Controversial Issues In Managing Locally Advanced Head And Neck Cancer ‘Oral Cavity Cancer’

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Disclosure slide

Nothing to declare
Oral Cancers - A Global Problem

300,373 cases annually worldwide
Problem of both developed and developing world
Hospital Registry Data 2013 - 9000 cases

Oral cavity 42%
- Oropharynx 16%
- Hypopharynx 16%
- Nasopharynx 2%
- Larynx 2%
- Paranasal sinuses 4%
- Salivary glands 2%
- Thyroid 6%
• 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

DFS at 6 months: 84.6%
12 months: 67.7%
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 T₆ 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, Shu-Hang Ng, Joseph Tung-Chieh Chang, Hung-Ming Wang, Chuen Hsueh, Li-Yu Lee, Chung-Kan Tsao, Wen-Ho Chen, I-How Chen, Chung-Jan Kang, Shiang-Fu Huang, Tzu-Chen Yen

T4b- Very Advanced Local disease
Involves: Masticator space, skull base, pterygoid plates, encasing Internal carotid.
## Neoadjuvant Chemotherapy

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Drugs</th>
<th>Arms</th>
<th>Number</th>
<th>End Point</th>
<th>Benefits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Licitra</td>
<td>2003</td>
<td>PF</td>
<td>Sx vs CT-Sx {±Adj}</td>
<td>195</td>
<td>OS: NS</td>
<td>Lesser mandibular resection (52% vs 31%) Lesser RT (46% vs 33%)</td>
</tr>
<tr>
<td>Zhong</td>
<td>2013</td>
<td>TPF</td>
<td>Sx+RT vs CT-Sx+ RT</td>
<td>256</td>
<td>OS: NS DFS: NS</td>
<td>Excellent response to CT ≤10% viable cells: superior OS</td>
</tr>
<tr>
<td>Zorat</td>
<td>2004</td>
<td>TP</td>
<td>CT-Sx+RT vs RT</td>
<td>237</td>
<td>OS: NS</td>
<td>Improves OS in inoperable cases</td>
</tr>
</tbody>
</table>
Borderline Operable
Neoadjuvant chemotherapy followed by surgery in very locally advanced technically unresectable oral cavity cancers.

Patil VM¹, Prabhakar K², Noronha V¹, Joshi A¹, Muddu V¹, Dhimal S¹, Arya S³, Juvekar S³, Chaturvedi P⁴, Chaukar D⁴, Pai P⁴, Kane S⁵, Patil A⁵, Agarwal JP⁶, Ghosh-Lashkar S⁶, Dcruz A⁴.

Review of 721 Stage IV cancers.

Selection criteria for NACT:

<table>
<thead>
<tr>
<th>Reason</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peritumoural edema to zygoma</td>
<td>484 (67.1%)</td>
</tr>
<tr>
<td>Peritumoural edema to hyoid</td>
<td>91 (12.6%)</td>
</tr>
<tr>
<td>Extention into valleculla</td>
<td>48 (6.7%)</td>
</tr>
<tr>
<td>Extention into high ITF</td>
<td>43 (6%)</td>
</tr>
<tr>
<td>Extensive skin infiltration</td>
<td>55 (7.6%)</td>
</tr>
</tbody>
</table>
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.

<table>
<thead>
<tr>
<th>Pathological details of resected specimen (n=294)</th>
<th></th>
</tr>
</thead>
</table>
| Margins                                         | >5mm:269(97.04%)  
|                                                  | <5mm:25(2.96%)   |
| pT                                              | No tumour:9(3.06%)  
|                                                  | Median reduction in size :50%(10-100%) |
| LN positivity                                   | 144(49%)  |
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

- Gross Paramandibular Disease
- No Bone Erosion
- Requires Bone Resection
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


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

195 patients

- 3 cycles cisplatin + fluorouracil followed by Surgery ± adjuvant RT
- Surgery ± adjuvant RT

• 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/m² + 5FU 1000mg/m² every 21 days
Paramandibular disease
Requiring segmental resection

Reduced tumor size enables marginal resection

NACT
Pre & Post NACT (External)
Trial Design

Randomization

Standard Arm

Segmental Mandibulectomy
+
Appropriate Adjuvant RT/ CTRT

Intervention Arm

NACT (2 Cycles)
T - Docetaxel – 75mg/m2 – Day -1
P - Cisplatin – 75mg/m2 – Day -1
F - 5 FU – 750mg/m2 – day 1-5

Reassess

Surgery
+
Adjuvant CTRT
## Demography

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

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

<table>
<thead>
<tr>
<th>Arm</th>
<th>Mean (Months)</th>
<th>At 24 Months</th>
<th>p value (Log Rank Test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard</td>
<td>35.81</td>
<td>66.5 %</td>
<td>0.39</td>
</tr>
<tr>
<td>Intervention</td>
<td>40.01</td>
<td>76.6 %</td>
<td></td>
</tr>
</tbody>
</table>

![Graph showing recurrence free survival](image-url)
Overall Survival

<table>
<thead>
<tr>
<th>Arm</th>
<th>Mean (Months)</th>
<th>At 24 Months</th>
<th>p value (Log Rank Test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard</td>
<td>37.22</td>
<td>58.8 %</td>
<td></td>
</tr>
<tr>
<td>Intervention</td>
<td>39.22</td>
<td>69.7 %</td>
<td>0.27</td>
</tr>
</tbody>
</table>
Mandible Preservation

• Standard arm – Nil

• Intervention Arm

48% (16/34)
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