What is the role of induction chemotherapy in locally advanced H&N cancer in 2013?

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## Disclosures

<table>
<thead>
<tr>
<th>Categories</th>
<th>Companies</th>
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</thead>
<tbody>
<tr>
<td>Grants to participate in scientific meetings or advisory boards</td>
<td>Boehringer Ingelheim, Novartis, Eurofarma, Merck Serono</td>
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<td>Investigator of sponsored clinical studies</td>
<td>Amgen, Eurofarma, Boehringer Ingelheim</td>
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<tr>
<td>Lectures</td>
<td>Merck Serono, Eurofarma</td>
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</tbody>
</table>
HNSCC 2013

- 333,400 deaths/year worldwide
- 7% of all cancer pts (3rd)

- Incidence and mortality are higher in developing countries
  - Tobacco and alcohol exposure
  - HPV infection
  - Most pts are diagnosed in advanced stages

Locally advanced HNSCC - Tx options

- Radical surgery
- Radiation therapy
  - Hyperfractionation
- Concurrent chemoradiation
  - Cisplatin-based
- Neoadjuvant (induction) chemotherapy, followed by (chemo-)RT
What is the role of neoadj-CT in HNSCC?

- To evaluate tumor response *in vivo*
- Early treatment of micrometastatic disease
- To predict response to RT
- To alleviate tumor-related symptoms, before RT
- Organ preservation
- To study predictive biomarkers
What is the role of neoadj-CT in HNSCC?

• To evaluate tumor response *in vivo* ✓
• Early treatment of micrometastatic disease
• To predict response to RT ✓
• To alleviate tumor-related symptoms, before RT ✓
• Organ preservation ✓
• To study predictive biomarkers ✓
• 31 studies on neoadjuvant CT
• No impact in SG
• 15 studies evaluated PF-induction
  ➢ HR 0.88
  ➢ IC 0.79 – 0.97
• Heterogeneous population
• Methodological concerns
• Study power
  ➢ FN results cannot be excluded
• Efficacy of neoadjuvant regimens

Pignon et al. Lancet 2000
MACH – NC 2009

Pignon et al., 2009

Non cancer death/person-years by period

<table>
<thead>
<tr>
<th></th>
<th>Years 0-2</th>
<th>Years 3-5</th>
<th>Years ≥ 6</th>
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</thead>
<tbody>
<tr>
<td>Control</td>
<td>187/2985</td>
<td>86/1769</td>
<td>37/544</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>201/3301</td>
<td>106/2330</td>
<td>34/727</td>
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</table>

Cancer death by period

<table>
<thead>
<tr>
<th></th>
<th>Years 0-2</th>
<th>Years 3-5</th>
<th>Years ≥ 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>1268</td>
<td>290</td>
<td>32</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>1049</td>
<td>278</td>
<td>28</td>
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</table>
### MACH – NC 2009

<table>
<thead>
<tr>
<th>Timing</th>
<th>No. Deaths / Entered</th>
<th>O-E</th>
<th>Variance</th>
<th>Hazard Ratio</th>
<th>HR [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LRT+CT</td>
<td>LRT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Concomitant</td>
<td>3171/4824</td>
<td>3389/4791</td>
<td>-326.4</td>
<td>1587.7</td>
<td>0.81 [0.78:0.86]</td>
</tr>
<tr>
<td>Induction</td>
<td>1877/2740</td>
<td>1813/2571</td>
<td>-40.0</td>
<td>900.7</td>
<td>0.96 [0.90;1.02]</td>
</tr>
<tr>
<td>Adjuvant</td>
<td>631/1244</td>
<td>661/1323</td>
<td>17.9</td>
<td>317.4</td>
<td>1.06 [0.95;1.18]</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>5679/8808</strong></td>
<td><strong>5863/8685</strong></td>
<td><strong>-348.5</strong></td>
<td><strong>2805.8</strong></td>
<td><strong>0.88 [0.85;0.92]</strong></td>
</tr>
</tbody>
</table>

