CASE DISCUSSION ON GASTRIC CANCER BASED ON ESMO GUIDELINES

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CLINICAL PRACTICE GUIDELINES

The Clinical Practice Guidelines (CPGs)

Number of ESMO CPGs:

- In Annals of Oncology
- On the ESMO website
- On the OncologyPRO website

Average downloads per manuscript during the 1st 6 months post-publication:

- 2009
- 2010
- 2011
- 2012
- 2013
- 2014
- 2015
CLINICAL PRACTICE GUIDELINES
2015 supplement to Annals of Oncology

- **Breast cancer**
  - Primary breast cancer

- **Lung cancer**
  - Malignant pleural mesothelioma *
  - Thymic epithelial tumours NEW

- **Gastrointestinal cancers**
  - Cancer of the pancreas

- **Haematological malignancies**
  - Chronic lymphocytic leukaemia
  - Philadelphia chromosome-negative chronic myeloproliferative neoplasms *NEW
  - Hairy cell leukaemia *NEW
  - Peripheral T-cell lymphomas NEW
  - Diffuse large B-cell lymphoma (DLBCL)

- **Genitourinary cancers**
  - Cancer of the prostate *

- **Melanoma**
  - Cutaneous melanoma

- **Cancers of unknown primary site**
  - Cancers of unknown primary site

- **Supportive and palliative care**
  - Management of oral and gastrointestinal mucosal injury *
  - Central venous access in oncology NEW
  - Treatment of dyspnoea in advanced cancer patients NEW
CONSENSUS GUIDELINES

Conferences and publications

Recent/coming soon consensus publications:

• ESMO Consensus Conference: Locally-advanced stage III non-small-cell lung cancer (NSCLC) - Published online 20 April 2015
• ESMO-ESGO-ESTRO consensus conference on endometrial cancer: diagnosis, treatment and follow-up – Submitted for publication July 2015
• ESMO consensus guidelines for the management of patients with metastatic colorectal cancer – accepted for publication

Recent consensus conferences:

• ESMO Consensus Conference on Malignant Lymphoma “Common open issues involving multiple mature lymphoid disorders” – June 2015
• MASCC/ESMO Consensus Conference: Prevention of chemotherapy and radiotherapy-induced nausea and vomiting – June 2015
POCKET GUIDELINES

2011 – 1 pocket guideline (Lung Cancer)

2012 – 6 pocket guidelines:

2013 – 7 pocket guidelines:

2014 – 9 pocket guidelines:
MOBILE APPS

All of the latest pocket guidelines are now available on the ESMO Cancer Guides app, available for iOS and Android.

The app also includes the ESMO Guides for Patients in several languages.

New for 2015: try out the ESMO Interactive Guidelines app

- Lung & Chest Tumours: available now
- Upper GI cancers: available now
- Lower GI cancers: coming soon
- Urogenital cancer: coming soon
GUIDES FOR PATIENTS

in collaboration with the Anticancer Fund

Guides for Patients based on ESMO Clinical Practice Guidelines, prepared in a format your patients can easily understand

The main goal of the project is to constantly help patients and their relatives to better understand the nature of different types of cancer and appreciate the best available treatment choices.

Patient guides are available in different languages (English, Dutch, French, Spanish). Other languages are available for some titles (Romanian, Polish, Portuguese).

Download from www.esmo.org or www.anticancerfund.org

**Online:** AML, bladder cancer, breast cancer, cervical cancer, CML, colorectal cancer, endometrial cancer, follicular lymphoma, head & neck cancer, liver cancer, melanoma, non-small-cell lung cancer, oesophageal cancer, ovarian cancer, pancreatic cancer, prostate cancer, and stomach cancer

Coming soon: Soft tissue sarcoma, Glioma, Bone sarcoma, Multiple myeloma

Pick up copies at the ESMO Booth and in the Patient Advocates area!
MANAGEMENT ON LOCALIZED GASTRIC CANCER

72 year old female PS1

No relevant previous comorbidities

Unspecific epigastric discomfort

Significant asthenia and weight loss for 3 months

Occasional vomiting and fullness after eating small amounts of food.

DIAGNOSTIC TESTS: Gastroscopy
MANAGEMENT ON LOCALIZED GASTRIC CANCER

GASTROSCOPY:
Ulcerated and infiltrating lesion of 5 cm in the corpus/antrum of the stomach

Multiple biopsies were done.

Poorly differentiated adenocarcinoma of intestinal type

Staging procedures were ordered
CT Scan
Chest: No lung or mediastinal metastasis
Abdominal-pelvic: No liver or peritoneal metastasis. Thickening of the whole gastric wall without invasion of any surrounding local structures.
Multiple perigastric lymph nodes, but no extraperigastric and paraortic nodes

An endoscopic ultrasonography and a laparoscopy were not considered

cT3cN+M0
Currently recommended approach to localised gastric cancer

- Clinical assessment and staging
- Multidisciplinary team discussion
- Preoperative treatment in all patients with clinical stage II and III
- Surgical resection after chemotherapy
- Pathology assessment and estimation of risk
- Postoperative chemotherapy if tolerated
- Participation in trials
Treatment for localised gastric cancer: What is standard of care according to Guidelines?

