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.

A Phase I/II Study of Afatinib/Carboplatin/Paclitaxel Induction Chemotherapy Followed by Standard Chemoradiation in HPV-Negative and High-Risk HPV-Positive Locally Advanced Stage III/IVa/IVb Squamous Cell Carcinoma of the Head and Neck

Institutional Principal Investigators: Shanthi Marur, MD, and Jill Gilbert, MD

Condition: Squamous cell carcinoma of the head and neck

Institutions: The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins and Vanderbilt-Ingram Cancer Center

This is a phase I/II prospective multicenter trial to investigate the efficacy and safety of afatinib with induction chemotherapy in primary unresected patients with human papillomavirus (HPV)–negative and high-risk HPV-positive locally advanced squamous cell carcinoma stage III or IVa/b of the oral cavity, oropharynx, hypopharynx, or larynx.

Eligible patients will begin with a 14-day lead-in period with afatinib alone. This will be followed immediately by 2 cycles of induction chemotherapy with carboplatin, area under the curve (AUC) 6 intravenously; paclitaxel, 175 mg/m^2 on day 1; and afatinib as a continuous daily dosing. Each cycle is repeated every 21 days. All patients will receive concurrent chemoradiotherapy with 70 Gy of intensity-modulated radiotherapy and weekly cisplatin, 40 mg/m^2 only beginning 2 to 3 weeks after the completion of the second cycle of induction chemotherapy.

Primary Objective, Phase I:

- Determine the maximum tolerated dose or the recommended phase II dose of daily oral afatinib that is safe in combination with carboplatin, AUC 6 and paclitaxel, 175 mg/m^2 every 21 days as an induction regimen

Primary Objective, Phase II:

- Estimate the objective tumor response rate and toxicity with induction therapy in patients treated with the afatinib dose determined in phase I

Secondary Objectives, Phase II:

- Overall response to entire treatment after completion of chemoradiotherapy
- Progression-free survival rate and overall survival at 2 years

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ClinicalTrials.gov Identifier: NCT01732640

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 NCCN.org/clinical_trials/clinicians.asp.

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A Phase I Trial of MEK Inhibitor Trametinib in Combination With Neoadjuvant 5-Fluorouracil Chemoradiation in the Treatment of KRAS-, BRAF-, and NRAS-Mutant Rectal Cancers

Principal Investigator: Evan Wuthrick, MD

Condition: Rectal cancer

Institutions: The Ohio State University Comprehensive Cancer Center - James Cancer Hospital and Solove Research Institute

This phase I trial studies the side effects and best dose of trametinib when given together with 5-fluorouracil (5-FU) and radiation therapy before surgery in treating patients with stage II–III rectal cancer. Many rectal cancers harbor mutations in key cancer proliferation proteins in the MAPK pathway. Trametinib is a MEK inhibitor that has robust preclinical activity in malignancies with MAPK pathway overexpression and may arrest tumor cell growth through blocking key proteins needed for cell growth and proliferation. Preclinically, MEK inhibitors are exciting candidates for radiosensitization. Trametinib will be used in combination with standard of care chemoradiation for locally advanced rectal cancer in this trial. The underlying hypothesis of the trial is that trametinib together with 5-FU and radiation therapy before surgery will make the tumor smaller, reduce the amount of normal tissue that needs to be removed, and improve pathologic response rates.

Patients receive trametinib orally alone once daily for a week and then concurrently with 5-FU intravenously continuously 5 days a week from days 1 through 38 of radiation therapy. The total radiation therapy dose is 50.4 Gy in 1.8-Gy daily fractions given 5 fractions per week. Patients then undergo surgery 6 to 10 weeks later.

Patients achieving negative surgical margins after complete resection of tumor receive postoperative chemotherapy comprising leucovorin calcium IV over 2 hours and 5-FU IV continuously over 46 hours on days 1 and 15 OR oxaliplatin IV over 2 hours, leucovorin calcium IV over 2 hours, and 5-FU IV continuously over 46 hours on days 1 and 15. Treatment repeats every 28 days for up to 4 courses in the absence of disease progression or unacceptable toxicity.

After completion of study treatment, patients are followed up every 3 months for 2 years, and then annually for 3 years.

Primary Objective:

- To identify the maximally tolerated dose of trametinib to be used in combination with 5-FU and radiation in patients with rectal cancers, to be used in a phase II trial

Secondary Objectives:

- Evaluation of tolerability and safety of the combination
- Evaluation of posttherapy pathologic response
- Evaluation of disease-free and overall survival
- Analysis of biomarkers: total mutations in KRAS, BRAF, and NRAS

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