Update in the Management of Head and Neck Cancer

Jan B. Vermorken, MD, PhD
Department of Medical Oncology
Antwerp University Hospital
Edegem, Belgium

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Limassol, Cyprus
• Participates in Advisory Boards of:
  Carrick Therapeutics Limited, Cue Biopharma, Debiopharm, Immunomedics, Innate Pharma, Merck-Serono, Merck Sharp & Dome Corp, PCI Biotech, Synthon Biopharmaceuticals, WntResearch

• Lecturer fee from:
  Merck-Serono, BMS, MSD
Head and Neck Cancer (HNC)  
A changing population

- Worldwide HNC is still increasing (>800,000 in 2016)
- Majority still tobacco and alcohol related
- Increase of viral-associated OPC, less so in elderly

- SEER data: 47% of SCCHN patients > 65 years of age
- The incidence of HNC among older patients is expected to increase 34% over the next 10 years, and 64% over the next 20 years.
- Most studies use the age of 70 (or even 75) as a cut-off for being old

## Head and Neck Cancer (HNC)

**A changing disease**

<table>
<thead>
<tr>
<th></th>
<th>HPV-pos</th>
<th>HPV-neg</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anatomical</strong></td>
<td>Tonsil, base of tongue</td>
<td>All sites</td>
</tr>
<tr>
<td><strong>Histology</strong></td>
<td>Non-keratinized</td>
<td>Keratinized</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td>Younger cohorts</td>
<td>Olders cohorts</td>
</tr>
<tr>
<td><strong>Sex ratio</strong></td>
<td>3:1 men</td>
<td>3:1 men</td>
</tr>
<tr>
<td><strong>Stage</strong></td>
<td>Tx, T1-2</td>
<td>Variable</td>
</tr>
<tr>
<td><strong>Risk factors</strong></td>
<td>Sexual behaviour</td>
<td>Alcohol, tobacco</td>
</tr>
<tr>
<td><strong>Incidence</strong></td>
<td>Increasing</td>
<td>Decreasing</td>
</tr>
<tr>
<td><strong>Survival</strong></td>
<td>Improved</td>
<td>Unchanging</td>
</tr>
</tbody>
</table>

*Marur et al, 2010*
Head and Neck Cancer (HNC)  
A changing treatment

• **Surgery**
  - reconstructive surgery
  - organ sparing techniques
  - TO(R)S

• **Radiotherapy**
  - altered fractionation schedules
  - Better targeting (CT-MRI, PET, IGRT)
  - New RT techniques (IMRT, STRT, PT)
  - Combined approaches: CT, TT, hypoxic cell modifiers

• **Systemic therapy**
  - New cytotoxic agents
  - Molecular targeted therapies
  - Immunotherapy
Multidisciplinary Team (MDT) Meetings

- Head and neck surgeon
- Radiation oncologist
- Medical oncologist
- Anesthesiologist, internist, general practitioner
- Radiologist
- Physical therapist, dietitian, social worker, psychologist a/o psychiatrist
- Biologist, pathologist
- Oncologic dentist
- Speech therapist

Guidelines

Clinical trials

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Decision Making during MDT Meetings

SCCHN patients

- **Disease factors** (e.g. site, stage, biology [HPV, EGFR], specific risk factors for locoregional or distant relapse)

- **Patient factors** (e.g. age, sex, performance status, nutritional status, comorbid chronic disease, oral health, lifestyle habits, socio-economic status)

- **Treatment factors** (surgery, radiotherapy, chemotherapy, immunotherapy, targeted therapy)

- **What do patients want?**
EBM for Treatment in Early Stage SCCHN

Selection treatment modality (ERT vs BT vs S) based on:

- Primary tumor site
- Age
- Comorbidity
- Occupation, preference and compliance
- Quality of life following the treatment
- Availability of expertise in RT or surgery
- History of a previous malignant lesion in the H&N

Corvò R, 2007 (ERT=external radiotherapy, BT=brachytherapy, S=surgery)
EORTC 1420-HNCG-ROG

Phase III study assessing the “best of” radiotherapy compared to the “best of” surgery (trans-oral surgery (TOS)) in patients with T1-T2, N0-N1 oropharyngeal, supraglottic carcinoma and with T1, N0 hypopharyngeal carcinoma.

