The Future is NRG!

After more than 2 years of intense work by hundreds of individuals, a vibrant new research organization was brought to full fruition on March 1 as NRG Oncology began conducting research as a research group of the National Cancer Institute (NCI) National Clinical Trials Network (NCTN). On March 3, the first day of business, clinical trial study participants were officially enrolled into NRG Oncology clinical trials.

The days leading up to the official unveiling were particularly charged with increased activity, with behind-the-scenes efforts being directed to ensure no interruption to study participant enrollment. NRG Oncology staff members have been quick to resolve the few hiccups that have arisen as a result of the transition, and the site research personnel have been very understanding and accommodating during this process.

Conducting research within the newly configured NCTN presents new ways to carry out multicenter clinical research. NRG Oncology will make every effort to keep affiliated research personnel informed about new programs and policies through the NRG Oncology Newsletter and eNews e-mail updates. Also, an archive of informational materials about this transition is available on the Transition News page of the NRG Oncology website.

Thank you to all for your ongoing support as NRG Oncology seeks to improve the lives of patients with cancer by conducting practice-changing multi-institutional clinical and translational research.

Well-Laid Plans Become a Reality

A majority of the nearly 1800 attendees at the NRG Oncology Semiannual Meeting held last month were present at the meeting’s General Session to learn more about the new group’s future. The full presentations highlighted below can be found on the NRG Oncology website.

Group Chair Philip J. DiSaia, MD, extended a warm welcome to all those participating in the expanded meeting. Emphasizing the depth and breadth of NRG Oncology, Group Chair Walter J. Curran, Jr, MD, described the overarching aims of the organization and presented the committees that will implement those aims.

Mitchell Machtay, MD, Deputy Group Chair for Research Strategy, acknowledged the challenges the new group faces in carrying out its scientific aims, given projected funding levels. He presented the critical factors the Research Strategy Committee will consider when reviewing new protocol concepts and full protocols (eg, compelling preclinical data, strong and intriguing phase I data, clinically meaningful end points, priority disease site status). J. Tate Thigpen, MD, Deputy Group Chair for Protocol Prioritization and Conduct, described the role of the Concept Prioritization Advisory Committee (CPAC) in prioritizing protocols approved by the Research Strategy Committee for implementation. The CPAC considers the studies’ scientific merits, feasibility scores, and rank among all the proposals developed within a respective committee in recommending which protocols should move forward. CPAC will also monitor study conduct and data reporting, and set and enforce deadlines.

Deborah Watkins Bruner, PhD, Deputy Group Chair for Publications and the contact principal investigator for the recently submitted National Cancer Institute (NCI) Community Oncology Research Program (NCORP) grant application, acknowledged the tremendous work by many individuals to prepare a proposal with strong scientific aims (see page 6). Group Chair Norman Wolmark, MD, concluded the General Session by emphasizing the collegiality and enthusiasm that have infused the development of NRG Oncology’s scientific research plan and the high levels of integrity and trust that have been key to the legacy groups’ successful integration.
Preparing to Navigate
The 10 National Cancer Institute (NCI) clinical trials cooperative groups have been collecting and archiving biospecimens from patients enrolled on clinical cancer trials for several decades. In an effort to provide better access to this material and to improve transparency the cooperative groups have been working on a new way to view and access this precious resource.

At the NRG Oncology meeting’s Translational Research session, Dave Billiter, director of the Research Informatics Core at Nationwide Children’s Hospital in Columbus, Ohio, presented an overview of “Navigator,” a new cancer research tool soon to be rolled out by the NCI. Navigator is designed to provide access to the comprehensive inventory of biospecimens across all National Clinical Trials Network (NCTN) research groups and the legacy clinical trial cooperative groups. The overarching goal of Navigator, under development since January 2013, is to improve the usability and efficiency of the biospecimen request process for the broad community of cancer researchers.

