LOCALLY ADVANCED

Clinical Trial Name: PurIST Classification-Guided Adaptive Neoadjuvant Chemotherapy by RNA Expression Profiling of EUS SAmples Study (PANCREAS)

Study Design: This is an open-label, single arm, phase II study in patients with resectable and borderline resectable pancreatic cancer. The study intervention involves molecular profiling Purity Independent Subtyping of Tumors (PurIST) subtyping of pretreatment Endoscopic Ultrasound Fine Needle Aspiration (EUS/FNA) samples to determine pancreatic cancer subtype. Neoadjuvant therapy is directed based on the molecular subtype (classical vs. basal). Patients with classical subtype will receive a standard chemotherapy (mFOLFIRINOX) and patients with basal subtype will receive an alternative standard therapy (gemcitabine/nab-paclitaxel).

NCT#: NCT04683315

Study PI:
Dr. Kathleen Christians

Clinical Research Coordinator:
Lauren Schmitz
Phone: 414-805-5175

Key Inclusion:

Eligibility for Treatment consent:

- ECOG performance status < 2
- Histologically confirmed adenocarcinoma. Biopsy must have been completed prior to start of treatment
- Clinical stage consistent with resectable or borderline resectable or locally advanced type A adenocarcinoma of the pancreas, based on CT or MRI findings
- Adequate organ and bone marrow function, as defined by: total leukocytes >3 x103/µL; ANC >1.5x 103/µL; HgB >9 g/dL; platelets >100 x 10e3/µL; creatinine clearance >60 mL/min or creatinine <1.5 mg/dL; bilirubin < 2 mg/dL; AST/SGOT & ALT/SGPT <3 x ULN

Key Exclusion:

- Received chemotherapy and/or radiation within three years prior to study enrollment
- Previous history of another malignancy w/in 3 years of study (other than cured basal or squamous cell carcinoma and other in situ carcinomas that were completely treated or localized prostate cancer with normal prostate specific antigen)

Clinical Trial Name: Testing Higher Dose Radiation Therapy for Locally Advanced Pancreatic Cancer (NRG-GI011)

Study Design: This phase III trial compares the effect of dose-escalated radiation therapy to usual care in patients with locally advanced unresectable pancreatic ductal adenocarcinoma who have received an initial 4-6 months of chemotherapy. Usual care options include additional chemotherapy, observation, or standard lower-dose radiation therapy. These treatments may delay tumor growth but have not been shown to improve survival. Radiation therapy uses high energy X-rays to kill cancer cells and shrink tumors. Dose-escalated radiation therapy involves the precise delivery of higher doses to the tumor, often over a shorter period of time. This trial assesses whether using dose-escalated radiation therapy can prolong survival.

NCT#: NCT06958328

Study PI:
Dr. William Hall

Clinical Research Coordinator:
Lauren Schmitz
Phone: 414-805-5175

Key Inclusion:

- At time of enrollment, the patient must have received 4-6 months of active chemotherapy with FOLFIRINOX or NALIRIFOX or gemcitabine/nab-paclitaxel. Patients are permitted to receive more than 1 type of chemotherapy for toxicity reasons, but not for disease progression. "Active chemotherapy" refers to time on chemotherapy not counting treatment breaks (i.e. if a patient had 1 month of chemotherapy followed by 1 month break, this would count as 1 month chemotherapy). Study registration must occur within 45 days of last day of chemotherapy cycle
- BASELINE PRE-ENTRY CHEMOTHERAPY REQUIREMENTS:
- Pathologically (histologically or cytologically) proven diagnosis of pancreatic ductal adenocarcinoma
- Locally advanced unresectable disease (as defined per the National Comprehensive Cancer Network [NCCN] guidelines and institutional tumor board review)
- Patients must have baseline pre-chemotherapy scans for staging. Options include: CT chest/abdomen/pelvis, CT chest/MRI abdomen/pelvis, CT chest/CT pelvis/MRI abdomen, or PET/CT performed prior to enrollment
- Age ≥ 18 years
- Performance status Eastern Cooperative Oncology Group (ECOG) 0-2
- Required initial laboratory values:

All laboratory values must be obtained any time prior to initiation of chemotherapy up to 30 days post initiation of chemotherapy

- Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) ≤ 3 x upper limit of normal (ULN)
- BASELINE CA19-9 AND BILIRUBIN REQUIREMENTS: The purpose is to obtain a baseline CA19-9 in the setting of a normal (or close to normal) bilirubin, since serologic response by serial CA19-9 measurements is part of post-chemotherapy eligibility criteria
  - If baseline CA19-9 > 37 U/mL the concurrent bilirubin must be ≤ 1.5 x ULN. (Note: if the bilirubin is not ≤ 1.5 x ULN both the CA19-9 and concurrent bilirubin can be repeated until bilirubin is ≤ 1.5 x ULN, as long as done within specified timeframe [up to 30 days post chemotherapy initiation])
  - If baseline CA19-9 U/mL ≤ 37, there are no restrictions on the required concurrent bilirubin level, and this can be the accepted baseline value
    - Prior radiation treatment
- Has the patient had prior radiotherapy to the region of the study cancer that would result in overlap of radiation therapy fields
- Prior non-overlapping radiation (e.g., breast, head and neck, extremity) is permitted

