ESMO Clinical Practice Guidelines

Treatment strategies in Gastric Cancer: Applying the ESMO Guidelines - Discussion -

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Disclosures

Yung-Jue Bang has declared no potential conflicts of interest
Case: Resectable GEJ cancer

• 48-years old man
• Presents with gastric pain, dysphagia, weight loss, and anemia
• GEJ adenocarcinoma, HER2 (-)
Q1: Staging investigations

What else is **undoubtedly** needed before decision making?

1. Nothing more - information are complete
2. Endoscopic ultrasound (EUS)
3. EUS plus diagnostic laparascopy
4. EUS plus PET
5. all of the above (EUS, Lap, PET)
## ESMO Clinical Practice Guidelines

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| Routine blood tests              | • Check for evidence of iron-deficiency anaemia  
                                  • Check hepatic and renal function to determine appropriate therapeutic options                                                  |
| Endoscopy + biopsy               | • Obtain tissue for diagnosis, histological classification and molecular biomarkers, e.g. HER-2 status.                                   |
| CT thorax + abdomen ± pelvis     | • Staging of tumour—particularly to detect local/distant lymphadenopathy and metastatic disease sites                                  |
| Endoscopic ultrasound (EUS)      | • Accurate assessment of T and N stage in potentially operable tumours  
                                  • Determine proximal and distal extent of the tumour                                                                                  |
| Laparoscopy + washings           | • To exclude occult metastatic disease involving the diaphragm/peritoneum                                                                 |
| Positron emission tomography (PET, if available) | • May improve detection of occult metastatic disease in some cases                                                                                                                                 |

18-21 December 2015
Singapore
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5. all of the above (EUS, Laparascopy, PET)
Question 2: Approach to operable, but locally advanced GEJ cancer (cT3N1)

1. Surgery alone
2. Surgery plus adjuvant Rtx* / CRtx* (if N+)
3. Preoperative CRtx*
4. Pre- / perioperative ECF / ECX / EOX /...
5. Pre- / perioperative other regimen
ESMO Clinical Practice Guidelines for esophageal cancer

T3-4 N0/N+ M0

SCC

- Fit(#) patient and Experienced Center
  - Preoperative Chemoradiation (41.4 – 45 Gy in 1.8 Gy fractions)
  - Surgery
    - R0
      - No further treatment
    - R1-2
      - Palliative CT for selected patients

- Unfit(#) patient or Non-exp. Center
  - Definitive Chemoradiation (at least 50.4 Gy in 1.8 Gy fractions)
  - Definitive Chemoradiation (at least 50.4 Gy in 1.8 Gy fractions)

Adenocarcinoma

- Fit #
  - Preoperative CRT or perioperative CT
    - 41.4 – 45 Gy in 1.8 Gy fractions + Carbo / Paclitaxel or FOLFOX or cis / FU (or Cis / Irinotecan)
    - 9 weeks Platinum / FU (+ E or D) + Surgery + 9 weeks Platinum / FU (+ E or D)

- Unfit #
  - Palliative therapy
    - Chemotherapy +/- Radiotherapy Local palliation

Phase III trial of preoperative CRT for esophageal or EGJ cancer

- Overall survival was significantly better in the chemoradiotherapy-surgery group (HR, 0.657; 95% CI, 0.495 to 0.871; P=0.003)

Q2: What would be your suggestion?

1. Surgery alone
2. Surgery plus adjuvant Rtx* / CRtx* (if N+)
3. Preoperative CRtx*
4. Pre- / perioperative ECF / ECX / EOX /...
5. Pre- / perioperative other regimen

* Rtx = radiotherapy; CRtx = chemo-radiotherapy
In Asia, other option includes

- Surgery
  - Total gastrectomy (D2 resection)
  - Abdominal approach (for Siewert II-III)
- Followed by adjuvant chemotherapy
  - XELOX for 6 months
  - S-1 for 1 year
Follow-up: relapse

- Treated with preop CRT with carbo/paclitaxel
- Followed by R0 surgery; ‘near CR’

- However, 4.5 months later, CEA 122 ng/mL
  - Relapse with a single liver metastasis
Question 3: chemotherapy of HER2-negative disease

1. Re-biopsy of liver lesion (HER2,...)
2. Start Ctx with FP* alone
3. Start Ctx with FP*/platinum
4. Start Ctx with FP*/ Platinum / Docetaxel
5. Start other treatment (Irinotecan, Ramucirumab,...)
Q3: What is your suggestion now?

