GI SLIDE DECK 2016
Selected abstracts on Non-Colorectal Cancer from:

18th World Congress on Gastrointestinal Cancer
29 June–2 July 2016 | Barcelona, Spain

Supported by Eli Lilly and Company.
Eli Lilly and Company has not influenced the content of this publication.
DEAR COLLEAGUES

It is my pleasure to present this ESDO slide set which has been designed to highlight and summarise key findings in digestive cancers from the major congresses in 2016. This slide set specifically focuses on the 18th World Congress on Gastrointestinal Cancer 2016 and is available in English and Japanese.

The area of clinical research in oncology is a challenging and ever changing environment. Within this environment, we all value access to scientific data and research that helps to educate and inspire further advancements in our roles as scientists, clinicians and educators. I hope you find this review of the latest developments in digestive cancers of benefit to you in your practice. If you would like to share your thoughts with us we would welcome your comments. Please send any correspondence to info@esdo.eu.

Finally, we are also very grateful to Lilly Oncology for their financial, administrative and logistical support in the realisation of this activity.

Yours sincerely,

Eric Van Cutsem
Wolff Schmiegel
Phillippe Rougier
Thomas Seufferlein
(ESDO Governing Board)
### COLORECTAL CANCERS

<table>
<thead>
<tr>
<th>Name</th>
<th>Affiliation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prof Eric Van Cutsem</td>
<td>Digestive Oncology, University Hospitals, Leuven, Belgium</td>
</tr>
<tr>
<td>Prof Wolff Schmiegel</td>
<td>Department of Medicine, Ruhr University, Bochum, Germany</td>
</tr>
<tr>
<td>Prof Thomas Gruenberger</td>
<td>Department of Surgery I, Rudolf Foundation Clinic, Vienna, Austria</td>
</tr>
</tbody>
</table>

### PANCREATIC CANCER AND HEPATOBLIARY TUMOURS

<table>
<thead>
<tr>
<th>Name</th>
<th>Affiliation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prof Jean-Luc Van Laethem</td>
<td>Digestive Oncology, Erasme University Hospital, Brussels, Belgium</td>
</tr>
<tr>
<td>Prof Thomas Seufferlein</td>
<td>Clinic of Internal Medicine I, University of Ulm, Ulm, Germany</td>
</tr>
</tbody>
</table>

### GASTRO-OESOPHAGEAL AND NEUROENDOCRINE TUMOURS

<table>
<thead>
<tr>
<th>Name</th>
<th>Affiliation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emeritus Prof Philippe Rougier</td>
<td>University Hospital of Nantes, Nantes, France</td>
</tr>
<tr>
<td>Prof Côme Lepage</td>
<td>University Hospital &amp; INSERM, Dijon, France</td>
</tr>
</tbody>
</table>

### BIOMARKERS

<table>
<thead>
<tr>
<th>Name</th>
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</tr>
</thead>
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<tr>
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</tr>
</tbody>
</table>
**Glossary**

1L  
5FU  
AE  
BCLC  
BID  
BSC  
CA-19.9  
Cap-RT  
CgA  
CI  
CR  
CRT  
CT  
D  
DCR  
ECC  
ECOG  
EGFR  
EOC  
EORTC-QLQC30  
EOX  
FOLFOX  
GC  
GEJ  
GemCap  
Gem-RT  
GI  
HCC  
HER2  
HR  
IHC  
ISH  
KPS  
LAR  
LLOQ  
Lu  
LV  
LV5FU2-CDDP  
MDT  
MSEC  
nal-IRI  
(P)NET  
NGS  
NR  
OR  
ORR  
ORR  
(m)OS  
PD  
PDAC  
PD-L1  
(m)PFS  
PR  
PS  
q(2/3/4/6/8)w  
QD  
QoL  
R  
RECIST  
RR  
RT  
SAE  
SRC  
SSA  
TTP  
VEGF  
W  
WHO

**Abbreviations:**

- **1L:** first line
- **5FU:** 5-fluorouracil
- **AE:** adverse event
- **BCLC:** Barcelona Clinic Liver Cancer
- **BID:** twice daily
- **BSC:** best supportive care
- **CA-19.9:** carbohydrate antigen-19.9
- **Cap-RT:** capecitabine + radiotherapy
- **CgA:** Chromogranin A
- **CI:** confidence interval
- **CR:** complete response
- **CRT:** chemoradiotherapy
- **CT:** chemotherapy
- **D:** day
- **DCR:** disease control rate
- **ECC:** epirubicin, cisplatin, capecitabine
- **ECOG:** Eastern Cooperative Oncology Group
- **EGFR:** endothelial growth factor receptor
- **EOC:** epirubicin, oxaliplatin, capecitabine
- **EORTC-QLQC30:** European Organization for Research and Treatment of Cancer core quality of life questionnaire
- **EOX:** epirubicin, oxaliplatin, capecitabine
- **FOLFOX:** leucovorin, fluorouracil, oxaliplatin
- **GC:** gastric cancer
- **GEJ:** gastroesophageal junction
- **GemCap:** gemcitabine, capecitabine
- **Gem-RT:** gemcitabine + radiotherapy
- **GI:** gastrointestinal
- **HCC:** hepatocellular carcinoma
- **HER2:** human epidermal growth factor receptor 2
- **HR:** hazard ratio
- **IHC:** immunohistochemistry
- **ISH:** in situ hybridisation
- **KPS:** Karnofsky performance status
- **LAR:** long-acting release
- **LLOQ:** lower limit of quantitation
- **Lu:** lutetium
- **LV:** leucovorin
- **LV5FU2-CDDP:** leucovorin, 5-fluorouracil, cisplatin
- **MDT:** multidisciplinary team
- **MSEC:** metastatic squamous-cell oesophageal cancer
- **nal-IRI:** nanoliposomal irinotecan
- **(P)NET:** (pancreatic) neuroendocrine tumour
- **NGS:** next generation sequencing
- **NR:** not reached
- **OR:** odds ratio
- **ORR:** overall response rate
- **(m)OS:** (median) overall survival
- **PD:** progressive disease
- **PDAC:** pancreatic ductal adenocarcinoma
- **PD-L1:** programmed death-ligand 1
- **(m)PFS:** (median) progression-free survival
- **PR:** partial response
- **PS:** performance status
- **q(2/3/4/6/8)w:** every (2/3/4/6/8) weeks
- **QD:** once daily
- **QoL:** quality of life
- **R:** randomised
- **RECIST:** Response Evaluation Criteria In Solid Tumors
- **RR:** response rate
- **RT:** radiotherapy
- **SAE:** serious adverse event
- **SRC:** signet ring cell
- **SSA:** somatostatin analogue
- **TTP:** time to progression
- **VEGF:** vascular endothelial growth factor
- **W:** week
- **WHO:** World Health Organization
Contents

