Perioperative Therapy for Resectable and Borderline-Resectable Pancreatic Adenocarcinoma With Molecular Correlates

CLINICALTRIALS.GOV IDENTIFIER	RECRUITMENT STATUS	FIRST POSTED	LAST UPDATE POSTED
NCT02723331	RECRUITING	MARCH 30, 2016	MARCH 8, 2021

STUDY DESCRIPTION

Brief Summary

The objective of this study is to estimate the R0 resection rate in patients with Resectable Pancreatic Ductal Adenocarcinoma (R-PDAC) as well as those with Resectable Pancreatic Ductal Adenocarcinoma (BR-PDAC) independently in response to neoadjuvant sequential therapy of combination nab-paclitaxel and gemcitabine followed by stereotactic body radiotherapy (SBRT).

Condition or Disease: Pancreatic Cancer
Pancreatic Adenocarcinoma
Pancreas Ductal Adenocarcinoma

Intervention/treatment: Drug: Nab-paclitaxel and gemcitabine for R-PDAC Patients
Drug: Nab-paclitaxel and gemcitabine for BR-PDAC Patients

Phase: Phase 2

DETAILED DESCRIPTION

Patients in both cohorts will receive a total of 3 cycles of neoadjuvant combination chemotherapy of nab-paclitaxel and gemcitabine, followed by re-staging CT scan, if re-staging CT does not show evidence of metastatic disease. Patients will receive SBRT and definitive surgical resection. Subsequently, patients will receive 3 cycles of adjuvant combination chemotherapy of nab-paclitaxel and gemcitabine. Each cycle of combination chemotherapy will be a total of 4 weeks. Patients will be evaluated for response at completion of the 3 cycles of neoadjuvant combination chemotherapy with CT scans of chest, abdomen and pelvis. Patients will undergo surveillance CT scan at 3-month intervals until evidence of disease progression.

STUDY DESIGN

Study Type: Interventional

Estimated Enrollment : 50 participants

Intervention Model : Parallel Assignment

Masking: None (Open Label) ()

Primary Purpose: Treatment

Official Title: Perioperative Therapy for Resectable Pancreatic Adenocarcinoma and Borderline Resectable Pancreatic Adenocarcinoma With Molecular Correlates

Actual Study Start Date: December 2016

Estimated Primary Completion Date: March 2022

Estimated Study Completion Date: May 2022

ARMS AND INTERVENTIONS

Arm	Intervention/treatment
Experimental: Nab-paclitaxel/Gemcitabine for R-PDAC Nab-paclitaxel and gemcitabine, for R-PDAC patients enrolled in this trial, will be given in combination as neoadjuvant combination chemotherapy, followed by SBRT. This is will be followed up by surgical resection and an additional combination chemotherapy of nab-paclitaxel and gemcitabine as adjuvant chemotherapy.	Drug: Nab-paclitaxel and gemcitabine for R-PDAC Patients Nab-paclitaxel and gemcitabine, for R-PDAC patients, will be given in combination as neoadjuvant and adjuvant chemotherapy. Nab-paclitaxel will be administered by IV infusion at a dose of 125 mg/m2 over 30 minutes on Days 1, 8, and 15 of every 28-day cycle. Gemcitabine will be administered by IV infusion, immediately after the administration of nab-paclitaxel, at a dose of 1000 mg/m2 over 30 minutes on Days 1, 8 and 15 of every 28-day cycle.
Experimental: Nab-paclitaxel/Gemcitabine for BR-PDAC Nab-paclitaxel and gemcitabine, for BR-PDAC patients enrolled in this trial, will be given in combination as neoadjuvant combination chemotherapy, followed by SBRT. This is will be followed up by surgical resection and an additional combination chemotherapy of nab-paclitaxel and gemcitabine as adjuvant chemotherapy.	Drug: Nab-paclitaxel and gemcitabine for BR-PDAC Patients Nab-paclitaxel and gemcitabine, for BR-PDAC patients, will be given in combination as neoadjuvant and adjuvant chemotherapy. Nab-paclitaxel will be administered by IV infusion at a dose of 125 mg/m2 over 30 minutes on Days 1, 8, and 15 of every 28-day cycle. Gemcitabine will be administered by IV infusion, immediately after the administration of nab-paclitaxel, at a dose of 1000 mg/m2 over 30 minutes on Days 1, 8 and 15 of every 28-day cycle.

OUTCOME MEASURES

Primary Outcome Measures: 1. R0 resection rates in each cohort as measured by macroscopically complete tumor removal with negative microscopic surgical margins [Time Frame: surgery]
R0 resection rates will be measured in patients with resectable PDAC and with patients with borderline-resectable PDAC, independently in response to neoadjuvant sequential therapy of combination of nab-paclitaxel and gemcitabine and SBRT, as perioperative therapy. R0 resection is determined by macroscopically complete tumor removal with negative microscopic surgical margins in the bile duct, pancreatic parenchyma, and superior mesenteric artery (SMA).

