LBA4004 **Oral Abstract Session**

Results of a randomized phase III trial of pre-operative chemotherapy with mFOLFIRINOX or PAXG regimen for stage I-III pancreatic ductal adenocarcinoma.

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Background: Preoperative mFOLFIRINOX is a treatment option for patients (pts) with resectable/borderline resectable (R/BR) pancreatic ductal adenocarcinoma (PDAC). **Methods:** CASSANDRA (NCT04793932) is a multicenter phase 3 superiority trial randomizing pts ≤75y with R/BR PDAC, stratified by site and CA19.9, in a 2 by 2 factorial design to receive either PAXG (oral daily capecitabine 1250 mg/m^2 with biweekly cisplatin 30 mg/m^2, nab-paclitaxel 150 mg/m^2, gemcitabine 800 mg/m^2; arm A) or mFOLFIRINOX (biweekly 5-fluorouracil 2400 mg/m^2, irinotecan 150 mg/m^2, oxaliplatin 85 mg/m^2; arm B; 1st random) for either 6 months before or 4 months before and 2 months after surgery (2nd random). The results of 1st random are presented. The primary endpoint is event-free survival (EFS = absence of progression, recurrence, 2 consecutive CA19.9 increases ≥20% separated by ≥ 4 weeks, unresectability, intraoperative metastasis, death) in the intention-to-treat population (ITT). Secondary endpoints are overall survival (OS), radiological, CA19.9, and pathological response rate, resection rate, toxicity, QoL in the ITT. With 173 events (260 pts) the study has a power of 80% to demonstrate a statistically significant difference at 5% two sided stratified logrank test under the alternative hypothesis of HR=0.65. EFS and OS were analyzed by Kaplan-Meier and log-rank test, HR estimated by Cox proportional hazard model. **Results:** Between Nov 2020 and Apr 2024, 260 eligible pts (tab 1) were randomly assigned to either arm A (N=132) or B (N=128). At data cutoff on March 1, 2025, with a median follow-up of 23.9 mos, 3y EFS was 30% (CI 20% – 40%) in arm A and 14% (CI 5% – 23%) in arm B with HR 0.66 (CI 0.49-0.89, p=0.005). In A/B, disease control rate was 98%/91% (p=0.009); CA19.9 reduction>50% 88/64% (p=<0.001); resection rate 75/67% (p=0.165); pathologic stage < II 35/23% (p=0.03); main G3-4 toxicity was: neutropenia 44/30%; fatigue 8/8%; diarrhea 2/5%; nausea/vomiting 7/10%; neuropathy 7/4%; AST/ALT 3/8%; infections 6/9%. **Conclusions:** Neoadjuvant PAXG significantly improved EFS compared to mFOLFIRINOX in pts with R/BR PDAC. Clinical trial information: NCT04793932. Research Sponsor: Non-Profit Patient Associations: MyEverest; Codice Viola; Per la Vita; Oltre la Ricerca; Associazione Pierluigi Natalucci.

	A	B
Age	65 (42-76)	63 (41-76)
Females	68 (52%)	62 (48%)
KPS 90-100	123 (93%)	117 (91%)
cStage I-II	119 (90%)	115 (90%)
III	13 (10%)	13 (10%)
R	63 (48%)	63 (49%)
BR	69 (52%)	65 (51%)
CA19.9 Normal	32 (24%)	43 (34%)
Increased Median	261	226