671O - Conversion rate in locally advanced pancreatic cancer (LAPC) after nab-paclitaxel/gemcitabine- or FOLFIRINOX-based induction chemotherapy (NEOLAP): Final results of a multicenter randomised phase II AIO trial

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Background
The optimal preoperative treatment for LAPC is unknown. This first prospective, randomised trial was designed to compare the efficacy and safety of nab-Paclitaxel and Gemcitabine (nPG) with Fluorouracil, Leucovorin, Irinotecan, Oxaliplatin (FOLFIRINOX) as induction chemotherapy in LAPC.

Methods
In this open-label, randomised, two-arm, phase 2 trial, treatment-naive patients (pts) with histologically/cytologically proven non-resectable LAPC were recruited from 33 German centres. After two cycles of nPG induction pts without progressive disease or unacceptable adverse events were randomly allocated (1:1) to receive either two additional cycles of nPG or four cycles of sequential un-modified sqFOLFIRINOX. Secondary resectability was assessed by surgical exploration in all pts with at least stable disease (SD) after completion of induction chemotherapy. The primary
endpoint was conversion rate (R0/R1 resection). Secondary endpoints included overall survival (OS) and safety.

Results

168 pts were registered and 130 were randomly allocated (64 to nPG and 66 to sqFOLFIRINOX). Disease control rate (DCR) after randomization was 82.3% in the nPG group and 75.0% % in the sqFOLFIRINOX group. Surgical exploration was performed in 62.5% of randomized pts in the nPG group and 63.6% in the sqFOLFIRINOX group. The conversion rate as primary endpoint was 30.6% in the nPG group and 45.0% in the sqFOLFIRINOX group (Odds ratio 0.54; 95% CI, 0.26 to 1.13; P = 0.135). At a median follow-up of 12.9 months, the median overall survival was 17.2 months in the nPG group and 22.5 months in the sqFOLFIRINOX group (adjusted Hazard ratio 0.73; 95% CI, 0.42 to 1.28; P = 0.268). Among all intention-to-treat pts (N = 165) conversion was associated with significant improved overall survival (27.4 vs. 14.2 months; P = 0.0035). Adverse events of ≥ grade 3 occurred in 54.7% of the patients in the the nPG group and in 53.0% of those in the in the sqFOLFIRINOX group.

Conclusions

Secondary resection after 4 months of induction combination chemotherapy followed by surgical exploration is feasible in about a third of pts with LAPC and associated with prolonged survival.

Clinical trial identification

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Legal entity responsible for the study

AIO-Studien-gGmbH.

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Nab-paclitaxel (Nab) plus gemcitabine (G) is more effective than G alone in locally advanced, unresectable pancreatic cancer (LAUPC): The GAP trial, a GISCAD phase II comparative randomized trial

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Background
The role of a combination therapy is defined in metastatic pancreatic cancer but not in LAUPC. Lacking dedicated randomized trials, evidence mostly comes from retrospective or phase II studies. G alone remains the standard option following a subgroup LAUPC analysis of a GERCOR/GISCAD trial (J Clin Oncol 2005).

Methods
GAP is a multicentre, open-label, randomized, comparative phase II trial testing the efficacy of NabG vs G. Patients ≤75 years, PS 0-1, were randomized 1:1 to Nab/G (Nab 125 mg/mq plus G 1000 mg/mq on days 1, 8 and 15 every 28 days for 3 cycles) or G (same schedule and doses). Patients not progressing after 3 cycles had to receive capecitabine plus radiotherapy for 5 weeks. Disease progression rate (DPR) according to RECIST 1.1 after 3 cycles of chemotherapy is the primary endpoint. With 80% power in detecting a reduction of DPR from 40% to 20%, one-tailed alpha=0.05, 124 patients were required. Progression-free survival (PFS) is a secondary endpoint; with 109 events the study has 80% power, with one-tailed alpha=0.05, to detect a 0.62 hazard ratio of PFS.
Results

124 patients were enrolled in this trial (4 withdrew consent after randomization in the G arm). Most of the patients were PS 0 (65.8%), and women (56.7%). The study met its primary endpoint DPR, with a reduction from 45.6% with G to 25.4% with Nab/G. There was no unexpected toxicity. One patient died during treatment with G due to a stroke.

**Table:**

<table>
<thead>
<tr>
<th>Arm</th>
<th>Patients</th>
<th>DPR</th>
<th>One-tail chi square</th>
<th>Median PFS (102 events)</th>
<th>HR of PFS (90% CI)</th>
<th>Progression at distant site</th>
<th>Median OS (82 events)</th>
<th>HR of OS (90% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>G</td>
<td>57</td>
<td>26  (45.6%)</td>
<td>P = 0.01</td>
<td>5.1 mos</td>
<td>0.71 (0.51-0.99)</td>
<td>18/26</td>
<td>10.7 mos</td>
<td>0.65 (0.44-0.94)</td>
</tr>
<tr>
<td>NabG</td>
<td>63</td>
<td>16  (25.4%)</td>
<td>7.6 mos</td>
<td>6/16</td>
<td>13.1 mos</td>
<td></td>
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</tbody>
</table>

**Conclusions**

NabG reduces the rate of LAUPC patients who progress after 3 cycles of chemotherapy compared with G, especially in terms of distant relapses, positively affecting PFS and overall survival. Nowadays it should be the therapeutic option in this setting.

**Clinical trial identification:** NCT02043730; 2013-002973-23.

**Legal entity responsible for the study**

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