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Poster # K8

Phase 2 Study of Pre-operative Chemotherapy with Nab-paclitaxel and Gemcitabine Followed by Chemo-radiation for Borderline Resectable or Node-positive Pancreatic Ductal Adenocarcinoma

Emerson Y. Chen, MD[1]; Garth W. Tormoen, MD, PhD[2]; Adel Kardosh, MD, PhD[1]; Nima Nabavizadeh, MD[2]; Bryan Foster, MD[3]; Skye C. Mayo, MD, MPH[4]; Kevin G. Billingsley, MD[4]; Erin W. Gilbert, MD, MCR[5]; Christian Lanciault, MD, PhD[6]; Aaron Grossberg, MD, PhD[2]; Kenneth G. Bensch, MD, PhD[7]; Erin Maynard, MD[7]; Eric C. Anderson, MD, PhD[1]; Brett C. Sheppard, MD[5]; Charles R. Thomas Jr., MD[2]; Charles D. Lopez, MD, PhD[1]; Gina M. Vaccaro, MD[1]; OHSU Gastrointestinal Cancer Disease Group

[1]Division of Hematology and Medical Oncology, Oregon Health & Science University, Knight Cancer Institute, Portland OR; [2]Department of Radiation Medicine, Oregon Health & Science University, Portland, Oregon, OR; [3]Department of Diagnostic Radiology, Oregon Health & Science University, Portland Oregon, OR; [4]Division of Surgical Oncology, Oregon Health & Science University, Knight Cancer Institute, Portland OR; [5]Division of Gastrointestinal and General Surgery, Oregon Health & Science University, Portland OR; [6]Department of Pathology, , Oregon Health & Science University, Portland, OR; [7]Portland VA Medical Center, Portland, OR

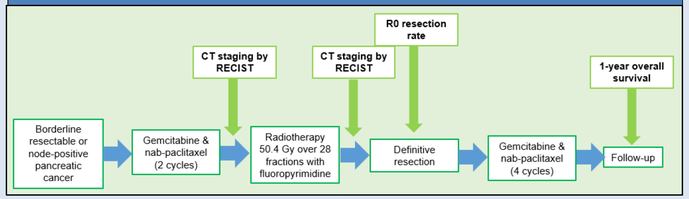
Background

- Resectable and borderline resectable pancreatic ductal adenocarcinoma (PDAC) has high risk of disease relapse after definitive surgery.
- Pre-operative therapy may eliminate micro-metastasis early and help achieve negative surgical margins (R0 resection rate).
- The present study assesses the feasibility and preliminary efficacy of gemcitabine & nab-paclitaxel followed by chemo-radiation with fluoropyridimine as a pre-operative treatment strategy for borderline resectable and clinical node-positive PDAC.

Methods

- Single-arm, open-label phase II trial **(NCT02427841)**
- Treatment-naïve, biopsy-proven, borderline resectable PDAC (AHPBA/SSO/SSAT* consensus criteria) or node-positive PDAC (abnormal regional lymph node visible on contrast CT)
- **Pre-operative and post-operative chemotherapy:** 2 cycles of gemcitabine 1000 mg/m^2 and nab-paclitaxel 125 mg/m^2 on days 1, 8, 15 every 28 days before surgery, and 4 cycles after surgery
- **Pre-operative chemo-radiation:** 50.4 Gy intensity-modulated radiation therapy over 28 fractions with concurrent 5-fluorouracil or capecitabine
- **Primary endpoint:** R0 resection rate
- **Secondary endpoints:** objective response rate, disease progressions during pre-operative therapy, rate of definitive resection, pathologic response, overall toxicities (CTCAE v.4.0), and survival endpoints

Figure 1. Study Schema



*American Hepato-Pancreato-Biliary Association (AHPBA); Society of Surgical Oncology (SSO); Society for Surgery of the Alimentary Tract (SSAT)

Results

Table 1. Baseline characteristics

N=19	Counts (%)
Age	68 (42-76)*
Sex	
Female	10 (53%)
Male	9 (47%)
Race	
Caucasian	15 (79%)
Asian	3 (16%)
African American	1 (5%)
ECOG functional status	
0	3 (16%)
1	16 (84%)
Primary tumor site	
Head	11 (58%)
Body or neck	5 (26%)
Tail	3 (16%)
Greatest Tumor diameter (cm)	4.0 (2.0-8.9)*
Vascular involvement	
Both arterial and venous	10 (53%)
Arterial only	6 (32%)
No vascular involvement	2 (11%)
Venous only	1 (5%)
Lymph node status	
Positive nodes on CAT scan	13 (68%)
Negative nodes on CAT scan	6 (32%)
Serum CA 19-9 (U/mL)	231 (4-12,414)*

*Median (range)

Figure 2. Consort Diagram

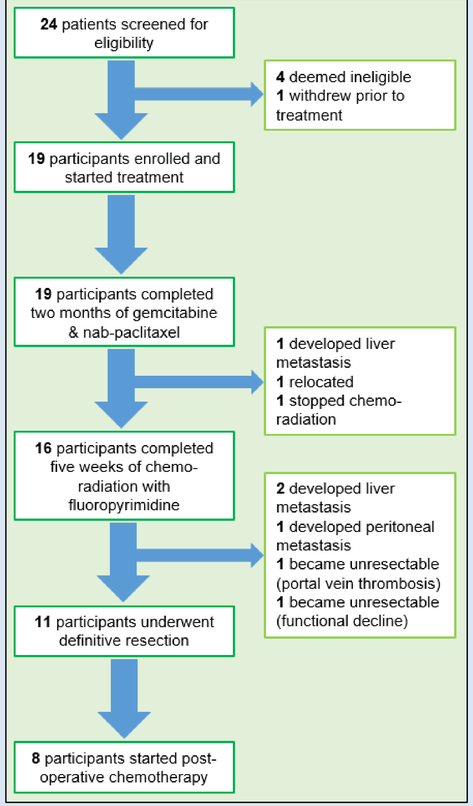


Table 2. Preliminary Efficacy

	Counts (%)
Best radiographic response rate (RECIST)	**N=19**
Partial response	4 (21%)
Stable disease	14 (74%)
Progressive disease	1 (5%)
Resection outcomes	**N=11**
R0 resection	8 (73%)
R1 resection	3 (27%)
Pathologic response	N=11
Near complete response	2 (18%)
Partial treatment response	7 (64%)

Table 3. Grade 3 & 4 Adverse Events

	Counts (%)
Pre-operative gemcitabine and nab-paclitaxel	**N=19**
Neutropenia	6 (32%)
Febrile neutropenia	2 (11%)
Elevated liver function tests	1 (5%)
Abdominal pain	1 (5%)
Encephalopathy	1 (5%)
Facial edema	1 (5%)
Flank pain	1 (5%)
Fatigue	1 (5%)
Hypokalemia	1 (5%)
Portal vein thrombosis	1 (5%)
Sepsis	1 (5%)
Pre-operative chemo-radiation with fluoropyrimidine	**N=17**
Lymphopenia	1 (6%)

Conclusions

- Borderline resectable and node-positive PDAC have high rates of disease progression.
- Multi-agent pre-operative chemotherapy is needed for early disease control prior to resection.
- Two cycles of gemcitabine & nab-paclitaxel followed by long-course radiation with single-agent fluoropyridimine provides modest R0 resection rates compared to other pre-operative treatment regimens.
- Pre-operative gemcitabine & nab-paclitaxel-based chemotherapy, perhaps of longer duration than two cycles, represents a feasible, alternate strategy to FOLFIRINOX-based therapy.

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Correspondence: cheem@ohsu.edu