Specific goals of the Navigator system include:
- Connect biospecimen inventory data with associated trial data and (when possible) clinical data to allow for the reasonable assessment of biospecimen availability based on trial design and clinical data end points
- Provide a secure, role-based, highly functional user interface for performing data queries and reporting according to the needs of the broad scientific community
- Provide a simple web-based interface for submitting and tracking biospecimen requests

Integral coordination of the biospecimen request process involves the NCI’s “Front Door Concierge,” which assigns the “Group Concierge” a role within the respective NCTN group(s). Once a request is submitted, the concierge role carries out three functions: (1) facilitate investigator access to NCTN specimens or make recommendations about other suitable specimen resources, when appropriate; (2) log and track all biospecimen requests and serve as a “time keeper” for the process; and (3) provide transparency to the request and review process. Assessment of the scientific merit of an applicant’s request for biospecimens will continue to be the responsibility of the respective cooperative group.

“Navigator and the Front Door Concierge represent an important and exciting step forward that will provide investigators better access to annotated biospecimens linked to specific trials across all the cooperative groups at one time. This will greatly improve the quality of research and ultimately positively impact patient care.”

RICHARD JORDAN, DDS, PHD, FRCPath
Director, RTOG Biospecimen Resource
Professor, Pathology and Radiation Oncology
University of California, San Francisco

The above graphic shows the flow of the Navigator biospecimen request, approval, and delivery process facilitated by the Front Door Concierge.
Educational Sessions Presented for Clinical Trial Nurses and Clinical Research Associates

The NRG Oncology Protocol Support Committee (PSC) provided educational sessions for the clinical trial nurses (CTNs) and clinical research associates (CRAs) attending the semiannual meeting. Approximately 400 nurses and CRAs attended these lectures. Jessica Lowenstein, MS, DABR, and Denise Manfredi, BS, RT, presented a session on the new National Clinical Trials Networks’ QA Service and the Imaging and Radiation Oncology Core (IROC) Group; Laura Covington, MS, CIP, provided an NCI Central Institutional Review Board (CIRB) Initiative overview; and a Medidata RAVE review was provided by Bill Elgie, MBA. An overview of NRG Oncology was presented by J. Tate Thigpen, MD, NRG Oncology Vice Chair. Molecular Testing and Targeted Therapy was presented by Anthony M. Magliocco, MD, FRCP, FCAP, from the H. Lee Moffitt Cancer Center. The speakers’ slides can be accessed on the NRG Oncology website at: PSC Presentations.

During the educational sessions, the new NRG Oncology PSC members were introduced. The primary functions of this committee include support and quality control for protocol-related activities, education and training of NRG Oncology members, and mentorship. Susan Nolte, PhD, CRNP, serves as the PSC Chair, and Nancy Knudsen RN, BSN, and Terry Thomas MS, CCRC, serve as co-chairs. The CRA and CTN subcommittees of the PSC are each composed of 15 members appointed from the legacy groups (NSABP, RTOG, and GOG). Co-chairs of the CRA Subcommittee are Sally Brown, RN, BSN, MGA; Joyce Neading RHIT, CTR; and Sharon Stockman BA, CCRP. Co-chairs of the CTN Subcommittee are Nancy Fusco, RN BSN, CCRP; Cindy Licavoli, RN, BSN, MA; and Bonnie Sauder, RN, BS, CCRP, OCN. The function, charge, and responsibilities of these subcommittees were presented by the respective co-chairs. A major charge of the subcommittees is to shepherd the PSC Working Groups.

The concept and activities of each of the Working Groups was discussed during breakout sessions. The four Working Groups—Protocol Review, Education and Training, Quality Control, and Mentorship—provide a unique opportunity for NRG Oncology members to participate in the activities of the PSC.

Call for Applications
CRAs and CTNs are encouraged to apply for membership in the PSC Working Groups. Additional information about the Working Groups, along with the requirements for membership and the Working Group Application, will be posted on the NRG Oncology website. The deadline to apply is April 21, 2014.

