Best of 2015: head and neck cancer

Jean-Pascal Machiels
Department of medical oncology
Disclosure slide

• Advisory board: Boehringer-Ingelheim, MSD, Debio
• Research grants: Novartis, Bayer, Janssen
Presentation outline

• The Cancer Genome Atlas project
• Anti-EGFR mAb with radiotherapy and HPV
• Nasopharyngeal cancer
• Oral cavity: elective neck dissection
• Recurrent/metastatic disease: immunotherapy
Candidate therapeutic targets and driver oncogenic events. Alteration events for key genes are displayed by sample (n = 279). TSG, tumor suppressor gene.

TCGA, Nature 2015
DKTK-ROG initiative

221 with oral cavity, hypopharynx, and oropharynx uniformly treated patients with surgery followed by chemoradiation

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Tinhofer, ASCO 2015
DKTK-ROG initiative

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Lower survival

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DKTK-ROG initiative

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Lower survival

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# Cetuximab improves overall survival

**Stage III/IV: curative intention**

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Regimens</th>
<th>3-y LRC</th>
<th>Median Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bonner Lancet Oncol 2010</td>
<td>213</td>
<td>Radiotherapy + Cetuximab versus Radiotherapy</td>
<td>47%</td>
<td>49 months</td>
</tr>
<tr>
<td></td>
<td>211</td>
<td>Radiotherapy</td>
<td>34%</td>
<td>29 months</td>
</tr>
</tbody>
</table>

Benefit of cetuximab may be more pronounced in p16+ patients

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<th>3-y Loco-regional control</th>
<th>p16+ oropharynx</th>
<th>p16- oropharynx</th>
</tr>
</thead>
<tbody>
<tr>
<td>RT + Cetuximab</td>
<td>87% (HR:0.31)</td>
<td>32% (HR: 0.78)</td>
</tr>
<tr>
<td>RT</td>
<td>65%</td>
<td>20%</td>
</tr>
</tbody>
</table>

Bonner, Lancet Oncology 2010
Rosenthal, ASCO 2014
Panitumumab and chemoradiation

Concert 1: chemoradiation vs chemoradiation plus panitumumab

Concert 2: Chemoradiation vs radiotherapy plus panitumumab

Mesia et al, Lancet Oncology 2015
Giralt et al, Lancet Oncology 2015
Panitumumab and chemoradiation

Concert 1: chemoradiation vs chemoradiation plus panitumumab

Concert 2: Chemoradiation vs radiotherapy plus panitumumab

Mesia et al, Lancet Oncology 2015
Giralt et al, Lancet Oncology 2015
Panitumumab + RT vs chemoradiation

NCIC CTG HN6
Stage III/IV

Primary endpoint = PFS

Conventional Radiation (70 Gy in 7 weeks)
Cisplatin 100 mg/m2 Day 1, 22, 43
N=160

Accelerated Radiation (70 Gy in 6 weeks)
Panitumumab 9 mg/kg one week before RT
and on days 15 and 36
N=160

L Siu et al. ASCO 2015
Primary Endpoint: PFS

<table>
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<tr>
<th>Study arm</th>
<th>2-year PFS</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Panitumumab</td>
<td>76.0%</td>
<td>68 – 82%</td>
</tr>
<tr>
<td>Cisplatin</td>
<td>73.0%</td>
<td>65 – 79%</td>
</tr>
</tbody>
</table>

HR 0.95 (95% CI = 0.60 – 1.50)
Stratified log rank p-value = 0.83

Overall Survival

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<th>Study arm</th>
<th>2-year OS</th>
<th>95% CI</th>
</tr>
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<tbody>
<tr>
<td>Panitumumab</td>
<td>88.0%</td>
<td>82 – 92%</td>
</tr>
<tr>
<td>Cisplatin</td>
<td>85.0%</td>
<td>78 – 90%</td>
</tr>
</tbody>
</table>

HR 0.89 (95% CI = 0.54 – 1.48)
Stratified log rank p-value = 0.66
This supports the investigation of treatment de-escalation in favorable HPV positive by replacing chemotherapy with anti-EGFR mAbs
De-intensification in HPV head and neck cancer?

