ESPAC-5F: Four arm, prospective, multicentre, international randomised phase II trial of immediate surgery compared with neoadjuvant gemcitabine plus capecitabine (GEMCAP) or FOLFIRINOX or chemoradiotherapy (CRT) in patients with borderline resectable pancreatic cancer.


ISRCTN: 89500674
EudraCT: 2013-003932-56
CRUK: C20203/A16186
**Study design**

- **Primary**
  1. Recruitment rate
  2. Resection rate (R1 + R0)

- **Secondary**
  1. R0 resection margin rate
  2. Toxicity
  3. Overall survival
  4. Post operative complication rate
  5. Post operative mortality rate
  6. Response rate
  7. Disease free survival rate
  8. Local disease free survival rate
  9. Quality of life

- **Chemoradiotherapy**
  CRT delivering a total dose of 50.4 Gy in 28 daily fractions over 5 1/2 weeks (1.8 Gy/# Mon – Fri) with **Capcitabine 830mg/m²** BD PO (Mon – Fri) throughout **Radiotherapy**

- **Gemcitabine, Oxaliplatin, Irinotecan, Leucovorin, 5-FU**
  - **Gemcitabine 1000mg/m²**
  - **Oxaliplatin 85mg/m²**
  - **Irinotecan 180mg/m²**
  - **Leucovorin 400mg/m²**
  - **5-FU 2400mg/m²**
  - **46 hour infuion**, repeated every 2 wks for 4 cycles

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- **Review of staging MDCT scan by central laboratory**
- **90 patients with borderline resectable pancreatic cancer**
- **Randomise - stratification by centre**
- **Restage CT scan**
- **Surgery**
- **Adjuvant therapy**
- **12 months follow up**

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Two patients excluded from the Full Analysis Set (one immediate surgery, one CRT)
Some data cleaning ongoing
## Primary outcome – resection rate (R0 + R1)

<table>
<thead>
<tr>
<th></th>
<th>No of resections</th>
<th>No of patients</th>
<th>Rate* (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediate Surgery</td>
<td>20</td>
<td>32</td>
<td>62% (44%, 79%)</td>
<td>0.668</td>
</tr>
<tr>
<td>Neoadjuvant treatment</td>
<td>31</td>
<td>56</td>
<td>55% (41%, 69%)</td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>51</td>
<td>88</td>
<td>58% (47%, 68%)</td>
<td></td>
</tr>
</tbody>
</table>

*Defined as R0 + R1 resections in patients included in the Full Analysis Set
Secondary outcomes - toxicity

9 (18%) neoadjuvant patients in the safety set reported 12 SAEs of Grade 3 or above

1 (6%) GEMCAP patients reported 1 SAE
5 (26%) FOLFIRINOX patients reported 6 SAEs
3 (21%) CRT patients reported 5 SAEs

<table>
<thead>
<tr>
<th>CTCAE Event Name</th>
<th>GEMCAP</th>
<th>FOLFIRINOX</th>
<th>CRT</th>
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<tbody>
<tr>
<td><strong>Grade 3-4</strong></td>
<td></td>
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<tr>
<td>Febrile neutropenia</td>
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<tr>
<td>Diarrhea</td>
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<tr>
<td>Gastritis</td>
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<td>0</td>
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<tr>
<td>Nausea</td>
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<tr>
<td>Hepatic infection</td>
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<td>0</td>
<td>0</td>
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<tr>
<td>Infections and infestations - Other(^1)</td>
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<td>0</td>
<td>1</td>
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<tr>
<td>Sepsis</td>
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<tr>
<td>Wound dehiscence</td>
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<tr>
<td>Metabolism and nutrition disorders – Other(^2)</td>
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<td>1</td>
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<tr>
<td><strong>Grade 5</strong></td>
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<tr>
<td>Sepsis</td>
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<td>1(^3)</td>
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</tbody>
</table>

\(^1\)Neutropenic sepsis
\(^2\)Diabetic ketoacidosis
\(^3\)SUSAR
Secondary outcomes - overall survival (II)

12-months survival estimate (95% CI)

- Immediate Surgery: 42% (27%, 64%)
- GEMCAP: 79% (62%, 100%)
- FOLFIRINOX: 84% (70%, 100%)
- CRT: 64% (43%, 95%)

Numbers at risk

<table>
<thead>
<tr>
<th>Treatment</th>
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<tbody>
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<td>21</td>
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<td>19</td>
<td>18</td>
<td>17</td>
<td>16</td>
<td>7</td>
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<tr>
<td>FOLFIRINOX</td>
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<td>19</td>
<td>17</td>
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<td>14</td>
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<td>14</td>
<td>13</td>
<td>11</td>
<td>10</td>
<td>8</td>
</tr>
</tbody>
</table>
Conclusions

• There was no statistical significant difference (p-value=0.668) in resection rate for immediate surgery (62%, [95% CI 44-79%]) versus neoadjuvant therapy (55%, [95% CI 41-69%])

• There was a significant survival advantage at one year for neoadjuvant therapy (77%, [95% CI 69-89%]) compared with immediate surgery (42%, [95% CI 22-64%])

• Among the neoadjuvant treatments, FOLFIRINOX demonstrated the best survival at one year versus immediate surgery (84%, [95% CI 70-100%]) compared with GEMCAP (79%, [95% CI 63-100%]) and CRT (64%, [95% CI 43-95%])

• Toxicity was higher in the FOLFIRINOX arm but overall was manageable.

• Neoadjuvant therapy should be considered for patients with borderline resectable pancreatic cancer