Alliance for Clinical Trials in Oncology
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Alliance Collaborates on NCI N01 Trials to Evaluate Rare Cancers

The Alliance for Clinical Trials in Oncology recently executed a successful collaboration to develop, activate and conduct four National Cancer Institute (NCI) N01 Program trials. The Alliance Central Protocol Operations Program (CPOP), Alliance Statistics and Data Center (SDC), and investigators worked collectively to open these trials using Medidata Rave® – a state-of-the-art data collection and management system that allows rapid trial assessment and possible modification. The trials involve investigational agents that are not commercially available and focus on rare patient populations, which is an area of interest for the Alliance Experimental Therapeutics Committee.

"This collaboration provides the Alliance access to novel targeted agents that would not be readily available under ordinary circumstances," said Gary K. Schwartz, MD, Chief of Melanoma and Sarcoma Service at Memorial Sloan-Kettering Cancer Center, who co-chairs the Alliance Experimental Therapeutics Committee with Charles Erlichman, MD, Professor of Oncology in the Mayo Clinic College of Medicine and Deputy Director of Clinical Research at the Mayo Clinic Cancer Center. "Not only does it make them available but it accelerates the process by which these agents can be evaluated for the first time in human cancers."

The N01 program advances phase II studies and pilot protocols that explore promising combination therapies and high priority studies that are pivotal for drug development. These studies, which examine rare solid tumors, rapidly evaluate the biologic effects of NCI-sponsored anticancer agents on their molecular targets and determine clinically relevant outcomes. They require accelerated initiation, completion, and data reporting.

"For the Alliance, such access is unparalleled in medical oncology. For the Experimental Therapeutics Committee, this brings new and exciting drugs to patients with orphan cancers (including such cancers as sarcomas, rare types of head and neck cancer, and specific types of melanoma such as ocular or uveal melanoma)," said Dr. Schwartz. "These are the cancers that are overlooked by pharmaceutical companies. Yet, orphan cancers make up 50 percent of all cancers in the United States. Furthermore, success with these agents in orphan cancers can be directly applied to the more common diseases such as breast, colon, lung and prostate – considered the big four."

The four Alliance/N01 trials include:

- A091104 A Phase II Study of MK-2206 in Patients with Progressive, Recurrent/Metastatic Adenoid Cystic Carcinoma *(activated in 7/23/12)*
- A091103 Phase II Study of the Angiopoietin-1 and -2 Peptibody AMG 386 for the Treatment of Angiosarcoma *(activated in 7/23/12)*
- A091102 Phase II Study of MLN8237 in Advanced/Metastatic Sarcoma *(activated in 8/22/12)*
- A091101 TPF Induction Chemotherapy and Veliparib—A Phase 1/Randomized Phase 2 Study in Patients with Locoregionally Advanced Squamous Cell Carcinoma of the Head and Neck (*in development*)

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Dedicated Information Systems Group Leader Departs Alliance to Pursue New Challenges

Kim Johnson

After more than 20 years of service, **Kim Johnson** leaves her position as Director of the Alliance Information Systems (IS) Group at Duke University in Durham, NC, and Information Technology (IT) Consultant at Alliance Statistics and Data Center in Rochester, MN, to pursue a career as an independent consultant in research informatics effective August 31, 2012. Josh Yoder, MBA, who has been the associate director of Duke IS for the last three years, will assume her role.

Johnson has worked at Duke since 1989, first as the Systems Programmer and later as IT Director for the Duke Comprehensive Cancer Center. Beginning in 1990, she led the transfer of information systems for the Cancer and Leukemia Group B (CALGB) to Duke under Stephen L. George, PhD, (former CALGB Group Statistician), setting up the first CALGB Information Systems group and hiring its first director. In 2004, she moved from the Cancer Center to become the IT Director for the CALGB. Her first project as Director was to complete the conversion of the CALGB database from Ingres to Oracle. She further integrated CALGB information systems by consolidating IT functions from both the CALGB Central Office at the University of Chicago and the CALGB Statistical Center at Duke into one comprehensive database that spanned all group functions. She was a key contributor to the development of both the Per-case Payment Application (PCPA) and the Specimen Tracking System (STS). Most recently, she was part of the leadership team that has worked to integrate information systems from CALGB, NCCTG, and ACOSOG to form the Alliance information systems.

