Introduction: nab-P in combination with gemcitabine is a standard of care for the first-line treatment of MPC. Recently, multi-agent nab-P-based regimens, including nab-P + 5-FU + leucovorin and nab-P in combination with 5-FU + leucovorin + oxaliplatin (FOLFOX), have yielded promising results in this patient population. In a small, single-center study of patients with advanced pancreatic cancer, treatment with a 5-agent regimen of metronomic 5-FU, nab-P, bevacizumab, leucovorin, and oxaliplatin (FABLOx) resulted in a 50% partial response rate and a median overall survival (OS) of 17 months; however, the regimen’s toxicity was substantial (Isacoff, ASCO 2012). This prospective, multicenter, phase 1/2 study will evaluate safety and efficacy of FABLOx in patients with MPC.

Methods: Trial Design: Chemo naive patients with MPC will be enrolled. Key eligibility criteria include age 18 - 65 years, Eastern Cooperative Oncology Group performance status ≤ 1, adequate organ function, no preexisting peripheral neuropathy grade > 1, and no brain metastasis or history of malignancy other than pancreatic cancer in the last 3 years. Phase 1 will determine the recommended phase 2 dose (RP2D). In phase 1, ≈ 6 -18 patients will be treated with the starting dose of FABLOx (bevacizumab 5 mg/kg days [d] 1, 15 → nab-P 75 mg/m² d 1, 8, 15 → oxaliplatin 40 mg/m² d 1, 8, 15 → leucovorin 20 mg/m² d 1, 8, 15 → continuous 5-FU 180 mg/m²/d 1 - 14). If > 1 of 6 pts experiences a dose-limiting toxicity (DLT) in cycle 1, the dose will be de-escalated to the next lower dose (dose level [DL]-1: bevacizumab 5 mg/kg d 1, 15 → nab-P 60 mg/m² d 1, 8, 15 → leucovorin 20 mg/m² d 1, 8, 15 → oxaliplatin 30 mg/m² d 1, 8, 15 → continuous 5-FU 135 mg/m²/d 1 - 14). If a DLT is experienced by > 1 of 6 pts at DL-2 (bevacizumab 5 mg/kg d 1, 15 → nab-P 50 mg/m² d 1, 8, 15 → leucovorin 20 mg/m² d 1, 8, 15 → oxaliplatin 20 mg/m² d 1, 8, 15 → continuous 5-FU 90 mg/m² d 1 - 14), the study will be terminated. The phase 1 primary endpoint is DLTs; the secondary endpoint is safety. In phase 2, ≈ 60 patients will be treated with the RP2D defined in phase 1. Treatment will continue until disease progression, withdrawal, or unacceptable toxicity. The phase 2 primary endpoint is 1-year survival rate; a ≥ 30% improvement (≥ 14.4% difference) over the historical 1-year survival rate (48%) will be considered clinically meaningful. Phase 2 secondary endpoints include safety, objective response rate, progression-free survival, OS, and patient-reported outcomes of symptom management. In both phase 1 and phase 2, a key exploratory endpoint is molecular tumor analyses. Patient enrollment is ongoing. ClinicalTrials.gov: NCT02620800.

Results: Conclusion: