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.

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

A Phase I/IB Study of AZD2171 (Cediranib) and Temsirolimus in Patients With Advanced Gynecological Malignancies

Principal Investigator: Susana M. Campos, MD, MPH

Condition: Endometrial cancer, ovarian cancer, cervical cancer, fallopian cancer and peritoneal cancer

Institution: Dana-Farber Cancer Institute/Brigham and Women's Cancer Center

The purpose of this research study is to determine the safety of combination cediranib and temsirolimus and the highest doses of these 2 drugs that can be given safely in combination. Cediranib may stop blood supply to the tumor and therefore help keep cancer cells from growing; temsirolimus may stop cancer cells from growing. Cediranib and temsirolimus have been used in research studies for ovarian and kidney cancer, and the results suggest that they may help to keep cancer from growing in this research study.

Primary Objective:

- Determine the maximum tolerated dose of cediranib with temsirolimus in patients with recurrent/refractory gynecologic malignancies

Secondary Outcome Measures:

- Determine the efficacy of combination cediranib and temsirolimus as measured by response rate or clinical benefit

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ClinicalTrials.gov Identifier: NCT01065662

Temsirolimus, an mTOR Inhibitor, to Reverse Androgen Insensitivity in Patients With Castration-Resistant Prostate Cancer

Principal Investigator: Sandhya Srinivas, MD

Condition: Prostate cancer

Institution: Stanford University

There is a clear need for novel, effective agents in castration-resistant prostate cancer (CRPC), an entity previously referred to as "androgen-insensitive" or "hormone-refractory" prostate cancer. Although numerous therapies impact biochemical response in this disease, none improve overall survival outside of chemotherapy. The mechanisms behind progression to castration resistance are unclear, but preclinical studies suggest that loss of the tumor suppressor gene *PTEN* and subsequent up-regulation of Akt, which is upstream of mTOR, may be involved in prostate cancer progression and metastasis.

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.

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Based on these observations, this study hypothesizes that inhibition of mTOR activity with an intravenous mTOR inhibitor, temsirolimus, may prolong hormone sensitivity and delay disease progression. Forty patients who have evidence of disease progression by prostate-specific antigen (PSA) or bony metastasis and who are currently receiving combined androgen blockade with bicalutamide will receive temsirolimus weekly for 13 weeks. Because evaluating new therapies in prostate cancer is uniquely challenging given its long natural history and relatively indolent nature, this study will use an established surrogate end point for efficacy—PSA. PSA will permit preliminary evaluation of this combination in fewer patients and in less time than would otherwise be possible, and additionally allows evaluation of secondary time-to-event outcomes. Co-targeting the androgen and PTEN/Akt/mTOR signaling pathways in CRPC provide great potential to impact this pervasive disease.

Primary Outcome Measure:

- PSA response at 13 weeks from day 1 dosing; PSA response is defined as a decrease ≥ 50% from baseline

Secondary Outcome Measures:

- Safety and tolerability as defined by percentage of patients who discontinue due to toxicity, time to PSA progression, median number of circulating tumor cells (CTCs) pre- and posttherapy, and characterization of pre- and posttherapy CTCs
- Time to PSA progression end point

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ClinicalTrials.gov Identifier: NCT01020305