Poster 185-P

Randomized Phase III trial of *nab*-Paclitaxel plus Gemcitabine vs Gemcitabine Alone as Adjuvant Therapy for Patients with Resected Pancreatic Cancer: APACT

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INTRODUCTION

- The goals of adjuvant therapy are to reduce relapse and improve survival following surgical resection[1]
- There are few ongoing trials of adjuvant therapy in pancreatic cancer (PC; Table 1)[2]

Table 1. Select Phase III Trials of Adjuvant Therapy in PC[a]

Trial No.	Treatment	Estimated Enrollment
NCT01013649[b]	Gem ± Erl or radiotherapy with Cape or 5-FU	N ≈ 950
NCT01526135	Gem vs mFOLFIRINOX[c]	N ≈ 490
NCT01150630[b]	Neoadjuvant and adjuvant Gem ± Cis, Epi, and Cape vs adjuvant Gem	N ≈ 370
NCT02355119	FOLFOXIRI	N ≈ 310

[a] Search terms: "adjuvant therapy" and "pancreatic cancer"; interventional; phase III; open. [b] Phase II/III. [c] Modified: oxaliplatin 85 mg/m^2, irinotecan 150 mg/m^2, leucovorin 400 mg/m^2, 5-FU 1200 mg/m^2/day (no bolus), q2w × 24 weeks.

- In the European Union and the United States, there are few adjuvant treatment recommendations
  - According to ESMO guidelines, Gem and 5-FU are category IA recommendations[3]
  - According to NCCN guidelines, Gem or 5-FU leucovorin are category 1 recommendations[4]
- Recurrence rates with adjuvant Gem were 76% and 81% in 2 phase III trials, suggesting a need for improved therapies[5,6]
- In the phase III MPACT trial in patients with metastatic PC, greater efficacy was observed with *nab*®-P + Gem than with Gem alone[7,8]
  - Median OS: 8.7 vs 6.6 months (HR 0.72; 95% CI, 0.62 - 0.83; $P < 0.001$)[8]
  - Median PFS: 5.5 vs 3.7 months (HR 0.69; 95% CI, 0.58 - 0.82; $P < 0.001$)[7]
  - ORR[7]
    - By independent review: 23% vs 7%; $P < 0.001$
    - By investigator review: 29% vs 8%; $P < 0.001$
- Based on the findings from the MPACT trial, the APACT trial will compare *nab*-P + Gem with Gem alone in patients with resected PC

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OBJECTIVES

Primary

- Compare DFS between patients randomized to *nab*-P + Gem vs Gem alone

Secondary

- Assess OS between patients randomized to *nab*-P + Gem vs Gem alone
- Assess safety and tolerability of the 2 treatment regimens

Exploratory

- Evaluate tumor markers to assess molecular heterogeneity
- Evaluate the effect of *nab*-P + Gem vs Gem alone on patients' quality of life

ENDPOINTS

Primary

- Independently assessed DFS (defined as the time from randomization to disease recurrence or death, whichever is earlier)

Secondary

- OS, safety

Exploratory

- Molecular profiling of tumor tissue to correlate tumor heterogeneity with clinical outcome
- Quality of life as measured by the EORTC QLQ-C30 and QLQ-PAN26

5-FU, 5-fluorouracil; CA19-9, carbohydrate antigen 19-9; Cape, capecitabine; Cis, cisplatin; CT, computed tomography; DFS, disease-free survival; ECOG PS, Eastern Cooperative Oncology Group performance status; EORTC, European Organisation for Research and Treatment of Cancer; Epi, epirubicin; Erl, erlotinib; ESMO, European Society for Medical Oncology; FOLFIRINOX, leucovorin, 5-FU, irinotecan, oxaliplatin; FOLFOXIRI, leucovorin, 5-FU, oxaliplatin, irinotecan; Gem, gemcitabine; HIV, human immunodeficiency virus; HR, hazard ratio; LN, lymph node; M, metastasis; MRI, magnetic resonance imaging; N, node; NCCN, National Comprehensive Cancer Network; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; q2w, every 2 weeks; QLQ, Quality of Life Questionnaire; qw 3/4, first 3 of 4 weeks; T, tumor.

