From the Leadership

Group Chair Philip J. DiSaia, MD, welcomed attendees to the General Session of the July 2014 NRG Oncology Semiannual Meeting, noting that more than 1300 people had registered to attend the meeting that took place July 10–13 in Chicago, Illinois. The General Session provided meeting attendees with an update on NRG Oncology activities since March 1, 2014, when the Group formally began conducting research as part of the National Cancer Institute (NCI) National Clinical Trials Network (NCTN).

In presenting the first NRG Oncology accrual performance data, Group Chair Walter J. Curran, Jr., MD, clarified that the intention of highlighting accrual results is to create a strong sense of membership identity, provide insight into enrollment trends and opportunities, and stimulate a healthy rivalry for top performance. He reported that accrual from March 1 through June 30 had exceeded expectations, with more than 2348 participants being enrolled into NRG Oncology clinical trials. Curran also presented accrual data that recognized the University of Oklahoma Health Sciences Center as the top-accruing Lead Academic Participating Site (LAPS), the New Mexico Minority-Based CCOP (MB-CCOP) as the top-accruing CCOP network, and Kaiser Permanente–Vallejo as the top-accruing site outside the LAPS and CCOP programs.

Deputy Group Chair for Research Strategy Mitchell Machtay, MD, reported that the NRG Oncology “pipeline” of trials includes 13 NCI-approved study concepts that are on the Operational Efficiency Working Group (OEWG) timeline and 15 concepts approved by the Research Strategy Committee that are in various stages of being submitted or resubmitted to NCI. Machtay commented that the trials in development are consistent with NCI’s goals for the NCTN of having fewer and earlier-phase trials.

Deputy Group Chair for Concept Prioritization and Conduct J. Tate Thigpen, MD, reviewed the functions and composition of the Concept Prioritization Advisory Committee (CPAC), including the prioritization scoring process, and highlighted the recently activated and preactivated trials.

Deputy Group Chair for Membership D. Lawrence Wickerham, MD, reviewed the requirements for NRG Oncology membership, emphasizing that beginning in 2015, voting members will be NRG Oncology Main Member institutions with annual accrual of at least 40 cases.

Exploring Solutions for Improved Clinical Trial Accrual

Eighty percent of clinical trials struggle with participant accrual. This fact led more than 240 people to attend the Saturday morning workshop entitled Clinical Trials Enrollment: Challenges and Opportunities. Workshop chair and moderator, Sandra E. Brooks, MD, MBA, engaged audience members and a panel of experts in the field of trial accrual in a valuable dialogue about critical issues affecting a patient’s decision to participate in a clinical trial.

Themes that cut across the exchange of ideas and experiences included the following:

• Addressing the concerns of the more than one third of women who are eligible for trials but do not enroll represents a significant opportunity for enhancing enrollment

• A critical mass of physician support and advocacy for trials is key, (eg, 33% of physicians enrolled 75% of a trial’s patients in a strong research support environment)

• A robust infrastructure (data management team, navigators to proactively address accrual barriers, and research associates) is vital to accrual success

Thank you to Dr. Brooks, co-moderator Carolyn Muller, MD, the panelists (Elise D. Cook, MD, MS; Sue Friedman, DVM; Worta McCaskill–Stevens, MD, MS; William A. Robinson, MD, PhD; Eleanor M. Walker, MD; Kate Yeager, PhD, RN), and the audience members for making the session a success.
Program Update

NRG Oncology Receives 5-Year NCORP Research Base Funding Award

NRG Oncology received formal notice that the Group is funded to carry out its scientific program as a National Cancer Institute (NCI) Community Oncology Research Program (NCORP) Research Base. The NRG NCORP research team has set plans in motion quickly to implement the research initiatives proposed in the Group’s application submitted in January 2014 and highlighted in the NRG Oncology Newsletter (Volume 1 2014). “Our application received a strong score, which reflects the importance of the scientific objectives we will pursue,” says Deborah Watkins Bruner, PhD, RN, FAAN, NRG NCORP Contact Principal Investigator (PI) and associate director of outcomes research at the Winship Cancer Institute of Emory University in Atlanta.