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Note: To jump to a section, right click on the number and ‘Open Hyperlink’
CANCERS OF THE OESOPHAGUS AND STOMACH
LBA-002: A multicenter randomized phase III trial of neo-adjuvant chemotherapy followed by surgery and chemotherapy or by surgery and chemoradiotherapy in resectable gastric cancer: First results from the CRITICS study – Verheij M, et al

**Study objective**
- To examine the effect of optimal local and systemic therapy on survival in patients with resectable GC

### Key patient inclusion criteria
- Stage Ib–IVa resectable GC or GEJ
- No distant metastases
- WHO PS ≤1
- Age ≥18 years (n=788)

### Stratification
- Centre
- Histological type
- Tumour localisation

### PRIMARY ENDPOINT
- OS

### SECONDARY ENDPOINTS
- PFS
- Safety, QoL

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*ECC (epirubicin 50 mg/m² D1; cisplatin 60 mg/m² D1; capecitabine 1000 mg/m² BID D1–14) or EOC (epirubicin 50 mg/m² D1, oxaliplatin 130 mg/m² D1, capecitabine 625 mg/m² BID D1–21); †Total/partial gastrectomy and en bloc N1 + N2 lymph nodes; ‡cisplatin 20 mg/m² qw, capecitabine 575 mg/m² BID.
LBA-002: A multicenter randomized phase III trial of neo-adjuvant chemotherapy followed by surgery and chemotherapy or by surgery and chemoradiotherapy in resectable gastric cancer: First results from the CRITICS study – Verheij M, et al

Key results

<table>
<thead>
<tr>
<th></th>
<th>CT</th>
<th>CRT</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-year OS, %</td>
<td>40.8</td>
<td>40.9</td>
</tr>
<tr>
<td>mOS, years</td>
<td>3.5</td>
<td>3.3</td>
</tr>
</tbody>
</table>

*Log-rank test.

LBA-002: A multicenter randomized phase III trial of neo-adjuvant chemotherapy followed by surgery and chemotherapy or by surgery and chemoradiotherapy in resectable gastric cancer: First results from the CRITICS study – Verheij M, et al

Key results (cont.)

Pre-operative AEs in ≥8% of patients

<table>
<thead>
<tr>
<th>Condition</th>
<th>Grade 3</th>
<th>Grade 4</th>
<th>Sum (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutropenia</td>
<td>171</td>
<td>76</td>
<td>247 (31)</td>
</tr>
<tr>
<td>Febrile neutropenia</td>
<td>53</td>
<td>10</td>
<td>63 (8)</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>94</td>
<td>5</td>
<td>99 (13)</td>
</tr>
<tr>
<td>Nausea</td>
<td>83</td>
<td>1</td>
<td>84 (11)</td>
</tr>
<tr>
<td>Anorexia</td>
<td>71</td>
<td>2</td>
<td>73 (9)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>58</td>
<td>3</td>
<td>61 (8)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>57</td>
<td>8</td>
<td>65 (8)</td>
</tr>
</tbody>
</table>

Grade 5 AEs, all

<table>
<thead>
<tr>
<th>Condition</th>
<th>Sum (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular</td>
<td>7</td>
</tr>
<tr>
<td>GI</td>
<td>3</td>
</tr>
<tr>
<td>Infectious</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>12 (2)</td>
</tr>
</tbody>
</table>

*Log-rank test.


5-year PFS, %

CT 38.5 CRT 39.5

mPFS, years

CT 2.3 CRT 2.5

*p=0.99
LBA-002: A multicenter randomized phase III trial of neo-adjuvant chemotherapy followed by surgery and chemotherapy or by surgery and chemoradiotherapy in resectable gastric cancer: First results from the CRITICS study – Verheij M, et al

Key results (cont.)

<table>
<thead>
<tr>
<th>Post-operative AEs in ≥10% of patients</th>
<th>CT (n=238)</th>
<th>CRT (n=248)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Grade 3</td>
<td>Grade 4</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>63</td>
<td>18</td>
</tr>
<tr>
<td>Febrile neutropenia</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Anorexia</td>
<td>20</td>
<td>0</td>
</tr>
<tr>
<td>Nausea</td>
<td>27</td>
<td>0</td>
</tr>
<tr>
<td>Fatigue</td>
<td>20</td>
<td>0</td>
</tr>
</tbody>
</table>

- Any surgery-related complications: 145 (22%) patients; in-hospital deaths: 15 (2%)

Conclusions

- No difference in OS was observed with CT vs CRT in patients with resectable GC
- The 5-year OS and mOS were comparable with other studies in Western countries
- Ongoing analyses may detect subgroups that specifically benefit from treatment, but the current data do not clearly identify any preferred adjuvant strategy
- As <50% of patients could complete full treatment, more emphasis on pre-operative strategies should be considered

*p<0.001.

LBA-04: The E-DIS study, a randomized discontinuation trial of first-line chemotherapy (CT) in patients with metastatic squamous-cell esophageal cancer (MSEC): efficacy and quality of life results – Adenis A, et al

Study objective

• To assess the benefit of 1L chemotherapy in MSEC patients free from progression after 6 weeks of chemotherapy

Key patient inclusion criteria

• MSEC
• ECOG PS ≤2
(n=67)

Primary endpoint

• 9-month survival rate

Secondary endpoints

• OS, PFS, QoL

Continuation arm
CT* continuation + BSC
(n=31)

Discontinuation arm
CT discontinuation + BSC
(n=33)

Note: Based on data from abstract only

*LV5FU2-CDDP q2w (n=7), FOLFOX (n=24).
### Key results

<table>
<thead>
<tr>
<th></th>
<th>Continuation (n=31)</th>
<th>Discontinuation (n=33)</th>
</tr>
</thead>
<tbody>
<tr>
<td>9-month survival rate, % (85% CI)</td>
<td>50 (37, 62)</td>
<td>48 (34, 60)</td>
</tr>
<tr>
<td>PFS, months (95% CI)</td>
<td>4 (2.8, 5.8)</td>
<td>1.4 (1.4, 2.7)</td>
</tr>
<tr>
<td>OS, months (95% CI)</td>
<td>8.5 (6.6, 12)</td>
<td>8.8 (5.9, 13.4)</td>
</tr>
<tr>
<td>Time until definite deterioration of global health status,* months (95% CI)</td>
<td>6.7 (3.3, 11.9)</td>
<td>4.4 (2.9, 6.3)</td>
</tr>
</tbody>
</table>

### Conclusion

- Both continuation and discontinuation of 1L chemotherapy were observed to be adequate for patients with MSEC

*Assessed with EORTC-QLCC30.

