Poster 186-P

International Phase II Trial of Weekly *nab*-Paclitaxel Plus Gemcitabine in Patients With Locally Advanced Pancreatic Cancer: LAPACT

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INTRODUCTION

- Locally advanced pancreatic cancer (LAPC) refers to a tumor that has expanded into nearby major blood vessels, without evidence of metastasis[1,2]
  - Approximately 30% of PC diagnoses[1]
  - Median overall survival (OS) of 8 to 14 months[1]
- In both the European Union and the United States, there are few recommended treatment options for patients (pts) with LAPC, based on extrapolations from metastatic PC (MPC) trials[2,3]
- Data from phase III trials in pts with LAPC suggest that chemotherapy alone is as effective or more effective than chemoradiation therapy[4,5]
- The phase III MPACT trial demonstrated superior efficacy of *nab*®-paclitaxel (*nab*-P) + gemcitabine (Gem) vs Gem alone for the first-line treatment of pts with MPC[6,7]
  - Primary endpoint was OS (median, 8.7 vs 6.6 months; HR 0.72; 95% CI, 0.62 - 0.83; $P < 0.001$)
- An evaluation of change from baseline in the primary tumor lesion showed a 3-fold greater benefit with *nab*-P + Gem than with Gem alone (Table 1), indicating that this regimen may be active in LAPC[8]

Table 1. Analysis of Primary Pancreatic and Nonpancreatic Target Lesions From the MPACT Trial[8]

Variable	*nab*-P + Gem	Gem
Primary pancreatic target lesions		
Pts, n	334	318
Sum of diameters at baseline, median (range), mm	50.75 (10.0 to 157.0)	49.50 (16.0 to 151.0)
Change at nadir from baseline, median (range), %	−22.15 (−100.0 to 52.2)	−7.02 (−77.0 to 107.1)
P value	< 0.001	
Metastatic target lesions		
Pts, n	328	326
Sum of diameters at baseline, median (range), mm	85.00 (12.0 to 342.0)	86.25 (10.0 to 364.0)
Change at nadir from baseline, median (range), %	−24.27 (−100.0 to 64.2)	−8.74 (−100.0 to 278.6)
P value	< 0.001	

- Based on the demonstrated efficacy and activity of *nab*-P + Gem in pancreatic lesions in the MPACT trial, the phase II LAPACT trial will evaluate the efficacy and safety of *nab*-P + Gem in pts with LAPC

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OBJECTIVES

Primary

- To evaluate TTF with *nab*-P + Gem as induction therapy followed by investigator's choice of treatment in pts with LAPC

Secondary

- Efficacy, measured as disease control rate after the first 6 cycles of *nab*-P + Gem; ORR; PFS; and OS
- Safety
- Health-related quality of life (QoL)

Exploratory

- Correlation between changes in circulating nucleic acids and disease progression/response to treatment

ENDPOINTS

Primary

- TTF—the time after the first dose of study therapy to therapy discontinuation due to PD, death (by any cause), or the start of a non–protocol-defined anti-cancer therapy

Secondary

- DCR after 6 cycles, ORR, PFS,[a] OS,[a] safety, and QoL[b]

Exploratory

- Correlation of changes in circulating nucleic acids with disease progression and response to treatment with *nab*-P + Gem subsequent chemoradiation

[a] Time-to-event analysis beginning at first dose of therapy. [b] QoL to be assessed by EORTC-QLQ-C30 and QLQ-PAN26 questionnaires.

Cape, capecitabine; CT, computed tomography; DCR, disease control rate; ECOG, Eastern Cooperative Oncology Group; EORTC, European Organisation for Research and Treatment of Cancer; HIV, human immunodeficiency virus; MRI, magnetic resonance imaging; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PS, performance status; qw 3/4, first 3 of 4 weeks; RECIST, Response Evaluation Criteria In Solid Tumors; SMA, superior mesenteric artery; SMV, superior mesenteric vein; TTF, time to treatment failure.