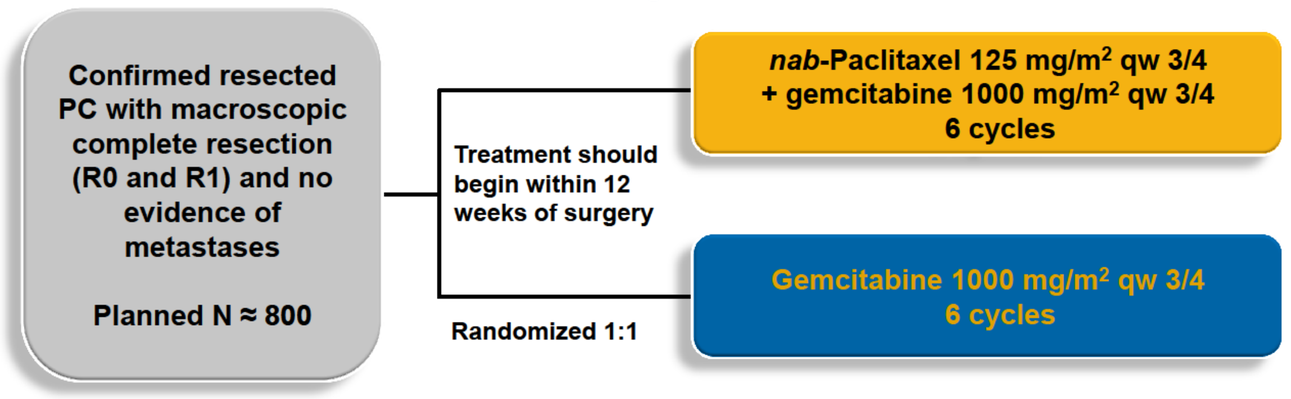
STUDY DESIGN

apact™

Adjuvant Pancreatic Adenocarcinoma Clinical Trial

albumin-bound paclitaxel (ABI-007) + gemcitabine

ClinicalTrials.gov NCT01964430



Stratification factors: resection status (R0 vs R1); nodal status (LN+ vs LN−); geographic region (North America vs Europe vs Australia vs Asia Pacific).

METHODS

Key Inclusion Criteria

- Histologically confirmed resected pancreatic adenocarcinoma with macroscopic complete resection (R0 and R1)
- Surgical staging: T1-3, N0-1, M0
- No prior neoadjuvant treatment or radiation therapy for pancreatic adenocarcinoma
- Able to begin treatment ≤ 12 weeks after resection
- Age ≥ 18 years
- ECOG PS ≤ 1
- Acceptable hematology and blood chemistry parameters
- CA19-9 < 100 U/mL assessed within 14 days of randomization

Key Exclusion Criteria

- Tumors of mixed origin
- Presence or history of metastatic PC
- Any other malignancy within 5 years of randomization, excluding adequately treated in situ cervical, uterine, or nonmelanomatous skin cancer
  - Treatment should have been completed > 6 months before randomization
- Active infection(s) requiring systemic therapy
- History of hypersensitivity to study drugs or their excipients
- Known history of hepatitis B or C or HIV infection or use of medications that could increase the risk of neutropenia

Dose Modifications

- Two dose reductions are allowed for hematologic and other toxicities (Table 2)
- Patients will be discontinued from the study if > 2 dose reductions are required

Table 2. Dose Reductions

Dose Level[a]	*nab*-P, mg/m^2	Gem, mg/m^2
Starting dose	125	1000
−1	100	800
−2	75	600

[a] Dose reductions may or may not be concomitant in the *nab*-P + Gem arm.

Patient Follow-Up

- DFS
  - CT/MRI scans will be performed at screening, every 8 weeks for the first 24 weeks, every 12 weeks for the first 3 years, then every 24 weeks until disease recurrence for up to 5 years from the last treatment
  - Patients who discontinue treatment in the absence of disease recurrence should undergo repeat imaging until disease recurrence, death, or the start of new therapy
- Posttreatment OS will be monitored every 3 months until death, withdrawal of consent, or the end of the study
- A data monitoring committee is in place for this trial

STATISTICAL ANALYSIS

- In 2 separate randomized phase III studies, the median DFS values for patients with surgically resected PC who received adjuvant Gem therapy were 13.4 months and 14.3 months[9,10]
- The planned enrollment of ≈ 800 patients in this trial was selected based on the following assumptions:
  - Gem will result in a median DFS of 14 months
  - *nab*-P + Gem will result in a median DFS of 19 months, representing an HR of 0.74
- At least 489 DFS events from 800 patients would allow 90% power to detect an HR of 0.74 at a 2-sided significance level of 0.05
- Two interim efficacy analyses are planned:
  - The first will assess futility after 163 DFS events
  - The second will assess both futility and superiority after 342 DFS events or the enrollment of 800 patients (whichever is later)
- One interim safety analysis is planned after 100 patients are treated (≥ 2 cycles)

CONCLUSIONS

- APACT (N ≈ 800) will determine whether *nab*-P + Gem is superior to Gem alone as adjuvant therapy in patients with resected pancreatic adenocarcinoma
- Primary endpoint is DFS
- This study may identify an effective treatment regimen for adjuvant PC
- This study will establish 1 of the largest collections of primary tumor tissue from patients with pancreatic adenocarcinoma for molecular analyses
- Current enrollment is 377 patients

ACKNOWLEDGMENTS

This study was supported by Celgene Corporation, Summit, NJ. The authors received editorial and production support in the preparation of this poster from MediTech Media, funded by Celgene Corporation. The authors are fully responsible for all content and editorial decisions for this poster.

DISCLOSURES

MAT: consultant or advisory role and research funding, Celgene, AstraZeneca, Champions Oncology, Roche, Myriad Genetics, NuCana Biomed, Targovax; DC: research funding, Synta, Incyte, Genentech, Celgene; AB: consultant or advisory role, Celgene, Clovis, Cure Forward; DG: research funding, Celgene, Pfizer, Amgen; MM: consultant or advisory role and research funding, Celgene; EMO: consultant or advisory role and speakers' bureau, Celgene, Roche, GSK, Bayer; PP: consultant or advisory role and research funding, Celgene; HR: consultant or advisory role, Celgene; TM: nothing to disclose; LY: employment or leadership position and stock ownership, Celgene; LL: employment or leadership position and stock ownership, Celgene; BL: employment or leadership position and stock ownership, Celgene.

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Poster presented at the European Society for Medical Oncology 17th World Congress on Gastrointestinal Cancer; July 1 - 4, 2015; Barcelona, Spain