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Note: Based on data from abstract only
LBA-06: IMAB362: A novel immunotherapeutic antibody targeting the tight-junction protein component CLAUDIN18.2 in gastric cancer – Al-Batran SE, et al

Study objective
• To evaluate the efficacy and safety of 1L IMAB362 + EOX compared with EOX alone in patients with advanced/recurrent gastric and GEJ cancer and CLDN18.2 expression

Key patient inclusion criteria
• Advanced/recurrent gastric and GEJ cancer
• CLDN18.2 expression of ≥2+ in ≥40% tumour cells by IHC
• No prior chemotherapy
• ECOG PS 0–1
• Not eligible for trastuzumab (n=246)

IMAB362 loading dose 800 mg/m², then 600 mg/m² D1, q3w + EOX* (n=77)

Stratification
• CLDN18.2 positivity, measurability of disease

EOX* (n=84)

Exploratory arm: IMAB362 1000 mg/m² + EOX* q3w (data not presented here) (n=85)

PRIMAR Y ENDPOIN T
• PFS

SECONDARY ENDPOINTS
• OS, safety

*Epirubicin 50 mg/m² + oxaliplatin 130 mg/m² D1 + capecitabine 625 mg/m² BID, D1–21; QD22).

LBA-06: IMAB362: A novel immunotherapeutic antibody targeting the tight-junction protein component CLAUDIN18.2 in gastric cancer – Al-Batran SE, et al

<table>
<thead>
<tr>
<th>Key results</th>
<th>IMAB362 + EOX</th>
<th>EOX</th>
<th>HR</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>mPFS (months)</td>
<td>7.9</td>
<td>4.8</td>
<td>0.47</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>mOS (months)</td>
<td>13.2</td>
<td>8.4</td>
<td>0.51</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

High CLDN18.2 expression subgroup*

| mOS (months) | 16.7 | 9.0 | 0.45 | <0.0005 |

*≥2+ intensity in ≥70% tumour cells.

LBA-06: IMAB362: A novel immunotherapeutic antibody targeting the tight-junction protein component CLAUDIN18.2 in gastric cancer – Al-Batran SE, et al

Key results (cont.)

• OS subgroup analysis

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Hazard ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>0.51 (0.36, 0.73)</td>
</tr>
<tr>
<td><strong>CLDN18.2</strong></td>
<td></td>
</tr>
<tr>
<td>2+</td>
<td>0.40 (0.22, 0.75)</td>
</tr>
<tr>
<td>3+</td>
<td>0.56 (0.36, 0.88)</td>
</tr>
<tr>
<td><strong>Tumor type</strong></td>
<td></td>
</tr>
<tr>
<td>Diffuse</td>
<td>0.40 (0.23, 0.70)</td>
</tr>
<tr>
<td>Intestinal</td>
<td>0.67 (0.36, 1.23)</td>
</tr>
<tr>
<td>Mixed</td>
<td>0.49 (0.17, 1.37)</td>
</tr>
<tr>
<td>Unknown</td>
<td>0.75 (0.24, 2.35)</td>
</tr>
<tr>
<td><strong>Measurable disease</strong></td>
<td></td>
</tr>
<tr>
<td>Measurable</td>
<td>0.51 (0.35, 0.76)</td>
</tr>
<tr>
<td>Non-measurable</td>
<td>0.48 (0.19, 1.22)</td>
</tr>
<tr>
<td><strong>Tumor location</strong></td>
<td></td>
</tr>
<tr>
<td>Esophagus</td>
<td>0.25 (0.03, 2.37)</td>
</tr>
<tr>
<td>Gastroesophageal junction</td>
<td>0.68 (0.29, 1.59)</td>
</tr>
<tr>
<td>Stomach</td>
<td>0.51 (0.34, 0.76)</td>
</tr>
<tr>
<td><strong>Previous gastrectomy</strong></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>0.40 (0.26, 0.62)</td>
</tr>
<tr>
<td>Yes</td>
<td>0.84 (0.43, 1.65)</td>
</tr>
<tr>
<td><strong>Before start of arm 3</strong></td>
<td></td>
</tr>
<tr>
<td>After start of arm 3</td>
<td>0.37 (0.14, 0.97)</td>
</tr>
<tr>
<td>Before start of arm 3</td>
<td>0.54 (0.36, 0.79)</td>
</tr>
<tr>
<td><strong>Stained cells</strong></td>
<td></td>
</tr>
<tr>
<td>&lt;70</td>
<td>0.75 (0.40, 1.43)</td>
</tr>
<tr>
<td>≥70</td>
<td>0.44 (0.29, 0.68)</td>
</tr>
</tbody>
</table>

Key results (cont.)
• Grade 3/4 events were not significantly increased by IMAB362

Conclusion
• IMAB362 + EOX significantly improved mPFS and mOS compared with EOX alone, and was well tolerated


Study objective

- To compare the molecular characteristics of oesophageal adenocarcinoma, oesophageal squamous cell carcinoma and gastric adenocarcinoma

Study design

- Between 2009 and 2015, 1892 gastroesophageal tumours were examined by Caris Life Sciences including IHC (protein expression), ISH (gene amplification) and NGS sequencing
- Only tumours with clear oesophageal or gastric origins were included
- Chi-square test was used to determine the differences between histological subtypes, and the Kaplan-Meier methodology was used to estimate survival

Key results

<table>
<thead>
<tr>
<th>Site, %</th>
<th>Oesophageal squamous cell adenocarcinoma (n=113)</th>
<th>Oesophageal adenocarcinoma (n=882)</th>
<th>Gastric adenocarcinoma (n=897)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary</td>
<td>70</td>
<td>65</td>
<td>67</td>
</tr>
<tr>
<td>Metastatic</td>
<td>30</td>
<td>34</td>
<td>30</td>
</tr>
<tr>
<td>Unclear</td>
<td>1</td>
<td></td>
<td>3</td>
</tr>
</tbody>
</table>

- Both oesophageal squamous cell adenocarcinomas (71% vs. 29%) and oesophageal adenocarcinomas (86% vs. 14%) were more prevalent in males than females (p<0.0001), respectively


Key results (cont.)

