NEOADJUVANT AND ADJUVANT THERAPY FOR GASTROESOPHAGEAL ADENOCARCINOMA

Prof. Andrés Cervantes
CONFLICT OF INTEREST DISCLOSURE

Employment: None; Stock Ownership: None

Consultant or Advisory Role: Merck Serono, Roche, Beigene, Bayer, Servier, Pierre Fabre, Novartis, Takeda, Astelas.

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Others: Executive Board member of ESMO, Director of Education ESMO, General and Scientific Director INCLIVA, Associate Editor: Annals of Oncology and ESMO Open, Editor in chief: Cancer Treatment Reviews.
“OLD” 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

<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) J Clin Oncol</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>Earle (2) Eur J Cancer</td>
<td>1999</td>
<td>13</td>
<td>1990</td>
<td>0.80</td>
<td>0.66–0.97</td>
<td>Small survival benefit In N+ patients</td>
</tr>
<tr>
<td>Mari (3) Ann Oncol</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>Janunger (4) Eur J Surg</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>
</tr>
<tr>
<td>Zhao et al (5) Cancer Invest</td>
<td>2008</td>
<td>15</td>
<td>3212</td>
<td>0.90</td>
<td>0.84-0.96</td>
<td>Significant benefit P: 0.001</td>
</tr>
<tr>
<td>Liu et al (6) Eur J Surg Oncol</td>
<td>2008</td>
<td>19</td>
<td>2286</td>
<td>0.85</td>
<td>0.80-0.96</td>
<td>Significant benefit P&lt;0.0001</td>
</tr>
<tr>
<td>Gastric Group (7) JAMA</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>
</tbody>
</table>

WHY HAS ADJUVANT CHEMOTHERAPY FAILED AFTER SURGERY IN WESTERN TRIALS?

Non standard surgery
High risk of local relapse
Chemotherapy nor 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

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Adjuvant S-1 in gastric cancer (ACTS-GC)

Overall survival (total population)

Patients with stage II & III gastric cancer; D2 or more dissection

S-1

Observation

n=529

n=530

S-1

HR, 0.669; 95% CI, 0.540 to 0.828

5-Year Overall Survival (%)

S-1 71.7
Surgery only 61.1

Time Since Random Assignment (years)

No. at risk
S-1 529 515 465 416 363 316
Surgery only 530 504 438 365 327 268

Sasako et al. J Clin Oncol 2011
ADJUVANT CAPECITABINE PLUS OXALIPLATIN

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

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

Addition of Docetaxel to Oral Fluoropyrimidine Improves Efficacy in Patients With Stage III Gastric Cancer: Interim Analysis of JACCRO GC-07

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

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>Radiochemotherapy</th>
<th>Control (surgery alone)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relapse Status</td>
<td>No.</td>
<td>%</td>
<td>No.</td>
</tr>
<tr>
<td>No relapse*</td>
<td>135</td>
<td>48</td>
<td>67</td>
</tr>
<tr>
<td>Relapse*</td>
<td>147</td>
<td>52</td>
<td>210</td>
</tr>
<tr>
<td>Sites of relapse (% of those randomly assigned)*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Local</td>
<td>7</td>
<td>2</td>
<td>21</td>
</tr>
<tr>
<td>Regional</td>
<td>62</td>
<td>22</td>
<td>109</td>
</tr>
<tr>
<td>Distant</td>
<td>46</td>
<td>16</td>
<td>49</td>
</tr>
<tr>
<td>Unknown site</td>
<td>32</td>
<td>11</td>
<td>31</td>
</tr>
<tr>
<td>Total</td>
<td>282</td>
<td></td>
<td>277</td>
</tr>
</tbody>
</table>

*Indicates statistically significant comparisons. \( P < .001 \) for relapse v. 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

Preoperative chemotherapy 3x EC/OC q 3 wks → D1 + surgery → 3x EC/OC q 3 wks

Preoperative chemotherapy 3x EC/OC q 3 wks → D1 + surgery → Chemoradiation

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-esophageal adenocarcinomas: The TOPGEAR Trial

Phase II/III (Part I= 120: Part II= 500)

- ECF (or ECX or EOX) x3 cycles or FLOT x 4 cycles
- ECF (or ECX or EOX) x2 cycles or FLOT x 3 cycles + chemoradiotherapy
- ECF (or ECX or EOX) x3 cycles or FLOT x 4 cycles
- ECF (or ECX or EOX) x3 cycles or FLOT x 4 cycles

Stratified by:
- Age: <50 yrs vs. 50 yrs – 70 yrs vs. >70 yrs
- Primary tumour site
- Clinical tumour stage: T1-2 vs. T3-4
- Clinical nodal stage: N+ve vs. N-ve
- Chemotherapy regimen: ECF/ECX vs. EOX vs. FLOT
- Gender, site, PET, EUS, laparoscopy
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
      - Preoperative chemotherapy
        - Surgery
        - Post-operative chemotherapy
  - Operable Stage >T1N0
    - Preferred pathway
      - Surgery
      - Adjuvant chemotherapy
      - Adjuvant chemoradiation

**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)

Recruitment: July 1994-April 2002

**Primary**
Overall survival

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

### 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 post-operative hospital stay</td>
<td>13 days</td>
<td>13 days</td>
</tr>
</tbody>
</table>

