LaBahn Pancreatic Cancer Program

CLINICAL TRIAL PORTFOLIO

PANCREATIC CANCER

RESECTABLE AND BORDERLINE RESECTABLE

A. Treatment Naïve
   I. CA19-9 Producer (CA 19-9 > 35 U/mL, when total bilirubin 2 mg/dL)
      a. PANC Trial - Phase II trial of adaptive neoadjuvant therapy
   II. CA19-9 Non-producer & Producer
      a. PANCREAS Trial – Tumor Subtype-directed Neoadjuvant Chemotherapy
      b. SOFT Trial - Phase II RCT of IMRT vs SBRT prior to surgery
B. Prior Neoadjuvant Chemotherapy
   I. SOFT Trial - Phase II, RCT of IMRT vs SBRT prior to surgery
   II. COLUMBIA-AAAU4206-AIRPANC- Neoadjuvant Therapy Targeting the Adenosine Immunosuppressive Pathway in Combination with Immune Checkpoint Blockade and Radiation Therapy in patients with PDAC
C. Post Surgical Resection
   I. PROTECT-PANC - Phase II, adjuvant therapy for patients at risk of cancer recurrence

LOCALLY ADVANCED

A. Type A – potentially operable
   I. SOFT Trial - Phase II, RCT of IMRT vs SBRT prior to surgery
   II. PANCREAS Trial – Tumor Subtype-directed Neoadjuvant Chemotherapy
B. Post Surgical Resection
   I. PROTECT-PANC - Phase II, adjuvant therapy for patients at risk of cancer recurrence

METASTATIC

A. Phase 1 and 2
   I. ASTELLAS-2138-CL-0101- Phase I/Ib, ASP2138 in Adults with Stomach Cancer or Pancreatic Cancer *(check for slot availability)*
   II. MIRATI 1719-001 - A Phase I/II Multiple Expansion Cohort Trial of MRTX1719 in Patients with Advanced Solid Tumors with Homozygous MTAP Deletion *(check for slot availability)*
   III. NEOGENE Trial-NT-112 – Phase I, Positive Adult Subjects with Unresectable, Advanced, And/ or Metastatic Solid Tumors Positive for the KRAS G12D Mutation
   IV. IIT-GEORGE-I-PREDICT- Phase I, Investigation of Profile-Related Evidence Determining Individualized Cancer Therapy for Patients

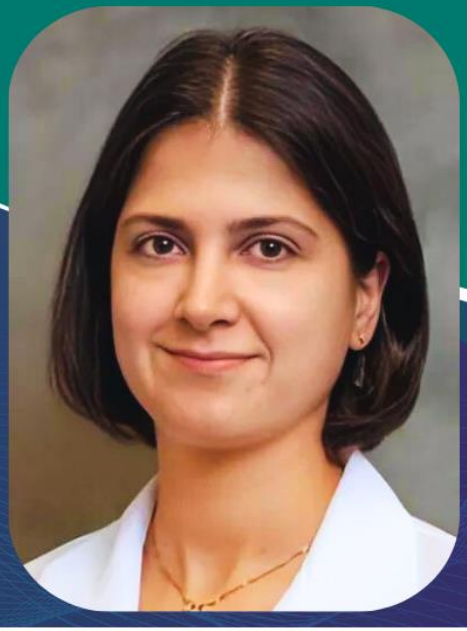
PANCREATIC NEUROENDOCRINE

I. ALLIANCE-A022001-PNETS- Lutetium LU 177 Dotatate PRRT vs Capecitabine and Temozolomide in PNET

PROTECT-PANC

For more information call 414-805-0789

The PROTECT-PANC study is a prospective, open-label, therapeutic interventional trial designed to determine the efficacy and safety of personalized matched therapy given adjuvantly in pancreatic cancer patients who have completed all intended multimodal therapy, including resection of the pancreatic cancer tumor.



