



# Controversial Issues In Managing Locally Advanced Head And Neck Cancer 'Oral Cavity Cancer'

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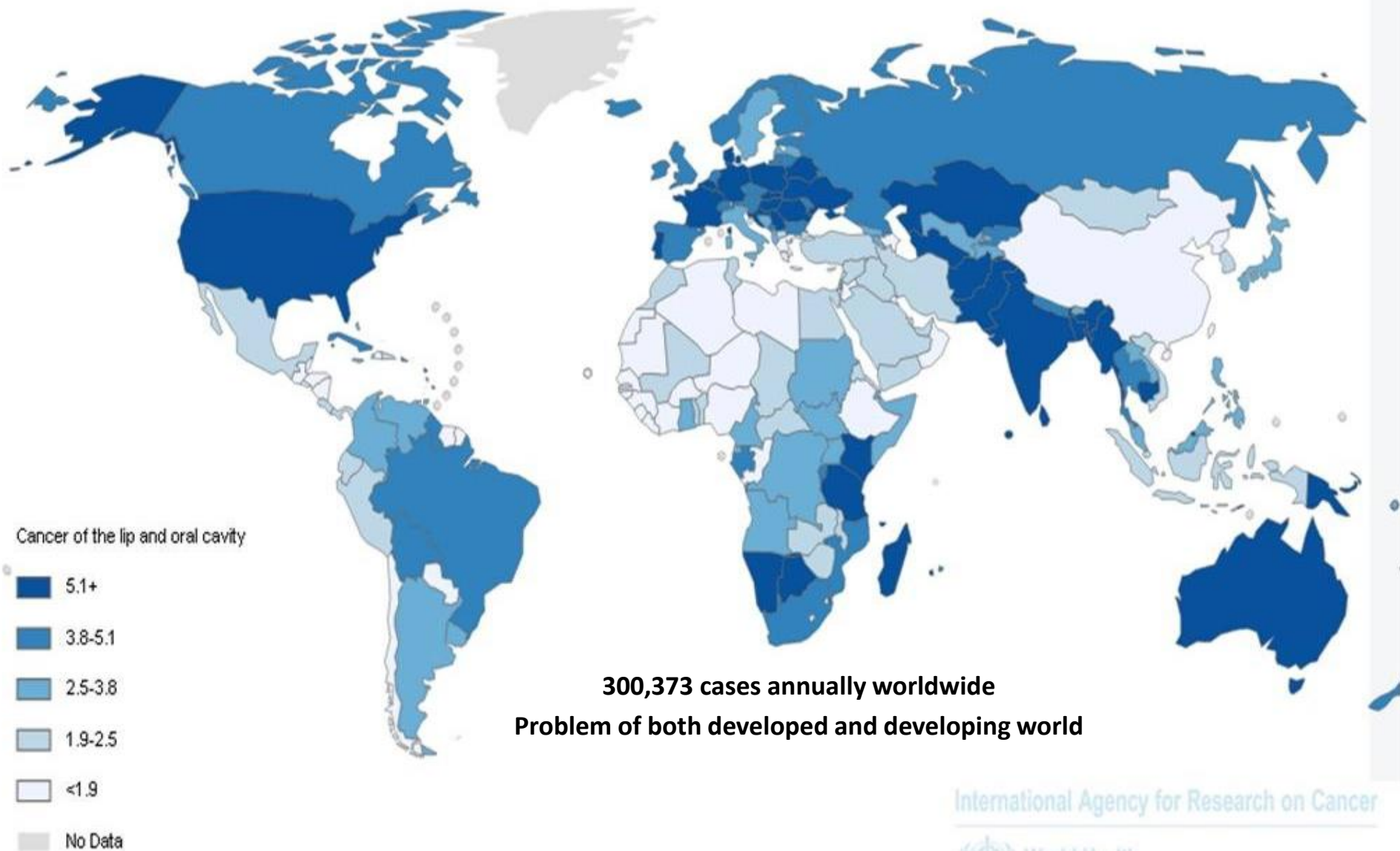
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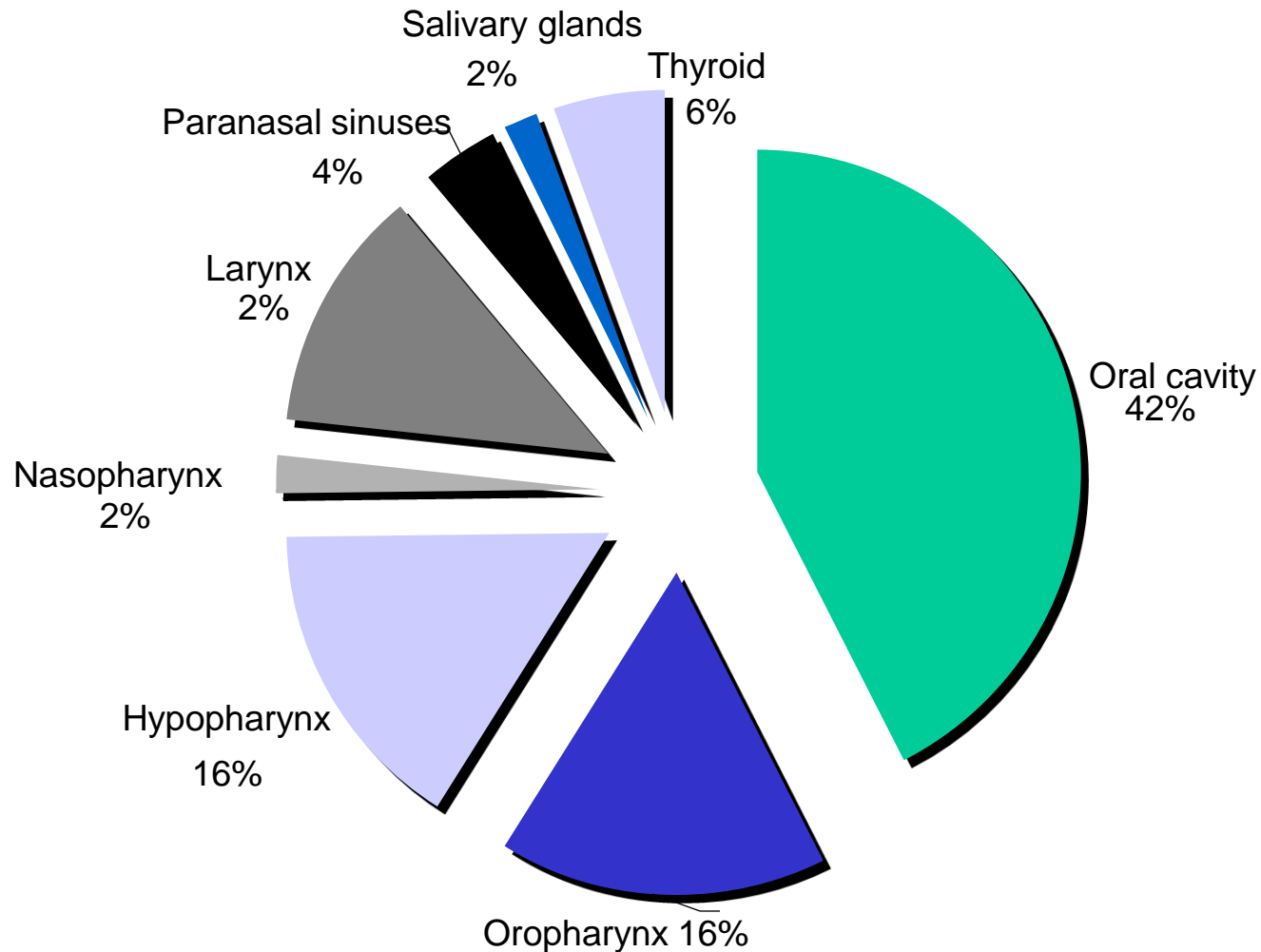
# Disclosure slide

