Larynx Hypopharynx

- Moderation: Rainald Knecht, Hamburg
- State of the art: Jean Louis Lefebvre, Lille
- Debate: pro CRT: Jan Klozar, Prague; contra CRT: Marshall Posner, Boston
- Clinical cases: all

Therapy algorithms
Head and neck carcinoma

Operable: OP → (C)RT → (C)RT, Neo-CT → (C)RT
Inoperable: OP → RT → CT
Recurrent/metastatic: OP → RT → CT

Why larynx preservation at all?

- Patient
  - Cancer control
  - Quality of life (swallow, speak, breathe)
  - Organ preservation
  - Function preservation (cognitive, sensory)
  - Adverse events (treatment-related, comorbidities)

- Social community
  - Treatment
  - Costs (rehabilitation, unemployment)

- Costs of life (economic, social, psychological)
main publications on nonsurgical larynx preservation


Lefebvre et al., J Natl Cancer Inst, 1996, 88:890-99 (Hypopharynx)

Forastiere et al., N Engl J Med 2003, 349:2091-2098 (Larynx)

1. Generation Larynx preservation (Larynx/Hypopharynx CA)

58% larynx preservation

Larynx preservation (Larynx/Hypopharynx CA)

RTOG 91-11 (Laryngeal Cancer, III-IV)

5-year Results (med follow up 6.9 yrs)

<table>
<thead>
<tr>
<th></th>
<th>CRT</th>
<th>I + RT</th>
<th>RT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lx Preserv</td>
<td>84%</td>
<td>70%</td>
<td>66%</td>
</tr>
<tr>
<td>LR Control</td>
<td>69%</td>
<td>55%</td>
<td>51%</td>
</tr>
<tr>
<td>Dist. Mets</td>
<td>13%</td>
<td>14%</td>
<td>22%</td>
</tr>
<tr>
<td>LF Survival</td>
<td>47%</td>
<td>45%</td>
<td>34%</td>
</tr>
<tr>
<td>DF Survival</td>
<td>39%</td>
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<tr>
<td>Survival</td>
<td>55%</td>
<td>59%</td>
<td>54%</td>
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</table>

Forastiere AA et. al. ASCO 2006 Atlanta, abstract # 5517; Forastiere A et. al. N Engl J Med 2003;349:2091-8
remission rate with induction chemotherapy in advanced HNSCC

<table>
<thead>
<tr>
<th></th>
<th>CR</th>
<th>PR</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cisplatin (100mg/m²)</td>
<td>33%</td>
<td>53%</td>
<td>68%</td>
</tr>
<tr>
<td>5- Fluorouracil (5000mg/m²)</td>
<td>43%</td>
<td>43%</td>
<td>86%</td>
</tr>
<tr>
<td>2 - 3 Zyklen</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EORTC, 1996</td>
<td></td>
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</tr>
<tr>
<td>Docetaxel (100mg/m²)</td>
<td>11%</td>
<td>31%</td>
<td>43%</td>
</tr>
<tr>
<td>1 - 8 Zyklen</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kienzer, 1998</td>
<td></td>
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</tr>
<tr>
<td>Cisplatin (100mg/m²)</td>
<td>25%</td>
<td>51%</td>
<td>76%</td>
</tr>
<tr>
<td>6 - 8 Zyklen</td>
<td></td>
<td></td>
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<tr>
<td>Baur, 1998</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Docetaxel (75mg/m²)</td>
<td>29%</td>
<td>26%</td>
<td>55%</td>
</tr>
<tr>
<td>1 - 3 Zyklen</td>
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<tr>
<td>Posner, 2000</td>
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<tr>
<td>Cisplatin (75mg/m²)</td>
<td>14%</td>
<td>60%</td>
<td>74%</td>
</tr>
<tr>
<td>3 - 4 Zyklen</td>
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<tr>
<td>Biakov, 2000</td>
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<tr>
<td>Docetaxel (80mg/m²)</td>
<td>17%</td>
<td>48%</td>
<td>65%</td>
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Hazard Ratio 0.67 (0.41-1.11)  P = 0.12

OS “Operable” Hypopharynx and Larynx Subanalysis Tax 324, Posner, 2007

Hazard Ratio 0.59 (0.37-0.85) P = .03
Phase III study: RT vs ERBITUX + RT (1)
Subanalysis of 171 patients with laryngeal and hypopharyngeal SCC

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<tr>
<th>Treatment</th>
<th>2-year rate</th>
<th>3-year rate</th>
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<tr>
<td>RT alone (n=78)</td>
<td>83%</td>
<td>80%</td>
</tr>
<tr>
<td>ERBITUX + RT (n=93)</td>
<td>92%</td>
<td>88%</td>
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State of the art?
primary treatment

Surgery Total LE only T4?
   TLS, CCS, CHEP at all?
   Neck dissection (XRT) when?
Radio/Chemo Therapy
   combined (CRT) or sequential (I+RT)
   normofract or hyperfract.accel RT
   bioradiation (EGFR): replacing or adding to
RTOG 91-11 (Laryngeal Cancer, III-IV)
5-year Results (med foll up 6.9 yrs)

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Larynx and Hypopharynx Overall Survival

Hazard Ratio 0.62 (0.41-0.94)  P = .024

OS “Operable” Hypopharynx and Larynx Subanalysis Tax 324, Posner, 2007

OS “Operable” Hypopharynx and Larynx Subanalysis Tax 324, Posner, 2007

Hazard Ratio 0.67 (0.41-1.11)  P = 0.12


Hazard Ratio 0.59 (0.37-0.85)  P = .03

Patients

Patients

Patients
Phase III study: RT vs ERBITUX + RT

Subanalysis of 171 patients with laryngeal and hypopharyngeal SCC


Updated information presented in poster

Hazard ratio = 0.51; p=0.13

Phase III study: RT vs ERBITUX + RT (1)
Subanalysis of 171 patients with laryngeal and hypopharyngeal SCC

58, male
Ca of the angle, N2b, M0
operable

Laryngoprotected study, Phase II
3 Cyel Induction TPF, Posner Prot.
CR
CRT, RTOG 91-11
3y result: no recurrence
no late toxicity
64 male
Multifocal microcarcinoma supraglottic bilateral operable

RT, 70Gy, normofractionation
3y result: free of tumor

53 male
Postcricoid carcinoma T2N2cM0 operable
53, male
Postcricoid carcinoma T2N2cM0 operable

Laryngoprotect Study, Phase II
3 Cyc Induction TPF, Posner Prot.
CRT, RTOG 91-11
3y result: no recurrence
no late toxicity

Vocal cord
T / T2
N0 / N2a / N2b / N2c

Surgery
CCA
CCF
Neck dissection comprehensive / selective

Radiation
3D CRT/IMRT
Standard
Hyperfractionated / Accelerated (protocol?)

Chemotherapy
Neoadjuvant / Concurrent (protocol?)
Adverse events (CTCAE v3.0)
Survival

Other therapy
Larynx preservation / Function / Tumor control

Vocal cord
T4a
N1 / N2a / N2b / N2c

Surgery
CCA
CCF
Neck dissection comprehensive / selective

Radiation
3D CRT/IMRT
Standard
Hyperfractionated / Accelerated (protocol?)

Chemotherapy
Neoadjuvant / Concurrent (protocol?)
Adverse events (CTCAE v3.0)
Survival

Other therapy
Larynx preservation / Function / Tumor control
Vocal cord/subglottis
T1 / T2a
N1 / N2a/b/ / N3

Surgery
CCS
TLS
SCPL

Radiation (3-D CRT/IMRT)

Chemotherapy

Other therapy

Larynx preservation / function
Lymphoma spread
PTOM and related

Supraglottis
T2 / T3 / T4a
N1 / N2a/b/c / N3

Surgery
CCS
TLS
SCPL

Radiation (3-D CRT/IMRT)

Chemotherapy

Other therapy

Larynx preservation / function
Lymphoma spread
PTOM and related

State of the art?

primary treatment

Surgery Total LE only T4?.......yes
TLS,CCS,CHEP at all?.......yes, contribution for CRT supravening
 Only

Neck dissection (XRT) when?.......RT in case is continuous
Radio-/chemo-therapy
    combined(RT) or sequential(RT) less support by studies
normofract or hyperfract accel RT...........useful
    bionradiation(EGFR): replacing or adding to....unknown more data