Journal of the National Comprehensive Cancer Network



## Highlights of the NCCN Oncology Research Program

The NCCN Oncology Research Program (ORP) strives to improve the quality of life for patients and reduce cancer-related deaths by advancing cancer therapies through research. Since the program's establishment in 1999, the NCCN ORP has brought millions of dollars in research grants to investigators at NCCN Member Institutions. Research grants are provided to NCCN through collaborations with pharmaceutical and biotechnology companies; these grants are in turn used to support scientifically meritorious cancer research efforts.

NCCN ORP studies typically explore new avenues of clinical investigation and seek answers to important cancer-related questions. All studies are approved and funded through a scientific peer-review process and are overseen by the ORP.

NCCN-sponsored studies funded through the grant mechanism are highlighted below.

### Phase I Trial of Chemoradiation With Capecitabine and Vorinostat in Pancreatic Cancer

**Principal Investigator:** Emily Chan, MD, PhD

**Condition:** Pancreatic cancer; periampullary adenocarcinoma

**Institution:** Vanderbilt-Ingram Cancer Center

Phase I dose-escalation trial studying the side effects and best dose of vorinostat when given together with capecitabine and radiotherapy (RT) for nonmetastatic pancreatic cancer. Patients receive oral capecitabine twice daily and undergo high-dose hypofractionated RT once daily on days 1–5 and 8–12. Patients also receive oral vorinostat once daily on days 1–5, 8–12, 15–19, and 22–26 if no disease progression or unacceptable toxicity. Patients are evaluated for surgery 6 weeks after completion of chemoradiotherapy. Patients with resectable disease proceed to surgery. Patients with unresectable disease may receive oral vorinostat once daily and oral capecitabine twice daily on days 1–14. Courses repeat every 21 days if no disease progression or unacceptable toxicity. Blood samples are collected periodically for correlative laboratory studies. Patients also undergo diffusion-weighted MRI for analysis of in vivo tumor cellularity. Patients are followed up for 5 years after completion of study therapy.

**Primary Outcome Measures:**

- Determine maximum tolerated dose of vorinostat given in combination with capecitabine and RT

**Secondary Outcome Measures:**

- Safety and side effect profile of combined vorinostat and capecitabine used with RT
- Response rate of combined vorinostat and capecitabine used with RT
- Correlative studies:
  - Whole-cell histone deacetylase (HDAC) activity levels on peripheral blood mononuclear cells comparing pre- and posttreatment samples
  - Assessment of chromatin structure and DNA damage in surgical samples
  - In vivo imaging to assess tumor cellularity

**Contact:** Clinical Trials Office, Vanderbilt-Ingram Cancer Center • 800-811-8480

**ClinicalTrials.gov Identifier:** NCT00983268

### Phase I Combination of Pazopanib and Everolimus in PI3KCA Mutation Positive/PTEN Loss Patients With Advanced Solid Tumors Refractory to Standard Therapy

**Principal Investigator:** Jennifer J. Wheler, MD

**Condition:** Solid tumors

The goal of the Highlights of the NCCN Oncology Research Program (ORP) is to provide readers with more information on the ORP, including studies currently accruing patients.

For more information on specific trials, including patient selection criteria, please use the contact information listed with each study.

For more information on the NCCN ORP, including a complete detailing of the clinical studies currently underway at NCCN Member Institutions, please access the NCCN ORP pages at http://www.nccn.org/clinical_trials/clinicians.asp.

**Institution:** The University of Texas MD Anderson Cancer Center

The goal of this clinical research study is to find the maximum tolerated dose (MTD) of combination pazopanib and everolimus that can be given to patients with advanced cancer, and to study the safety of these drugs. Pazopanib is designed to block different receptors in the cancer cells that ultimately are responsible for growth of the tumor and its blood vessels. Everolimus is designed to block the protein mTOR inside the cancer cells, which is also involved in cancer growth.

**Primary Objectives:**

- Determine a reasonable dose of the combination treatment pazopanib and everolimus, including MTD and toxicity profiles, via a brief initial "run-in" dose escalation
- Evaluate the antitumor activity (tumor response) of this combination
- At the MTD expansion phase, evaluate response in patients with tumors that have either *PI3K* mutations and/or *PTEN* loss and/or *PTEN* mutation

**Secondary Objectives:**

- Perform correlative studies, including pharmacokinetic evaluation (pre- and postdosing time-points), to determine biologic effects of the combination treatment and elucidate molecular responses with a specific emphasis on antiangiogenesis activity and pathways
- Correlate *PI3K* mutation status, *PTEN* loss (immunohistochemistry), *PTEN* mutation status (and signaling aberrations) with toxicity and response
- Identify vascular endothelial growth factor polymorphisms using peripheral blood mononuclear cells and correlate with toxicity and response

**Contact:** Jennifer J. Wheler, MD • 713-745-9246

**ClinicalTrials.gov Identifier:** NCT01430572

### Phase I Study of Bendamustine With Concurrent Whole Brain Radiation Therapy in Patients With Brain Metastases From Solid Tumors

**Principal Investigator:** Edward Pan, MD

**Condition:** Brain metastases

**Institution:** H. Lee Moffitt Cancer Center & Research Institute

Study patients will receive a weekly dose of intravenous bendamustine with whole brain radiation therapy (WBRT) for 3 weeks, and then a fourth dose of intravenous bendamustine 1 week after completion of WBRT. The first dose of intravenous bendamustine will be given when WBRT is initiated. Once the maximum tolerated dose (MTD) is determined, 3 to 6 study patients will be enrolled to receive a lumbar puncture immediately after the fourth bendamustine dose to determine whether bendamustine penetrates into the cerebrospinal fluid.

**Primary Objectives:**

- Determine the MTD of bendamustine with concurrent WBRT
- Determine the plasma pharmacokinetics of bendamustine in study patients
- Determine presence of bendamustine in study patients' cerebrospinal fluid

**Secondary Objectives:**

- Determine 6-month progression-free survival
- Determine overall survival
- Assess neurocognitive function and quality of life throughout the study

**Contact:** Pam A. Smith, CCRP • 813-745-3951 • pam.smith@moffit.org

**ClinicalTrials.gov Identifier:** NCT00879073