Johnson has also significantly contributed to projects at the national level. She was part of the National Cancer Institute Cancer (NCI) Biomedical Informatics Grid (caBIG®) Clinical Trial Management Systems (CTMS) Steering Committee and the Strategic Planning Workspace, and was a co-lead for the caBIG CTMS Knowledge Center at Duke. caBIG was an initiative launched by NCI in 2004 to develop a network of tools, data, and researchers to support translational and clinical research in oncology, with an ultimate goal to improve cancer care for patients.

Johnson was one of five leaders for the Electronic Data Capture (EDC) vendor review project coordinated by the Coalition of Cooperative Groups that chose Medidata RAVE as the EDC software of choice for the cooperative groups. She also has and continues to serve as a member of the Group Banking Committee Informatics Subcommittee as well as serving on a number of other national committees.

Johnson has been an incredible asset to the CALGB and the Alliance throughout the years. Her contributions have provided a strong IT foundation, from which the Alliance will continue to benefit.

Alliance Collaborates on N01 Trials

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NCI #8129, Phase I/II Trial of IMC-A12 in Combination with Temsirolimus in Patients with Metastatic Breast Cancer, an N01 trial that activated separately in early August but not included in Medidata Rave, is also key to this collaboration.

What follows is a brief summary of each trial. Trials are available on the CTSU menu (ctsu.org) to all Alliance members. Refer to the protocols for complete information about the trial design and patient eligibility.

A091102 Phase II Study of MLN8237 in Advanced/Metastatic Sarcoma

Study Chair: Mark A. Dickson, MD
Memorial Sloan-Kettering Cancer Center
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There are limited active treatment options for patients with metastatic soft tissue sarcomas. One interesting new target for anticancer therapies is Aurora Kinase A, an enzyme that is required for centrosome maturation and division, and mitotic spindle formation. Researchers at Memorial Sloan-Kettering (MSKCC) have shown that Aurora Kinase A is commonly overexpressed in soft tissue sarcomas, and that inhibiting Aurora Kinase A inhibits proliferation in soft tissue sarcoma cells in culture.

MLN8237 is an orally available inhibitor of Aurora Kinase A and its activity will tested in this phase II trial. Six different cohorts will separately test for activity of the drug in patients with liposarcomas, non-uterine leiomyosarcomas, undifferentiated sarcomas, malignant peripheral nerve sheath tumors.

MLN8237 has a benzodiazepine structure and side effects such as drowsiness, GI toxicities and myelosuppression. An unlimited number of prior therapies is permitted; measurable disease is required. At this time, only patients at MSKCC will have optional pre- and post-treatment biopsies and optional FLT-PET scans to correlate potential clinical benefit with markers of Aurora Kinase inhibition in tumor tissue and with changes in FLT-PET uptake after one week of treatment.

A091103 Phase II Study of the Angiopoietin-1 and -2 Peptibody AMG 386 for the Treatment of Angiosarcoma

Study Chair: Sandra P. D'Angelo, MD
Memorial Sloan-Kettering Cancer Center
E-mail: dangelos@mskcc.org

Angiosarcomas are particularly rare and aggressive tumors that account for only about 1 to 2 percent of soft tissue sarcomas. Antiangiogenic therapies are of interest, and single agent bevacizumab was reported to produce a response rate of 12 percent *(Agulnik et al, Proc ASCO 2009).*

AMG 386 is a novel, intravenously administered peptide-Fc fusion protein that binds to and sequesters angiopoietin 1 and 2, thereby preventing their interaction with TIE2 and inhibiting tumor endothelial cell growth. Angiosarcomas are known to have high expression of angiopoietin 2 and up-regulation of TIE2.

AMG 386 has a unique toxicity of edema, including ascites and pleural effusion. Allergic responses occurred.

This straightforward single-arm phase II trial enrolls patients with measurable disease; up to four prior systemic treatment regimens are allowed. At MSKCC only, optional pre- and post-cycle 1 biopsies will be obtained to explore correlation of baseline expression and changes in expression of angiopoietin 2 and TIE2 in tumor with benefit from therapy.

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A091101 TPF Induction Chemotherapy and Veliparib—A Phase 1/Randomized Phase 2 Study in Patients with Locoregionally Advanced Squamous Cell Carcinoma of the Head and Neck *(in development)*

Study Chair: Jonas A. de Souza, MD
University of Chicago
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Veliparib, formerly known as ABT888, is an orally available small molecule PARP inhibitor. Phase I of the trial seeks to determine the MTD of veliparib when combined with TPF (docetaxel, cisplatin, 5-FU) induction therapy. The subsequent randomized placebo-controlled phase II portion will compare response rates to two cycles of induction chemotherapy with and without veliparib. The trial has a flexible design, in which one of two chemoradiotherapy regimens after induction is permitted, and either IMRT or 3-D conformal radiation is acceptable.