Nothing to declare

# Oral Cancers- A Global Problem



# Hospital Registry Data 2013 -9000 cases



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# HPV DNA, E6/E7 mRNA, and p16<sup>INK4a</sup> detection in head and neck cancers: a systematic review and meta-analysis



*Cathy Ndiaye\*, Marisa Mena\*, Laia Alemany, Marc Arbyn, Xavier Castellsagué, Louise Laporte, F Xavier Bosch, Silvia de Sanjosé, Helen Trottier*

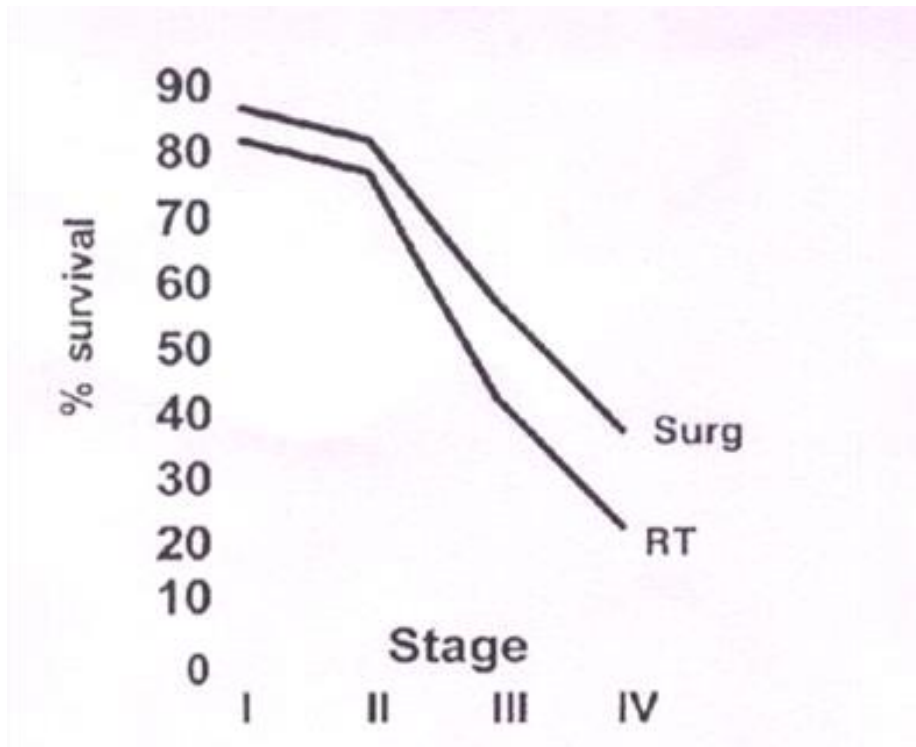
- Studies that used PCR for detection of HPV DNA > 20 biopsies between 1990-2012
- 148 studies with 12163 patients 44 countries
- Where data not present authors contacted
- Pooled HPV DNA prevalence estimates were
  - 45.8% for oropharynx ( tonsil highest 53. 9 % CI 95% )
  - 22.1% for larynx (including hypopharynx)
  - 24.2% for oral cavity

# HPV and Oral Cancer

## International Cancer Genomic Consortium

- 23 % at Tatas for Oral Cancers ( ICGC Project)
- High risk HPV Types 16,18 and 31
- Only one patient with no habits

# Management Locally Advanced Oral Cancers



**Combined Modality Therapy**

**Surgery + RT / CT-RT**

# T4a – Inoperability ?



T4a – Moderately advanced local disease

Tumor invades adjacent structures

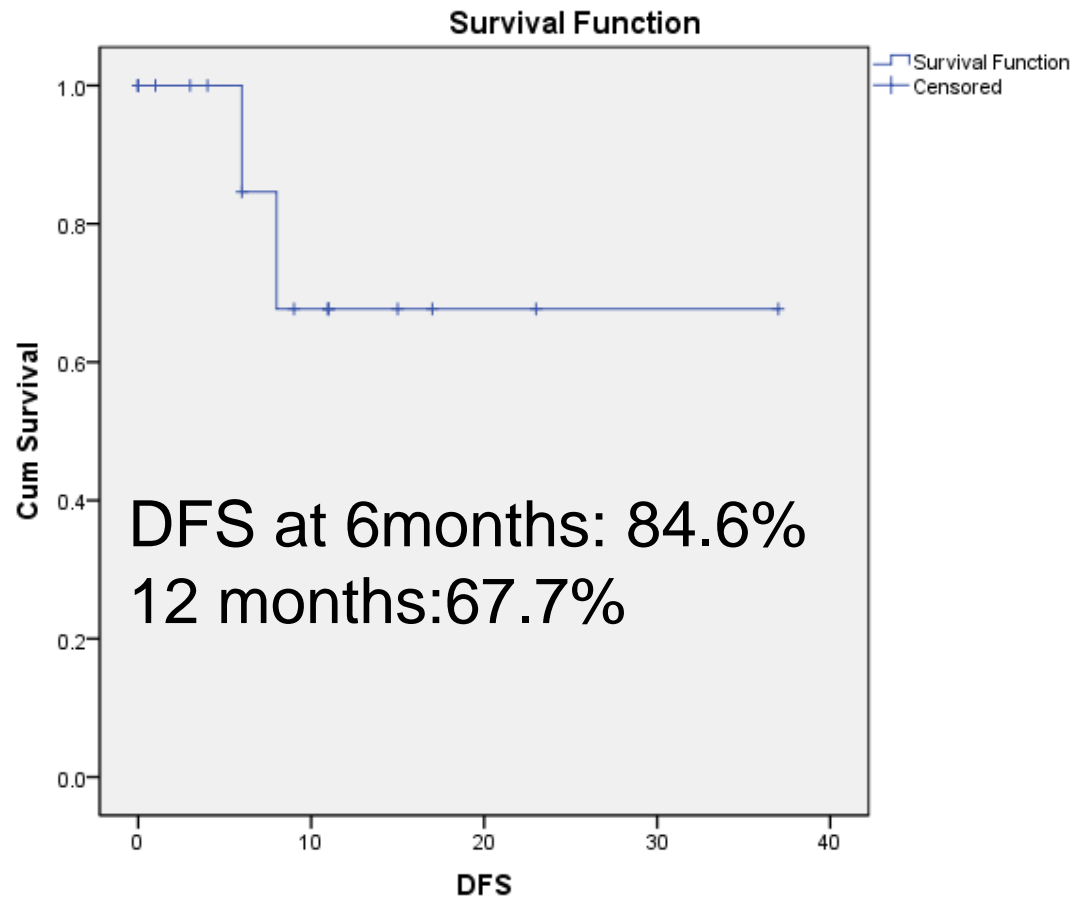
Tongue: Deep muscles (extrinsic)