STUDY DESIGN

lapact™

Locally **A**dvanced **P**ancreatic **A**denocarcinoma **C**linical **T**rial
albumin-bound paclitaxel (ABI-007) + gemcitabine
followed by investigator choice

ClinicalTrials.gov NCT02301143

Previously untreated, locally advanced, unresectable pancreatic cancer

Planned N = 110

→ ***nab*-P 125 mg/m² qw 3/4 + Gem 1000 mg/m² qw 3/4 × 6 cycles**

→ **For pts without disease progression or unacceptable toxicity after 6 cycles, investigator's choice:**

***nab*-P + Gem, chemoradiation,[a] or surgical resection**

→ **Periodic follow-up for PFS, OS**

- All pts will have a CT or MRI scan every 8 weeks; tumor response defined by RECIST v1.1
- Pts will be followed by CT or MRI until PD, withdrawal of consent, loss to follow-up, or death
- If continued *nab*-P + Gem is chosen, treatment should follow the same schedule as prior cycles until PD or unacceptable toxicity
- ≥ 3 weeks must have passed between last cycle of *nab*-P + Gem and initiation of chemoradiation[a]
- Surgical intervention may occur prior to completing the planned 6 cycles of *nab*-P + Gem if pts experience a major therapeutic response

[a] Concurrent Cape or Gem + radiation according to institutional practice.

METHODS

Key Inclusion Criteria

- Histologically or cytologically confirmed pancreatic adenocarcinoma (no endocrine or mixed origin)
  - Unresectable according to radiographic criteria or exploration:
    - SMV and portal vein: occlusion, thrombosis, or encasement extending several centimeters
    - SMA: tumor abutment > 180° or thrombosis of artery
    - Celiac axis: abutment or encasement
    - Lymph nodes: involvement
- ECOG PS of 0 or 1
- Adequate organ function

Key Exclusion Criteria

- Distant metastasis
- Prior anti-cancer therapy for pancreatic carcinoma
- Any other malignancy within 5 years of enrollment[a]
- Any active infection requiring systemic therapy
- Known infection with hepatitis B/C or history of HIV infection or treatments that might increase the risk of serious neutropenic complications
- Hypersensitivity to Gem, *nab*-P, or any of their excipients
- Grade > 1 peripheral neuropathy
- Clinically significant ascites
- Plastic biliary stent (metal stents allowed)

[a] With the exception of adequately treated in situ carcinoma of the prostate (Gleason score ≤ 7), cervix, uterus, or nonmelanomatous skin cancer (treatments completed > 6 months prior to enrollment).

Statistical Design

- The LAPACT trial is a global study that will enroll ≈ 110 pts in the United States, Canada, France, Spain, and Italy (Figure 1)
- A sample size of 100 pts (planned enrollment of 110 assumes a 10% dropout rate) will have 80% power at a 1-sided alpha of 0.05 to detect a 30% increase in median TTF from 5.1 months (median TTF in the phase III MPACT study) to 6.6 months

Follow-Up

- When pts discontinue *nab*-P + Gem (for any reason), they will have a safety visit 28 days after discontinuation
- If a pt undergoes chemoradiation or surgery, they will have an additional safety visit 28 days after discontinuation
- Pts who have PD will be followed for OS and post-study anti-cancer therapies ≈ every 90 days

Figure 1. Global Representation of LAPACT Participants

CONCLUSIONS

- LAPACT is a phase II trial to evaluate 6 cycles of *nab-P* + Gem followed by investigator's choice as first-line therapy for LAPC
- The planned enrollment for this trial is ≈ 110 pts
- The estimated study length, with treatment and follow-up for OS, is 3.5 years or until up to 95% of survival data have been collected, whichever occurs first
- The first pt was enrolled in April of 2015

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DISCLOSURES

PP: consultant or advisory role, honoraria, speakers bureau, and research funding, Celgene; LK: employment, stock ownership Celgene; TN: employment, stock ownership, Celgene; DP: employment and stock ownership, Celgene; PH: consultant or advisory role, honoraria, and travel, accommodations, expenses, Celgene.

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