nab-Paclitaxel (*nab*-P) plus gemcitabine (Gem) vs Gem alone as adjuvant therapy for resected pancreatic cancer (PC) in a global phase III trial (APACT)

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Background: Gem monotherapy after surgery improves both survival rates and disease-free survival (DFS) in patients with PC. However, disease recurrence is common, indicating a need for improved treatment. *nab*-P + Gem demonstrated superior efficacy over Gem alone in a phase III trial (MPACT) of patients with metastatic PC, including the primary endpoint of overall survival (OS; median 8.7 vs 6.6 months; hazard ratio [HR] 0.72; $P < 0.001$). Toxicities were manageable. Based on the activity demonstrated in the metastatic setting, *nab*-P + Gem will be compared with Gem alone in the adjuvant setting.

Trial design: Approximately 800 patients from North America, Europe, Australia, and Asia Pacific with histologically confirmed PC, macroscopic complete resection (R0 or R1), and no evidence of metastasis will be enrolled. Key eligibility criteria include staging of T1-3, N0-1, M0; Eastern Cooperative Oncology Group performance status of 0 or 1; acceptable hematologic parameters; and CA19-9 < 100 U/mL. Patients with neuroendocrine tumors, any other malignancy within 5 years of randomization, infection with human immunodeficiency virus or hepatitis B or C, or prior neoadjuvant treatment or radiation therapy for PC are ineligible. Eligible patients will be randomized 1:1 to receive 6 cycles of either *nab*-P 125 mg/m^2 + Gem 1000 mg/m^2 or Gem alone 1000 mg/m^2 on days 1, 8, and 15 of each 28-day cycle. Stratification factors are resection status (R0 vs R1), nodal status (LN+ vs LN−), and geographic region (North America, Europe, and Australia vs Asia Pacific). Study treatment will start as early as when the patient has adequately recovered from surgery but no later than 12 weeks after surgery. The primary endpoint is independently assessed DFS, and secondary endpoints are OS and safety. Exploratory endpoints include molecular profiling of tumor tissue to correlate tumor heterogeneity with clinical outcome and quality of life as assessed by the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaires (EORTC QLQ-C30 and EORTC QLQ-PAN26). At least 489 DFS events from 800 patients will allow 90% power to detect an HR for DFS of 0.74 at a 2-sided significance level of 0.05. One interim safety analysis and 2 interim efficacy analyses (the first for futility and the second for both futility and efficacy) will be performed. More than 450 patients had been enrolled as of August 2015. Eighty percent of all activated study sites (n = 141) had randomized ≥ 1 patient. Thirty-one sites had randomized ≥ 5 patients. Of the 674 patients who were screened, 27% were found to be ineligible mainly due to disease recurrence. Patient enrollment is ongoing. ClinicalTrials.gov identifier NCT01964430.