ADVANCES IN GASTRIC CANCER
How to approach localised disease?

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University of Valencia, Spain
CLASSICAL APPROACH TO LOCALISED GASTRIC CANCER

Surgical resection
Pathology assessment and estimation of risk
Treatment based upon classical TNM stage
Postoperative chemotherapy of doubtful versus no value
Postoperative chemoradiation
META-ANALYSIS OF TRIALS OF ADJUVANT CHEMOTHERAPY VS. SURGERY ALONE

In localised gastric cancer

<table>
<thead>
<tr>
<th>Meta-analysis</th>
<th>Year</th>
<th>No. trials</th>
<th>No. pts</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hermanns (1)</td>
<td>1993</td>
<td>11</td>
<td>2096</td>
<td>0.88</td>
<td>0.78-1.08</td>
<td>No benefit</td>
</tr>
<tr>
<td>J Clin Oncol</td>
<td></td>
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<td></td>
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<tr>
<td>Earle (2)</td>
<td>1999</td>
<td>13</td>
<td>1990</td>
<td>0.80</td>
<td>0.66–0.97</td>
<td>Small survival benefit</td>
</tr>
<tr>
<td>Eur J Cancer</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td>In N+ patients</td>
</tr>
<tr>
<td>Mari (3)</td>
<td>2000</td>
<td>20</td>
<td>3658</td>
<td>0.82</td>
<td>0.75–0.89</td>
<td>Small survival benefit</td>
</tr>
<tr>
<td>Ann Oncol</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Janunger (4)</td>
<td>2002</td>
<td>21</td>
<td>3962</td>
<td>0.84</td>
<td>0.74–0.96</td>
<td>Very heterogeneous group of trials</td>
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<tr>
<td>Eur J Surg</td>
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<tr>
<td>Zhao et al (5)</td>
<td>2008</td>
<td>15</td>
<td>3212</td>
<td>0.90</td>
<td>0.84–0.96</td>
<td>Significant benefit</td>
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<tr>
<td>Cancer Invest</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td>P: 0.001</td>
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<tr>
<td>Liu et al (6)</td>
<td>2008</td>
<td>19</td>
<td>2286</td>
<td>0.85</td>
<td>0.80-0.90</td>
<td>Significant benefit</td>
</tr>
<tr>
<td>Eur J Surg Oncol</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>P&lt;0.0001</td>
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<tr>
<td>Gastric Group (7)</td>
<td>2010</td>
<td>17</td>
<td>3871</td>
<td>0.82</td>
<td>0.76-090</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>JAMA</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

WHY HAS ADJUVANT CHEMOTHERAPY FAILED TO SHOW ANY POSITIVE EFFECT AFTER SURGERY...

... In gastric cancer?

Non standard surgery
High risk of local relapse
Chemotherapy not very active in advanced disease: Complete response rate less than 10%
Heterogeneous samples, low size samples, most patients n-
Inadequate statistical design
Prolonged and slow accrual
META-ANALYSIS

Individual data of trials involving adjuvant chemotherapy versus surgery alone for gastric cancer

Overall survival estimate after any chemotherapy or surgery alone truncated at 10 years

Reproduced with permission from JAMA 2010;303:1729–37. The Gastric Group. Copyright©2010 American Medical Association. All rights reserved.
ADJUVANT CAPECITABINE PLUS OXALIPLATIN
For gastric cancer after D2 gastrectomy versus surgery alone:
5-year follow-up of a randomised phase III trial

ADJUVANT CAPECITABINE PLUS OXALIPLATIN

For gastric cancer after D2 gastrectomy versus surgery alone: 5-year follow-up of a randomised phase III trial

THE ROLE OF RADIATION IN THE POSTOPERATIVE SETTING

Adjuvant chemoradiotherapy for gastric cancer after surgery versus surgery alone: A randomised Phase III Trial

Study design

- Surgery
- Stratification
  - T 1–4
  - NODES
    - 0, 1–3, >3
- No treatment
- CT+ CT-RT + CT

ADJUVANT CHEMORADIOThERAPY FOR GASTRIC CANCER AFTER SURGERY VERSUS SURGERY ALONE

A randomised Phase III Trial

Overall survival among all eligible patients, according to treatment-group assignment

ADJUVANT CHEMORADIOThERAPY FOR GASTRIC CANCER AFTER SURGERY VERSUS SURGERY ALONE
Long term results of a randomised Phase III Trial

Overall survival by arm

Relapse-free survival by arm

Patterns of failure by arm

<table>
<thead>
<tr>
<th></th>
<th>Radiochemo-therapy</th>
<th>Control (surgery alone)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relapse Status</td>
<td>No.    %</td>
<td>No.        %</td>
<td>No.   %</td>
</tr>
<tr>
<td>No relapse*</td>
<td>135   48</td>
<td>67         24</td>
<td>202   36</td>
</tr>
<tr>
<td>Relapse*</td>
<td>147   52</td>
<td>210        76</td>
<td>357   64</td>
</tr>
<tr>
<td>Sites of relapse (% of those randomly assigned)*</td>
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<tr>
<td>Local</td>
<td>7     2</td>
<td>21         8</td>
<td>28    5</td>
</tr>
<tr>
<td>Regional</td>
<td>62    22</td>
<td>109        39</td>
<td>171   31</td>
</tr>
<tr>
<td>Distant</td>
<td>46    16</td>
<td>49         18</td>
<td>95    17</td>
</tr>
<tr>
<td>Unknown site</td>
<td>32    11</td>
<td>31         11</td>
<td>63    11</td>
</tr>
<tr>
<td>Total</td>
<td>282   -</td>
<td>277        -</td>
<td>559   -</td>
</tr>
</tbody>
</table>

*Indicates statistically significant comparisons. P <.001 for relapse vs. no relapse ($\chi^2$); P=.012 for sites of relapse (among those with sites reported, $\chi^2$ test for trend).

FU, fluorouracil; RT, radiotherapy.
ARTIST: THE ROLE OF RADIATION IN THE POSTOPERATIVE SETTING

Adjuvant cisplatin and capecitabine versus chemoradiation for gastric cancer after surgery: A randomised phase III Trial

Disease-free survival

Overall survival

XP, capecitabine plus cisplatin; XPRT, concurrent chemoradiotherapy with capecitabine plus cisplatin.

CRITICS TRIAL

Design: 788 pts: 393 CT and 395 CRT

Stratified for:
- Center
- Histological type
- Localisation of tumour

45 Gy/25 fx + capecitabine cisplatin

FINAL RESULTS FROM CRITICS

ASSESSING PREOPERATIVE CHEMORADIATION VS. CHEMOTHERAPY ALONE

In gastro-oesophageal adenocarcinomas: The TOPGEAR Trial

EORTC Clinical Trial Database. Available at: https://www.eortc.org/research_field/clinical-detail/1707/. Accessed May 2019
TREATMENT FOR LOCALISED GASTRIC CANCER

What is standard of care?

Algorithm for the management of gastric cancer

Gastric cancer (adenocarcinoma)

Operable Stage T1N0

Consider endoscopic/limited resection

Operable Stage >T1N0

Preferred pathway

Preoperative chemotherapy

Surgery

Post-operative chemotherapy

Surgery

Adjuvant chemoradiation

Adjuvant chemotherapy

Eligible patients:
- Adenocarcinoma of the stomach or lower third of the oesophagus (from 1999), suitable for curative resection
- Non-metastatic disease
- Stage II or greater

Chemotherapy (ECF):
- Epirubicin 50 mg/m², IV day 1
- Cisplatin 60 mg/m², IV day 1
- 5-FU 200 mg/m²/day, continuous infusion, days 1-21
(cycles repeated every 3 weeks)

Study entry and randomisation
- S arm N=253
- CSC arm N=250

Primary
- Overall survival

Secondary
- Progression-free survival
- Surgical resectability
- Quality of Life

Recruitment: July 1994-April 2002

## MAGIC TRIAL

Postoperative morbidity/mortality

<table>
<thead>
<tr>
<th></th>
<th>CSC</th>
<th>S</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postoperative deaths</td>
<td>6% (14/219)</td>
<td>6% (15/240)</td>
</tr>
<tr>
<td>Postoperative complications</td>
<td>46%</td>
<td>46%</td>
</tr>
<tr>
<td>Median duration of postoperative hospital stay</td>
<td>13 days</td>
<td>13 days</td>
</tr>
</tbody>
</table>

