Squamous Cell Cancer of the Esophagus
Definitive Chemoradiotherapy

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A Case from Last Week

- 09/2017 Diagnosis in a female, 58 ys, **Esophageal Squamous Cell Cancer**
  Location: **middle third, T3 N+ M0**, 10cm length, stenotic, without airway infiltration

- 10-11/2017 **Cisplatin/5-FU + 60Gy (fr 2Gy)**

- 6/2018: **Recurrence/tumor persistence** in the esophageal wall (in a 'radiogenic stenosis').

- Diagnosis with repeated bite-on-bite biopsies

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CT Thorax/Abdomen 7 June 2018
A Case from Last Week

To be discussed

• Was the decision for definitive RCTx correct?

• Was the treatment regimen correct? Cisplatin/5-FU + 60Gy (fr 2Gy)

• How to treat local recurrence?
1. Was the Decision for Definitive RCTx Correct?

ESMO Guidelines
Esophageal Cancer

Randomized Trials – Postoperative Mortality

**FRENCH FFCD9102**


**GERMAN**

- Def. CRTx 66 Gy
- 46 Gy + SURG
- 40 Gy + SURG
- Def. CRTx 65 Gy

Randomized Trials – Postoperative Mortality

**FRENCH FFCD9102**

90-day mortality 9.3% vs. 0.8%

**GERMAN**

Tx.-rel. mortality 12.8% vs. 3.5%


Contemporary Postoperative Mortality

Scandinavia 2016
NeoRes Study*
Cisplatin/5-FU + 40 Gy → Surgery

90-day mortality (6/78)
8%

*N ESCC 28%, AC 72% included in analysis

Netherlands 2017
Extended CROSS eligibility criteria**
Carbo/Paclitaxel + 41.4 Gy → Surgery

90-day mortality (7/72)
10%

**N ESCC 21%, AC 79% included in analysis

QoL post Esophagectomy vs Def. RCTx (FFCD9102)

Physical functioning and fatigue scores were not restored to pre-esophagectomy levels

Most QoL domains were restored to pre RCTx levels

To be discussed

- Was the decision for definitive RCTx correct?
- Was the treatment regimen correct? Cisplatin/5-FU + 60Gy (fr 2Gy)
- How to treat local recurrence?
Standard versus Higher Radiation Dose

USA INT 0123 (2002)

Conclusion: Chemoradiation with a dose of 50.4 Gy remains standard for definitive treatment. No evidence of benefit for dose escalation > 50.4 Gy

Xu YZW, et al. ASCO 2018; #4013
Cisplatin-5FU versus FOLFOX + RTx

France - PRODIGE5 / ACCORD17

Cisplatin-5FU x 4 + 50Gy (fr 2Gy)

FOLFOX x 6 + 50Gy (fr 2Gy)

## Better Chemotherapy in Definitive RCTx?

<table>
<thead>
<tr>
<th>Study</th>
<th>Regimen</th>
<th>OS Standard</th>
<th>OS Experimental</th>
<th>HR and P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK SCOPE-1</td>
<td>Cisplatin 60 mg/m² d1 Capecitabine 625 mg/m² 2x/d (d1–21) + 50 Gy/2.0 Gy +/- Cetuximab</td>
<td>Median 25.4 months</td>
<td>Median 22.1 months</td>
<td>HR 1.53 [95% CI 1.03–2.27]; p=0.035)</td>
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<tr>
<td>USA RTOG 0436</td>
<td>Cisplatin (50mg/m²), Paclitaxel (25mg/m²), + 50.4 Gy/1.8 Gy +/- Cetuximab</td>
<td>2 years: 44% 3 years: 28%</td>
<td>2 years: 45% 3 years: 34%</td>
<td>HR, 0.90; 95%CI, 0.70-1.16; P = 0.47</td>
</tr>
</tbody>
</table>

**Conclusion:** Chemotherapy with Cisplatin and 5-FU + RTx + ~50 Gy remains standard. No evidence of greater efficacy for any other regimen.

To be discussed

• Was the decision for definitive RCTx correct?

• Was the treatment regimen correct?
  Cisplatin/5-FU + 60Gy (fr 2Gy)

• How to treat local recurrence?
What is the Treatment of Relapse?

ESMO Guidelines
Esophageal Cancer

Probability of complete response
48% for ESCC
(according to CROSS study)

Salvage versus Planned Surgery

<table>
<thead>
<tr>
<th></th>
<th>SALV</th>
<th>NCRS</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-hospital mortality</td>
<td>8.4%</td>
<td>9.3%</td>
<td></td>
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<tr>
<td>Anastomotic leak rate</td>
<td>17.2%</td>
<td>10.7%</td>
<td>0.007</td>
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<tr>
<td>3-y-OS</td>
<td>43.3%</td>
<td>40.1%</td>
<td>0.542</td>
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<tr>
<td>3-y-DFS</td>
<td>39.2%</td>
<td>32.8%</td>
<td>0.232</td>
</tr>
</tbody>
</table>

Salvage Surgery

- High mortality (16% vs 6%) in low vs high volume centers
- High mortality (28% vs 4%) after > 55Gy radiation

Pre Sano Trial

Selection of patients for a watch-and-wait strategy

- Endoscopy
- Bite-on-bite biopsy
- Endosonography
- Fine needle aspiration
- PET-CA

Clinical Response Evaluation
week 6 and week 12

- Sensitivity 90%
- Specificity 72%

**Ongoing Phase II / Phase III Studies**

**NL SANO TRIAL**

- Inclusion
  - nCRT
  - CRE-I
  - CRE-II
  - cCR
  - "Treatment allocation"*

  - Surgery
  - Active surveillance

**FRANCE PRODIGE-32 ESOSTRATE FFCD-1401**

- Registration
- (RCT) treatment at choice of site
- E: Assessment of the response 5-6 weeks after RCT
- R: Monitoring (Salvage surgery in case of resectable recurrence)
- Translational research: Blood samples and biopsies sent to EPIGENETEC

- If complete response: randomization


https://clinicaltrials.gov/ct2/show/NCT02551458
SUMMARY – Definitive Chemoradiotherapy for ESCC

• Definitive chemoradiation is a recommended standard (ESMO 2016)
• Cisplatin-5FU + 50.4 Gy has the best evidence
• No evidence for higher radiation doses
• Salvage surgery for local recurrence is an option
• To be done in highly experienced expert centers, and if possible
• In ongoing phase II/III clinical trials