The NRG Oncology NCORP Research Base will support the design and conduct of multicenter studies of cancer prevention, control, screening, and posttreatment surveillance, as well as cancer care delivery research (CCDR). “The majority of the 34 NCORP Community Sites and 12 Minority/Underserved Community Sites have named NRG NCORP as their research base,” says D. Lawrence Wickerham, MD, NRG NCORP PI/Steering Committee Chair, associate professor of human oncology at the Pittsburgh Campus of the Drexel University School of Medicine, and the section chief of cancer genetics and prevention at Allegheny General Hospital in Pittsburgh. “These sites have histories of strong accrual across the 3 legacy groups, and we look forward to their continued active participation in the practice-defining research planned for the NRG NCORP.”

Cancer Care and Delivery Research Committee Adds Expanded Research Dimension

The Cancer Care and Delivery Research (CCDR) Committee held its inaugural meeting at the July 2014 NRG Oncology Semiannual Meeting. One of 3 NRG Oncology Non-Disease Site Scientific Committees and a key component of the NRG Oncology NCORP Research Base, the new program is co-chaired by two distinguished researchers—David E. Cohn, MD and Joseph Lipscomb, PhD. Cohn is associate professor of gynecologic oncology in the Department of Obstetrics and Gynecology and director of the Division of Gynecologic Oncology at The Ohio State University College of Medicine in Columbus. He also was co-chair of GOG’s Health Outcomes Research Committee. Lipscomb is professor of health policy and management at Emory University’s Rollins School of Public Health and associate director for population sciences at Emory’s Winship Cancer Institute in Atlanta. Lipscomb previously served as chief of the NCI Outcomes Research Branch.

Cohn and Lipscomb presented the definition of CCDR as “a multidisciplinary field of investigation that studies how complex, multilevel forces — operating at the patient, provider, and health system levels — influence cancer care access, quality, and cost." They explained how the Institute of Medicine report (Delivering High-Quality Cancer Care: Charting a New Course for a System in Crisis) provided the conceptual framework for the NRG Oncology CCDR program. An ambitious first-year plan proposed for discussion focused on data infrastructure development, including the conduct of several proof-of-concept CCDR studies with one or more NCORP Community Sites with highly developed, well-integrated data systems. To learn more about the committee’s proposed plans, view the meeting’s discussion slide set.  

continued
patients who received a placebo. Additionally, at the July 2014 NRG Oncology Semianual Meeting in Chicago, NRG NCORP presented a translational science workshop on the fallopian tube as the etiology of ovarian cancer to introduce the NCORP research team to an upcoming study on interval salpingectomy, prior to oophorectomy, in women who are BRCA1 and BRCA2 mutation carriers. This ovarian cancer prevention study is expected to open in 2015.

“We are particularly excited to expand research activities in the area defined by NCI as cancer care delivery research—a focus of the legacy groups’ CCOPs for some time,” says NRG NCORP PI/Executive Committee Chair Joan L. Walker, MD, a gynecologic oncologist at the Stephenson Cancer Center at the University of Oklahoma Health Sciences Center in Oklahoma City. As an example, Walker cites GOG’s analyses of quality of life and other patient-reported outcome data that have contributed substantially to the interpretation of overall risks and benefits of ovarian cancer treatment regimens. (See sidebar about NRG Oncology’s new CCDR committee, page 2.)

An immediate challenge faced by all 7 NCORP research bases is how to accomplish their research aims in light of significant funding reductions. The funding level for the NRG NCORP is 40% below the aggregate funding level of the NSABP, RTOG, and GOG CCOP Research Base programs. “The research team is working intensely to develop strategies to maximize the resources at hand while maintaining the exceptional menu of cancer prevention and control studies,” says Bruner.

For information about NRG Oncology NCORP Research Base strategic goals, visit NRG Oncology website.

For more information about NCORP, visit the newly launched NCORP website.

In the News

GOG Study Results Lead to Expeditious Approval of Bevacizumab for Advanced Cervical Cancer

On August 14, the US Food and Drug Administration (FDA) approved bevacizumab (Avastin) for the treatment of patients with persistent, recurrent, or late-stage cervical cancer. The decision was based on the results of the GOG 240 trial, which showed an overall survival of 16.8 months for participants who received chemotherapy in combination with Avastin as compared with 12.9 months for those receiving chemotherapy alone. Trial Principal Investigator Krishnansu S. Tewari, MD, FACOG, FACS, professor and director of research in the Division of Gynecologic Oncology at the University of California, Irvine, shares his thoughts about the drug’s approval.