NRG-GI011 (Continued)	• If uncertain about prior overlap, please contact the study principal investigator, Dr. Nina Sanford ◦ POST PRE-ENTRY CHEMOTHERAPY REQUIREMENTS: ◦ If baseline CA19-9 is elevated (defined as > 37 u/mL) the post-pre-entry chemotherapy CA19-9 must be less than 37 u/mL or a 50% decline from pre-chemotherapy level with absolute value less than 100u/mL ◦ If baseline CA19-9 is not elevated (defined as ≤ 37 u/mL) the post-pre-entry chemotherapy CA19-9 must remain ≤ 37 u/mL ◦ No active duodenal or gastric ulcers ◦ No direct tumor invasion of the bowel or stomach ◦ Restaging scans showing at least stable disease (no progression). Options for scans include: CT chest/abdomen/pelvis, CT chest/MRI abdomen/pelvis, or CT chest/CT pelvis/MRI abdomen, or PET/CT performed prior to enrollment, with restaging CT showing at least stable disease ◦ Not pregnant and not nursing ◦ No cardiac condition that was the primary reason for hospitalization in the last 6 months ◦ New York Heart Association Functional Classification II or better (NYHA Functional Classification III/IV are not eligible) (Note: Patients with known history or current symptoms of cardiac disease, or history of treatment with cardiotoxic agents, should have a clinical risk assessment of cardiac function using the New York Heart Association Functional Classification.) ◦ HIV-infected patients on effective anti-retroviral therapy with undetectable viral load within 6 months are eligible for this trial

Clinical Trial Name: Molecular Profile-related Individualized Targeted Therapy in Resected Pancreatic Cancer with High-Risk of Cancer Recurrence (PROTECT-PANC)

Study Design: This is a prospective, open-label therapeutic interventional investigation designed to interrogate the efficacy and safety of individualized matched therapies in patients with pancreatic cancer at high risk of disease recurrence post-surgery.

NCT#: NCT06228599

Study PI:
Dr. Mandana Kamgar

Clinical Research Coordinator:
Dawn Carini
Phone: 414-805-0789

Key Inclusion:

- Pathologically confirmed pancreatic cancer (excluding neuroendocrine histology).
- Pancreatic tumor is surgically removed and
  - Patient has received multimodal therapy (neoadjuvant, sandwich or adjuvant chemotherapy ± radiation) or
  - Patient is ineligible for or refuses multimodal therapy
- Patient has one of the following:
  - Post-surgical cancer antigen (CA) 19-9 elevation (> 35 U/mL at least 6 weeks post-surgical resection) in the setting of bilirubin < 2 mg/dL (unless bilirubin elevation is consistent with Gilbert's syndrome) OR
  - High-risk pathological features, defined as positive surgical margin or lymph node involvement in cancer.
- Patient has no definitive measurable disease recurrence or metastatic disease at the time of first post-surgical imaging (in those with high-risk pathological features) or within four weeks of elevated CA 19-9 value as evidenced by appropriate imaging
- Laboratory values:
  - Absolute neutrophil count (ANC) ≥ 1.0 × 109/L
  - Platelet count ≥ 75,000/mm^3 (125 × 109/L)
  - Hemoglobin (Hgb) ≥ 8 g/dL
  - aspartate aminotransferase (AST) serum glutamic-oxaloacetic transaminase (SGOT), alanine transaminase (ALT) serum glutamate-pyruvate transaminase (SGPT) ≤ 5 × upper limit of normal range (ULN)
  - ECOG Performance Status < 3
  - At the time of treatment, patient should be off other anti-tumor agents for at least five half-lives of the agent or three weeks from the last day of treatment, whichever is shorter
  - Patient must be presented at the Molecular Tumor Board (MTB) and agree to receive the MTB-recommended therapy

Key Exclusion:

- CA 19-9 non-producers, unless high-risk pathological features present.
- Receiving concomitant investigational agent(s) for pancreatic ductal adenocarcinoma (PDAC)
- Radiographic evidence of metastatic disease
- Inability to ingest study drugs by mouth
- Diarrheal bowel movements > 6 per day postoperatively on maximal medical therapy
- Patient has active, untreated, or uncontrolled bacterial, viral, or fungal infection(s) requiring systemic intravenous therapy
- Patient has undergone or planned major surgery other than diagnostic surgery (i.e., surgery done to obtain a biopsy for diagnosis without removal of an organ) within four weeks prior to Day 1 of study therapy
- Uncontrolled concurrent illness, including, but not limited to, unstable angina pectoris, uncontrolled and clinically significant cardiac arrhythmia, or psychiatric illness/social situations that would limit compliance with study requirements