A091104 A Phase II Study of MK-2206 in Patients with Progressive, Recurrent/ Metastatic Adenoid Cystic Carcinoma

Study Chair: Alan L. Ho, MD, PhD
Memorial Sloan-Kettering Cancer Center
E-mail: hoa@mskcc.org

Adenoid cystic carcinomas (ACC) are tumors that most commonly originate in the salivary glands. No effective therapies are known. Recently, it has been discovered that there is a t(6;9) translocation in ACC that creates a gene fusion of the the c-myb and NFIB transcription factors, leading to up-regulation of c-myb expression. C-myb is an oncogene, and it is hypothesized that targeting Akt will inhibit the c-myb network. MK-2206 is an orally administered Akt inhibitor; this nonrandomized phase II trial requires measurable disease, and allows any number of prior treatment regimens. Toxicities include rash, diarrhea, mucositis, conjunctivitis, hyperglycemia, QTc prolongation, and bradycardia.

NCI #8129 Phase I/II Trial of IMC-A12 in Combination with Temsirolimus in Patients with Metastatic Breast Cancer

Study Chairs: Cynthia Ma, MD, PhD
Washington University School of Medicine
E-mail: cma@im.wustl.edu

Despite the fact that PI3K/AKT/mTOR pathway activation is activated in breast cancers through multiple mechanisms, mTOR inhibitors as single agents have had limited activity. It is hypothesized that one of the mechanisms of resistance to single agent mTOR inhibition may be feedback up-regulation of AKT activity mediated by the insulin-like growth factor receptor (IGF-1R/IGF) pathway, and combinations may be more promising.

The U.S. Food and Drug Administration (FDA) has recently approved everolimus in combination with exemestane in the treatment of postmenopausal women with aromatase inhibitor-pretreated estrogen receptor positive breast cancers. This phase II trial combines an intravenous mTOR inhibitor, temsirolimus, with the anti IGF-1R antibody, IMC-A12 (Cixutumumab) in women with measurable breast cancer who have received one or two prior chemotherapy regimens for metastatic disease.

What's New? Public Result Summaries Now Available On Alliance Website

The Alliance for Clinical Trials in Oncology has launched an initiative to make results of published Alliance and legacy group studies more accessible to the general public by making plain language summaries of the studies available on the Alliance website. This initiative, spearheaded by the Alliance Publications Committee, provides patients and healthcare professionals with relevant, up-to-date information about the Alliance's progress and discoveries.

The summaries are drafted by the respective study chairs, reviewed by the publications committee, in collaboration with Alliance Patient Advocate and Oncology Nursing committees, and respective faculty statisticians.

Each summary adheres to a formatted template containing sections that address what the study is about, why the study was done, study results, what the results mean, and subsequent scientific publications about the study.

Once a study summary is complete, it is posted in newsletters and on the publications page on the Alliance website. Currently, there are 10 plain language summaries posted about the following studies:

- CALGB 9840 (breast)
- CALGB 49907 (breast)
- CALGB 70601 (cancer control)
- CALGB 70602 (cancer control)
- CALGB 80303 (GI)
- CALGB 9720 (leukemia)
- CALGB 59804 (lymphoma)
- CALGB 60301 (experimental therapeutics)
- CALGB 30402 (respiratory)
- CALGB 100104 (transplant)

More public result summaries will be available in the coming months and once the protocol catalog is released on the website's member side next year, they will will be made available on study pages. Here's a quick link to the current selection: http://www.allianceforclinicaltrialsinoncology.org/main/public/publications/results_summaries.xhtml.

Next Alliance Meeting

2012 Fall Committee Meetings

Open to Alliance committee members only

November 15-17, 2012
InterContinental Chicago O'Hare
Rosemont, IL 60018

- The Alliance Neuro-Oncology Committee will not meet at the 2012 Fall Committee Meetings. It will meet at the Society for Neuro-Oncology (SNO) meeting in Washington, DC, on Thursday, November 15, 4:30-7:30 pm, in the Columbia 1 meeting room at the Washington Hilton Hotel.
- See Alliance website for draft meeting schedule

For meeting and travel queries, contact Katherine Faherty:
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For more information on the Alliance and updates to meeting information, visit allianceforclinicaltrialsinoncology.org