<table>
<thead>
<tr>
<th></th>
<th>Oesophageal squamous cell adenocarcinoma (n=113)</th>
<th>Oesophageal adenocarcinoma (n=882)</th>
<th>Gastric adenocarcinoma (n=897)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ISH-HER2, %</td>
<td>0</td>
<td>21*</td>
<td>10*</td>
</tr>
<tr>
<td>IHC-HER2/Neu, %</td>
<td>0</td>
<td>12*</td>
<td>6*</td>
</tr>
</tbody>
</table>

*p < 0.05.

Key results (cont.)

- TP53 is the most mutated gene in all three cancer types (70% in both oesophageal squamous and oesophageal adenocarcinomas and 46% in gastric adenocarcinoma).
- KRAS mutation occurred more frequently in oesophageal (p=0.01) and gastric adenocarcinomas (p=0.03) than oesophageal squamous cell adenocarcinoma, where it was completely absent.
- APC occurred more frequently in oesophageal adenocarcinoma (p=0.04) and was completely absent in oesophageal squamous cell adenocarcinoma.

Conclusions

- This molecular comparison of gastroesophageal tumours demonstrated that the tumour profile of oesophageal adenocarcinomas is similar to that of gastric adenocarcinomas, but differs from that of oesophageal squamous cell carcinoma, which suggests that treatment of gastroesophageal tumours should be based on its histological subtype rather than anatomical site.
- Low frequency mutations in several druggable genes may have potential therapeutic value including HER2, PD-L1, BRCA1/2, PIK3CA, PTEN, FGFR2.


Study objective

- To assess compare the impact of gastric cancer histologies on survival in a large sample of patients with resectable gastric cancer in the US

Study design

- Patients with stages 0–III gastric cancer who underwent definitive surgical resection between 2003 and 2012 were identified from the ACS National Cancer Database
- Treatment groups were stratified based on commonly presented histology, including intestinal type, diffuse type, signet ring cell (SRC), mucinous and mixed cell type
- Based on tumour aggressiveness, histology cohorts were combined to form two distinct cohorts – intestinal/mucinous and diffuse/SRC
- Propensity score matching was performed to determine mortality rates after matching for demographic, surgery-related and tumour-related variables

Note: Based on data from abstract only

Key results

- Of 8367 patients with resectable cancer, 2328 (27.8%) had intestinal type, 916 (10.9%) had diffuse type, 654 (7.8%) had mucinous, 4008 (47.9%) had SRC and 461 (5.6%) had mixed cell type

<table>
<thead>
<tr>
<th>Intestinal/mucinous</th>
<th>Diffuse/SRC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Older</td>
<td>Younger</td>
</tr>
<tr>
<td>More comorbidities</td>
<td>Less comorbidity</td>
</tr>
<tr>
<td></td>
<td>More frequently underwent total gastrectomy</td>
</tr>
<tr>
<td>Negative surgical margins</td>
<td>Positive surgical margins</td>
</tr>
<tr>
<td>No lymph node involvement</td>
<td>Diffuse type more frequently lymph node positive</td>
</tr>
<tr>
<td>Stage I no difference in mortality</td>
<td></td>
</tr>
<tr>
<td>Stage II mortality 40.06%</td>
<td>Stage II mortality 50.50% (p&lt;0.0001)</td>
</tr>
<tr>
<td>Stage III mortality 52.43%</td>
<td>Stage III mortality 65.70% (p&lt;0.0001)</td>
</tr>
</tbody>
</table>

Note: Based on data from abstract only
Conclusions

• Patients with gastric tumours with diffuse type and SRC histologies have worse survival than those with intestinal type and mucinous tumours, regardless of other prognostic factors and therapeutic intervention

• Further research is required to determine whether a different or more aggressive treatment strategy should be employed for these patients
**Study objective**

- To evaluate the predictive and prognostic value of plasma markers in patients with advanced GC

**Key patient inclusion criteria**

- Patients with advanced GC (RAINBOW trial) (n=665)

**Subanalysis of the RAINBOW trial:**

- VEGF markers and cytokines were assessed
- Patient data were divided into low- and high-marker subgroups, using:
  - The lower limit of quantitation as the cut-off point for those markers with >20% of samples below the limit of quantitation
  - The median marker level as the cut-off point

O-007: Biomarker analyses of second-line Ramucirumab in patients with advanced gastric cancer from RAINBOW, a global, randomized, double-blind, phase 3 study – Van Cutsem E, et al

Key results

<table>
<thead>
<tr>
<th>Analysis of predictive markers</th>
<th>Cut-off point (value, pg/mL)</th>
<th>OS, interaction p-value</th>
<th>PFS, interaction p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>VEGF-C</td>
<td>LLOQ (261.8)</td>
<td>0.2723</td>
<td>0.9946</td>
</tr>
<tr>
<td>VEGF-D</td>
<td>LLOQ (656.1)</td>
<td>0.9165</td>
<td>0.9530</td>
</tr>
<tr>
<td>sVEGFR-1</td>
<td>Median (119.0)</td>
<td>0.6590</td>
<td>0.9864</td>
</tr>
<tr>
<td>sVEGFR-2</td>
<td>Median (11625.0)</td>
<td>0.5295</td>
<td>0.7852</td>
</tr>
<tr>
<td>Placental growth factor</td>
<td>Median (21.2)</td>
<td>0.6693</td>
<td>0.3303</td>
</tr>
</tbody>
</table>

Percentage change from baseline in selected biomarkers

LLOQ, lower limit of quantitation.

O-007: Biomarker analyses of second-line Ramucirumab in patients with advanced gastric cancer from RAINBOW, a global, randomized, double-blind, phase 3 study – Van Cutsem E, et al

Key results (cont.)