PI: Mandana Kamgar, MD

Sponsored by:
SEENA
Magowitz Foundation

NEW PATIENT COORDINATOR: (414) 805-6849

RESECTABLE & BORDERLINE RESECTABLE

Clinical Trial Name: Adaptive Modification of Neoadjuvant Therapy Based on Clinical Response in Patients with Localized Pancreatic Cancer (PANC Trial)

Study Design: This is a single arm, Phase II clinical trial utilizing neoadjuvant therapy and surgery for patients with resectable and borderline resectable pancreatic adenocarcinoma which utilizes a total neoadjuvant therapy approach with adaptive modification of the chemotherapy regimen based on radiographic response (CT scan), biochemical response (CA19-9 decline), and performance status (as measured by a short physical performance battery).

NCT#: NCT03322995

Study PI: Dr. Kathleen Christians

Clinical Research Coordinator: Megan Graham

Phone: 414-805-8921

Key Inclusion

- ECOG performance status of < 2
- Histologically confirmed adenocarcinoma of the pancreas
- Clinical stage resectable or borderline resectable pancreatic adenocarcinoma
- Must be CA19-9 producer (pretreatment CA19-9 > 35 U/mL when total bilirubin ≤ 2 mg/dL)

Key Exclusion:

- Received chemotherapy and/or radiation within 3 years prior to study enrollment
- History of prior malignancy except for adequately treated in situ cancer of the cervix or basal cell or squamous cell skin cancer or localized prostate cancer with a normal PSA within the last 3 years

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

Research Coordinator: Sara Riel

Phone: 414-805-3326

Key Inclusion

Eligibility for screening consent:

- Suspicion of PDAC and plan for endoscopic biopsy or enough archival tissue to be requested from previous screening endoscopic biopsy. Agrees to additional EUS biopsy at the first restaging and tissue collection from surgical specimen

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: Stereotactic Body Radiation Therapy or Conventionally Fractionated Concurrent Chemotherapy and Radiation Therapy Preoperatively for Resectable or Borderline Resectable Pancreatic Adenocarcinoma (SOFT Trial)	
Study Design: This study is a prospective, open-label, randomized, parallel, two-arm, phase II clinical trial. Patients meeting the eligibility criteria will be randomized after a minimum of two months of induction chemotherapy. These patients will be required to have no biopsy-proven distant disease on repeat staging studies before randomization. Patients who have radiologically equivocal evidence of distant metastatic disease (small lung nodules, or liver lesions that cannot be definitively characterized, etc.) are also eligible for enrollment. Patients with biopsy-proven metastatic disease are not eligible.	
NCT#: NCT03704662 **Study PI:** Dr. William Hall **Research Coordinator:** Grace Westerman **Phone:** 414-805-8986	***Key Inclusion*** • Confirmed, resectable/borderline resectable, locally advanced Type A pancreatic adenocarcinoma • Patients with and without regional adenopathy are eligible • No evidence of distant metastatic disease • ≥ 1 cycle of systemic chemotherapy without evidence of distant progression ***Key Exclusion***: • Distant metastatic disease • Prior invasive malignancy within the last 3 years • Prior radiotherapy to the region of the study cancer that would result in overlap of radiation therapy fields • Major surgery within 28 days prior to study entry

Clinical Trial Name: Neoadjuvant Therapy Targeting the Adenosine Immunosuppressive Pathway in Combination with Immune Checkpoint Blockade and Radiation Therapy in patients with PDAC (COLUMBIA-AAAU4206-AIRPANC)	
Study Design: A Phase 2, Open-Label, Multicenter, Randomized Study Evaluating Neoadjuvant Therapy Targeting the Adenosine Immunosuppressive Pathway in Combination with Immune Checkpoint Blockade and Radiation Therapy in Patients with Advanced PANCreatic Ductal Adenocarcinoma Who Are Candidates for Surgical Resection	
NCT#: NCT06048484	***Key Inclusion:***