Multi-center, randomized phase 3 trial

Max 2 weeks

Planning (max 4 weeks)

Follow-up

MDT Registration Randomization Treatment Year 1 Year 2-5

T1-T2, N0-N1, M0 Oropharyngeal, Supraglottic or T1, N0, M0 Hypopharyngeal squamous cell carcinoma Resectable Treatment naive

Baseline MDADI

Lab tests Questionnaires Pregnancy test Videoendoscopy/water swallow test

RTQA

R 1:1

IMRT with definitive dose of 70Gy; elective dose 54.45 Gy in 6 weeks (moderately accelerated)

TOS (TLM, TORS, conventional) with selective neck node dissection

Surgery QA

Primary endpoint: MDADI at 4.5, 6, 9, 12 months

Secondary endpoints:
- Treatment related toxicity
- QOL based on patient's priorities for selected domains
- Quality surgery and radiotherapy
- Cost-effectiveness

Total sample size = 170 pts (85 per arm)
Treatment Strategies in Locoregionally Advanced SCCHN

- **Definitive CCRT** (planned or optional surgery [PS or OpS])
  - MACH-NC meta-analysis
- Surgery → adjuvant RT or concurrent CRT (CCRT)
  - MARCH meta-analysis
- Altered fractionation radiotherapy (PS or OpS)
  - DAHANCA meta-analysis
- Hypoxic modification of radiotherapy (PS or OpS)
  - DAHANCA meta-analysis
- Definitive RT + cetuximab (BRT; with PS or OpS)
- Induction CT → definitive local therapy (S/RT, CCRT, BRT)

*all 3 approaches have level IA evidence*

CRT = chemoradiation with cisplatin; BRT = bioradiation
## Clinical Practice Guidelines for Patients with Locoregionally Advanced SCCHN
### Standard options

<table>
<thead>
<tr>
<th>Treatment Option</th>
<th>Level of evidence</th>
<th>Grade of recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery $\rightarrow$ RT or CCRT</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Concomitant CT and RT*</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Cetuximab plus RT</td>
<td>II</td>
<td>B</td>
</tr>
<tr>
<td>CCRT or ICT $\rightarrow$ RT for organ preservation</td>
<td>II</td>
<td>A</td>
</tr>
<tr>
<td>ICT $\rightarrow$ CCRT (sequential therapy)</td>
<td></td>
<td>Still under evaluation</td>
</tr>
</tbody>
</table>

*in case of mutilating surgery and in nonresectable disease;  
*Cisplatin dose: 100 mg/m² x3 during CF-RT*  

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CCRT: Late Toxicity

- Analysis of 230 patients receiving CRT in 3 studies (RTOG 91-11, 97-03, 99-14)

MVA: significant variables correlating with severe late toxicity were: older age (OR, 1.05 per year; p=.001), advanced T-stage (OR, 3.07; p=.0036), larynx/hypopharynx primary site (OR, 4.17; p=.0041) and neck dissection (OR, 2.39; p=.018)  Machtay M, et al. J Clin Oncol 2008; 26: 3582–3589
How to Improve on Cisplatin/RT in LA-HNSCC

Reducing toxicity (in particular for HPV-positive OPC)
- Other dose schedules than high-dose cisplatin for CCRT
- Less toxic cytotoxic agents than cisplatin during CCRT
- Replacing cisplatin by targeted therapy?
- Integrating immunotherapy?

Increasing efficacy (in high-risk HPV-negative patients)
- Adding more cytotoxics?
- Adding targeted agents to cytotoxics?
- Adding hypoxic sensitizers to CCRT?
- Adding immunotherapy to standard therapies?
Discussion on Dose & Schedule of Cisplatin

- LD vs HD cisplatin. Lessons learned from 59 CCRT trials
  Stzurz et al, Front Oncol 2019 Feb 21; 9: 86

- Once-a-week vs once-every-three weeks: prospective phase III trial
  Noronha et al, J Clin Oncol 35, 2017

- LD-weekly (40 mg/m^2) vs HD-3-weekly postoperatively in high-risk patients with LA-SCCHN (JCOG#1008;ASCO 2020)
  Kiyota (personal communication)