<table>
<thead>
<tr>
<th></th>
<th>OS</th>
<th></th>
<th>PFS</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR* (95% CI)</td>
<td>p-value</td>
<td>HR* (95% CI)</td>
<td>p-value</td>
</tr>
<tr>
<td>C-reactive protein</td>
<td>2.1 (1.6, 2.7)</td>
<td>&lt;0.0001</td>
<td>1.5 (1.2, 2.0)</td>
<td>0.0007</td>
</tr>
<tr>
<td>Hepatocyte growth factor</td>
<td>1.9 (1.3, 2.7)</td>
<td>0.0007</td>
<td>1.8 (1.3, 2.6)</td>
<td>0.0009</td>
</tr>
<tr>
<td>Intercellular adhesion molecule-3</td>
<td>1.4 (1.0, 1.8)</td>
<td>0.0377</td>
<td>1.4 (1.0, 1.8)</td>
<td>0.0382</td>
</tr>
<tr>
<td>Interleukin-8</td>
<td>1.5 (1.1, 1.9)</td>
<td>0.0039</td>
<td>1.3 (1.0, 1.7)</td>
<td>0.0401</td>
</tr>
<tr>
<td>Serum amyloid A</td>
<td>1.8 (1.4, 2.4)</td>
<td>&lt;0.0001</td>
<td>1.3 (1.0, 1.7)</td>
<td>0.0420</td>
</tr>
<tr>
<td>Vascular cell adhesion molecule-1</td>
<td>1.6 (1.3, 2.0)</td>
<td>0.0001</td>
<td>1.4 (1.1, 1.7)</td>
<td>0.0074</td>
</tr>
</tbody>
</table>

*High vs low expression level.

Conclusions

- There are no known consistently predictive biomarkers to guide patient selection, despite multiple approved anticancer therapies that target angiogenesis.
- The exploratory plasma analyses available from the RAINBOW study do not identify a predictive biomarker for ramucirumab.
- However, this analysis revealed pharmacodynamic trends with VEGF-D, PIGF + ANG2.
- Several prognostic markers were identified.

CANCERS OF THE PANCREAS, SMALL BOWEL AND HEPATOBILIARY TRACT
Cancers of the pancreas, small bowel and hepatobiliary tract

PANCREATIC CANCER

Study objective

• To characterise the trends, factors and outcomes associated with utilisation of palliative therapies among patients with metastatic pancreatic adenocarcinoma in the US

Study design

• Patients with clinical stage 4 pancreatic adenocarcinoma were identified from the US National Cancer Database between 2003 and 2011
• Patients were stratified by receipt of palliative therapy (surgery, radiation, systemic therapy, pain management or a combination thereof) and compared with those without these designations
• Linear regression, multivariable logistic regression, and survival analyses using multivariate proportional hazards models were performed

Note: Based on data from abstract only
Key results

• A total of 68,075 patients with stage IV disease were identified, 10,105 (14.8%) of whom received specified palliative therapy

• Among the palliative cohort, the majority received systemic therapy (42.2%), followed by a surgical intervention (21.6%), pain management alone (17.3%), radiation (9.1%) and a combination of modalities (9.8%)

• Utilisation of palliative therapies increased from 12.2% in 2003 to 15.9% in 2011 (p<0.001)
  – This trend was not observed among patients with inoperable stage 1 (7.2–8.5%, p=0.646), stage 2 (10.1–10.2%, p=0.204) or stage 3 disease (13.5–12.5%, p=0.651)

• Patients were less likely to undergo palliation with age >60 years (OR 0.88, p<0.001), and particularly for those >80 years (OR 0.66, p<0.001)

• Utilisation did not differ between males and females (p=0.58). Lower utilisation of palliative measures was observed for black (OR 0.83, p<0.001) and Hispanic (OR 0.79, p<0.001) ethnicities vs Caucasians
Key results (cont.)

- Palliative therapy was used more in the presence of associated comorbidities, with 10% higher odds in those with one comorbidity (95% CI 1.05, 1.16), and 14% higher odds in those with two or more (95% CI 1.06, 1.23).
- Utilisation was lower for privately insured patients compared with patients with government or no insurance (OR 0.92, p=0.004).
- Community cancer centres were less likely to offer palliative therapies than comprehensive community and academic centres and there were significant regional variations.
- Overall, survival was slightly worse in patients receiving palliative therapies (HR 1.02; 95% CI 1.01, 1.05), with median survival of 3.6 months.
- When stratifying by type of palliative therapy, those receiving surgery or combination therapy had similar survival to non-palliative patients.
  - Those undergoing systemic palliative therapy, however, demonstrated prolonged survival (median 4.7 months, HR 0.88; 95% CI 0.85, 0.91), while those undergoing palliative radiation (median 3.2 months, HR 1.12; 95% CI 1.05, 1.20) or pain management alone (median 1.6 months, HR 1.79; 95% CI 1.71, 1.89) experienced worse survival.

Note: Based on data from abstract only.
Conclusions

- Palliation of symptoms remains underutilised in the US, particularly in non-Caucasian, older patients with more comorbidities, and across all stages of inoperable disease, despite the continued dismal prognosis of pancreatic cancer.
- Although palliation does not improve survival, increased awareness of palliative options may help increase its utilisation for end-of-life symptom control.

Note: Based on data from abstract only
**O-003: Long-term outcome from the SCALOP trial: A multi-centre randomized phase II trial of Gemcitabine or Capecitabine-based chemoradiation (CRT) for locally advanced pancreatic cancer (LAPC) – Mukherjee S, et al**

**Study objective**

- To evaluate the efficacy and safety of CRT with gemcitabine vs capecitabine following induction CT in patients with locally advanced pancreatic cancer

**Key patient inclusion criteria**

- Locally advanced pancreatic adenocarcinoma
- Responding/stable disease after 3 cycles GemCap*
- WHO PS 0–2
- Maximum tumour diameter 7 cm (n=74)

**Primary endpoint**

- 9-month PFS (reported previously)

**Secondary endpoints**

- OS, PFS (time to event), ORR (RECIST)
- Safety, treatment compliance

**Stratification**

- Centre
- WHO performance status [0 vs 1]
- Disease location [head vs body or tail]

**Cap-RT**

GemCap* (1 cycle) followed by Capecitabine (830 mg/m² BID on RT days) + RT† (n=38)

**Gem-RT**

GemCap* (1 cycle) followed by Gemcitabine (300 mg/m² qw) + RT† (n=36)

*Gemcitabine 1000 mg/m² D1,8,15 + capecitabine 830 mg/m² BID D1–21 of 28-day cycle; †50.4 Gy in 28 fractions.