Study PI: Dr. Ben George **Research Coordinator:** Grace Westerman **Phone:** 414-805-8986	• Histological or pathological confirmation of pancreatic adenocarcinoma Cytologic or histologic proof of pancreatic ductal adenocarcinoma (PDAC) needs to be verified by the treating institution pathologist. A pathological report from non-treating institutions is sufficient to consent and to initiate investigational therapy if tissue sample is unavailable for evaluation at time of consent or enrollment. However, in such a case, PDAC diagnosis should be confirmed by the treating institution pathologist at a later time. • Completed 8 cycles of neoadjuvant modified FOLFIRINOX. Omission of oxaliplatin due to adverse events may be allowed in cycles 5-8 with consultation with the principal investigator. • Patients with surgically resectable PDAC who are considered appropriate to undergo the applicable operation. MCW's criteria of borderline resectable meets this inclusion criteria. • Eligible to undergo SBRT. • Measurable disease as per Response Evaluation Criteria in Solid Tumors (RECIST) 1.1. • No prior surgical, systemic, or radiotherapy for PDAC except for mFOLFIRINOX. • ECOG: 0 or 1. ***Key Exclusion***: • Prior treatment with T-cell co-stimulating or immune checkpoint blockade therapies, including but not limited to anti-CTLA-4, anti-PD-1, and anti-PD-L1 therapeutic antibodies. • Uncontrolled pleural effusion, pericardial effusion, or ascites. • Uncontrolled hypercalcemia (ionized calcium > 1.5 mmol/L, calcium > 12 mg/dL, or corrected serum calcium > ULN) or symptomatic hypercalcemia requiring continued use of bisphosphonate therapy. • Active or history of autoimmune disease or immune deficiency, including, but not limited to, myasthenia gravis, myositis, autoimmune hepatitis, systemic lupus erythematosus, rheumatoid arthritis, inflammatory bowel disease (Crohn's disease or ulcerative colitis), antiphospholipid antibody syndrome, Wegener granulomatosis, Sjögren's syndrome, Guillain-Barré syndrome, or multiple sclerosis (some exceptions permissible as outlined per protocol). • History of idiopathic pulmonary fibrosis, interstitial lung disease, organizing pneumonia (e.g., bronchiolitis obliterans), drug-induced pneumonitis, or idiopathic pneumonitis, or evidence of active pneumonitis on screening chest CT scan. • History of radiation pneumonitis in the radiation field (fibrosis) is permitted. • Positive HIV test at screening or at any time prior to screening. • Active hepatitis B virus (HBV) infection (chronic or acute), defined as having a positive hepatitis B surface antigen (HBsAg) test at screening. • Active hepatitis C virus (HCV) infection, defined as having a positive HCV antibody test followed by a positive HCV RNA test at screening. The HCV RNA test will be performed only for patients who have a positive HCV antibody test. • History of allergy or hypersensitivity to oxaliplatin, irinotecan, leucovorin, fluorouracil, pegfilgrastim, or any excipients. • History of Gilbert's disease or known genotype UGT1A1 *28/*28.

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

LOCALLY ADVANCED

Clinical Trial Name: Stereotactic Body Radiation Therapy or Conventionally Fractionated Concurrent Chemotherapy and Radiation Therapy Preoperatively for Resectable or Borderline Resectable Pancreatic Adenocarcinoma (SOFT Trial)

Study Design: This study is a prospective, open-label, randomized, parallel, two-arm, phase II clinical trial. Patients meeting the eligibility criteria will be randomized after a minimum of two months of induction chemotherapy. These patients will be required to have no biopsy-proven distant disease on repeat staging studies before randomization. Patients who have radiologically equivocal evidence of distant metastatic disease (small lung nodules, or liver lesions that cannot be definitively characterized, etc.) are also eligible for enrollment. Patients with biopsy-proven metastatic disease are not eligible.

NCT#: NCT03704662

Study PI: Dr. William Hall

Research Coordinator: Kathryn Hallada

Phone: 414-805-0124

Key Inclusion:

- Confirmed, resectable/borderline resectable, locally advanced Type A pancreatic adenocarcinoma
- Patients with and without regional adenopathy are eligible
- No evidence of distant metastatic disease
- ≥ 1 cycle of systemic chemotherapy without evidence of distant progression

Key Exclusion:

- Distant metastatic disease
- Prior invasive malignancy within the last 3 years
- Prior radiotherapy to the region of the study cancer that would result in overlap of radiation therapy fields
- Major surgery within 28 days prior to study entry

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NCT#: NCT04683315

Study PI: Dr. Kathleen Christians

Key Inclusion

Eligibility for screening consent:

- Suspicion of PDAC and plan for endoscopic biopsy or enough archival tissue to be requested from previous screening endoscopic biopsy. Agrees to additional EUS biopsy at the first restaging and tissue collection from surgical specimen

Eligibility for Treatment consent:

Research Coordinator: Sara Riel **Phone** 414-805-3326	• 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)

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  - High-risk pathological features, defined as positive surgical margin or lymph node involvement in cancer.
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- 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
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- 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

METASTATIC

PHASE I/II STUDIES

Clinical Trial Name: A Phase 1/1b Study of ASP2138 in Participants with Metastatic or Locally Advanced Unresectable Gastric or Gastroesophageal Junction (GEJ) Adenocarcinoma or Metastatic Pancreatic Adenocarcinoma (ASTELLAS).

Study Design: A Phase 1/1b Study of ASP2138 in Participants with Metastatic or Locally Advanced Unresectable Gastric or Gastroesophageal Junction (GEJ) Adenocarcinoma or Metastatic Pancreatic Adenocarcinoma Whose Tumors Have Claudin (CLDN) 18.2 Expression.

NCT #:

NCT05365581

Study PI: Dr. Mandana Kamgar

Research Coordinator: Morgan Ward

Phone: 414-805-6345

***Key Inclusion**:*

- Tumor sample is positive for claudin (CLDN)18.2 expression by central immunohistochemistry (IHC) testing.
- Radiographically-confirmed, locally advanced, unresectable or metastatic disease within 28 days prior to the first dose of study intervention
- Measurable disease according to Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 within 28 days prior to the first dose of study intervention. For participant with only 1 measurable lesion and prior radiotherapy, the lesion must be outside the field of prior radiotherapy or must have documented progression following radiation therapy.
- QT interval by Fredericia (QTcF) =< 470 msec.
- Participant has ECOG performance status of 0 or 1.
- Disease Specific Criteria: Pancreatic Cancer
    - Participant has histologically or cytologically confirmed pancreatic adenocarcinoma.
    - Participant with pancreatic adenocarcinoma who has progressed, is intolerant, has refused, or for whom there is no standard approved therapies that impart significant clinical (no limit to the number of prior treatment regimens).

***Key Exclusion**:*

- Prior severe allergic reaction or intolerance to known ingredients of ASP2138 or other antibodies, including humanized or chimeric antibodies.
- Received systemic immunosuppressive therapy, including systemic corticosteroids 14 days prior to first dose of study intervention.
- Complete gastric outlet syndrome or a partial gastric outlet syndrome with persistent/recurrent vomiting.
- Gastric bleeding and/or untreated gastric ulcers that exclude the participant from participation.
- Symptomatic CNS metastases or participant has evidence of unstable CNS metastases even if asymptomatic.
- Known HIV infection.
- Participant is known to have active hepatitis B (positive hepatitis B surface antigen [HBsAg]) or hepatitis C infection. Testing is required for known history of these infections or as mandated by local requirements.
- Negative for HBsAg, but hepatitis B core antibody (HBc Ab) positive, a hepatitis B virus (HBV) deoxyribonucleic acid (DNA) test will be performed and if positive the participant will be excluded.
- Positive hepatitis C virus (HCV) serology, but negative HCV ribonucleic acid (RNA) test results are eligible.
- Treated for HCV with undetectable viral load results are eligible.
- Within 6 months prior to first dose of study intervention any of the following: unstable angina, myocardial infarction, ventricular arrhythmia requiring intervention or hospitalization for heart failure.
- Active infection requiring systemic therapy that has not completely resolved within 7 days prior to the start of study intervention.