MAGIC TRIAL RESULTS

2 year survival 5 year survival Median survival
CSC 50% 36% 24 mo
S 41% 23% 20 mo
Benefit to CSC arm 9% 13% 4 mo

On multivariate analysis, treatment effect unchanged after adjustment for age, performance status, site of primary and gender

Hazard ratio for death
- Adjusted: 0.74 (95%CI: 0.59-0.93)
- Unadjusted: 0.75

In operable gastric and lower oesophageal cancer, perioperative chemotherapy with ECF:

- Leads to downsizing of primary tumour
- pCR rate 8%
- Significantly improves progression-free survival
- Significantly improves overall survival

PERIOPERATIVE CHEMO
FNLCC 94012-FFCD 9703 Trial

Randomisation N=224

CT + S

FP (°) x 2/3 every 28 days

4 - 6 weeks

Resection

4 – 6 weeks

FP x 3/4 or no treatment

Follow-up

S

Within 4 weeks

Resection

FP x 3/4 or no treatment

Follow-up

Trial accrual 1995-2003
Median FU 5.7 yrs

*5-Fluorouracil 800 mg/m² d1-5*
+ Cisplatin 100 mg/m² day 1

# SUMMARY OF PHASE III CONTROLLED TRIALS

Perioperative chemotherapy for localised oesophago-gastric cancer

<table>
<thead>
<tr>
<th>Trial</th>
<th>CT</th>
<th>No. pts control</th>
<th>No. pts CT</th>
<th>5-year survival control</th>
<th>5-year survival CT</th>
<th>HR (CI at 95%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cunningham D, N Eng J Med 2006</td>
<td>ECF</td>
<td>253</td>
<td>250</td>
<td>23%</td>
<td>36%</td>
<td>0.75 (0.60-0.93) p=0.009</td>
</tr>
<tr>
<td>Ychou M, J Clin Oncol 2011</td>
<td>CDDP</td>
<td>111</td>
<td>113</td>
<td>24%</td>
<td>38%</td>
<td>0.69 (0.50-0.95) p=0.021</td>
</tr>
<tr>
<td>Allum W, J Clin Oncol 2009</td>
<td>CDDP</td>
<td>402</td>
<td>400</td>
<td>17.6%</td>
<td>25.5%</td>
<td>0.84 (0.72-0.98) P=0.03</td>
</tr>
</tbody>
</table>

REGRESSION GRADE AFTER NEOADJUVANT ECF AND OVERALL SURVIVAL

In oesophago-gastric cancer in MAGIC

ASSESSING POSTOPERATIVE IMMUNOTHERAPY VS. CHEMOTHERAPY

In gastro-oesophageal adenocarcinomas with poor regression after neoadjuvant chemotherapy: The VESTIGE Trial

Phase II, n=240

GC or EGJ
N+ or R1
After neoadj.CT
D2 Lymph

1:1

Stratification by:
- Location (gastric vs. EG junction)
- Histology (intestinal vs. non-intestinal)
- R0 versus R1 status
- Preoperative chemotherapy (FLOT vs. non-FLOT)

Nivolumab 1 mg/kg IV Q3W plus Ipilimumab 3 mg/kg IV Q3W for 4 cycles (3 months)

Nivolumab 480 mg flat-dose IV Q4W for 9 months

Control arm: Completion of the perioperative treatment according to the 2016 ESMO GUIDELINES

EORTC Clinical Trial Database. Available at: https://www.eortc.org/research_field/clinical-detail/1707/. Accessed May 2019
THE MOLECULAR CLASSIFICATION OF GASTRIC CANCER ACCORDING TO THE CANCER GENOME ATLAS

50% CIN
- Intestinal histology
- TP53 mutation
- RTK-RAS activation

9% EBV
- PIK3CA mutation
- PD-L1/2 overexpression
- EBV-CIMP
- CDKN2A silencing
- Immune cell signalling

20% GS
- Diffuse histology
- CDH1, RHOA mutations
- CLDN18–ARHGAP fusion
- Cell adhesion

22% MSI
- Hypermutation
- Gastric-CIMP
- MLH1 silencing
- Mitotic pathways
OVERALL SURVIVAL