Mukherjee et al. Ann Oncol 2016; 27 (suppl 2): abstr O-003
O-003: Long-term outcome from the SCALOP trial: A multi-centre randomized phase II trial of Gemcitabine or Capecitabine-based chemoradiation (CRT) for locally advanced pancreatic cancer (LAPC) – Mukherjee S, et al

Key results

<table>
<thead>
<tr>
<th></th>
<th>Cap-RT</th>
<th>Gem-RT</th>
</tr>
</thead>
<tbody>
<tr>
<td>mPFS, months</td>
<td>17.6</td>
<td>14.6</td>
</tr>
<tr>
<td>HR (95% CI); p-value</td>
<td>0.73 (0.46, 1.18); 0.203</td>
<td></td>
</tr>
</tbody>
</table>

Mukherjee et al. Ann Oncol 2016; 27 (suppl 2): abstr O-003
O-003: Long-term outcome from the SCALOP trial: A multi-centre randomized phase II trial of Gemcitabine or Capecitabine-based chemoradiation (CRT) for locally advanced pancreatic cancer (LAPC) – Mukherjee S, et al

Key results (cont.)

<table>
<thead>
<tr>
<th>OS by variables at baseline</th>
<th>HR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;65 years</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>≥65 years</td>
<td>0.54 (0.33, 0.88)</td>
<td>0.013</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>1.12 (0.69, 1.80)</td>
<td>0.654</td>
</tr>
<tr>
<td>WHO PS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>1–2</td>
<td>2.09 (1.24, 3.52)</td>
<td>0.006</td>
</tr>
<tr>
<td>CA19.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;613</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>≥613</td>
<td>4.11 (2.38, 7.12)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GHS*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-</td>
<td>0.95 (0.85, 1.06)</td>
<td>0.395</td>
</tr>
<tr>
<td>Tumour diameter†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-</td>
<td>1.28 (1.08, 1.51)</td>
<td>0.005</td>
</tr>
</tbody>
</table>

*HRs were calculated for every 10-point difference in scores; †HRs were calculated for every 1 cm increase.

Mukherjee et al. Ann Oncol 2016; 27 (suppl 2): abstr O-003
O-003: Long-term outcome from the SCALOP trial: A multi-centre randomized phase II trial of Gemcitabine or Capecitabine-based chemoradiation (CRT) for locally advanced pancreatic cancer (LAPC) – Mukherjee S, et al

Key results (cont.)

<table>
<thead>
<tr>
<th>OS treatment arm at start of CRT</th>
<th>Patients, n</th>
<th>mOS, months</th>
<th>HR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capecitabine-RT</td>
<td>25</td>
<td>13.9</td>
<td>0.40 (0.17, 0.91)</td>
<td>0.029</td>
</tr>
<tr>
<td>Gemcitabine-RT</td>
<td>29</td>
<td>9.5</td>
<td>1.00</td>
<td>-</td>
</tr>
</tbody>
</table>

Conclusions

• In the overall population, survival with capecitabine-RT was no longer superior to gemcitabine-RT in patients with locally advanced pancreatic cancer compared with the initial survival analysis
• However, in patients receiving CRT, survival was significantly superior with capecitabine-RT vs gemcitabine-RT
• Age, WHO PS, tumour diameter and CA-19.9 levels all significantly influenced OS

Mukherjee et al. Ann Oncol 2016; 27 (suppl 2): abstr O-003
**Study objective**

- To evaluate the impact on QoL of nal-IRI (MM-398) with 5FU + leucovorin compared with 5FU + leucovorin alone in patients with metastatic pancreatic ductal adenocarcinoma (PDAC).

**Key patient inclusion criteria**

- Metastatic PDAC
- PD after prior gemcitabine or gemcitabine-containing therapy
- KPS ≥70%

**Primary endpoint**

- OS (previously reported)

**Secondary endpoints**

- QoL and global health (EORTC-QLQ-C30)

**Combinations and dosages**

- **R 1:1**
  - *nal-IRI 80 mg/m² + 5FU 2400 mg/m² + Leucovorin 400 mg/m² q2w (n=71)*
  - *5FU 2000 mg/m² + Leucovorin 200 mg/m² q6w combination control (n=83)*

**Abbreviations**

- PD: Progression Disease
- OS: Overall Survival
- KPS: Karnofsky Performance Status
- PDAC: Pancreatic Ductal Adenocarcinoma
- QoL: Quality of Life
- EORTC: European Organisation for Research and Treatment of Cancer

**Notes**

- nal-IRI, nanoliposomal irinotecan.
O-004: Effects of nal-IRI (MM-398) ± 5-fluorouracil on quality of life (QoL) in NAPOLI-1: A phase 3 study in patients with metastatic pancreatic ductal adenocarcinoma (mPDAC) previously treated with gemcitabine – Hubner R, et al

**Key results**

<table>
<thead>
<tr>
<th>Global health status and functional scale</th>
<th>Nal-IRI + 5FU/LV (n=71)</th>
<th>5FU/LV (n=57)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improvement</td>
<td>Improvement</td>
<td>Improvement</td>
</tr>
<tr>
<td>Stable</td>
<td>Stable</td>
<td>Stable</td>
</tr>
<tr>
<td>Worsening</td>
<td>Worsening</td>
<td>Worsening</td>
</tr>
</tbody>
</table>

**Symptom scale**

<table>
<thead>
<tr>
<th>Symptom scale</th>
<th>Nal-IRI + 5FU/LV (n=71)</th>
<th>5FU/LV (n=57)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>Improvement</td>
<td>Improvement</td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td>Stable</td>
<td>Stable</td>
</tr>
<tr>
<td>Pain</td>
<td>Worsening</td>
<td>Worsening</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>Improvement</td>
<td>Improvement</td>
</tr>
<tr>
<td>Insomnia</td>
<td>Stable</td>
<td>Stable</td>
</tr>
<tr>
<td>Appetite loss</td>
<td>Worsening</td>
<td>Worsening</td>
</tr>
<tr>
<td>Constipation</td>
<td>Improvement</td>
<td>Improvement</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>Stable</td>
<td>Stable</td>
</tr>
</tbody>
</table>

*Benjamini-Hochberg-adjusted p-value.