	• Active autoimmune disease that has required systemic immunosuppressive treatment within the past 1 month prior to the start of study intervention. • Major surgical procedure 28 days before start of study intervention and has not fully recovered. • Received radiotherapy for locally advanced unresectable or metastatic gastric or GEJ or metastatic pancreatic adenocarcinoma 14 days prior to start of study intervention and has NOT recovered from any related toxicity. • Received an CLDN18.2-targeted investigational agent (e.g., zolbetuximab or chimeric antigen receptor CLDN18.2-specific T cells) prior to first dose of study intervention administration is not eligible for dose escalation cohorts. However, a participant who has received an CLDN18.2-targeted investigational agent greater than 28 days or 5 half-lives (whichever is longer) prior to first dose study intervention administration is eligible for dose expansion cohorts only, except for participants who have experienced Grade >= 3 gastrointestinal (GI) toxicity after receiving an CLDN18.2-targeted investigational agent. • History or complication of interstitial lung disease.

Clinical Trial Name: MRTX1719 in Patients With Advanced Solid Tumors With Homozygous MTAP Deletion (MIRATI 1719-001)	
Study Design: The study is a Phase 1/2, open-label, multicenter, study of the safety, tolerability, PK, PD, and anti-tumor activity of MRTX1719 patients with advanced, unresectable or metastatic solid tumor malignancy with homozygous deletion of the MTAP gene.	
NCT #: NCT05245500 **Study PI:** Dr. Ben George **Research Coordinator:** Nicholas Pucek **Phone:** 414-805-4639	***Key Inclusion:*** • Histologically confirmed diagnosis of a solid tumor malignancy with homozygous deletion of the MTAP gene detected in tumor tissue or ctDNA • Unresectable or metastatic disease • Patients must have received standard therapies appropriate for their tumor type and stage with disease progression on or after the most recent treatment ▪ Phase 1 dose escalation, RECIST 1.1 measurable or evaluable disease ▪ Phase 1b and Phase 2 cohorts, RECIST 1.1 measurable disease • Presence of a tumor lesion amenable to mandatory biopsy for pharmacodynamic evaluation at baseline and on-study unless Sponsor-confirmed as medically unsafe or infeasible • ECOG: 0 or 1 ***Key Exclusion:*** • Prior treatment with a PRMT5 or MAT2A inhibitor therapy. • Active brain metastases or carcinomatous meningitis. • History of significant hemoptysis or hemorrhage within 4 weeks of the first dose of study treatment. • Major surgery within 4 weeks of first dose of study treatment. • History of intestinal disease, inflammatory bowel disease, major gastric surgery, or other gastrointestinal conditions (eg, uncontrolled nausea, vomiting, malabsorption syndrome) likely to alter absorption of study treatment or result in inability to swallow oral medications • Cardiac abnormalities

Clinical Trial Name: A Study of NEOGENE Trial-NT-112 in HLA-C*08:02-Positive Adult Subjects with Unresectable, Advanced, And/ or Metastatic Solid Tumors Positive for the KRAS G12D Mutation (NEOGENE Trial)

Study Design: This is a Phase 1, open-label, multicenter study to evaluate the safety and preliminary antitumor activity of NEOGENE Trial-NT-112 in HLA-C*08:02 subjects with unresectable, advanced, and/or metastatic NSCLC, colorectal adenocarcinoma, pancreatic adenocarcinoma, endometrial cancer, or any other solid tumor histology that is positive for the KRAS G21D mutation

NCT #:

NCT06218914

Study PI: Mandana Kamgar

Research Coordinator:

Lauren Winkowski

Phone:

414-805-8937

Key Inclusion:

- Age ≥18 years
- Diagnosed with NSCLC, Colorectal adenocarcinoma, Pancreatic adenocarcinoma, Endometrial Cancer or any other solid tumor
- Tumors must harbor a KRAS G12D variant mutation and subject must be HLA-C*08:02 positive
- Subject has advanced solid cancer, defined as unresectable, advanced, and/or metastatic disease (Stage III or IV) after at least 1 line of approved systemic standard of care (SOC) treatment regimen and for which there are no available curative treatment options.
- Presence of at least 1 measurable lesion per RECIST v1.1
- Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 1 at the time of enrollment

Key Exclusion:

- Any other primary malignancy within the 3 years prior to enrollment (except for non-melanoma skin cancer, carcinoma in situ (eg, cervix, bladder, breast) or low-grade prostate cancer
- Known, active primary central nervous system (CNS) malignancy
- History of prior adoptive cell and gene therapy, allogeneic stem cell transplant or solid organ transplantation.
- History of stroke or transient ischemic attack within the 12 months prior to enrollment.
- History of clinically significant cardiac disease within the 6 months prior to enrollment or heart failure at any time prior to enrollment.
- Systemic therapy within at least 2 weeks or 3 half-lives, whichever is shorter, prior to enrollment.
- Any form of primary immunodeficiency.
- Active immune-mediated disease requiring systemic steroids or other immunosuppressive treatment (except if related to prior checkpoint inhibitor therapy)
- Female of childbearing potential who is lactating or breast feeding at the time of enrollment

Clinical Trial Name: Investigation of Profile-Related Evidence Determining Individualized Cancer Therapy for Patients (IIT-GEORGE-I-PREDICT)

Study Design: The purpose of this study is to learn more about personalized cancer therapy, including response to treatment and its side effects. Personalized cancer therapy is the practice of making decisions about what kind of treatment patients should receive based on the characteristics of their tumor.

NCT #:

NCT05674825

Study PI: Ben George

Research Coordinator:

Paola Gonzalez Quevedo

Phone: 414-805-2674

Key Inclusion:

- Patient with aggressive solid malignancy must meet at least one of the following:
  - Malignancy with ≥30% two-year cancer-associated mortality as estimated by the treating oncologist and one of the study investigators and/or, where appropriate, according to accepted data sets in the field (e.g., NCDB). Diseases include but are not limited to: ampullary carcinoma, appendiceal cancer, colorectal cancer (CRC), extrahepatic cholangiocarcinoma (EHCC), esophageal adenocarcinoma, gallbladder cancer (GBCA) gastric adenocarcinoma, head and neck cancer, hepatocellular carcinoma (HCC), intrahepatic cholangiocarcinoma (IHCC), melanoma, non-KIT gastrointestinal stromal tumor (GIST), non-small cell lung cancer (NSCLC), ovarian cancer, pancreatic ductal adenocarcinoma (PDAC), sarcoma (high-grade), small bowel adenocarcinoma (including duodenal), triple-negative breast cancer (TNBC), urothelial cancer
  - Refused standard therapies, OR
  - Cancer of unknown primary or a rare tumor (i.e., fewer than 4 cases per 100,000 per year) with no approved therapies.
- Patient with aggressive solid malignancy irrespective of two-year mortality who, in the opinion of the investigator, has no treatment option expected to yield significant clinical benefit.
- Patient must have at least one of the following for a diagnosis/disease status:
  - Unresectable disease, as determined by a disease-appropriate multidisciplinary tumor board.
  - Medically unfit for surgical resection but with an expected survival of > three months.
  - Localized disease and are eligible for neoadjuvant treatment.
  - Metastatic disease.
  - Disease where no conventional therapy leads to a survival benefit > six months in the respective cohort and line of therapy for which the patient is otherwise eligible.
- Patient is either:
  - Treatment naïve for their newly diagnosed malignancy (for enrollment to Groups 1 or 2), or
  - Status post one or more systemic therapy regimens, whether matched or unmatched (for enrollment to Group 3). Note: There are no limitations on the number of prior local therapies.
- Patient must have measurable disease for malignancy: defined as at least one lesion that can be accurately measured in at least one dimension (longest diameter to be recorded for non-nodal lesions and short axis for nodal lesions) as ≥20 mm with conventional techniques or as ≥10 mm with spiral CT scan, positron emission tomography (PET) -CT, MRI, or calipers by clinical exam.
- ECOG:0-2
- New York Heart Association (NYHA) Functional Classification I-II
- Adequate organ and marrow function as defined below:
  - Absolute neutrophil count ≥ 1.0 x 109/L
  - Platelet count ≥ 75 x 109/L
  - Total bilirubin ≤ 2.0 x institution's upper limit of normal (ULN)
  - Patients without underlying liver disease: alanine transaminase (ALT) and aspartate aminotransferase (AST) ≤ 3 x institutional ULN
  - Serum creatinine ≤ 2.0 x institution's ULN or 24-hour creatinine clearance ≥ 30 ml/min
- At the time of treatment, patient should be off other anti-tumor agents for at least five half-lives of the agent or two weeks from the last day of treatment, whichever is shorter to enroll in Group 3. Patient must not have been treated with anti-tumor agents to enroll in Group 1 or Group 2. Patient must be off prior antibody therapy for at least three half-lives before starting treatment.
- If actionable or appropriate molecular profiling has not already been performed, patient must have or provide evaluable tissue and/or blood for molecular profiling. This could be obtained during the standard of care tumor diagnosis or tumor staging evaluation. Tissue and/or blood is to be procured based on clinical discretion and discussion with the patient.