Buccal Mucosa: Cortical bone, floor of mouth, Skin involvement



# Is this surgery worth it ?

## Survival analysis 45 cases over 2 years



# Locally advanced Oral cancers!

## Selection of patients

- Surgeon must be reasonably certain of negative margins
- Good Reconstruction should be feasible to ensure a good QOL
- Biologically favourable tumours

# Managing the T<sub>6</sub> Cancer!

## Biological Criteria

- Skin – no dermal nodules/ lymphedema
- Grade / Aggressive histology
- Neck nodes – bulky nodes ( PET Scan)
- Should be suitable for adjuvant treatment



## T4b oral cavity cancer below the mandibular notch is resectable with a favorable outcome

Chun-Ta Liao <sup>a,j</sup>, Shu-Hang Ng <sup>b,j</sup>, Joseph Tung-Chieh Chang <sup>c,j</sup>,  
Hung-Ming Wang <sup>d,j</sup>, Chuen Hsueh <sup>e,j</sup>, Li-Yu Lee <sup>e,j</sup>, Chung-Kan Tsao <sup>f,j</sup>,  
Wen-Ho Chen <sup>g,j</sup>, I-How Chen <sup>a,j</sup>, Chung-Jan Kang <sup>a,j</sup>,  
Shiang-Fu Huang <sup>a,j</sup>, Tzu-Chen Yen <sup>h,i,j,\*</sup>

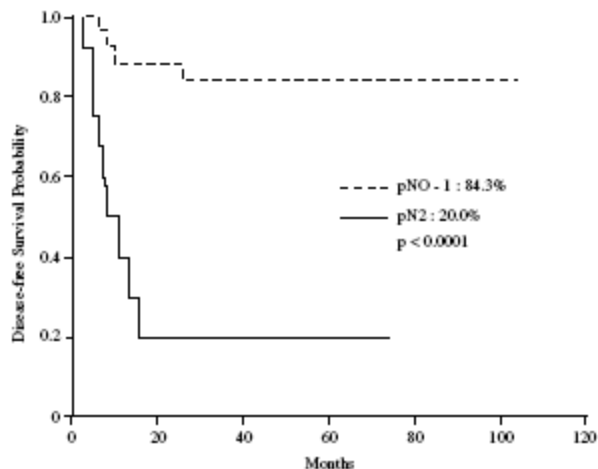
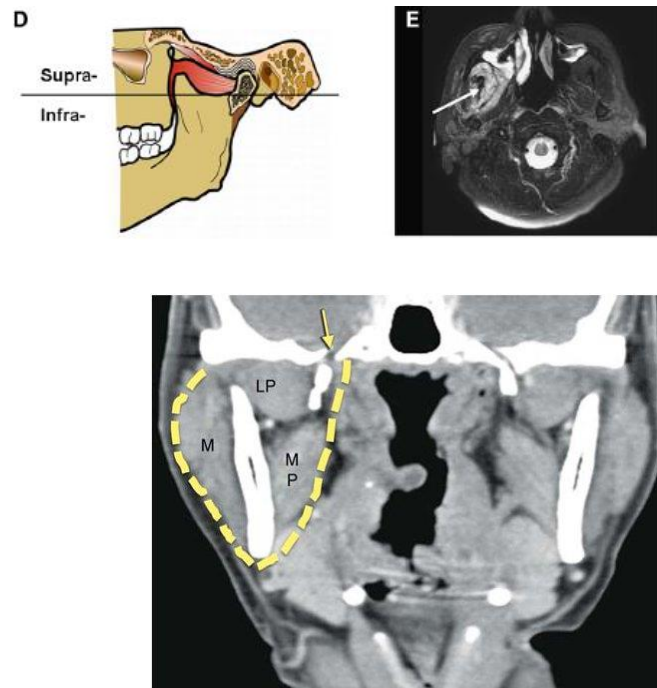


Figure 3 Disease-free survivals of infra-notch patients (pN0-1 vs. pN2).



