ESPAC-5F: Four-arm, prospective, multicenter, international randomized 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.

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Abstract Disclosures

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Background:
Patients with borderline resectable pancreatic cancer have poor survival and low resection rates. Neoadjuvant therapy may improve the outcome for these patients. The aim of this trial was to determine the feasibility and efficacy of a comparison of immediate surgery versus neoadjuvant GEMCAP or FOLFIRINOX or CRT.

Methods:
Eligible patients with NCCN defined borderline resectable (following central review of the baseline CT scan) and biopsy proven pancreatic cancer were randomised (stratified by centre) to receive
immediate surgery, or neoadjuvant therapy of either 2 cycles of GEMCAP, or 4 cycles of FOLFIRINOX or 50.4Gy capecitabine-based CRT in 28 daily fractions over 5 ½ weeks. Patients were restaged at 4-6 weeks and underwent surgical exploration if still borderline resectable. Resected patients received adjuvant therapy. Follow up was 12 months. There was quality assurance of surgery and CRT. Primary endpoints were recruitment rate and resection rate (R1/R0). Secondary endpoints included overall survival and toxicity. A target of 90 patients was set to determine feasibility and resection rates. Rates will be presented as point estimates and survival compared across treatment arms using a log-rank test. Analyses will be on an ITT basis.

Results:
Between August 2014 and December 2018, 90 patients were randomised with 88 included in the full analysis set (32 immediate surgery, 20 GEMCAP, 20 FOLFIRINOX, 16 CRT). Median age was 63 years, 44% were men. WHO performance status was 0 and 1 in 45% and 55% respectively. Median CA19-9 was 603 kU/L at baseline. 44 (79%) patients completed neoadjuvant therapy. Recruitment rate $= 21$ patients per year. Resection rate was 62% for immediate surgery and 55% for neoadjuvant therapy ($p=0.668$). R0 resection rate on resected patients was 15% and 23% respectively ($p=0.721$). One year survival rate was 40% [95% CI, 26% – 62%] for immediate surgery and 77% [95%CI, 66% - 89%] for neoadjuvant therapy. Log-rank analysis showed an HR=0.27 [95% CI, 0.13 – 0.55]; $\chi^2 (1) = 14.91$, $P<0.001$. 9 out of the 51 neoadjuvant patients included in the safety set reported 12 serious adverse events of grade 3 or above.

Conclusions:
There was no difference in resection rate between arms, however neoadjuvant therapy had a significant survival benefit compared with immediate surgery. Clinical trial information: 89500674.