Scientific Session Highlights

The NRG Oncology Semiannual Meeting was an opportunity to showcase recent study results. Following is a recap of three presentations made during the meeting’s Scientific Session, along with an overview of recently published results in the New England Journal of Medicine.

Tool Shows Predictive Promise

Greg Yothers, PhD, a biostatistician in NRG Oncology’s Statistical and Data Management Center, presented results from the NSABP R-04 trial validating the newly developed Neoadjuvant Rectal (NAR) cancer score, a tool developed as a potential surrogate endpoint for survival in patients with rectal cancer treated with neoadjuvant therapy. Yothers and his coauthors developed this score based partially on information from nomograms developed by Valentini, et al.1 Inputs to the score include pathologic nodal stage and downstaging of tumor (T) from pretherapy clinical T to posttherapy pathologic T (ct–pT). The R-04 study presented an opportunity to validate the proposed score independently.

Both the new NAR score and the traditionally used surrogate end point of pathologic complete response (pCR) were highly statistically significantly associated with survival in NSABP R-04, demonstrating patient-level association. The NAR score proved to be a statistically superior predictor of survival compared with pCR in this data set based on Akaike information criterion (P<.0001). Yothers and colleagues are currently actively engaged in assembling a

continued
meta-analysis to demonstrate trial-level association of the NAR score, as well as of pCR, with survival. This study demonstrated the NAR score to be a viable surrogate end point for survival in early-phase trials of neoadjuvant treatment for rectal cancer.

Preserving Memory

Preclinical and clinical evidence suggesting that the dose of radiotherapy received by the hippocampus during whole brain radiotherapy (WBRT) may play a role in radiotherapy-induced cognitive decline led investigators to develop the research study RTOG 0933. Co-led by Vinai Gondi, MD, co-director of the Cadence Health Brain Tumor Center and associate research director at the Cadence Health Proton Center, the single-arm, phase II trial was designed to determine if employing a hippocampal avoidance technique with intensity-modulated radiotherapy (IMRT) would achieve the therapeutic benefits of WBRT while still preserving memory function.

Gondi presented results showing that study participants with brain metastases in whom the hippocampal region was avoided during WBRT experienced, on average, a 7% memory score decline at 4 months post-treatment, as measured by the Delayed Recall scale of the Hopkins Verbal Learning Test. In comparison, a historical control group of patients with brain metastases who underwent conventional WBRT without avoiding the hippocampus experienced a 30% memory score decline. The results suggest that, by minimizing radiation dose to the hippocampus during WBRT, patient memory function can essentially be preserved. Gondi noted that a 7% memory score decline is within the standard error of measurement for the Delayed Recall scale, suggesting that the hippocampal-avoidance WBRT technique resulted in minimal impact on patients’ memory.

Treatment Improves Survival of Patients With Advanced Cervical Cancer

Vascular endothelial growth factor (VEGF) promotes angiogenesis, a mediator of disease progression in cervical cancer. The GOG 240 study evaluated the effectiveness of bevacizumab (an anti-VEGF monoclonal antibody) in patients with recurrent, persistent, or metastatic cervical cancer. Patients (N=452) were assigned randomly to chemotherapy with or without bevacizumab at a dose of 15 mg per kilogram of body weight. Chemotherapy consisted of cisplatin at a dose of 50 mg/m², plus paclitaxel at a dose of 135 or 175 mg/m² or topotecan at a dose of 0.75 mg/m² on days 1 to 3, plus paclitaxel at a dose of 175 mg/m² on day 1. Cycles were repeated every 21 days until documentation of disease progression, unacceptable toxic effects, or complete response. The primary end point was overall survival; a reduction of 30% in the hazard ratio (HR) for death was considered clinically important.