T4b- Very Advanced Local disease

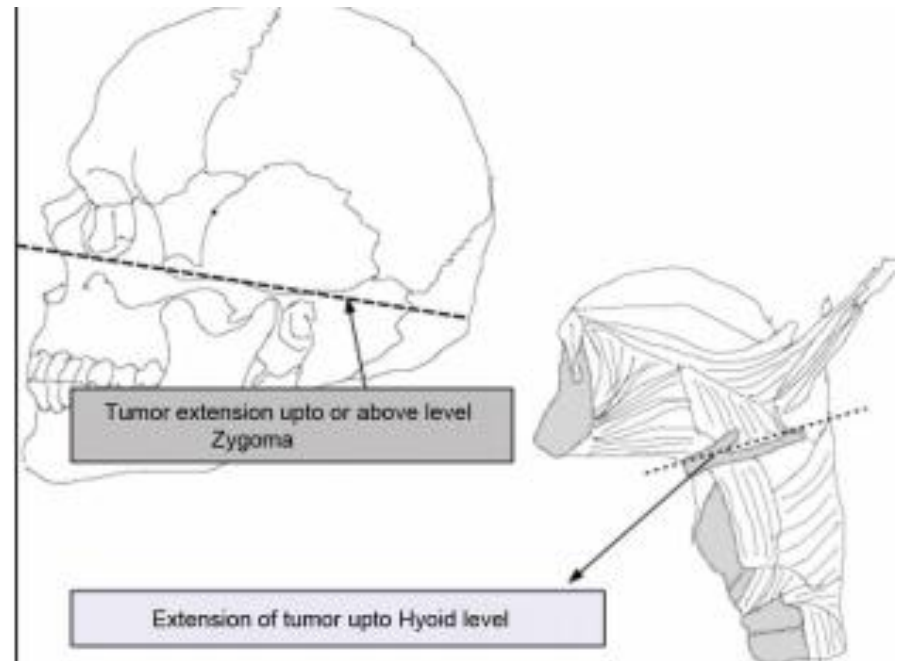
Involves: Masticator space, skull base, pterygoid plates, encasing Internal carotid.

# Chemotherapy Oral Cancers – RCTS

## Neoadjuvant Chemotherapy

Study	Year	Drugs	Arms	Number	End Point	Benefits
Licitra	2003	PF	Sx vs CT-Sx {±Adj}	195	OS: NS	Lesser mandibular resection (52% vs 31%) Lesser RT (46% vs 33%)
Zhong	2013	TPF	Sx+RT vs CT-Sx+ RT	256	OS: NS DFS: NS	Excellent response to CT ≤10% viable cells: superior OS
Zorat	2004	TP	CT-Sx+RT vs RT	237	OS: NS	Improves OS in inoperable cases

# Borderline Operable



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

Patil VM<sup>1</sup>, Prabhash K<sup>2</sup>, Noronha V<sup>1</sup>, Joshi A<sup>1</sup>, Muddu V<sup>1</sup>, Dhumal S<sup>1</sup>, Arya S<sup>3</sup>, Juvekar S<sup>3</sup>, Chaturvedi P<sup>4</sup>, Chaukar D<sup>4</sup>, Pai P<sup>4</sup>, Kane S<sup>5</sup>, Patil A<sup>5</sup>, Agarwal JP<sup>6</sup>, Ghosh-Lashkar S<sup>6</sup>, Dcruz A<sup>4</sup>.

Review of 721 Stage IV cancers.

Selection criteria for NACT:

Reason	Percentage
Peritumoural edema to zygoma	484 (67.1%)
Peritumoural edema to hyoid	91 (12.6%)
Extention into vallecula	48(6.7%)
Extention into high ITF	43(6%)
Extensive skin infiltration	55(7.6%)

2 drug (89.8%) /3 drug regimen

43% (310) patients had size reduction and were suitable for surgery

Of the others:

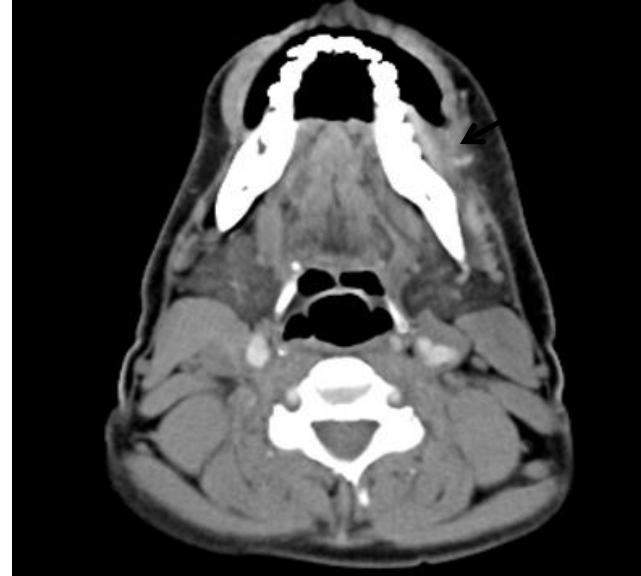
167 received CRT, 3 radical RT and 241 palliative treatment alone.

