Efficacy and Safety of Folfirinox in pancreatic metastatic cancer

Introduction

Efficacy and safety of a combination chemotherapy (CT) regimen consisting of oxaliplatin, irinotecan, fluorouracil and leucovorin (FOLFIRINOX) have been investigated in metastatic pancreatic cancer in real practice.

Our study endpoints are:
- Objective response and disease stabilization rates
- Progression Free Survival (PFS) / Overall Survival (OS)
- Toxicities

Methods/Population description (1)

- 340 patients included between July 2010 and June 2012 amongst 22 private institutions and public hospitals of Brittany and Pays de la Loire

Group 1:
- 241 patients (71%) according to Prodigie 4 criteria (Conroy et al, 2011).
- Age between 18-75 years
- Metastatic pancreatic adenocarcinoma (histo/cytologically confirmed)
- In metastatic first-line therapy
- Performance status score: 0 or 1
- Good haematological and renal function
- Subnormal bilirubin level (possible biliary drainage) with bilir<1.5 ULN

Group 2:
- 26 patients (7%) did not respected at least one Prodigie 4 criteria
- Age >75 years old / abnormal bilir
- Metastatic pancreatic adenocarcinoma (histo/cytologically confirmed)
- In metastatic first-line therapy
- Performance status score: 0 or 1
- Good haematological and renal function
- Subnormal bilirubin level (possible biliary drainage) with bilir<1.5 ULN

Group 3:
- 59 patients (17%) had a locally advanced cancer

Group 4:
- 14 patients (4%) have been treated in 2nd metastatic line.
- Treatment: oxaliplatin (85 mg/m²), leucovorin (400 mg/m²), irinotecan (180 mg/m²) and 5-FU (400 mg/m²) bolus plus 2 400 mg/m² infusion over 46 hours) biweekly

Population description (2)

- 75% patients with synchronous metastasis in group 1 vs 86% in group 2

<table>
<thead>
<tr>
<th>Age ≤75</th>
<th>Group 1 (n=261)</th>
<th>Group 2 (n=26)</th>
<th>Group 3 (n=59)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PFS (%)</td>
<td>241 (100%)</td>
<td>18 (69%)</td>
<td>55 (93%)</td>
</tr>
<tr>
<td>Good haematological/renal function</td>
<td>241 (100%)</td>
<td>25 (96%)</td>
<td>58 (98%)</td>
</tr>
<tr>
<td>Subnormal bilirubin level (&lt;1.5ULN)</td>
<td>241 (100%)</td>
<td>17 (65%)</td>
<td>51 (86%)</td>
</tr>
<tr>
<td>Median age (years)</td>
<td>62 (15-75)</td>
<td>64 (29-79)</td>
<td>64 (39-81)</td>
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<tr>
<td>Synchronous metastasis</td>
<td>181 (73%)</td>
<td>22 (85%)</td>
<td>NA</td>
</tr>
<tr>
<td>Overall Response Rate (ORR)</td>
<td>95 (36%)</td>
<td>4 (16%)</td>
<td>23 (39%)</td>
</tr>
<tr>
<td>Complete Response (CR)</td>
<td>6 (2%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Partial Response (PR)</td>
<td>89 (34%)</td>
<td>4 (16%)</td>
<td>23 (39%)</td>
</tr>
<tr>
<td>Stable Disease (SD)</td>
<td>63 (26%)</td>
<td>10 (41%)</td>
<td>25 (42%)</td>
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<tr>
<td>Unchanged</td>
<td>31 (13%)</td>
<td>5 (19%)</td>
<td>5 (8%)</td>
</tr>
<tr>
<td>Treatment ongoing</td>
<td>2 (1%)</td>
<td>0</td>
<td>2 (3%)</td>
</tr>
<tr>
<td>Median cycle number</td>
<td>9 (1-27)</td>
<td>6 (1-12)</td>
<td>7 (5-20)</td>
</tr>
<tr>
<td>Dose adjustment at CI</td>
<td>98 (41%)</td>
<td>13 (56%)</td>
<td>29 (49%)</td>
</tr>
<tr>
<td>Dose adjustment after CI</td>
<td>90 (42%)</td>
<td>6 (24%)</td>
<td>20 (34%)</td>
</tr>
<tr>
<td>Grade III and IV toxicities</td>
<td>77 (31%)</td>
<td>10 (46%)</td>
<td>28 (48%)</td>
</tr>
</tbody>
</table>

Data Base: Baseline Characteristics and clinical benefit of Patients (p<0.0107; *p<0.0166)

Results

- 241 patients (100%) included between July 2010 and June 2012 amongst 22 private institutions and public hospitals of Brittany and Pays de la Loire
- Metastatic pancreatic adenocarcinoma (histo/cytologically confirmed)
- In metastatic first-line therapy
- Performance status score: 0 or 1
- Good haematological and renal function
- Subnormal bilirubin level (possible biliary drainage) with bilir<1.5 ULN

Grade III and IV toxicities

- 21 patients (9%) had Grade III and IV toxicities
- 7 patients (3%) had Asthenia grade III and IV toxicities
- 6 patients (3%) had Thromboembolic grade III and IV toxicities
- 1 patient (0.5%) has had other grade III and IV toxicities

Reason of folfirinox treatment arrest

- 14 patients (4%) have been treated in 2nd metastatic line.
- Treatment: oxaliplatin (85 mg/m²), leucovorin (400 mg/m²), irinotecan (180 mg/m²) and 5-FU (400 mg/m²) bolus plus 2 400 mg/m² infusion over 46 hours) biweekly

Discussion

- Efficacy of Folfirinox in pancreatocancer in real practice
- Toxicities of Folfirinox in pancreatocancer in real practice

Conclusion

- Our study shows a high rate of dose adjustment before the first cure (>40%) in all groups while in most cases DPD and/or UGT mutations have not been reported. What is the reason?
- Our study tends to prove that PFS and OS decrease significantly in case of non respect of Prodigie 4 criteria with a lower response rate.
- For group 2, with a high rate of dose adjustment, it will be interested to compare in a prospective trial modified Folfirinox versus Gemcitabine or Gemcitabine Nab-paclitaxel.