Alternatives for High-Dose Cisplatin in CCRT

- Other cisplatin schedules (daily, weekly, dailyx5, etc)
- Other platinum drugs (CBDCA/5-FU [GORTEC], CBDCA)
- Other cytotoxics (taxanes w/wo cetuximab, gemcitabine)
- Targeted therapies (cetuximab, nimotuzumab)
  - Both RTOG#1016 and De-ESCAlaTE showed inferior results

Mehanna et al, Lancet 2018
How to Improve on Cisplatin/RT in LA-HNSCC

Reducing toxicity (in particular for HPV-positive OPC)
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Increasing efficacy (in high-risk HPV-negative patients)
- Adding more cytotoxics?
- Adding targeted agents to cytotoxics?
- Adding hypoxic sensitizers to CCRT?
- Adding immunotherapy to standard therapies?
# Adding Checkpoint Inhibitors to RT or CCRT Studied with ≥100 patients

<table>
<thead>
<tr>
<th>Trial</th>
<th>Setting</th>
<th>Regimens</th>
</tr>
</thead>
<tbody>
<tr>
<td>PembroRad</td>
<td>IIR (definitive)</td>
<td>Pembro+RT vs Cet +RT*</td>
</tr>
<tr>
<td>PATHWay</td>
<td>IIR (adjuvant)</td>
<td>Pembro vs placebo</td>
</tr>
<tr>
<td>RTOG 3504</td>
<td>I/III (def.+adj)</td>
<td>Nivo+CRT (LD-P) vs Nivo+CRT (HD-P) vs Nivo+Cet+RT vs Nivo+RT</td>
</tr>
<tr>
<td>REACH</td>
<td>III (definitive)</td>
<td>P+RT vs Cet+Ave+RT* vs Cet+RT</td>
</tr>
<tr>
<td>KEYNOTE-412</td>
<td>III (definitive)</td>
<td>Pembro+P+RT vs Placebo+P+RT</td>
</tr>
<tr>
<td>JAVELIN HN-100</td>
<td>III (definitive)</td>
<td>Ave+P+RT vs Placebo+P+RT</td>
</tr>
</tbody>
</table>

Modified from Szturz and Vermorken, BMC Medicine 2017 (*separately in NPC and Oral cavity cancer)

Pembro=pembrolizumab (anti-PD1); Cet= cetuximab; P=cisplatin; RT=radiotherapy; CRT=chemoradiation
Nivo= nivolumab (anti-PD1); Ave= avelumab (anti-PD-L1) * Presented at ASCO 2018 (abstract #6018)
## Development of Chemotherapy in R/M SCCHN

**First breakthrough in first-line in 2008**

1977: cisplatin shows efficacy in 1\textsuperscript{st}-line SCCHN

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Regimen</th>
<th>ORR (%)</th>
<th>Median OS (months)</th>
<th>Significant OS benefit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grose et al 1985</td>
<td>100</td>
<td>Methotrexate, Cisplatin</td>
<td>16</td>
<td>5.0</td>
<td>No</td>
</tr>
<tr>
<td>Forastiere et al 1992</td>
<td>277</td>
<td>Cisplatin + 5-FU, Carboplatin + 5-FU, Methotrexate</td>
<td>32*</td>
<td>6.6</td>
<td>No</td>
</tr>
<tr>
<td>Clavel et al 1994</td>
<td>382</td>
<td>CABO, Cisplatin + 5-FU, Cisplatin</td>
<td>34*</td>
<td>7.3</td>
<td>No</td>
</tr>
<tr>
<td>Gibson et al 2005</td>
<td>218</td>
<td>Cisplatin + 5-FU, Cisplatin + paclitaxel</td>
<td>27</td>
<td>8.7</td>
<td>No</td>
</tr>
<tr>
<td>Vermorken et al 2008</td>
<td>442</td>
<td>Platinum + 5-FU, Platinum + 5-FU + Cetuximab</td>
<td>20</td>
<td>7.4</td>
<td>Yes</td>
</tr>
</tbody>
</table>