In stage I-III gastro-oesophageal adenocarcinoma according to MSI status

Martinez-Ciarpaglini C, et al. ESMO Open 2019 in press. Reproduced under the terms of the Creative Commons Attribution-Non Commercial 4.0 International (CC BY-NC 4.0). Available at: http://creativecommons.org/licenses/by-nc/4.0/; accessed May 2019.
NEOADJUVANT ECF AND OVERALL SURVIVAL IN MAGIC ACCORDING TO MSI STATUS

Overall survival by microsatellite instability (MSI) status and treatment arm in the study patients

Reproduced with permission from JAMA Oncol. 2017;3(9):1197–1203. Copyright©2017 American Medical Association. All rights reserved.
Response to Adjuvant Chemotherapy According to MSI Status

- The benefit from adjuvant chemotherapy was not clear in MSI-H gastric cancer.
- In sharp contrast, the prognosis of patients treated with chemotherapy was significantly better than that of patients treated with surgery only in the MSS gastric cancer group.

5-FU, LEUCOVORIN, OXALIPLATIN AND DOCETAXEL VS. ECF/ECX AS PREOPERATIVE CHEMOTHERAPY
For gastro-oesophageal adenocarcinoma: The FLOT-4 Study

Randomised, multicentre, Phase II/III Study

- Gastric or EGJ cancer typ I-III
- Medically and anatomically operable
- cT2-4/cN-any/cM0 or cT-any/cN+/cM0

Stratification:
- ECOG (0 or 1 vs. 2), localisation (GEJ Type I vs. Type II/III vs. Gastric), age (< 60 vs. 60-69 vs. ≥70 years) and nodal status (cN+ vs. cN-)

23% had Siewert type I
33% had Siewert type II/III

FLOT: Docetaxel 50mg/m², d1; 5-FU 2600 mg/m², d1; Leucovorin 200 mg/m², d1; Oxaliplatin 85 mg/m², d1, q2w

ECF/ECX: Epirubicin 50 mg/m², d1; Cisplatin 60 mg/m², d1; 5-FU 200 mg/m² (or Capecitabin 1250 mg/m² p.o. divided in 2 doses d1-d21), q2w

n=716

5-FU, LEUCOVORIN, OXALIPLATIN AND DOCETAXEL VS. ECF/ECX AS PREOPERATIVE CHEMOTHERAPY

For gastro-oesophageal adenocarcinoma: The FLOT-4 Study

Results on overall survival

Reprinted from The Lancet, 393(10184), Al-Batran SE, et al. Perioperative chemotherapy with fluorouracil plus leucovorin, oxaliplatin, and docetaxel versus fluorouracil or capecitabine plus cisplatin and epirubicin for locally advanced, resectable gastric or gastro-oesophageal junction adenocarcinoma (FLOT4): a randomised, phase 2/3 trial, 1948–57. Copyright 2019, with permission from Elsevier.
# 5-FU, LEUCOVORIN, OXALIPLATIN AND DOCETAXEL VS. ECF/ECX AS PREOPERATIVE CHEMOTHERAPY