Test for heterogeneity: $\chi^2_{107} = 179.8$, $p < 0.0001$  
Test for interaction: $\chi^2_{2} = 26.60$, $p < 0.0001$  
LRT+CT effect: $p < 0.0001$

Pignon et al., 2009
## TPF Regimens

<table>
<thead>
<tr>
<th>Local therapy</th>
<th>Tax 323, 2007</th>
<th>Tax 324, 2007</th>
<th>Hitt, 2005</th>
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<tbody>
<tr>
<td></td>
<td>n 358</td>
<td>n 501</td>
<td>n 382</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Induction</th>
<th>PF</th>
<th>TPF</th>
<th>p</th>
<th>PF</th>
<th>TPF</th>
<th>p</th>
<th>PF</th>
<th>PCF</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>TR</td>
<td>54%</td>
<td>68%</td>
<td>0.006</td>
<td>64%</td>
<td>72%</td>
<td>0.07</td>
<td>68%</td>
<td>80%</td>
<td>&lt;0.001</td>
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<tr>
<td>PFS (mo.)</td>
<td>8.2</td>
<td>11.0</td>
<td>0.0071</td>
<td>13</td>
<td>36</td>
<td>0.004</td>
<td>12.0</td>
<td>20</td>
<td>0.003</td>
</tr>
<tr>
<td>OS (mo.)</td>
<td>14.2</td>
<td>18.6</td>
<td>0.0052</td>
<td>30</td>
<td>71</td>
<td>0.006</td>
<td>36.8</td>
<td>42.4</td>
<td>0.031</td>
</tr>
</tbody>
</table>

*PF: DDP + 5-FU; TPF: Docetaxel + PF; PCF: Paclitaxel + PF*

TPF regimen

• 100 pts
• IC: 3 x CDDP 75 mg/m² + PTX 175 mg/m² q21d
• CRT: 70 Gy + CDDP 100 mg/m² d1,22, 43
• 94 pts T3–4 & 70 pts N2–3; OP 50 pts, L 30 pts
• RR – IC: 81%
• 79/94 pts completed CRT
  - Median delivered RT dose: 70 Gy in 61 d
  - Median number of concurrent CDDP cycles: 2
• BMI > 22 kg/m² and no FT remained significant as favorable prognostic factors in terms of OS in MV analysis

• Cohen et al.: DeCIDE: A phase III randomized trial of docetaxel (D), cisplatin (P), 5-fluorouracil (F) (TPF) induction chemotherapy (IC) in patients with N2/N3 locally advanced squamous cell carcinoma of the head and neck (SCCHN)

• Haddad et al.: The PARADIGM trial: A phase III study comparing sequential therapy (ST) to concurrent chemoradiotherapy (CRT) in locally advanced head and neck cancer (LANHC)
Overall Survival

Progression Free Survival

Haddad et al. Lancet Oncol 2013
Squamous cell carcinoma of the head and neck: EHNS–ESMO–ESTRO Clinical Practice Guidelines for diagnosis, treatment and follow-up

V. Grégoire¹, J.-L. Lefebvre², L. Licitra³ & E. Felip⁴
On behalf of the EHNS–ESMO–ESTRO Guidelines Working Group*

The role of induction chemotherapy (ICT) has been reconsidered since the introduction of taxane–platinum-based (TPF) combinations that have proved to be superior to platinum–fluorouracil PF schedule in loco-regionally advanced disease [I, A]. However, at present, induction chemotherapy is not considered standard treatment in advanced disease. ICT followed by RT-CT (so-called sequential CT-RT) is still under evaluation. The overall toxicity of this approach can be substantial thus compromising the final result.
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Conclusions

• Neoadjuvant CT can be considered as investigative in the treatment of locally advanced HNSCC
• Head-to-head comparisons with concurrent cisplatin-based chemoradiation are pending
• Patient selection remains critical
• Some scenarios seem to be interesting
  ➢ OP
  ➢ Bulky cervical disease
• Biomarkers must be studied