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.

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 Study Determining the Safety and Tolerability of Combination Therapy With Pazopanib, a VEGFR/PDGFR/Raf Inhibitor, and GSK 1120212, an MEK Inhibitor, in Advanced Solid Tumors Enriched With Patients With Advanced Differentiated Thyroid Cancer**

**Principal Investigators:** Nilofer S. Azad, MD, and Razelle Kurzrock, MD

**Conditions:** Solid tumors, advanced thyroid cancer

**Institutions:** The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, and The University of Texas MD Anderson Cancer Center

This trial has a dose escalation component and expansion cohort at the maximum tolerated dose (MTD). The dose-escalation portion will include patients with solid tumors; the expansion cohort is limited to those with differentiated thyroid cancer. A total of 6 dose levels are defined for the phase I study. Three dose levels of pazopanib (400 mg, 600 mg, and 800 mg qd) with the GSK1120212 dose held constant (1 mg qd) will be tested, followed by 3 dose levels where the pazopanib dose is held constant (800 mg qd) and GSK 1120212 is escalated (1 mg, 1.5 mg, and 2 mg qd). Three patients will be treated per dose level in a standard 3 + 3 dose escalation design. The MTD is defined as the highest dose at which 1 or fewer dose-limiting toxicities (DLTs) are observed in 6 patients. A total of 6 patients will be treated at the MTD. The target toxicity with this type of design is less than 30%. At least 3 patients must be treated for 4 weeks without the development of a DLT prior to treating a new cohort at a higher dose level.

**Primary Objective:**

- Determine the safety and toxicity of combination pazopanib and GSK 1120212 in patients with solid tumors and advanced thyroid cancer, and identify the MTD for phase II study.

**Secondary Objectives:**

Secondary objectives and correlative studies will be evaluated only in the expansion cohort, which will comprise of patients with advanced thyroid cancer being treated at the MTD.

- Response rate: preliminary efficacy of this treatment combination will be assessed by the objective response rate at 6 months.
- Progression-free survival (PFS): will be a secondary measure of efficacy and will be defined from the date of study entry to the date of progression or death. The median PFS will be compared with a historical median, estimated to be 11.7 months.
- Pharmacokinetic (PK) data, pharmacodynamic (PD) markers, tumor genotype and subtype: exploratory end points include correlation of PK data with radiographic response, PD markers, and the impact of tumor histologic subtype and tumor genotype on radiographic response.

Cont. on page xxxvi.
A Multicenter Phase II Study of Ofatumumab and Bortezomib in Previously Untreated Patients With Waldenström Macroglobulinemia

Principal Investigator: Seema Bhat, MD

Conditions: Waldenström macroglobulinemia

Institution: Roswell Park Cancer Institute

This phase II trial examines ofatumumab together with bortezomib (OB) in patients with previously untreated Waldenström macroglobulinemia. Monoclonal antibodies, such as ofatumumab, can block cancer growth in different ways. Some block the ability of cancer cells to grow and spread. Others find cancer cells and help kill them or carry cancer-killing substances to them. Combination ofatumumab and bortezomib, which has known activity against Waldenström macroglobulinemia, may be a better way to block cancer growth.

Induction phase: patients receive ofatumumab intravenously on days 1, 8, and 15, and bortezomib subcutaneously on days 8 and 15. Beginning on course 2, patients receive ofatumumab intravenously on days 1 and 15, and bortezomib subcutaneously on days 1, 8, and 15. Treatment repeats every 28 days for up to 4 courses in the absence of disease progression or unacceptable toxicity.

Maintenance phase: beginning 8 weeks after course 4 of the induction phase, patients receive ofatumumab intravenously on day 1 and bortezomib subcutaneously on days 1, 8, and 15. Treatment repeats every 28 days for up to 8 courses in the absence of disease progression or unacceptable toxicity.

After completion of study treatment, patients are followed up at 30 days, and then every 3 months for 5 years.

Primary Objective:
- Determine overall response rate (complete remission [CR] + partial response [PR] + minor response) of OB.

Secondary Objectives:
- Determine CR, near CR, very good partial remission, and PR rates per new criteria.
- Determine 5-year PFS.
- Determine time to progression and duration of response to OB.
- Determine safety of OB.
- Conduct laboratory correlates.

Contact: Roswell Park  •  877-275-7724  •  AskRPCI@roswellpark.org

ClinicalTrials.gov Identifier: NCT01536067