CABO, cisplatin, methotrexate, bleomycin, vincristine

*significant

## EXTREME: Efficacy Data

<table>
<thead>
<tr>
<th>Variable</th>
<th>PF+cetuximab n=222</th>
<th>PF n=220</th>
<th>HR or OR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Survival – mo</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>overall</td>
<td>10.1 (8.6 -11.2)</td>
<td>7.4 (6.4-8.3)</td>
<td>HR 0.80 (0.60-0.99)</td>
<td>0.04</td>
</tr>
<tr>
<td>progression-free</td>
<td>5.6 (5.0 - 6.0)</td>
<td>3.3 (2.9-4.3)</td>
<td>HR 0.54 (0.43-0.67)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Best response - %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>overall</td>
<td>36 (29-42)</td>
<td>20 (15-25)</td>
<td>OR 2.33 (1.50-3.60)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>disease control</td>
<td>81 (75-86)</td>
<td>60 (53-67)</td>
<td>OR 2.88 (1.87-4.44)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Time to TRT failure - mo</td>
<td>4.8 (4.0-5.6)</td>
<td>3.0 (2.8-3.4)</td>
<td>HR 0.59 (0.48-0.73)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Duration of response</td>
<td>5.6 (4.7-6.0)</td>
<td>4.7 (3.6-5.9)</td>
<td>HR 0.76 (0.50-1.17)</td>
<td>0.21</td>
</tr>
</tbody>
</table>

*PF=cisplatin or carboplatin + 5-FU; HR=hazard ratio; OR: odds ratio*

EXTREME: Toxicity of PFE vs PF

Grade 3 and 4 AEs with a frequency ≥5%† in either arm of the safety population

*Platinum-based CT, consisting of cisplatin/carboplatin + 5-FU;
†p=0.05 vs CT alone; ‡p=0.02 vs CT alone; §p<0.001 vs CT alone
AE, adverse event

EXTREME – Overall Survival
Long-term follow-up

Vermorken et al. ASCO 2014 (abstr. #6021)
## CheckMate-141 and KEYNOTE-040 Trials
### Second breakthrough 2nd-Line in 2016

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Second-line Chemother&lt;sup&gt;1&lt;/sup&gt;</th>
<th>Nivolumab Checkmate 141&lt;sup&gt;1&lt;/sup&gt;</th>
<th>Pembrolizumab KEYNOTE 040&lt;sup&gt;2&lt;/sup&gt;</th>
<th>Second-line Chemother&lt;sup&gt;2&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR</td>
<td>5.8%</td>
<td>13.3%</td>
<td>14.6%</td>
<td>10.1%</td>
</tr>
<tr>
<td>CR</td>
<td>0.8%</td>
<td>2.5%</td>
<td>1.6%</td>
<td>0.4%</td>
</tr>
<tr>
<td>PR</td>
<td>5.0%</td>
<td>10.8%</td>
<td>13.0%</td>
<td>9.7%</td>
</tr>
<tr>
<td>Median PFS</td>
<td>2.3 months</td>
<td>2.0 months</td>
<td>2.1 months</td>
<td>2.3</td>
</tr>
<tr>
<td>6-month PFS</td>
<td>9.0%</td>
<td>19.7%</td>
<td>25.9%</td>
<td>19.5%</td>
</tr>
<tr>
<td>Median OS</td>
<td>5.1 months</td>
<td>7.5 months</td>
<td>8.4 months</td>
<td>7.1 months</td>
</tr>
<tr>
<td>12-months</td>
<td>16.6%</td>
<td>36.0%</td>
<td>37.3.0%</td>
<td>27.2%</td>
</tr>
</tbody>
</table>

CheckMate-141 vs KEYNOTE-040: median time to response 2.1 vs 4.5 months; response duration 9.7 vs 18.4 months

<sup>1</sup> From CheckMate 141 (Ferris et al, NEJM 2016)

<sup>2</sup> From KEYNOTE-040 (Cohen et al, ESMO abstract LBA-45, 2017 and Lancet Oncol 2018)
## CheckMate-141: Treatment-related Adverse Events