	• Patients presented at Molecular Tumor Board (MTB) up to two weeks prior to signing consent are eligible to be treated on study based on the MTB recommendations and do not need to be represented at MTB prior to starting therapy on trial (unless six months elapsed between consent and start of study treatment). ***Key Exclusion:*** • Two oncologists disagree on prognosis or resectability. • Severe or uncontrolled medical disorder that would, in the investigator's opinion, confound study analyses of treatment response (i.e., uncontrolled diabetes, chronic renal disease, chronic pulmonary disease or active, uncontrolled infection, psychiatric illness/social situations that would limit compliance with study requirements). • Is pregnant or breastfeeding or any patient with childbearing potential not using adequate pregnancy prevention. Whole brain radiation or stereotactic radiotherapy to CNS metastases within 14 days prior to start of study treatment.

PANCREATIC NEUROENDOCRINE

Clinical Trial Name: ALLIANCE-A022001-PNETS Lutetium LU 177 Dotatate PRRT vs Capecitabine and Temozolomide in PNET

Study Design: This is a phase II randomized, prospective trial of Lutetium LU 177 Dotatate PRRT versus Capecitabine and Temozolomide in well-differentiated pancreatic neuroendocrine tumors.

NCT#:
NCT05247905

Study PI: Dr. Callisia Clarke

Research Coordinator:
Barb Dion

Phone: 414-805-4639

Key Inclusion

- Histologic or pathologic documentation of well-differentiated pancreatic neuroendocrine tumor (G1, G2, or well-differentiated G3) confirmed by local histology and/or pathology. Functional or nonfunctional tumors are allowed.
- Stage: locally unresectable or metastatic disease.
- Tumor Site: neuroendocrine tumor of pancreatic primary site.
- Radiologic evaluation: tumor must have shown somatostatin receptor (SSTR) positivity on 68Ga-DOTATATE PET or other SSTR-PET scan in the 12 months prior to registration; however, documentation of SSTR positivity in the 6 months prior to registration is preferred. SSTR positivity is defined as uptake greater than background liver in all measurable lesions.
- Patients are eligible if they meet one of the following criteria:
  - Previously untreated patients with grade 2 or 3 disease AND with symptoms of either disease bulk causing pain, anorexia, early satiety, large effusions/ascites, abdominal pain, abdominal fullness due to hepatomegaly, dyspnea) OR incompletely controlled symptoms of hormone excess despite somatostatin analogue (SSA) and supportive care (including but not limited to: diarrhea, hypercalcemia, hypoglycemia, hyperglycemia, flushing, Cushing's syndrome). Patient may have been started on SSA for up to 2 months for attempted symptom control without disease progression prior to registration.
  - Patients previously treated with SSA only and with disease progression by RECIST in prior 12 months.
  - Patients previously treated with SSA and one or more prior systemic therapy must have received prior anti-vascular endothelial growth factor (VEGF) pathway therapy inhibitor OR have contraindication to anti-VEGF therapy (including but not limited to: uncontrolled hypertension [systolic blood pressure [SBP] > 150 and/or diastolic blood pressure [DBP] > 90 despite medical management], stage IIB or greater heart disease, angina pectoris, prior arterial [ATE] and venous thromboembolic [VTE] events in the past 6 months, gastrointestinal [GI] bleed in the last 6 months) and disease progression by RECIST in prior 12 months.
  - Patients previously treated with more than 2 lines of therapy, not including anti VEGF therapy, but with NET related symptoms as outlined in first bullet (pain, anorexia, early satiety, large effusions/ascites, abdominal pain, abdominal fullness due to hepatomegaly, anorexia, early satiety, dyspnea) OR incompletely controlled symptoms of hormone excess despite somatostatin analogue (SSA) and supportive care (including but not limited to: diarrhea, hypercalcemia, hypoglycemia, hyperglycemia, flushing, Cushing's syndrome).
  - Any patient with disease progression by RECIST criteria in < 4 months.
- Patients must have measurable disease per RECIST v1.1 by computer tomography (CT) scan or magnetic imaging (MRI). Any lesions which have undergone percutaneous therapies or radiotherapy after starting protocol therapy should not be considered measurable unless the lesion has clearly progressed since the procedure.
- Lesions must be accurately measured in at least one dimension (longest diameter to be recorded) as >= 1 cm with CT or MRI (or shortest diameter >= 1.5 cm for lymph nodes). Non-measurable disease includes disease smaller than these dimensions or lesions considered truly non- measurable including: leptomeningeal disease, bone metastases, ascites, pleural or pericardial effusion, lymphangitic involvement of skin or lung.