<b>Pathological details of resected specimen (n=294)</b>	
<b>Margins</b>	<b>&gt;5mm:269(97.04%) &lt;5mm:25(2.96%)</b>
<b>pT</b>	<b>No tumour:9(3.06%) Median reduction in size :50%(10-100%)</b>
<b>LN positivity</b>	<b>144(49%)</b>

# Survival

- DFS at 24 months:
  - 32% for NACT followed by Surgery, 15% for those undergoing non surgical treatment (p value 0.0001)
- Median O.S:
  - 19.6 months in surgery group and 8.16 months in non surgical treatment group ( p value 0.0001)
  - 24 months survival rate for operated patients was 45 %

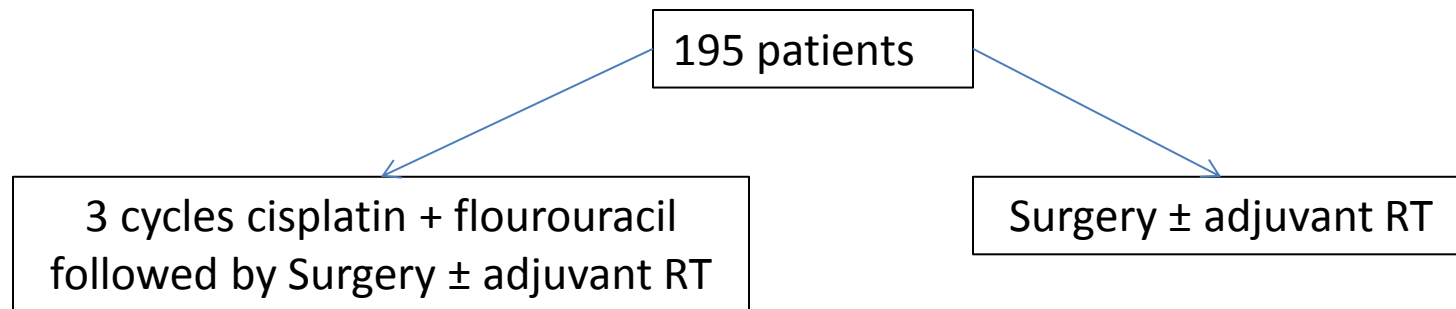
# Advanced Oral Cancer Organ Preservation



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

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  
*J Clin Oncol* 21:327-333.