MAGIC TRIAL RESULTS

**PFS**

Logrank p-value = 0.0001

Hazard Ratio = 0.66

(95% CI 0.53 - 0.81)

**Overall**

Logrank p-value = 0.009

Hazard Ratio = 0.75

(95% CI 0.60 - 0.93)

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

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MAGIC TRIAL

Conclusions

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

### 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 No CT</td>
<td>250</td>
<td>23%</td>
<td>36 %</td>
<td>0.75</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.60-0.93</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>p=0.009</td>
</tr>
<tr>
<td>Ychou M, J Clin Oncol 2011</td>
<td>CDDP</td>
<td>111 No CT</td>
<td>113</td>
<td>24%</td>
<td>38%</td>
<td>0.69</td>
</tr>
<tr>
<td></td>
<td>5-FU</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.50-0.95</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>p=0.021</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</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.72-0.98</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>P=0.03</td>
</tr>
</tbody>
</table>

REGRESSION GRADE AFTER NEOADJUVANT ECF AND OVERALL SURVIVAL

In oesophagogastric cancer in MAGIC

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THE MOLECULAR CLASSIFICATION OF GASTRIC CANCER ACCORDING TO THE CANCER GENOME ATLAS

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

GE Junction

Fundus

Cardia

Pylorus

Antrum

Body


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

MSI
- Hypermutation
- Gastric-CIMP
- MLH1 silencing
- Mitotic pathways

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

50% 9%

20% 22%
INDIVIDUAL DATA PATIENT META-ANALYSIS OF MSI STATUS IN LOCALIZED GASTRIC CANCER

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

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 type 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

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></td>
<td>Grade 1 or 2</td>
<td>Grade 3 or 4</td>
<td>Grade 1 or 2</td>
</tr>
<tr>
<td>Diarrhoea</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 (-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>121 (34%)</td>
<td>1 (-1%)</td>
<td>116 (33%)</td>
</tr>
<tr>
<td>Serum ALT</td>
<td>55 (16%)</td>
<td>1 (-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>34 (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>59 (16%)</td>
<td>1 (-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>--</td>
<td>2 (+1%)</td>
<td>--</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>
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<tbody>
<tr>
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<td>ECF</td>
<td>253 No CT</td>
<td>250</td>
<td>23%</td>
<td>36 %</td>
<td>0.75 (0.60-0.93) p=0.009</td>
</tr>
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<td>Ychou M, J Clin Oncol 2011</td>
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<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>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) P=0.03</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) P=0.012</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 Eng 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 localized Esophago-gastric cancer: a new standard

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

**Form 1:** for new approaches to adjuvant therapy or new potentially curative therapies

| Name of study: | |
| Study drug: | Indication: |
| First author: | Year: | Journal: |
| Name of evaluator: | |

**Grade A**

9% (> 5%) increase in OS at 3 years from 48% for ECF/ECX to 57% for FLOT: Grading A

No concerns from toxicity

PRODIGY: Randomised phase III study in gastric and GEJ adenocarcinoma of peri-op vs. post-op chemotherapy

Histologically confirmed cT2, 3 / N(+) or cT4N\textsubscript{any} gastric or GEJ adenocarcinoma

Primary endpoint: 3-year PFS

HR = 0.70 (95% CI 0.52–0.95) 
p=0.0230, stratified log-rank

Median follow-up 37.4 months

Overall survival

HR = 0.84 (95% CI 0.60–1.19) 
p=0.3383, stratified log-rank 
<30% OS events observed thus far, therefore very low power

Kang et al ESMO 2019
Randomised phase III study in gastric and GEJ adenocarcinoma of peri-operative SOX vs. post-op SOX vs. post-op CAPOX (RESOLVE)

Histologically confirmed cT4aN1 or cT4bNany gastric or GEJ adenocarcinoma

Arm A
D2 surgery → CAPOX ×8 cycles

Arm B
D2 surgery → SOX ×8 cycles

Arm C
SOX ×3 → D2 surgery → SOX ×5 followed by S-1 ×3 cycles

Primary endpoint: 3-year DFS
Arms A vs. C: superiority; A vs. B: non-inferiority

Ji et al ESMO 2019
RESOLVE Primary comparisons

ARMs A vs. C

<table>
<thead>
<tr>
<th></th>
<th>3y-DFS</th>
<th>HR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>A: D2→XELOX</td>
<td>54.78%</td>
<td>0.79</td>
<td>0.0</td>
</tr>
<tr>
<td>C: SOX→D2→SOX</td>
<td>62.02%</td>
<td>(0.62,0.99)</td>
<td></td>
</tr>
</tbody>
</table>

ARMs A vs. B

<table>
<thead>
<tr>
<th></th>
<th>3y-DFS</th>
<th>HR (95% CI)</th>
<th>NI*</th>
</tr>
</thead>
<tbody>
<tr>
<td>A: D2→XELOX</td>
<td>54.78%</td>
<td>0.85</td>
<td>1.33</td>
</tr>
<tr>
<td>B: D2→SOX</td>
<td>60.29%</td>
<td>(0.67,1.07)</td>
<td></td>
</tr>
</tbody>
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Ji et al ESMO 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
EXPERIMENTAL APPROACHES IN LOCALISED GASTRO-OESOPHAGEAL ADENOCARCINOMAS

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!
Thanks