	• Prior treatment with tyrosine kinase inhibitors (TKIs) such as mammalian target of rapamycin (mTOR) inhibitors (e.g. everolimus, temsirolimus, etc.) or VEGF pathway inhibitors (e.g. sunitinib, pazopanib, cabozantinib, bevacizumab, etc.) are allowed. • Prior treatment with hepatic intra-arterial embolic therapies is allowed if there is recovery from all toxicities, measurable lesions do not include embolized liver unless there has been clear subsequent progression, all measurable lesions are somatostatin receptor avid, and treatment completed at least 2 months prior to registration. • Prior treatment with cryoablation or thermal/radiofrequency ablation of metastases is allowed if there is recovery from all toxicities, measurable lesions do not include treated metastases, and treatment completed at least 2 months prior to registration. • ECOG = 0-2. • Absolute neutrophil count (ANC) >= 1,500/mm^3, Platelet count >= 100,000/mm^3, Hemoglobin >= 9.0 g/dL, Creatinine =< 1.5 x upper limit of normal (ULN) OR calculated (calc.) creatinine clearance >= 30 mL/min (calculated by the Cockcroft-Gault equation), Total bilirubin =< 1.5 x ULN (in patients with liver metastases or known Gilbert's syndrome, total bilirubin must be =< 3.0 x ULN), Aspartate aminotransferase (AST) (serum glutamic-oxaloacetic transaminase [SGOT]) and alanine aminotransferase (ALT) (serum glutamate pyruvate transaminase [SGPT]) =< 3.0 x ULN, Albumin >= 3.0 g/dL. • Concurrent somatostatin analog use while on protocol therapy is allowed provided that the patient: ▪ Has a functional tumor (evidence of peptide hormones and/or bioactive substances associated with a clinical hormone syndrome such as carcinoid syndrome or Cushing's syndrome). ▪ Has been on a stable dose of somatostatin analog therapy for at least three months. ▪ Has previously demonstrated radiographic disease progression while on somatostatin analog therapy. For subjects receiving lutetium Lu 177 dotatate, there should be a minimum of 14 days between long-acting somatostatin analogue and lutetium Lu 177 dotatate dosing. Short-acting somatostatin analogs should not be administered within 24 hours of lutetium Lu 177 dotatate dosing. Following lutetium Lu 177 dotatate dosing, long-acting somatostatin analogs may be administered between 4 and 24 hours after each dose. ***Key Exclusion:*** • Patients with poorly differentiated neuroendocrine carcinoma (large cell histology or small cell histology) are not eligible. • No prior temozolomide, dacarbazine, capecitabine, 5-FU, or any PRRT for treatment of the pNET. • No uncontrolled congestive heart failure (New York Heart Association [NYHA] II, III, IV). • No "currently active" second malignancy other than non-melanoma skin cancers or cervical carcinoma in situ. Patients are not considered to have a "currently active" malignancy if they have completed therapy or are on adjuvant hormonal therapy and are free of disease for >= 3 years. • No known medical condition causing an inability to swallow and no known impairment of gastrointestinal function that may significantly alter the absorption of an oral agent.