For reasons not completely clear, the experiences of our patients with advanced cervical cancer stand out in our memories. Perhaps we view their suffering as needless because of the preventable nature of the disease, or the fact that so many are young women with little children at home may be especially heartbreaking. The FDA’s approval of bevacizumab for advanced cervical cancer represents a regulatory milestone and underscores the FDA’s commitment to bring promising therapies to patients expeditiously. This achievement was made possible through the vision of the GOG leadership, the provision of the drug by Genentech, and, most importantly, the dedication to clinical research shown by GOG 240 investigators who discussed the study with their patients. Much more work needs to be done, but we have finally identified a potential therapeutic window through which patients with advanced cervical cancer who derive benefit from bevacizumab can be treated with newer targeted agents or immunotherapy before they experience disease progression. This work, although not signifying the end of cervical cancer, represents the beginning of the end.

To learn more about study results, click here. | To read the FDA news release, click here.
Clinical Trials Update

Newly Activated Trials

**NRG-BR001: SBRT for Treating Multiple Metastases**

Oligometastasis describes an intermediate state of cancer spread between localized disease and widespread metastases.\(^1\) During the last decade, evidence has emerged that patients with controlled primary tumors and limited metastases may survive longer through aggressive treatment of oligometastatic disease prior to or during standard palliative systemic therapy. Experimental and clinical observations suggest that select patients with newly diagnosed metastatic breast, prostate, and lung cancer may benefit from treatment of all oligometastases with stereotactic body radiotherapy (SBRT) and/or surgery. Although the safety and toxicity of SBRT for treating patients with single sites of metastasis within individual organs is known, only a few single-institution studies have attempted, to date, to assess the safety and tolerability associated with treating multiple and potentially overlapping sites of disease simultaneously.

With the recent activation of the phase I NRG-BR001 trial, investigators seek to determine the safety and tolerability of SBRT for treating patients with primary breast, prostate, and non-small cell lung cancer who have multiple metastases in 1 of 7 anatomical sites—peripheral lung, central lung, mediastinal/cervical lymph node, liver, spinal/paraspinal region, osseous tissue, and abdominopelvic cavity. SBRT or ablative radiotherapy approaches have been studied in 4 prior RTOG clinical trials for single lesions in lung, liver, and spinal metastases. These trials have provided a framework for successful delivery and quality assurance of complex radiotherapy in the cooperative group setting.

If acceptable toxicity and tolerance is demonstrated, a planned phase II/III randomized trial can be expanded to include patients with more extensive metastases.

http://jco.ascopubs.org/content/31/11/1384.full.pdf+html.

---

**NRG-BR001 Images of Treatment Planning for Multiple Metastases**

Click here to view a larger version.

**Coronal and Axial Images Displaying Radiation Dose Distributions for Patients With Multiple Metastases**

A patient with multiple pulmonary metastases (2 in the right lung, 1 in the left lung) is shown in axial and coronal planes. Multiple coronal images are seen to visualize all tumors. Each tumor is being treated with SBRT. Care is taken to minimize dose to the lung, heart, esophagus, and spinal cord, while ensuring coverage of all tumors.

Images courtesy of Steven Chmura, MD

---

**Study Objectives**  
**Protocol Documents**
**Newly Activated Trials (continued)**

**Children's Oncology Group and NRG Oncology Team**

**Up to Evaluate a New Treatment Option for a Rare Cancer**

The Children's Oncology Group (COG) and NRG Oncology have collaborated in the development of a clinical trial exploring a new treatment option for patients diagnosed with nonrhabdomyosarcoma soft tissue sarcomas (NRSTS). Activated on July 11, 2014, this jointly conducted study is a unique and unprecedented opportunity to advance the treatment of both pediatric and adult patients with NRSTS, a disease classified as having a low incidence rate. NRSTS comprise 4% of all childhood malignancies and less than 1% of all adult malignancies. This trial builds on the backbones of 2 recently successfully completed clinical trials on NRSTS conducted by NRG Oncology (RTOG 0630) and by COG ARST0332.