- Randomized multicentric trial
- Resectable T2-4, N0-2, M0 SCC oral cavity



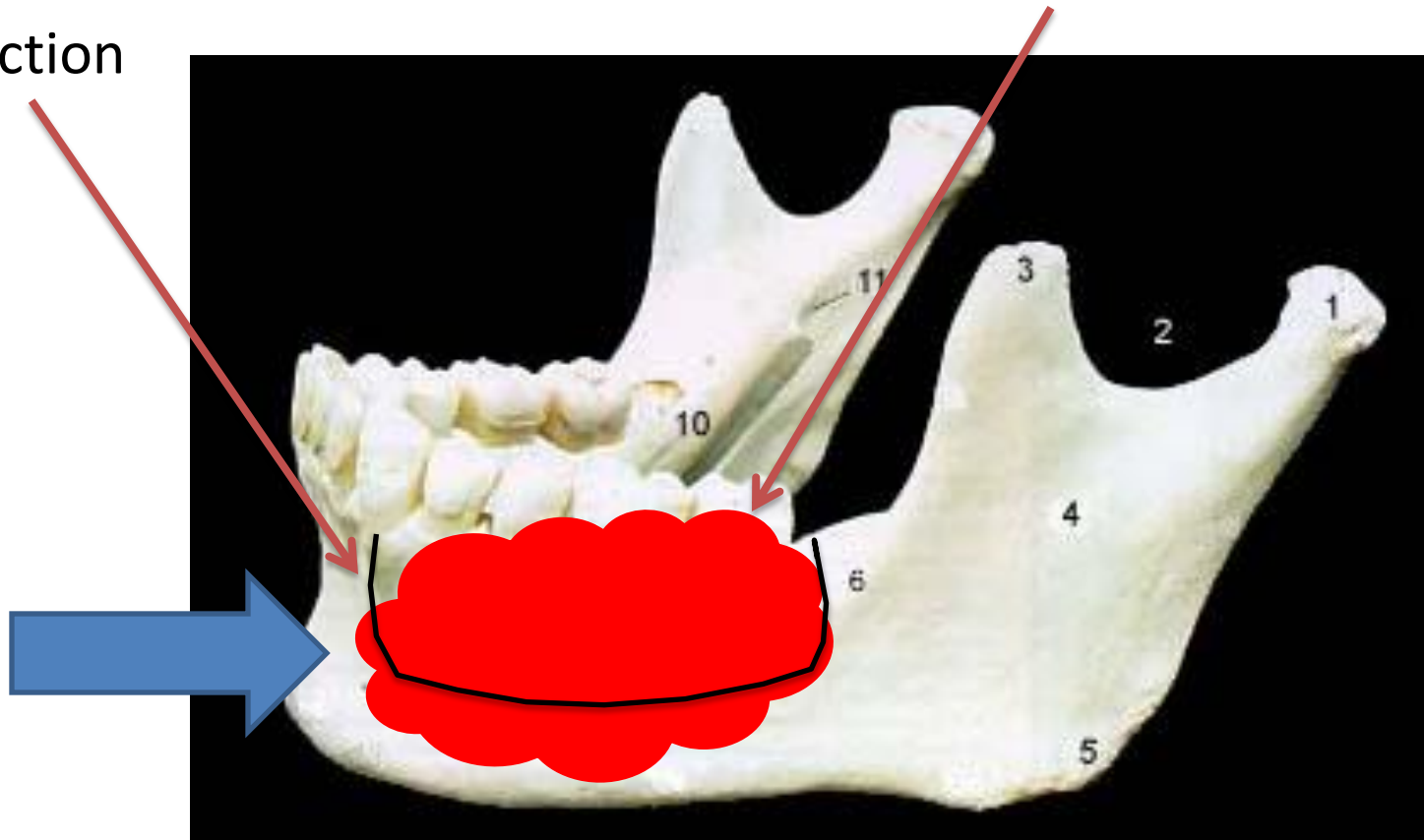
- 5 year survival rate was 55% in both the arms
- 3 toxic deaths in Arm A
- Postoperative RT: 33% in chemotherapy arm versus 46% in control arm
- Mandibular resection: 31% chemotherapy arm versus 52% in control arm

Cisplatin 100mg/m<sup>2</sup> + 5FU 1000mg/m<sup>2</sup> every 21 days

Paramandibular disease  
Requiring segmental resection

Reduced tumor size enables  
marginal resection

**NACT**



# Pre & Post NACT (External)



# Trial Design

Randomization

Standard Arm

Intervention Arm

Segmental Mandibulectomy  
+  
Appropriate  
Adjuvant RT/ CTRT

NACT (2 Cycles)

T - Docetaxel – 75mg/m<sup>2</sup> – Day -1  
P - Cisplatin – 75mg/m<sup>2</sup> – Day -1  
F - 5 FU – 750mg/m<sup>2</sup> – day 1-5