- De-intensification of systemic therapy
  - Cetuximab versus cisplatin (RTOG1016, TROG1201, De-escalate)

- De-intensification of radiation therapy
  - Surgery to select for de-intensification of radiation (ECOG331, ADEPT)
  - Induction chemotherapy to select for de-intensification of radiation (ECO1308, Quarterback study)
HPV+ oropharynx: low-risk group

- T0-T3,N0-N2c, M0, HPV + or p16 +, less than 10 pack-years
- Radiotherapy 60 Gy + cisplatin 30 mg/m²/week
- Primary endpoint was pCR, N=49
- pCR = 86%, all the patients alive (median follow-up 15 months)

NOT A STANDARD OF CARE: we need randomized trials

Chera et al. ASCO 2015
T4 N3 disease
Presentation outline

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• Recurrent/metastatic disease: immunotherapy
Post-IMRT 8 weeks and 6 months undetectable plasma EBV DNA

<table>
<thead>
<tr>
<th></th>
<th>Undetectable EBV DNA</th>
<th>Detectable EBV DNA</th>
</tr>
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<tbody>
<tr>
<td>N=289</td>
<td>8 weeks</td>
<td>6 months</td>
</tr>
<tr>
<td>3-year Survival</td>
<td>95%</td>
<td>97%</td>
</tr>
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Lee et al. ASCO 2015
Plasma EBV DNA

Concurrent chemoradiation

EBV DNA after treatment

- Negative
  - Adjuvant CT
  - No adjuvant CT

- Positive
  - Cisplatin/5FU
  - Paclitaxel/gemcitabine

NRG-HN001/NCTC02135042
Presentation outline

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Elective versus therapeutic neck dissection in oral cavity

Elective neck dissection (ipsilateral, level I-III)
N=298

Primary endpoint = Overall survival

Therapeutic neck dissection
N=298

cT1-2, cN0
Oral cavity

D’Cruz et al. ASCO 2015
D’Cruz et al, NEJM 2015
Elective versus therapeutic neck dissection in oral cavity

Overall survival

Disease-free survival

Hazard ratio, 0.64 (95% CI, 0.45–0.92)
P = 0.01

Hazard ratio, 0.45 (95% CI, 0.34–0.59)
P < 0.001

243  195  143  110  86
253  197  129  105  86

D’Cruz et al. ASCO 2015
D’Cruz et al, NEJM 2015
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The priming phase

Activation signal

Inactivation signal

Cellule T naïve

Dendritic cell

Dendritic cell

B7

CD28

Anti-CTLA-4

The effector phase

Inactivation signal

Inactivation signal

Cellule tumorale

Activated T-cell

Cellule tumorale

PD-L1

PD-1

PD-1

Anti-PD-L1

Anti-PD-1
antii-PD1 and anti-PD-L1 in recurrent head and neck cancer

<table>
<thead>
<tr>
<th>Pembrolizumab Anti-PD-1</th>
<th>Total N=117</th>
<th>HPV+ N=34</th>
<th>HPV- N=81</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR</td>
<td>24.8%</td>
<td>20.6%</td>
<td>27.2%</td>
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<tr>
<th>MEDI4736 Anti-PD-L1</th>
<th>Total N=62</th>
<th>PD-L1+ N=22</th>
<th>PD-L1- N=37</th>
</tr>
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<tr>
<td>ORR</td>
<td>11%</td>
<td>18%</td>
<td>8%</td>
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Seiwert et al, ASCO 2015
Segal et al., ASCO 2015
Pembrolizumab

MEDI4736

Seiwert et al, ASCO 2015
Segal et al., ASCO 2015
PD-L1 positive recurrent nasopharyngeal cancer

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Hsu et al. ECCO 2015
Conclusions

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• Nasopharyngeal cancer: plasma EBV
• Oral cavity: elective neck dissection
• Recurrent/metastatic disease: immunotherapy