Journal of the National Comprehensive Cancer Network

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.

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.

Phase I/II Trial of Torisel and Liposomal Doxorubicin in Patients With Advanced Soft Tissue and Bone Sarcomas

Principal Investigator: David Loeb, MD, PhD

Condition: Sarcoma

Institution: The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins

The effectiveness of treatments for recurrent sarcomas is quite limited. One hypothesis to explain the refractory nature of recurrent sarcomas is the existence of chemotherapy-resistant sarcoma stem cells. This study is designed to test the hypothesis that Torisel will increase the effectiveness of liposomal doxorubicin in killing sarcoma cells, including sarcoma stem cells.

Primary Outcome Measures:

- Incidence of dose-limiting toxicities
- Objective response rate

Secondary Outcome Measures:

- Describe the pharmacokinetics of Torisel when administered with liposomal doxorubicin
- Determine progression-free survival
- Measure time to clinical benefit rate
- Assess overall survival
- Assess the activity of the mTOR signaling pathway before and after therapy with Torisel and liposomal doxorubicin
- Measure the proportion of cells with stem cell properties in tumors before and after treatment with Torisel and liposomal doxorubicin

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ClinicalTrials.gov Identifier: NCT00949325

A Phase I Trial of Vorinostat Concurrent with Stereotactic Radiotherapy in Treatment of Brain Metastases from Non–Small Cell Lung Cancer

Principal Investigator: Griffith Harsh, MD

Condition: Brain metastases, non–small cell lung cancer

Institution: Stanford Cancer Institute

Vorinostat is an oral histone deacetylase inhibitor with anticancer activity in several different cancers. Given the potentially debilitating negative effects and the lack

of survival benefit of whole-brain irradiation for treatment of brain metastases, there is a growing movement towards using stereotactic radiosurgery (SRS) alone for patients with a limited number of brain metastases. The hypothesis behind this study is that vorinostat, given concurrently with SRS, will improve local tumor control and decrease distant brain failure. The purpose of this study is to determine the maximum tolerated dose (MTD) of vorinostat given concurrently with SRS to treat non–small cell lung cancer brain metastases in patients with 1 to 4 lesions.

Primary Outcome Measures:

- Determine the MTD of vorinostat concurrent with radiosurgery
- Confirm the safety of the MTD during the expanded phase I portion of the study
- Determine the local control and distant intracranial control rates

Secondary Outcome Measures:

- Determine the short-term (< 30 days posttreatment) and long-term (> 30 days posttreatment) adverse effects
- Determine the overall survival rate

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ClinicalTrials.gov Identifier: NCT00946673

Phase I Study of the HDAC Inhibitor Vorinostat With Chemotherapy and Radiation Therapy for the Treatment of Locally Advanced Non–Small Cell Lung Cancer

Principal Investigators: Ranee Mehra, MD; Mary Pinder-Schenck, MD; and Keisake Shirai, MD

Condition: Locally advanced non–small cell lung cancer

Institutions: Fox Chase Cancer Center, H. Lee Moffitt Cancer Center & Research Institute, and Medical University of South Carolina

This phase I trial will escalate doses of the histone deacetylase inhibitor (HDAC) vorinostat combined with a chemoradiation platform of cisplatin, pemetrexed, and radiation to a dose of 66 Gy in non–small cell lung cancer (NSCLC) patients with unresectable IIIA and dry IIIB disease.

Primary Outcome Measures:

- Assess the safety and maximally tolerated dose of vorinostat in combination with chemoradiation for unresectable locally advanced NSCLC

Secondary Outcome Measures:

- Investigate progression-free survival
- Evaluate response rates with this combination
- Assess if pretreatment tumor expression of TS, ERCC1, and HDAC1, 2, 3 are associated with response rate

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ClinicalTrials.gov Identifier: NCT01059552