Abstract 384156: A PHASE Ib/2a TRIAL OF CEND-1 IN COMBINATION WITH NEOADJUVANT FOLFIRINOX BASED THERAPIES IN PANCREATIC, COLON AND APPENDICEAL CANCERS (CENDIFOX), NCT05121038

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BACKGROUND

- Efficacy of chemotherapy is often compromised due to poor penetration of drugs.
- Tumor microenvironment, consists of extracellular matrix creates a physical barrier to penetration of anti-cancer drugs especially desmoplastic stroma in Pancreatic Ductal Adenocarcinoma (PDAC) and plasma peritoneal barrier in peritoneal metastases from Colorectal/Appendiceal adenocarcinoma.
- CEND-1 is a tumor-penetrating peptide (scientifically also known as iRGD) has demonstrated in in vitro and in vivo preclinical models that penetration of chemotherapy agents is enhanced by binding to integrins and activating the transporter neuropilin-1.
- Higher delivery and concentration of chemotherapeutics selectively in the tumor, while sparing normal tissue.
- Improves the efficacy of anti-cancer therapies and reduce side effects through increased specificity and sensitivity.
- We hypothesize that CEND-1 may become a powerful adjuvant that safely enhances standard anti-neoplastic therapy in the neoadjuvant setting for this population.

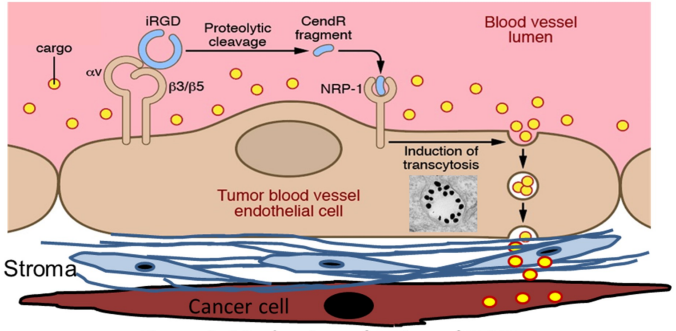
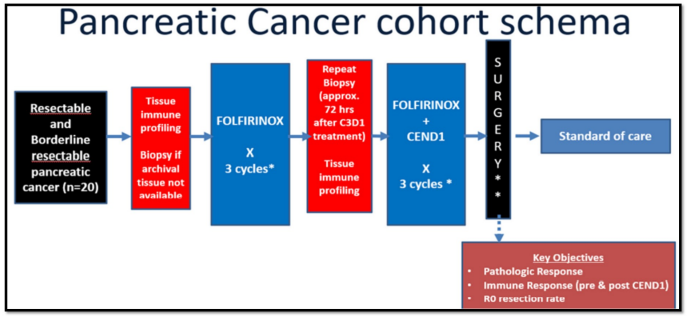
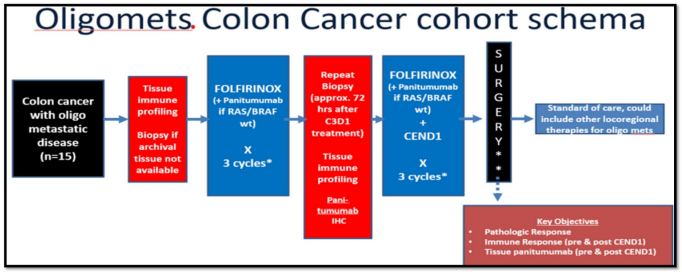


Figure 1: Mechanism of action of CEND-1

METHODS

Methods	
Protocol Number	IIT-2021-CENDIFOX
Phase	1b / 2a
Design	Open label, non-randomized, 3 cohorts
Study Duration	4 years in total with 2 years for accrual Participants to be followed for 1 year and 2 years for DFS and OS
Study Center(s)	The University of Kansas Cancer Center
Number of Participants	50 participants (20 with pancreatic adenocarcinoma, 15 with colon peritoneal metastases, 15 with oligometastatic colon cancer





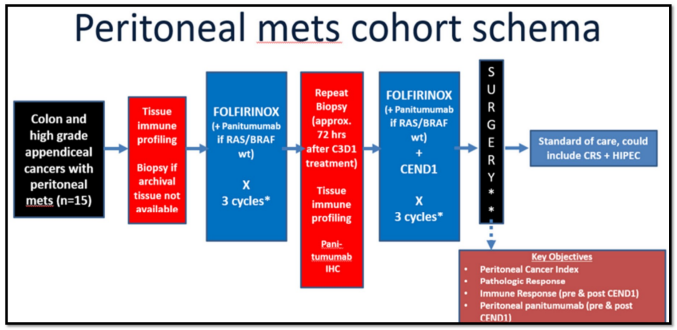


Figure 2: Schema for the Pancreatic cancer, Oligometastatic colon cancer and peritoneal metastases from Colorectal/Appendiceal adenocarcinoma cohorts

INCLUSION CRITERIA

Diagnosis and Key Inclusion Criteria
Histologically confirmed PDAC, colon and appendiceal adenocarcinoma
ECOG PS 0 - 1
1 or more lesions evaluable on MRI, PET/CT, or CT scan according to RECIST v1.1
Eligible for treatment with FOLFIRINOX
Adequate archival tissue from prior biopsy for biomarker evaluation or willingness to undergo biopsy before treatment starts and on treatment
Patients eligible for planned surgery at end of treatment

OBJECTIVES

Primary Objectives
Determine safety and biological activity of CEND-1 when given in combination with standard of care FOLFIRINOX based chemo for pancreatic, colon, appendiceal cancers

Correlative/Exploratory studies
Examine tumor biomarkers for predicting the response to CEND-1 therapy, and/or correlation with clinical response
Determine pathologic response, tissue immune response, EGFR expression pre and post CEND-1
Determine the tumor tissue-to-plasma concentration ratio of panitumumab prior to and following CEND-1 co-administration and changes in correlative study biomarkers

DOSE ESCALATION

- A starting CEND-1 dose of 3.2 mg/kg in combination with the standard doses of FOLFIRINOX (+/- Panitumumab if RAS/RAF wild type) will be used for the safety lead in.
- CEND-1 dose will be lowered for phase II if >1/6 patients experienced DLTs.
- Participants will receive standard doses of FOLFIRINOX q2w +/- Panitumumab q2w 6mg/kg IV q2w (14-day cycles) for Cycles 1-3, followed by a research biopsy, CEND-1 will be given IV at RP2D q2w for cycles 4-6 along with standard chemo, and followed by CEND-1 +/- Panitumumab ~72h prior to resection.

Assessments
Assessment of tumor response using RECIST v1.1 will be done every 3 cycles.

STUDY PROGRESS

Enrollment to the CENDIFOX trial is currently ongoing.

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NCT05121038. (For more information contact akasi@kumc.edu)