- Algorithm for the management of gastric cancer

Gastric cancer (adenocarcinoma)

Operable/resectable Stage >T1N0

Preoperative chemotherapy

Surgery

Adjuvant chemoradiation

Adjuvant chemotherapy

Operable Stage T1N0

Consider endoscopic/limited resection

Preoperative chemotherapy

Surgery

Post-operative chemotherapy

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MANAGEMENT ON LOCALIZED GASTRIC CANCER

Three courses of preoperative CT with CAPE-OX were given
With good tolerance

A D2 surgical resection with partial gastrectomy was performed. No liver or peritoneal metastasis were detected.

The pathology report indicated poorly differentiated adenocarcinoma of intestinal subtype invading till the muscular layer, but not beyond.
1+/16 lymph nodes in the peri-gastric fat.
0/12 LN in the extra peri-gastric regions
No Veinous or Neural invasion

ypT2 ypN1/28 M0
MANAGEMENT ON LOCALIZED GASTRIC CANCER

Three courses of postperative CT with CAPE-OX were planned after surgery.

Due to surgical related morbidities no post-operative chemotherapy could be administered.

The patient is doing well with no evidence of relapsing disease 48 months after surgical resection.
<table>
<thead>
<tr>
<th>Procedure</th>
<th>Purpose</th>
</tr>
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<tbody>
<tr>
<td>Full blood count</td>
<td>Assess for iron deficiency anaemia</td>
</tr>
<tr>
<td>Renal and liver function</td>
<td>Assess renal and liver function to determine appropriate therapeutic</td>
</tr>
<tr>
<td></td>
<td>options</td>
</tr>
<tr>
<td>Endoscopy and biopsy</td>
<td>Obtain tissue for diagnosis, histological classification and molecular</td>
</tr>
<tr>
<td></td>
<td>biomarkers, e.g. HER2 status</td>
</tr>
<tr>
<td>CT thorax + abdomen ± pelvis</td>
<td>Staging of tumour—to detect local/distant lymphadenopathy and metastatic</td>
</tr>
<tr>
<td></td>
<td>disease or ascites</td>
</tr>
<tr>
<td>EUS</td>
<td>Accurate assessment of T and N stage in potentially operable tumours</td>
</tr>
<tr>
<td></td>
<td>Determine the proximal and distal extent of tumour</td>
</tr>
<tr>
<td>Laparoscopy ± washings</td>
<td>Exclude occult metastatic disease involving peritoneum/diaphragm</td>
</tr>
<tr>
<td>PET, if available</td>
<td>May improve detection of occult metastatic disease in some cases</td>
</tr>
</tbody>
</table>

CT, computed tomography; EUS, endoscopic ultrasound; PET, positron emission tomography
Perioperative chemotherapy

- Perioperative (pre- and postoperative) chemotherapy with a platinum and fluoropyrimidine combination is recommended for patients with ≥ stage IB resectable gastric cancer [I, A]
- Since capecitabine avoids the need for an indwelling central venous access device, and is non-inferior to 5-FU in the advanced disease setting, capecitabine-containing regimens can also be suggested in the perioperative setting [IV, C]

Adjuvant treatment

- For patients with ≥ stage IB gastric cancer who have undergone surgery without administration of preoperative chemotherapy, postoperative CRT or adjuvant chemotherapy is recommended [I, A]
- Adjuvant therapy with 5-FU/leucovorin plus conventionally fractionated RT resulted in improved OS years compared with surgery alone. After 10 years of follow-up, this OS improvement remains significant [I, A]
- Postoperative CRT may (mainly) be compensating for suboptimal surgery [II, B]. However, some data suggest potential benefits from postoperative CRT event after optimal D2 dissection [I, B]
- In patients who have had a microscopically incomplete resection, significant improvements in OS and local recurrence rates with the use of CRT after an R1 resection have been seen [IV, B]
- RT should preferably be given as a concomitant regimen of fluoropyrimidine-based CRT to a total dose of 45 Gy in 25 fractions of 1.8 Gy, 5 fractions/week by intensity-modulated RT techniques [IV, A]. The clinical target volume encompasses the gastric bed, anastomoses and draining regional lymph nodes [I, B]
METASTATIC GASTRIC CANCER

Case provided by Ian Chau (Royal Marsden UK)
Case history 1

- 55 years old male
- Presented shortness of breath, lethargy, anaemia with 6kg weight loss
- OGD showed 6cm ulcer in gastric fundus
- Biopsy showed poorly differentiated intestinal type adenocarcinoma; HER2 -ve
Pre-treatment

T4N1M1 with retroperitoneal lymphadenopathy
clínica práctica guías

Cáncer gástrico: Guías Clínicas de Práctica Clínica de la ESMO para diagnóstico, tratamiento y seguimiento†

doi:10.1093/annonc/mdw350
Case history 1 (cont’d)

- CT → T4N1M1 gastric adenocarcinoma with coeliac axis, retroperitoneal lymphadenopathy
- Commenced on ECX
Case history 1 (cont’d)

- CT → T4N1M1 gastric adenocarcinoma with coeliac axis, retroperitoneal lymphadenopathy
- Commenced on ECX
- ECX 4 cycles with PD in primary tumour, malignant lymphadenopathy plus new peritoneal deposits
- PS =1
What treatment would you recommend?