Groups were well balanced with respect to age, histologic findings, performance status, previous use or nonuse of a radiosensitizing platinum agent, and disease status. The addition of bevacizumab to chemotherapy was associated with increased overall survival (17.0 months vs 13.3 months; HR for death, 0.71) and higher response rates (48% vs 36%). Bevacizumab, as compared with chemotherapy alone, was associated with an increased incidence of hypertension of grade 2 or higher (25% vs 2%), thromboembolic events of grade 3 or higher (8% vs 1%), and gastrointestinal fistulas of grade 3 or higher (3% vs 0%).

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In Focus: NRG Oncology's Developmental Therapeutics Committee

The Developmental Therapeutics Committee (DTC) of NRG Oncology is responsible for phase I and II evaluation of novel therapies. This is carried out in collaboration with the Cancer Therapy Evaluation Program (CTEP) of the National Cancer Institute (NCI) and the pharmaceutical industry.

The Phase I Committee of the DTC oversees safety lead-ins for phase II studies and conducts phase IB trials in collaboration with the NRG Oncology disease site committees and the Translational Science Committee, with an aim toward future randomized phase II and phase III studies. Phase IB studies include combination studies (multimodality studies that include radiation therapy) and dose- and schedule-finding studies. The Phase I Committee has particular expertise in evaluating multimodality therapy (eg, concurrent chemotherapy/targeted therapy and radiation therapy trials focused on curative intent).

The phase II program is driven by the scientific priorities of the disease site committees (breast cancer, brain tumor, gastrointestinal cancer, genitourinary cancer, gynecologic cancer, head and neck cancer, and lung cancer) and the Translational Science Committee. The internationally recognized NRG Oncology investigators have extensive experience and a fund of knowledge across the seven disease sites that make up the focus of the group. Site leaders for each disease site have been identified to provide communication between the disease site committees and the DTC.

Integral and integrated biomarkers and exploratory translational research in phase I and II studies involves a team science approach in which the NRG Oncology committees, the biorepository, SPORE/PO1 sites, cancer centers, and other funded laboratories actively collaborate. Integral and integrated biomarkers and imaging are used for patient selection, validating targets, and/or predicting effectiveness of treatments.

Throughout the protocol development process, the DTC also interacts with the scientific core committees (medical oncology, pathology, radiation oncology and medical physics, surgical oncology, protocol support [clinical research associates and nursing], patient advocates, and special populations).

Developmental Therapeutics Leadership

Carol Aghajanian, MD, Chair
Memorial Sloan Kettering Cancer Center

Samuel Jacobs, MD, Co-chair
University of Pittsburgh

David Raben, MD, Co-chair
University of Colorado

Russell Schilder, MD, Chair of Phase I Subcommittee
Thomas Jefferson University

“NRG Oncology has a unique web-based system for effectively managing phase I trials and safety lead-ins in real time. This allows us to bring the right trials to the right patients early in the drug development process. Precision medicine trials are informed by the individual patient’s genetics, the tumor’s genetics, and now by multiple genetic targets at once.”

CAROL AGHAJANIAN, MD
Professor of Medicine, Weill Cornell Medical College
Chief, Gynecologic Medical Oncology Service
Memorial Sloan Kettering Cancer Center
New York, NY

“Personalized medicine, utilizing genomic and proteomic platforms with high sensitivity and specificity, is now used to identify targetable alterations. Early-phase studies not only establish dose, but should also give a signal of activity in selected populations.”

SAMUEL JACOBS, MD
Developmental Therapeutics Co-chair
Clinical Professor
University of Pittsburgh
Pittsburgh, PA

“It really is time to search out new and innovative paradigms for integrating biologically driven anticancer agents with radiation. What has been done in the past—simply combining the next “promising agent” with chemoradiation backbones—has not been successful.”

DAVID RABEN, MD
Developmental Therapeutics Co-chair
Professor of Radiation Oncology
University of Colorado Cancer Center
Aurora, CO

“NRG Oncology Newsletter is a collaboration of the Communications Committee with contributions from members and staff.