Secondary Outcome Measures:	1. Number of participants with treatment related adverse events as assessed by CTCAE v.4.03 [Time Frame: 24 months] 2. Number of participants with progression-free occurence [Time Frame: Up to 5 years] The progression-free survival (PFS) will be assessed for all participants using Response Evaluation Criteria in Solid Tumors (RECIST v1.1). 3. Number of participants with disease recurrence [Time Frame: Up to 5 years] Disease-free survival will be assessed for all participants using Response Evaluation Criteria in Solid Tumors (RECIST v1.1).

ELIGIBILITY CRITERIA

Ages Eligible for Study: 18 to 101 Years (Adult, Older Adult)

Sexes Eligible for Study: All

Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:
1. Histologically confirmed resectable or borderline resectable pancreatic adenocarcinoma.
2. No evidence of distant metastasis representing stage IV metastatic disease.
3. R-PDAC: No evidence of distant metastasis and tumor mass showing no extension to superior mesenteric artery (SMA) and hepatic artery. There must be a clearly defined fat plane between SMA and celiac axis. Patent superior mesenteric vein (SMV/portal vein (PV) with no distortion of venous architecture.
4. BR-PDAC: defined as localized PDAC with 1 or more of the following features: a) an interface between the primary tumor and superior mesenteric vein (SMV)-portal vein (PV) measuring 180o or greater of the circumference of the vein wall, and/or b) short-segment occlusion of the SMV-PV with normal vein above and below the level of obstruction that is amenable to resection and venous reconstruction and/or c) short-segment interface of any degree between tumor and hepatic artery with normal artery proximal and distal to the interface that is amenable to resection and arterial reconstruction and/or d) an interface between the tumor and SMA or celiac trunk measuring less than 180o of the circumference of the artery wall.
5. Age > 18 years old
6. Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1
7. Patients must have adequate bone marrow function:
- Platelets >100,000 cells/mm3
- Hemoglobin > 9.0 g/dL
- Absolute Neutrophil Count > 1,500 cells/mm3
8. Patients must have adequate liver function:
- aspartate aminotransferase (AST) and Alanine Aminotransferase (ALT) < 2.5 X upper limit of normal - Alkaline phosphatase < 2.5 X upper limit of normal, unless bone metastasis is present in the absence of liver metastasis - Total bilirubin < 1.5 mg/dL 9. Patients must have adequate renal function: creatinine 50 mL/min calculated using the Cockcroft-Gault equation.
10. Women of childbearing potential and sexually active males must use an effective contraception method during treatment and for three months after completing treatment.
11. Negative serum or urine β-human chorionic gonadotropin (hCG) pregnancy test at screening for patients of childbearing potential.
12. Patients must have grade 1).
8. Patients with clinically significant cardiac disease (New York Heart Association Classification III or IV and cardiac arrhythmias not well controlled with medication), or myocardial infarction within the previous six months.
9. Serious, uncontrolled, concurrent infection(s) requiring antibiotics.
10. Pregnant or breastfeeding women: positive pregnancy test within 7 days of starting treatment.
11. Treatment for other carcinomas within the last five years, except cured non-melanoma skin and treated in-situ cervical cancer.
12. Participation in any investigational drug study within 4 weeks preceding the start of study treatment.
13. Patients with external biliary drains.

CONTACTS AND LOCATIONS

Contacts

Contact:

Locations

United States, Arizona	Mayo Clinic Hospital	Scottsdale
United States, Arizona	University of Arizona	Tucson
United States, Colorado	University of Colorado Cancer Center	Aurora
United States, New York	New York University	New York

Sponsors and Collaborators

Academic Thoracic Oncology Medical Investigators Consortium

Celgene Corporation

Criterium, Inc.

University of Colorado, Denver

Investigator

Principal Investigator : Wells Messersmith, MD University of Colorado, Denver

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MORE INFORMATION

Responsible Party :	Academic Thoracic Oncology Medical Investigators Consortium
ClinicalTrials.gov Identifier :	NCT02723331
Other Study ID Numbers :	15-0150.cc
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Individual Participant Data (IPD) Sharing Statement:	
Plan to Share IPD:	No
Keywords provided by Academic Thoracic Oncology Medical Investigators Consortium:	*Stereotactic Body Radiation Therapy* *Perioperative Therapy* *Resectable Pancreas Ductal Adenocarcinoma* *Abraxane* *Borderline Resectable Pancreas Ductal Adenocarcinoma Nab-paclitaxel* *Gemcitabine* *Neoadjuvant Therapy* *Adjuvant Therapy*
Additional relevant MeSH terms :	*Adenocarcinoma*