O-004: Effects of nal-IRI (MM-398) ± 5-fluorouracil on quality of life (QoL) in NAPOLI-1: A phase 3 study in patients with metastatic pancreatic ductal adenocarcinoma (mPDAC) previously treated with gemcitabine – Hubner R, et al

Key results (cont.)

- No appreciable change from baseline in either arm
  - Observed median change from baseline to week 6 in physical functioning score was 6.7 points in both arms
  - Observed median change from baseline to week 6 in fatigue score was ~11 points in the nal-irinotecan + 5-FU + leucovorin arm

O-004: Effects of nal-IRI (MM-398) ± 5-fluorouracil on quality of life (QoL) in NAPOLI-1: A phase 3 study in patients with metastatic pancreatic ductal adenocarcinoma (mPDAC) previously treated with gemcitabine – Hubner R, et al

Conclusions

• Overall, over 12 weeks, patients treated with nal-IRI + 5FU + leucovorin had no deterioration in QoL
• No significant difference in global health status and functional scale scores were observed between treatment arms at baseline, or over the 12 weeks of the study
• As nal-IRI has been previously shown to improve OS, these data support it as a new treatment option for patients with metastatic PDAC previously treated with gemcitabine-based therapy

Cancers of the pancreas, small bowel and hepatobiliary tract

HEPATOCELLULAR CARCINOMA
**Study objective**
- To evaluate the efficacy and safety of regorafenib in patients with intermediate or advanced HCC who had disease progression on sorafenib

**Key patient inclusion criteria**
- HCC BCLC stage B or C
- Received and tolerated sorafenib for ≥20 days at ≥400 mg/day
- Documented radiological progression on sorafenib
- Child-Pugh A liver function
- ECOG PS 0–1 (n=573)

**Regorafenib 160 mg/day**
- W1–3 of each 4-week cycle + BSC (n=379)

**Placebo QD**
- W1–3 of each 4-week cycle + BSC (n=194)

**Stratification**
- Geographic region (Asia vs ROW)
- ECOG PS, α-fetoprotein, extra-hepatic spread, macroscopic vascular invasion

**Primary endpoint**
- OS

**Secondary endpoints**
- PFS, TTP, RR and DCR

**Note:** Based on data from abstract only
LBA-03: Efficacy and safety of regorafenib versus placebo in patients with hepatocellular carcinoma (HCC) progressing on sorafenib: Results of the international, randomized phase 3 RESORCE trial – Bruix J, et al

Key results

<table>
<thead>
<tr>
<th></th>
<th>Regorafenib (n=379)</th>
<th>Placebo (n=194)</th>
<th>HR</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median OS, months</td>
<td>10.6</td>
<td>7.8</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Median PFS, months</td>
<td>3.1</td>
<td>1.5</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Median TTP, months</td>
<td>3.2</td>
<td>1.5</td>
<td>0.44</td>
<td>0.36, 0.55</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ORR, %</td>
<td>10.6</td>
<td>4.1</td>
<td>–</td>
<td>–</td>
<td>0.005</td>
</tr>
<tr>
<td>DCR*, %</td>
<td>65.2</td>
<td>36.1</td>
<td>–</td>
<td>–</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

- There was a 38% reduction in the risk of death in the regorafenib group compared with the placebo group (HR 0.62; 95% CI 0.50, 0.78; p<0.001)
- Compared with placebo, the risk of progression or death with regorafenib reduced by 54% (HR 0.46; 95% CI 0.37, 0.56; p<0.001)

Note: Based on data from abstract only

*Complete and partial responses + stable disease by mRECIST.

LBA-03: Efficacy and safety of regorafenib versus placebo in patients with hepatocellular carcinoma (HCC) progressing on sorafenib: Results of the international, randomized phase 3 RESORCE trial – Bruix J, et al

Key results (cont.)

<table>
<thead>
<tr>
<th></th>
<th>Regorafenib (n=379)</th>
<th>Placebo (n=194)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade ≥3 AEs, %</td>
<td>79.7</td>
<td>58.5</td>
</tr>
<tr>
<td>Most common grade ≥3 AE, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>15.2</td>
<td>4.7</td>
</tr>
<tr>
<td>Hand-foot skin reaction</td>
<td>12.6</td>
<td>0.5</td>
</tr>
<tr>
<td>Fatigue</td>
<td>9.1</td>
<td>4.7</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>3.2</td>
<td>0</td>
</tr>
<tr>
<td>Dose modifications due to AEs, %</td>
<td>68.2</td>
<td>31.1</td>
</tr>
<tr>
<td>Death up to 30 days after last dose, %</td>
<td>13.4</td>
<td>19.7</td>
</tr>
</tbody>
</table>

Note: Based on data from abstract only
Conclusions

- In patients with HCC who had progressed under sorafenib, treatment with regorafenib significantly improved OS
- Regorafenib therapy was well tolerated and observed AEs were in line with its known safety profile

Note: Based on data from abstract only
Cancers of the pancreas, small bowel and hepatobiliary tract

NEUROENDOCRINE TUMOUR
Study objective

- To evaluate the efficacy and safety of $^{177}$Lu-dotatate compared with octreotide LAR in patients with advanced, progressive somatostatin receptor positive midgut NETs.

Key patient inclusion criteria
- Grade 1–2 metastatic or locally advanced midgut NET
- PD on octreotide LAR
- KPS ≥60 (n=230)

$^{177}$Lu-Dotatate 7.4 GBq q8w (x4) + SSAs (n=115)

Primary endpoint
- PFS (RECIST 1.1)

Secondary endpoints
- ORR, OS, TTP, safety and QoL


Key results

<table>
<thead>
<tr>
<th></th>
<th>177Lu-Dotatate</th>
<th>Octreotide LAR</th>
</tr>
</thead>
<tbody>
<tr>
<td>mPFS, months</td>
<td>NR</td>
<td>8.4</td>
</tr>
<tr>
<td>HR (95% CI); p-value</td>
<td>0.21 (0.13, 0.33); &lt;0.0001</td>
<td>+ censored</td>
</tr>
</tbody>
</table>


Key results (cont.)

