgery received concurrent chemoradiation except for those who achieved pCR

Issues post Induction/ Ne-adjuvant Chemotherapy in Advanced Disease……..

- Avoiding radiotherapy in a patient with an SCC of the oral cavity with a clinical stage of cT2N1M0 (UICC TNM) that downstages to ypT2N0 post-chemotherapy and surgery is unclear.
- Clinically evident extranodal extension (ENE) at the baseline may show up as negative ENE in the

Adoption of chemoradiotherapy for all doubtful cases might result in overtreatment, increased toxicities, and wastage of resources.

- The number of nodes resected, a mismatch between node positivity on clinico-radiological correlation versus the resection specimen (pathological ypN0 for any clinically evident nodal disease
- The size of the tumour after NACT and its extensions
- The pathological status of the cut margins

Are the classical indications of postoperative chemoradiotherapy in head and neck squamous cell cancers valid in the era of neoadjuvant chemotherapy?

What we know from evidence:

- There is a definite role of NACT/ Induction chemotherapy in some locally advanced OCSCC
- Response to chemotherapy is the most robust indicator of outcome
- Patients who can undergo surgery after chemotherapy have the best outcomes

What we do not know:

- Patients who will respond to chemotherapy
- Optimal adjuvant therapy post surgery after Induction/ NACT

Factors to consider when deciding on adjuvant therapy:

- Primary: Size, DoI
- Other adverse features: PNI, LVE, WPOI, C/M status

- Node: Number, levels, ENE

- Patient: Tolerance

- Counselling

- Volumes, Doses, Total package time

THANK YOU
????