For gastro-oesophageal adenocarcinoma: The FLOT-4 Study

## Treatment related toxicities according to treatment arm

<table>
<thead>
<tr>
<th></th>
<th>ECF/ECX (n=354)</th>
<th>FLOT (n=354)</th>
<th>Difference in grade 3 or 4 events (p value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhoea</td>
<td>Grade 1 or 2</td>
<td>Grade 3 or 4</td>
<td>Grade 1 or 2</td>
</tr>
<tr>
<td></td>
<td>103 (29%)</td>
<td>13 (4%)</td>
<td>182 (52%)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>102 (29%)</td>
<td>27 (8%)</td>
<td>113 (32%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>215 (61%)</td>
<td>55 (16%)</td>
<td>211 (60%)</td>
</tr>
<tr>
<td>Constipation</td>
<td>86 (24%)</td>
<td>1 (&lt;1%)</td>
<td>75 (21%)</td>
</tr>
<tr>
<td>Stomatitis or mucositis</td>
<td>107 (30%)</td>
<td>10 (3%)</td>
<td>99 (28%)</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>175 (49%)</td>
<td>75 (21%)</td>
<td>180 (51%)</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>93 (26%)</td>
<td>139 (39%)</td>
<td>84 (24%)</td>
</tr>
<tr>
<td>Anaemia</td>
<td>282 (80%)</td>
<td>20 (6%)</td>
<td>283 (80%)</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>123 (35%)</td>
<td>11 (3%)</td>
<td>137 (39%)</td>
</tr>
<tr>
<td>Serum AST</td>
<td>41 (12%)</td>
<td>1 (&lt;1%)</td>
<td>116 (33%)</td>
</tr>
<tr>
<td>Serum ALT</td>
<td>55 (16%)</td>
<td>1 (&lt;1%)</td>
<td>127 (36%)</td>
</tr>
<tr>
<td>Fever</td>
<td>29 (8%)</td>
<td>2 (1%)</td>
<td>77 (22%)</td>
</tr>
<tr>
<td>Peripheral neuropathy</td>
<td>120 (34%)</td>
<td>7 (2%)</td>
<td>228 (64%)</td>
</tr>
<tr>
<td>Pain</td>
<td>171 (48%)</td>
<td>14 (4%)</td>
<td>166 (47%)</td>
</tr>
<tr>
<td>Alopecia*</td>
<td>147 (42%)</td>
<td>74 (21%)</td>
<td>122 (35%)</td>
</tr>
<tr>
<td>Renal</td>
<td>99 (28%)</td>
<td>1 (&lt;1%)</td>
<td>38 (11%)</td>
</tr>
<tr>
<td>Infections</td>
<td>62 (18%)</td>
<td>30 (9%)</td>
<td>61 (17%)</td>
</tr>
<tr>
<td>Thromboembolic</td>
<td>31 (9%)</td>
<td>21 (6%)</td>
<td>13 (4%)</td>
</tr>
<tr>
<td>Toxic death†</td>
<td>2 (&lt;1%)</td>
<td>2 (&lt;1%)</td>
<td>2 (&lt;1%)</td>
</tr>
</tbody>
</table>

Reprinted from The Lancet, 393(10184), Al-Batran SE, et al. Perioperative chemotherapy with fluorouracil plus leucovorin, oxaliplatin, and docetaxel versus fluorouracil or capecitabine plus cisplatin and epirubicin for locally advanced, resectable gastric or gastro-oesophageal junction adenocarcinoma (FLOT4): a randomised, phase 2/3 trial, 1948–57. Copyright 2019, with permission from Elsevier.
# FLOT as Perioperative Chemotherapy for Localised Oesophago-Gastric Cancer

A new standard

<table>
<thead>
<tr>
<th>Trial</th>
<th>CT</th>
<th>No. pts control</th>
<th>No. pts CT</th>
<th>5-year survival control</th>
<th>5-year survival CT</th>
<th>HR (CI at 95%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cunningham D, N Eng J Med 2006</td>
<td>ECF</td>
<td>253 No CT</td>
<td>250</td>
<td>23%</td>
<td>36 %</td>
<td>0.75 (0.60-0.93)</td>
</tr>
<tr>
<td>Ychou M, J Clin Oncol 2011</td>
<td>CDDP 5-FU</td>
<td>111 No CT</td>
<td>113</td>
<td>24%</td>
<td>38%</td>
<td>0.69 (0.50-0.95)</td>
</tr>
<tr>
<td>Allum W, J Clin Oncol 2009</td>
<td>CDDPFU</td>
<td>402 No CT</td>
<td>400</td>
<td>17.6%</td>
<td>25.5%</td>
<td>0.84 (0.72-0.98)</td>
</tr>
<tr>
<td>Al-Batran SE, Lancet 201</td>
<td>FLOT</td>
<td>360 ECF</td>
<td>356 FLOT</td>
<td>36%</td>
<td>45%</td>
<td>0.77 (0.63-0.94)</td>
</tr>
</tbody>
</table>