<table>
<thead>
<tr>
<th></th>
<th>177Lu-Dotatate (n=101)</th>
<th>Octreotide LAR (n=100)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR, n</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>PR, n</td>
<td>17</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>ORR, % (95% CI)</td>
<td>18 (10, 25)</td>
<td>3 (0, 6)</td>
<td>0.0008</td>
</tr>
<tr>
<td>OS (interim), HR (95% CI)</td>
<td>0.398 (0.21, 0.77)</td>
<td>0.0043</td>
<td></td>
</tr>
</tbody>
</table>

Treatment-related AEs, n (%)

<table>
<thead>
<tr>
<th></th>
<th>177Lu-Dotatate (n=111)</th>
<th>Octreotide LAR (n=110)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any AE</td>
<td>95 (86)</td>
<td>34 (31)</td>
</tr>
<tr>
<td>SAE</td>
<td>10 (9)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Withdrawal</td>
<td>5 (5)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

Key results (cont.)

<table>
<thead>
<tr>
<th>Grade 3/4 AEs occurring in ≥1%, %</th>
<th>^177^Lu-Dotatate (n=111)</th>
<th>Octreotide LAR (n=110)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Vomiting</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Fatigue/asthenia</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Lymphopenia</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

Conclusions

- ^177^Lu-Dotatate was superior to octreotide LAR for PFS and OS in patients with progressive metastatic midgut NETs
- ^177^Lu-Dotatate showed a favourable tolerability profile with no clinically relevant findings
- ^177^Lu-Dotatate may be a major therapeutic benefit for these patients who have limited treatment options after progressing under SSAs

Study objective
• To evaluate in the US population, the survival impact of selected factors Chromogranin A levels (CgA), mitotic rate and histologic grade of the tumour in patients with non-functional pancreatic neuroendocrine tumours (PNETs)

Study design
• The US National Cancer Data Base was reviewed between 1998 and 2012 to identify patients with stages 1–3 non-functional PNETs of ≤2 cm
• Clinicopathologic characteristics were collected for the identified patient population
• Statistical analysis comprised univariate and multivariate survival analyses

Note: Based on data from abstract only

Key results

<table>
<thead>
<tr>
<th></th>
<th>Well differentiated (n=824)</th>
<th>Moderately differentiated (n=94)</th>
<th>Poorly differentiated (n=54)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Earlier clinical stage disease (Stage I), %</td>
<td>93.2</td>
<td>86.2</td>
<td>85.2</td>
<td>0.015</td>
</tr>
<tr>
<td>Lower mitotic rate, %</td>
<td>31.7</td>
<td>12.8</td>
<td>1.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Undergoing surgery, %</td>
<td>88.0</td>
<td>68.1</td>
<td>31.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Positive lymph nodes, n</td>
<td>0.35</td>
<td>0.56</td>
<td>0.94</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Earlier pathological stage disease (Stage I), %</td>
<td>61.0</td>
<td>38.3</td>
<td>9.3</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

- Patients with high mitotic rates had poorer differentiated disease (p<0.001) and were less likely to undergo surgery (p<0.0001) than those with medium or low mitotic rates.
- After controlling for disease characteristics only mitotic rate >20 mitoses/10 HPF significantly impacted survival (HR 10.6; p=0.002).
- Patients with low CgA values (≤100 ng/mL) had fewer comorbidities, well differentiated disease, lower mitotic rate and tended to undergo surgical resection (all p<0.0001) than those with high CgA levels (>100 ng/mL).

Note: Based on data from abstract only

*Well differentiated vs moderately and poorly differentiated.
Conclusions

- Both grade and very high CgA levels were significantly associated with survival in patients with non-functional, small PNETs.
- Survival appeared to be negatively impacted by mitotic rate >20 mitoses/10 HPF only, although this was a rare occurrence.
- In this select population, both poor grade and elevated CgA levels should be considered as poor prognostic indicators, but surgical resection appears to improve survival in these patients.

Note: Based on data from abstract only
Cancers of the pancreas, small bowel and hepatobiliary tract
O-001: The influence of multidisciplinary teams on diagnosis and treatment – Basta Y, et al

Study objective
• To assess the influence of MDTs on the diagnosis and management of patients with potential GI cancers

Study design
• A total of 551 patients were prospectively discussed 691 times at 74 GI oncology MDT meetings over a 6-month period
• Diagnoses by MDTs were validated using pathology or follow-up
• Factors influencing correct diagnosis were identified with a Poisson regression model
• Implementation of MDT-decisions was assessed using electronic patient records and reasons to deviate from these decisions were searched manually in the records

O-001: The influence of multidisciplinary teams on diagnosis and treatment – Basta Y, et al

Key results

Diagnosis formulated by MDT

- Imaging/lab (n=64)
- Pathology (n=451)

Correct (n=515)

Referrals (n=551)

Inaccurate (n=30)

No diagnosis (n=6)

Benign (n=14)

Malignant (n=16)

O-001: The influence of multidisciplinary teams on diagnosis and treatment – Basta Y, et al

Key results (cont.)

Referral diagnosis rectified by MDT

- Correct (n=431)
- Referrals (n=551)
- Incorrect (n=109)
- No diagnosis (n=11)

- Diagnosis + M± (n=17)
- M± (n=27)
- Diagnosis (n=67)

M±, alteration of stage.

Key results (cont.)

<table>
<thead>
<tr>
<th>Factors influencing correct decision</th>
<th>RR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treating physician</td>
<td>1.2 (1.02, 1.47)</td>
<td>0.045</td>
</tr>
<tr>
<td>Additional tests needed</td>
<td>0.8 (0.75, 0.93)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Number of patients discussed</td>
<td>1.0 (0.98, 1.01)</td>
<td>-</td>
</tr>
<tr>
<td>Duration of meeting</td>
<td>1.0 (0.99, 1.00)</td>
<td>-</td>
</tr>
</tbody>
</table>

Reason for deviation from advised treatment plan, n

<table>
<thead>
<tr>
<th>Reason for deviation from advised treatment plan, n</th>
<th>N=32</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient wishes</td>
<td>15</td>
</tr>
<tr>
<td>Patient physical condition</td>
<td>14</td>
</tr>
<tr>
<td>Second opinion</td>
<td>1</td>
</tr>
<tr>
<td>Incorrect diagnosis</td>
<td>2</td>
</tr>
</tbody>
</table>

Conclusions

• In patients with potential GI cancers, MDTs rectified 21.8% of referral diagnoses
• The presence of the treating physician was the most important factor to ensure a correct diagnosis
• The number of correct diagnoses were not influenced by the number of patients discussed or the duration of the meeting