

Enrolling Clinical Trials: Combination Chemotherapy/Immunotherapy for Patients with Previously Untreated Metastatic Pancreatic Ductal Adenocarcinoma

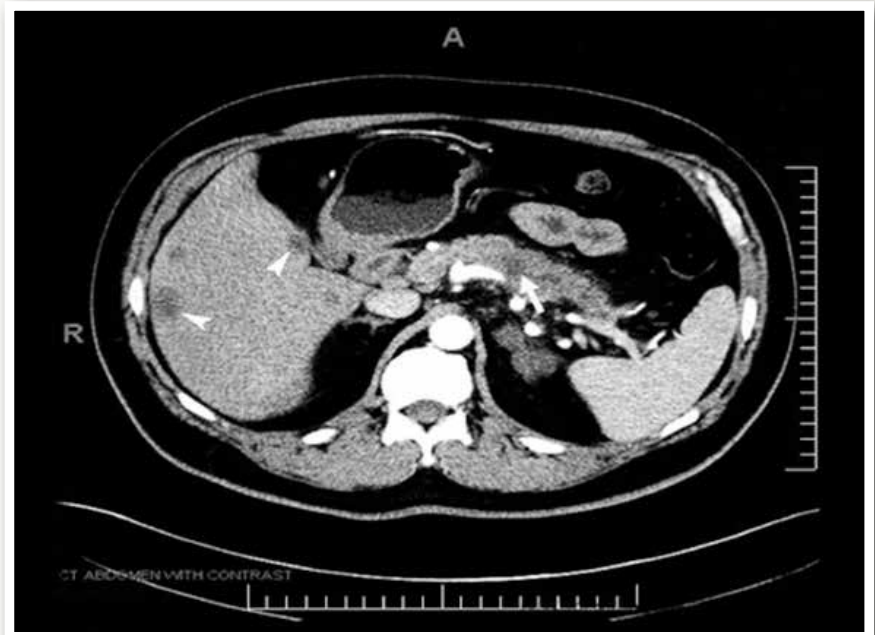
► Researchers at the Abramson Cancer Center are participating in a multi-center clinical trial to determine the safety and benefit of an investigational anti-CD40 agonist antibody when added to the chemotherapeutics nab-paclitaxel and gemcitabine in patients with newly diagnosed resectable pancreatic ductal adenocarcinoma (PDA). The primary investigator for this study is Robert H. Vonderheide, MD, DPhil, Director of the Abramson Cancer Center and the John H. Glick, MD, Abramson Cancer Center Director's Professor.

Dr. Vonderheide leads a laboratory at the Perelman School of Medicine devoted to advancing the understanding of tumor immunology and the development of novel immunotherapies for cancer. Basic research at the Vonderheide laboratory encompasses pancreatic cancer, breast cancer, and melanoma, with a focus on the regulation of immune surveillance and the tumor microenvironment by CD40 and other oncogenic pathways. A costimulatory protein found on the surface of antigen presenting cells, CD40 binds to CD40L, a ligand expressed primarily by T cells, and is over-expressed in more than half of carcinomas and melanomas, and almost all hematological B cell malignancies.

PDA is notoriously resistant to standard cancer therapies, and is now the third leading cause of cancer-related deaths in the United States. Unfortunately, pancreatic tumors lack the mechanisms for endogenous T cell infiltration. Thus, the immunotherapies that have altered the treatment paradigm for many cancers (including anti-PD-1 and anti-CTLA-4) have little effect in pancreatic cancers.

With the discovery that PDA tumors contain infiltrating macrophages that express CD40, however, agonistic anti-CD40 antibody therapy has emerged as an area of keen investigation. At the Vonderheide laboratory, anti-CD40 immunotherapy has proved capable of converting tumors devoid of T cells to tumors sensitive to T cell-mediated destruction.

Agonist anti CD40 antibody therapy has limited efficacy as monotherapy. Recent studies at the Vonderheide Lab have thus focused on the combination of anti-CD40 agonists with other immunotherapeutics and chemotherapies, including gemcitabine (Gem), an agent that has shown clinical promise in metastatic PDA



► Figure 1: Pancreatic adenocarcinoma (arrow) with liver metastases (indicators, left).

when combined with another antineoplastic, nab-paclitaxel (nP). In combination studies, agonistic anti-CD40 has demonstrated the capacity to drive T cell infiltration and T cell-dependent regression of established tumors when administered 48 hours after treatment with Gem.

The Vonderheide laboratory is participating in a clinical trial (NCT03214250) to explore the combination of nP/Gem with two agents individually, a novel anti-CD40 antibody and an anti-PD-1 checkpoint inhibitor. A cohort of patients, in addition, will receive all four agents. Dr. Vonderheide is the national principal investigator for this trial, which, like much of the research originating from the Vonderheide laboratory, represents a classical effort in translational medicine, fulfilling a core mission of the Abramson Cancer Center.

The primary research leading to this trial was performed at the Vonderheide laboratory by Katelyn T. Byrne, PhD, a 2017 recipient of the prestigious Parker Fellowship. This trial is an initiative of the Parker Institute for Cancer Immunotherapy, in collaboration with Bristol-Myers Squibb (BMS) and biotech company Apexigen.

To refer patients, or for more information about this trial, please call 215-615-0537, or visit <https://www.med.upenn.edu/pccr/>.

FACULTY TEAM

The Abramson Cancer Center (ACC) at Penn Medicine is a world leader in cancer research, patient care, and education. Led by Director Ben Stanger, MD, PhD, the Pancreatic Cancer Research Center (PCRC) at the ACC is comprised of a multidisciplinary team of medical oncologists, translational scientists, surgeons, gastroenterologists, radiation oncologists, pathologists and dedicated nurse navigators who work together to bring discoveries from the lab to the patient's bedside.

► Pancreatic Cancer Research at the Abramson Cancer Center

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