LOCALLY ADVANCED

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:
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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