<table>
<thead>
<tr>
<th>Event</th>
<th>Nivolumab n = 236</th>
<th>Investigator’s Choice n = 111</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Any Grade n (%)</td>
<td>Grade 3–4 n (%)</td>
</tr>
<tr>
<td>Any treatment-related AE in ≥10% of patients</td>
<td>139 (58.9)</td>
<td>31 (13.1)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>33 (14.0)</td>
<td>5 (2.1)</td>
</tr>
<tr>
<td>Nausea</td>
<td>20 (8.5)</td>
<td>0</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>16 (6.8)</td>
<td>0</td>
</tr>
<tr>
<td>Anemia</td>
<td>12 (5.1)</td>
<td>3 (1.3)</td>
</tr>
<tr>
<td>Asthenia</td>
<td>10 (4.2)</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Mucosal inflammation</td>
<td>3 (1.3)</td>
<td>0</td>
</tr>
<tr>
<td>Alopecia</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Treatment-related select AEs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin</td>
<td>37 (15.7)</td>
<td>0</td>
</tr>
<tr>
<td>Endocrine</td>
<td>18 (7.6)</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>16 (6.8)</td>
<td>0</td>
</tr>
<tr>
<td>Hepatic</td>
<td>5 (2.1)</td>
<td>2 (0.8)</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>5 (2.1)</td>
<td>2 (0.8)</td>
</tr>
<tr>
<td>Hypersensitivity/infusion reaction</td>
<td>3 (1.3)</td>
<td>0</td>
</tr>
<tr>
<td>Renal</td>
<td>1 (0.4)</td>
<td>0</td>
</tr>
</tbody>
</table>

CheckMate-141: Quality of Life and Symptom Burden

Ongoing Randomized first-line Trials with Checkpoint Inhibitors in R/M-SCCHN (≥100 pts)

<table>
<thead>
<tr>
<th>Trial</th>
<th>Setting</th>
<th>No</th>
<th>Regimens</th>
</tr>
</thead>
<tbody>
<tr>
<td>CheckMate-714</td>
<td>IIR</td>
<td>315</td>
<td>Nivo+Ipi vs Nivo+placebo</td>
</tr>
<tr>
<td>KESTREL</td>
<td>III</td>
<td>760</td>
<td>Durva vs Durva+Treme vs PFE</td>
</tr>
<tr>
<td>KEYNOTE-048</td>
<td>III</td>
<td>825</td>
<td>Pembro vs Pembro+PF vs PFE</td>
</tr>
<tr>
<td>CheckMate-651</td>
<td>III</td>
<td>490</td>
<td>Nivo+Ipi vs PFE</td>
</tr>
</tbody>
</table>

Modified from Szturz and Vermorken, BMC Medicine, 2017

Nivo= nivolumab (anti-PD1); Ipi= ipilimumab (anti-CTLA-4); Durva= durvalumab (anti-PD-L1); Treme= tremelimumab (anti-CTLA-4); Pembro= pembrolizumab (anti-PD1)
KEYNOTE-048: A Breakthrough in 1st-Line?

**KEYNOTE-048 Study Design (NCT02358031)**

**Key Eligibility Criteria**
- SCC of the oropharynx, oral cavity, hypopharynx, or larynx
- R/M disease incurable by local therapies
- ECOG PS 0 or 1
- Tissue sample for PD-L1 assessment\(^a\)
- Known p16 status in the oropharynx\(^b\)

**Stratification Factors**
- PD-L1 expression\(^a\) (TPS ≥50% vs <50%)
- p16 status in oropharynx (positive vs negative)
- ECOG performance status (0 vs 1)

\(^a\)Assessed using the PD-L1 IHC 22C3 pharmDx assay (Agilent). TPS = tumor proportion score = % of tumor cells with membranous PD-L1 expression. \(^b\)Assessed using the CINtec p16 Histology assay (Ventana); cutpoint for positivity = 70%. \(^c\)Following a loading dose of 400 mg/m\(^2\).