Reassess

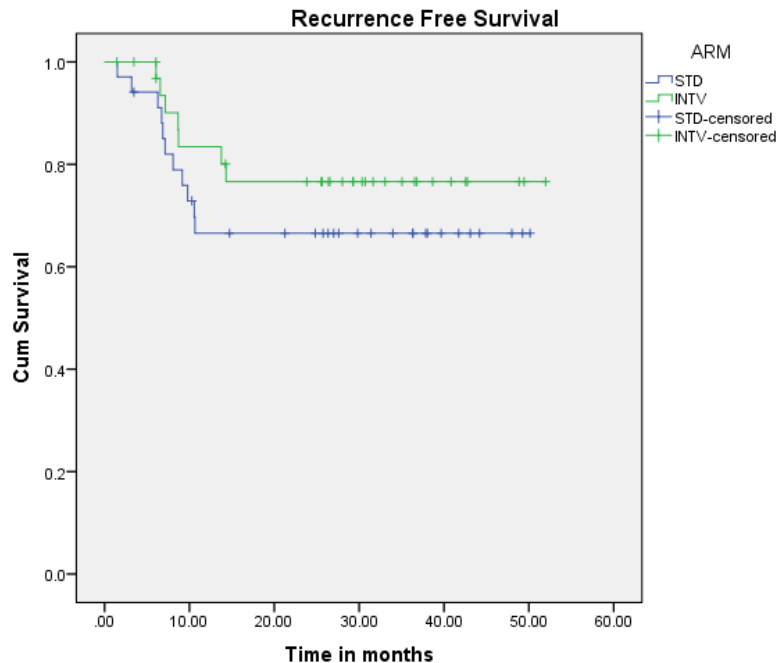
Surgery  
+  
Adjuvant CTRT

# Demography

	Standard Arm number (%)	Intervention Arm number (%)
<b>Gender</b>		
Male	29 (85%)	33 (97%)
Female	5 (15%)	1 (3%)
<b>Site</b>		
Bucco-alveolar complex	32 (94%)	32 (94%)
Tongue +FOM	2 (6%)	2 (6%)
<b>Clinical T stage</b>		
T2	9 (26%)	5 (15%)
T3	6 (18%)	8 (23%)
T4	19 (56%)	21 (62%)
<b>Clinical N stage</b>		
N0	19 (56%)	11 (32%)
N1	10 (29%)	12 (35%)
N2b	4 (12%)	9 (27%)
N2c	1 (3%)	2 (6%)

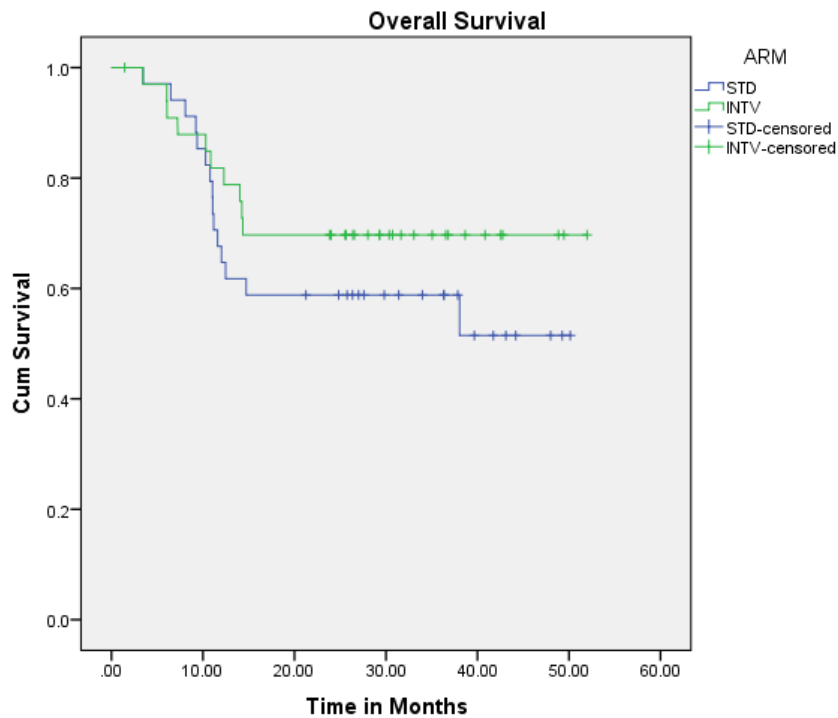
# Disease Free Survival

Median Follow up Period - 26.5 Months ( 1.5-52 months)



Arm	Mean (Months)	At 24 Months	p value (Log Rank Test)
Standard	35.81	66.5 %	0.39
Intervention	40.01	76.6 %	

# Overall Survival



Arm	Mean (Months)	At 24 Months	p value (Log Rank Test)
Standard	37.22	58.8 %	0.27
Intervention	39.22	69.7 %	

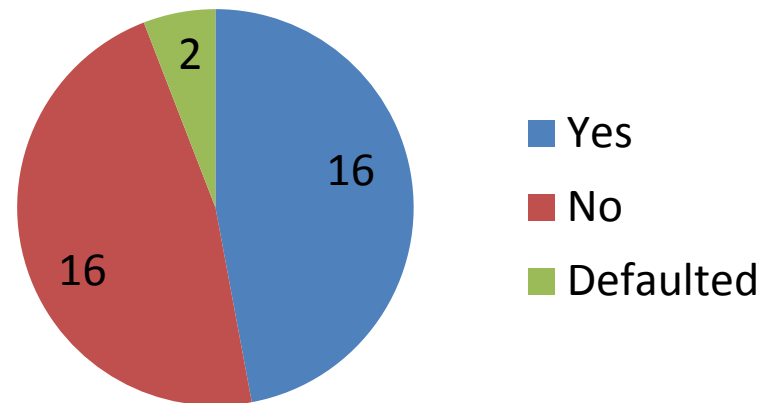
# Mandible Preservation

- Standard arm – Nil

- Intervention Arm

48 % ( 16 / 34 )

**Mandible Preservation**



# Oral Cancers Conclusions

- Global problem
- Role of HPV undefined
- Surgery main stay of treatment – Some changes in staging required
- Chemotherapy may play some role

Thank You