FLOT AS PERIOPERATIVE CHEMOTHERAPY FOR LOCALISED OESOPHAGO-GASTRIC CANCER
A new standard

<table>
<thead>
<tr>
<th>Trial</th>
<th>CT Experimental</th>
<th>No. pts</th>
<th>pCR Control vs. Experimental</th>
<th>5-year survival Control vs. Exp</th>
<th>HR (CI at 95%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cunningham D, N Engl J Med 2006</td>
<td>ECF</td>
<td>503</td>
<td>0% vs. 8%</td>
<td>23% vs. 36%</td>
<td>0.75 (0.60-0.93), p=0.009</td>
</tr>
<tr>
<td>Al-Batran SE, Lancet 2019</td>
<td>FLOT</td>
<td>716</td>
<td>5.8% vs. 15.6%</td>
<td>36% vs. 45%</td>
<td>0.77 (0.63-0.94), P=0.012</td>
</tr>
<tr>
<td>Alderson D, Lancet Oncol 2017</td>
<td>ECX</td>
<td>897</td>
<td>3% vs. 11%</td>
<td>39% vs. 42%*</td>
<td>0.90 (0.77-1.05), 0.19</td>
</tr>
<tr>
<td>Cunningham D, Lancet Oncol 2017</td>
<td>BEV-ECX</td>
<td>1063</td>
<td>8% vs. 11%</td>
<td>50% vs. 48%*</td>
<td>1.09 (0.91-1.29), 0.36</td>
</tr>
</tbody>
</table>

FLOT AS PERIOPERATIVE CHEMOTHERAPY FOR LOCALISED OESOPHAGO-GASTRIC CANCER: A NEW STANDARD

**ESMO Magnitude of Clinical Benefit Scale v1.1**

<table>
<thead>
<tr>
<th>Name of study:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Study drug:</td>
<td>Indication:</td>
</tr>
<tr>
<td>First author:</td>
<td>Year:</td>
</tr>
<tr>
<td>Name of evaluator:</td>
<td></td>
</tr>
</tbody>
</table>

**Grade A**

- >5% improvement of survival at ≥3 years follow-up
- Improvements in DFS alone (primary endpoint) (HR <0.65) in studies without mature survival data

9% (> 5%) INCREASE IN OS AT 3 YEARS
FROM 48% FOR ECF/ECX TO 57% FOR FLOT: GRADING A
NO CONCERNS FROM TOXICITY

ASSESSING THE ADDITION OF TRASTUZUMAB VS. TRASTUZUMAB PERTUZUMAB

To preoperative chemotherapy in HER2 amplified gastro-oesophageal adenocarcinomas: The INNOVATION Trial

FLOT, CapOx or mFOLFOX6 (Cisplatin/5FU Korea)

FLOT, CapOx or mFOLFOX6+ Trastuzumab (Cisplatin/5FU Korea)

FLOT, CapOx or mFOLFOX6+ Trastuzumab+ Pertuzumab (Cisplatin/5FU Korea)

Surgery D2

FLOT, CapOx or mFOLFOX6 (Cisplatin/5FU Korea)

FLOT, CapOx or mFOLFOX6 + Trastuzumab (Cisplatin/5FU Korea)

FLOT, CapOx or mFOLFOX6 + Trastuzumab + Pertuzumab (Cisplatin/5FU Korea)

Observation

Trastuzumab

Trastuzumab + Pertuzumab

Phase II, n=215

1:2:2

EORTC Clinical Trial Database. Available at: https://www.eortc.org/research_field/clinical-detail/1203/. Accessed May 2019
Conclusions

Perioperative chemotherapy:
- Induces downstaging
- May increase the R0 resection rate
- Prolongs disease free survival
- Improves overall survival

Evidence level I based upon 2 well designed and properly conducted randomised trials.
FLOT is current standard of care
Preoperative therapy is better tolerated than postoperative
Quality of surgery essential
Localised gastric cancer requires a multidisciplinary team approach
Adjuvant or neoadjuvant chemotherapy does not seem to benefit patients with MSI
Postoperative chemoradiation of limited value if D2 surgery performed or preoperative chemotherapy given

Preoperative chemoradiation under scrutiny in TOPGEAR trial

Radiotherapy still experimental

No biological agents (bevacizumab) to be used in this setting

Further research on biological predictive factors is needed

The addition of trastuzumab vs. trastuzumab/pertuzumab under investigation in the INNOVATION trial

Immunotherapy experimental
CURRENTLY RECOMMENDED APPROACH TO LOCALISED GASTRIC CANCER

Clinical assessment and staging
Multidisciplinary team discussion
FLOT preoperative treatment in clinical stage II and III patients
Surgical resection after FLOT chemotherapy
Pathology assessment and estimation of risk
Postoperative chemotherapy if tolerated
THANK YOU!