Pembrolizumab 200 mg Q3W for up to 35 cycles

Pembrolizumab 200 mg + Carboplatin AUC 5 OR Cisplatin 100 mg/m\(^2\) + 5-FU 1000 mg/m\(^2\)/d for 4 days for 6 cycles (each 3 wk)

Cetuximab 250 mg/m\(^2\) Q1W + Carboplatin AUC 5 OR Cisplatin 100 mg/m\(^2\) + 5-FU 1000 mg/m\(^2\)/d for 4 days for 6 cycles (each 3 wk)

Pembrolizumab 200 mg Q3W for up to 35 cycles total

Cetuximab 250 mg/m\(^2\) Q1W

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Burtness B. et al Presented at ESMO, 22.10.2018
Rischin D, et al. Presented at ASCO, 31.05.2019
**KEYNOTE- 048**

**Overall Survival**

- In the PD-L1 CPS ≥ 20 population (A), CPS ≥ 1 population (B), population (C) at 2nd IA, at FA (D)

**Progression-free Survival**

- In the PD-L1 CPS ≥ 20 population (A), CPS ≤ 1 population (B) Total and in the total population (C)

**Pembro alone vs cetuximab + chemotherapy (A t/m D)**

In total population at 2nd IA (E), in PD-L1 CPS ≥ 20 population (F) and in CPS ≥ 1 population at FA

**Pembro + chemotherapy vs cetuximab + chemotherapy (E t/m G)**

In PD-L1 CPS ≥ 20 population (D), CPS ≥ 1 population, and in the total population (F)
KEYNOTE-048: Worrying and Promising

**Response Summary, P vs E, Total Population**

<table>
<thead>
<tr>
<th>Confirmed Response, n (%)</th>
<th>Pembro N = 301</th>
<th>EXTREME N = 300</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR</td>
<td>51 (16.9)</td>
<td>108 (36.0)</td>
</tr>
<tr>
<td>CR</td>
<td>14 (4.7)</td>
<td>8 (2.7)</td>
</tr>
<tr>
<td>PR</td>
<td>37 (12.3)</td>
<td>100 (33.3)</td>
</tr>
<tr>
<td>SD</td>
<td>82 (27.2)</td>
<td>102 (34.0)</td>
</tr>
<tr>
<td>PD</td>
<td>122 (40.5)</td>
<td>37 (12.3)</td>
</tr>
<tr>
<td>Non-CR/non-PD(^a)</td>
<td>14 (4.7)</td>
<td>11 (3.7)</td>
</tr>
<tr>
<td>Not evaluable or assessed(^b)</td>
<td>32 (10.6)</td>
<td>42 (14.0)</td>
</tr>
</tbody>
</table>

**Duration of Response**

Median (range)
- P: 22.6 mo (1.5+ to 43.0+)
- E: 4.5 mo (1.2+ to 38.7+)

\(^a\)Patients without measurable disease per central review at baseline who did not have CR or PD. \(^b\)Patients who did not have a post-baseline imaging assessment evaluable for response or who did not have post-baseline imaging. Response assessed per RECIST v1.1 by blinded, independent central radiologic review. FA (data cutoff date: Feb 25, 2019).

*Rischin et al. ASCO 2019, abstract #6000*
Management of Recurrent / Metastatic SCCHN
EORTC 1559 - Umbrella trial: Personalized biomarker-based treatment strategy or immunotherapy in patients with recurrent/metastatic HNSCC «UPSTREAM»

Informed consent must be taken at 2 timepoints; 1. At registration; 2. After allocation to patient cohort and before randomization, when applicable: in the scheme indicated with ★

Presented by Rachel Galot (ESMO 2019)
Take-Home Messages: LA-SCCHN

- Concurrent chemoradiation (CCRT) with HD-CDDP standard
- MTD meetings necessary for individualized approach
- Discussion on optimal cisplatin dose and schedule still open - randomized trials on this issue eagerly awaited
- De-escalation in HPV+ LA-OPSCC experimental and not indicated outside clinical trials
- Intensification in HPV- OPSCC and non-OPSCC experimental - Pembrolizumab/RT less toxic than cetuximab/RT, efficacy?
- Cetuximab added to CCRT with HD-CDDP no benefit
Take-Home Messages: R/M-SCCHN

- EXTREME changed the scene for R/M-SCCHN in 1st-line, but response duration and long-term survival are disappointing.

- Immune checkpoint inhibitors have made a major change:
  - inducing durable responses
  - prolonging overall survival in both 1st and 2nd line
  - showing a more favorable safety profile and a better QoL

- Confirmatory trials are needed, as are studies to define the optimal sequence of the different treatment options.

- Precision medicine (personalized) new research direction.