1) Weekly paclitaxel
2) Best supportive care
3) Paclitaxel + ramucirumab
4) Irinotecan
5) Ramucirumab monotherapy
6) Docetaxel
7) Others
Case history 2

- 45 years old male
- June 2010 Diagnosed with metastatic adenocarcinoma OGJ with widespread lymphadenopathy
- July 2010 Started on E-Carbo-X (another institution)
- August 2010-January 2011 EOX × 7 cycles with complete (metabolic) response
- October 2013 Recurrence on OGJ primary, but no distant metastases
- Repeat biopsy → HER2 positive
- October 2013-January 2014 Folfiri/Trastuzumab x6 cycles
- January-March 2014 Folfiri/Trastuzumab cycles 7 and 8 (treatment interrupted because of cardiac arrest).
April-May 2014 Carboplatin/Raltitrexed/Trastuzumab (GI bleed).

Chemoradiation to primary, 54Gy in 30 fractions (concomitant Raltitrexed/Carboplatin), completed 05.08.2014.

October 2014: Reassessment endoscopy showed regression in oesophageal tumour within radiation field but some progression of a proximal tumour which appears to be separate and outside radiation field.

Chemoradiation to encompass oesophageal disease 25-28cm plus bilateral supraclavicular fossae 54Gy/30# with concomitant Raltitrexed/Carboplatin completed December 2014.
Case history 2 (cont’d)

- June 2015 Repeat OGD showed residual adenocarcinoma
- CT and PET scans showed retroperitoneal lymphadenopathy and lung metastases
- Performance status: 0
What treatment would you recommend?

1) Weekly paclitaxel
2) Best supportive care
3) Paclitaxel + ramucirumab
4) Irinotecan
5) Ramucirumab monotherapy
6) Docetaxel
7) Others
Case history 2 (cont’d)

- June 2015 Repeat OGD showed residual adenocarcinoma
- CT and PET scans showed retroperitoneal lymphadenopathy and lung metastases
- Performance status: 0
- 6 cycles of Paclitaxel plus ramucirumab with good partial response
- Patient wanted a treatment break
Case history 2 (cont’d)

- April 2016 small volume lung metastases progression on surveillance CT
- Performance status: 0
What treatment would you recommend?

1) Watch and Wait
2) Rechallenge with paclitaxel + ramucirumab
3) Irinotecan
4) Ramucirumab monotherapy
5) Docetaxel
Management of advanced/metastatic disease

First-line treatment
- Doublet or triplet platinum/floropyrimidine combinations are recommended for fit patients with advanced gastric cancer [I, A]
- Patients with inoperable locally advanced and/or metastatic (stage IV) disease should be considered for systemic treatment (chemotherapy), which has shown improved survival and quality of life compared with best supportive care alone [I, A]. However, comorbidities, organ function and PS must always be taken into consideration [II, B]
- Capcitabine is associated with improved OS compared with infused 5-FU within doublet and triplet regimens [I, A]
- DCF in a 3-weekly regimen was associated with improved OS, but also added significant toxic effects including increased rates of febrile neutropenia [I, C]

Elderly patients with gastric cancer
- Regimens that have been specifically addressed in phase II trials in elderly patients with comparable survival results include capcitabine and oxaliplatin, FOLFOX, single-agent capcitabine and S1 (in Asian patients) [III, B]
- The FLOT regimen is associated with a trend towards improved PFS but also with increased toxicity [II, B]

Second- and further-line treatment
- Second-line chemotherapy with a taxane (docetaxel, paclitaxel), or irinotecan, or ramucirumab as a single agent or in combination with paclitaxel is recommended for patients who are of PS 0–1 [I, A]
- Similar efficacy has been demonstrated for weekly paclitaxel and irinotecan [I, A]
- In patients with disease progression >3 months following first-line chemotherapy, it may be appropriate to consider a rechallenge with the same drug combination [IV, C]
- In patients with symptomatic locally advanced or recurrent disease, hypofractionated RT is an effective and well-tolerated treatment modality that may palliate bleeding, obstructive symptoms or pain [III, B]

Personalised medicine and targeted therapy
- Trastuzumab is recommended in conjunction with platinum- and floropyrimidine-based chemotherapy for patients with HER2-positive advanced gastric cancer [I, A]