1. Re-biopsy of liver lesion (HER2,...)
2. Start Ctx with FP* alone
3. Start Ctx with FP*/platinum
4. Start Ctx with FP*/Platinum / Docetaxel
5. Start other treatment (Irinotecan, Ramucirumab,...)

* FP = any Fluoropyrimidine (inf. 5FU, Capecitabine, S1, others)
**V-325 trial: Overall survival**

- **p=0.0201**
- **HR: 1.293 (95% CI: 1.041-1.606)**
- **Risk reduction: 22.7%**

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<th>Months</th>
<th>Survival Probability (%)</th>
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<tbody>
<tr>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>3</td>
<td>90</td>
</tr>
<tr>
<td>6</td>
<td>80</td>
</tr>
<tr>
<td>9</td>
<td>70</td>
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<tr>
<td>12</td>
<td>60</td>
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<td>24</td>
<td>20</td>
</tr>
<tr>
<td>27</td>
<td>10</td>
</tr>
<tr>
<td>30</td>
<td>0</td>
</tr>
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- **TCF**
  - Median (months): 9.2 (95% CI: 8.38-10.58)
  - 1-year survival: 40.2%
  - 2-year survival: 18.4%

- **CF**
  - Median (months): 8.6 (95% CI: 7.16-9.46)
  - 1-year survival: 31.6%
  - 2-year survival: 8.8%

- **p=0.0201**
- **HR: 1.293 (95% CI: 1.041-1.606)**
- **Risk reduction: 22.7%**

- **DCF was associated with higher incidence of grade ¾ neutropenia with fever and/or infection 29% vs 12%), and grade ¾ diarrhea (19% vs 8%)**
**FOLFIRI vs. ECX: French study**

**Primary endpoint: TTF**

- **HR, 0.77; 95% CI, 0.63 to 0.93; P = .008**

- **TTF**
  - FOLFIRI: 5.08 m
  - ECX: 4.24 m
  - HR: 0.77
  - P: 0.008

- **PFS**
  - FOLFIRI: 5.75 m
  - ECX: 5.29 m
  - HR: 0.99
  - P: 0.96

- **OS**
  - FOLFIRI: 9.72 m
  - ECX: 9.49 m
  - HR: 1.01
  - P: 0.95

- **ORR**
  - FOLFIRI: 37.8%
  - ECX: 39.2%

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Guimbaud R et al. JCO 2014;32:3520-26
Follow-up: 2\textsuperscript{nd} relapse

- Treated with FLOT $\rightarrow$ PR (for 4.5 months)
  $\rightarrow$ Capecitabine d/t neuropathy (for 4 months)
  $\rightarrow$ Observation

- 4 months later, increased pre-existing lesion without any new lesions
Question 4: 2\textsuperscript{nd}-line treatment

1. Re-Induce FP +/- Oxaliplatin +/- Taxane
2. Start „2nd line“ Taxane
3. Start „2nd line“ Taxane plus Ramucirumab
4. Start „2nd line“ Ramucirumab
5. Start „2nd line“ Irinotecan (+/- FP)
6. Consider ablative treatment to the liver met (surgery, RFTA, etc.)
2\textsuperscript{nd}-Line chemotherapy trials

![Bar graph showing overall survival in months for various therapies.](image-url)

- **BSC**
- **Irinotecan**
- **Docetaxel or Irinotecan**
- **ASC**
- **Docetaxel**
- **Irinotecan**
- **Weekly paclitaxel**

Overall Survival, months:
- BSC: 2.4
- Irinotecan: 4.0
- BSC: 3.8
- Docetaxel or Irinotecan: 5.3
- ASC: 3.6
- Docetaxel: 5.2
- Irinotecan: 8.4
- Weekly paclitaxel: 9.5

References:
4. Hironaka S et al. JCO 2013
Q4: What is your suggestion now?

1. Re-Induce FP +/- Oxaliplatin +/- Taxane
2. Start „2nd line“ Taxane
3. Start „2nd line“ Taxane plus Ramucirumab
4. Start „2nd line“ Ramucirumab
5. Start „2nd line“ Irinotecan (+/- FP)
6. Consider ablative treatment to the liver met (surgery, RFTA, etc.)
Other option includes

- Chemotherapy
  - Resume fluoropyrimidine/platinum doublet only if, neuropathy < Grade II
  - Paclitaxel + ramucirumab
  - FOLFIRI or others

- Clinical trial
  - PARP inhibitor, STAT3 inhibitor etc
  - Immune check-point blocking agents