

## **Phase II Study of Neoadjuvant Modified FOLFOXIRI in Locally Advanced Pancreatic Cancer**

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**Context** FOLFIRINOX has shown high activity in metastatic pancreatic cancer patients and therefore the regimen could be of interest also for patients with inoperable locally advanced disease. Our group had developed a very similar schedule in colorectal cancer named FOLFOXIRI with no bolus 5-fluorouracil and a slight lower dose of irinotecan with good tolerance and activity. **Objective** We have performed a phase II trial in order to prospectively evaluate the activity of a modified (m)FOLFOXIRI regimen in locally advanced pancreatic cancer. **Methods** mFOLFOXIRI consisted of: oxaliplatin 85 mg/m<sup>2</sup>, irinotecan 150 mg/m<sup>2</sup> and folinic acid 200 mg/m<sup>2</sup> on day 1, plus infusional 5-fluorouracil 2,800 mg/m<sup>2</sup> administered in 48 hours on days 1 to 3, with cycle repeated every 14 days. The study enrolled patients with diagnosis of pancreatic cancer, stage III locally advanced disease without evidence of metastatic disease, ECOG performance status (PS) 0 or 1, age 18-75 years. The primary endpoint of the study was the percentage of patients who achieve radical surgical resection after chemotherapy; the trial was designed with a percentage of low activity of 30% and a percentage of interest of 50% with an  $\alpha$

and  $\beta$  errors of 0.05 and 0.20, respectively. **Results** Twenty-five patients have been so far enrolled; M/F: 8/17; PS 0/1: 10/15. Median age was 60 years (range: 44-75 years). Celiac axis was involved in 9 patients, superior mesenteric artery in 11 cases, both arteries in 5 patients. Baseline computer tomography showed pathological nodes in 21 patients. Twenty-one patients have been evaluated, with 9 partial responses (43%) and 12 stable disease (57%). A local treatment after chemotherapy was received by 13 patients until now: 8 (38%) underwent to radical surgery; 1 had an explorative laparotomy with evidence of liver metastases; 4 received concomitant chemoradiotherapy with gemcitabine. Median progression-free survival was 24.5 months and median overall survival was 30.1 months. **Conclusion** Chemotherapy with mFOLFOXIRI seems active in locally advanced pancreatic cancer patients and may allow to obtain a downstaging of disease leading some patients to achieve a curative surgical resection. Longer follow-up is needed to better evaluate long-term outcome of this strategy.