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Please send information about special achievements of NRG Oncology members or research teams, suggestions for future articles, and regular features you would like to see in future issues of the NRG Oncology Newsletter to: info@nrgoncology.org

www.nrgoncology.org
NRG Oncology Develops NCORP Research Base Blueprint

Considerable team effort went into the preparation of NRG Oncology’s grant application, submitted this past January, to participate as a research base in the future National Cancer Institute (NCI) Community Oncology Research Program (NCORP). The NRG NCORP Research Base proposal draws upon the more than 100 years of combined Community Clinical Oncology Program (CCOP) research base experience across the three groups that now comprise NRG Oncology. The research plans for the NRG NCORP are well integrated into NRG Oncology’s scientific program, which includes a unique focus on both women’s health and radiation therapy.

Overarching research themes the NRG NCORP plans to pursue include the following:

- Developing cancer prevention and symptom intervention trials in which biomarker status determines eligibility and/or treatment response
- Testing and further validating patient-reported measures across many cancer disease types to evaluate and design interventions to improve the quality of life of cancer survivors
- Improving early detection and diagnostic techniques that avoid overdiagnosis and underdiagnosis of cancers
- Leveraging NRG Oncology’s therapeutic trials to provide a unique research portfolio—with particular foci on women’s cancers and radiation oncology innovation—to NRG Oncology’s research community and across the National Clinical Trials Network (NCTN)
- Reducing disparities in cancer care outcomes among minority and underserved populations

The proposal’s three principal investigators (PIs) include:

- Contact PI Deborah Bruner, PhD, RN, FAAN, who is PI of the RTOG CCOP Research Base, NRG Oncology Deputy Group Chair for Publications, and associate director for outcomes research at the Winship Cancer Institute of Emory University
- PI/Executive Committee Chair Joan L. Walker, MD, who is a gynecologic oncologist at the Stephenson Cancer Center at the University of Oklahoma Health Sciences Center
- PI/Executive Committee Chair D. Lawrence Wickerham, MD, who is NRG Oncology Deputy Group Chair for Membership, and an associate professor of human oncology at the Pittsburgh Campus of the Drexel University School of Medicine

Expected to launch in the fall of 2014, NCORP combines the work carried out by the CCOP and elements of the NCI Community Cancer Centers Program (NCCC) into one program network. An NCORP research base will provide scientific and statistical leadership for developing, implementing, and analyzing multi-institutional clinical trials. For more information about the NCORP program, view the slide presentation.

“The real strength of the NCORP NCORP is the exemplary multidisciplinary team of expert investigators and patient advocates, all working together to carry out practice- and policy-changing research while enhancing community access to treatment, symptom management, cancer control, and cancer care delivery trials.”

DEBORAH BRUNER
Principal Investigator
RTOG CCOP Research Base
Associate Director for Outcomes Research
Winship Cancer Institute of Emory University
Atlanta, GA

D. LAWRENCE WICKERHAM
Associate Professor of Human Oncology
Drexel University School of Medicine
Pittsburgh, PA

“We are pleased that the initial group of Main Members in NRG Oncology includes 43 CCOPs and 9 Minority-Based CCOPs (MB-CCOPs). The new NCORP Program will allow NRG Oncology investigators and their patients continued access to high-quality studies that are clinically interesting and scientifically important.”

Joan L. Walker
George Lynn Cross Research Professor
The James A. Merrill Chair in Ob/Gyn
Stephenson Cancer Center
The University of Oklahoma
Oklahoma City, OK

“The NCORP Research Base application, including the new Cancer Care Delivery Research (CCDR) component, is very important to our NRG Oncology research program. This funding would enhance the efforts of our investigators to deliver state-of-the-art cancer care in the most effective, least expensive, and yet patient-centered manner; reduce cancer health outcomes disparities; improve cancer prevention programs and strategies; and improve the quality of the lives of cancer survivors.”

Joan L. Walker
George Lynn Cross Research Professor
The James A. Merrill Chair in Ob/Gyn
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