At initial diagnosis, 40% of patients with NRSTS have intermediate- to high-risk disease. Despite the use of multimodality therapy, overall survival rates for these patients are approximately 50% in children and 15% in adults. Response rates and outcomes remain poor for patients with large, high-grade tumors and for those with unresectable or metastatic disease. Further, the lack of homogeneous chemotherapy sensitivity across all NRSTS subtypes suggests the need for a more histologic-specific treatment approach.

The COG-NRG ARST1321 study will first determine the feasibility of administering pazopanib, a tyrosine kinase inhibitor approved by the FDA for single-agent use in metastatic sarcoma, in combination with radiation or chemoradiation in pediatric and adult patients newly diagnosed with unresected intermediate- and high-risk NRSTS.

Subsequently, the study will compare the rates of near-complete pathologic response (>90% tumor necrosis) in 2 parallel cohorts

- Preoperative pazopanib plus chemoradiation versus preoperative chemoradiation alone for potentially resectable high-risk (grade 3, >5 cm) NRSTS of chemotherapy-sensitive histologic subtypes
- Pazopanib plus preoperative radiotherapy versus preoperative radiotherapy alone for all other potentially resectable intermediate- to high-risk NRSTS

The study will also evaluate the feasibility of standardizing preoperative radiotherapy through the incorporation of high-quality MRI image fusion, consensus-based clinical target volume definition, and accurate delivery using image-guidance technology. The correlative studies will collect data from the largest sample of pediatric and adult NRSTS tumor tissue and blood in an effort to understand the similarities and differences between pediatric and adult NRSTS and to identify other potential actionable targets for future development.

For more information see:
- **Study Objectives**
- **Protocol Documents**

---

**Clinical Trial Spotlight**

**About the e³ Breast Cancer Study**

The e³ breast cancer study—evaluating everolimus with endocrine therapy—is a randomized, placebo-controlled phase III adjuvant therapy trial that assesses the benefits of adding 1 year of everolimus to adjuvant endocrine therapy in patients with high-risk hormone receptor-positive and HER2/neu-negative breast cancer. Also known as SWOG S1207/NSABP B-53, the e³ trial is being led by SWOG and NRG Oncology within the National Cancer Institute (NCI) National Clinical Trials Network (NCTN).

The trial also includes a Behavioral and Health Outcomes (BAHO) study. The BAHO component provides the opportunity to determine whether the use of everolimus delays or retards recovery of energy and functioning after primary breast cancer treatment and, if so, what symptoms and quality of life domains are impaired.

Priya Rastogi, MD, one of the study chairs for the trial, states, “Everolimus has been shown to increase the activity of endocrine therapy in patients with metastatic breast cancer. S1207/B-53 is evaluating whether 1 year of everolimus added to endocrine therapy can lower the risk of recurrence in women with early-stage breast cancer.”

Eligibility criteria for the trial include:

- Completion of either breast-conserving surgery or total mastectomy, with negative margins and appropriate axillary staging
- A histologically confirmed diagnosis of estrogen receptor-and/or progesterone receptor-positive (ER+ and/or PgR+) and human epidermal growth factor receptor 2-negative (HER2-) invasive breast carcinoma for which standard adjuvant endocrine therapy is planned
- Patients with multifocal, multicentric, primary inflammatory, or synchronous bilateral breast cancer

The study, which opened to enrollment on September 3, 2013, will enroll 3500 patients over 3.5 years. Please consider the e³ breast cancer study for your patients with breast cancer who have completed their primary treatment for breast cancer. Protocol and supporting documents for this study can be found on the [Cancer Trials Support Unit (CTSU) website](http://www.ctsu.cancer.gov).
NRG Oncology Science at ASTRO 2014

NRG Oncology-affiliated researchers will have a strong presence at the American Society for Radiation Oncology’s 56th Annual Meeting taking place September 14–17 in San Francisco, with research results being presented in more than 20 scientific sessions. Nine disease sites are covered in 16 oral presentations—including a plenary session presentation—and 7 poster sessions. The broad range of research results to be presented address trial primary end points, patient outcomes, quality assurance, physics, a new gynecologic treatment planning atlas, and trial secondary end points and secondary analyses. The following 4 primary end point presentations are included in the meeting’s program:

Plenary Session Presentation
• RTOG 0126: A Phase III Randomized Trial of High-Dose (79.2 Gy) vs. Standard-Dose (70.2 Gy) Radiation Therapy (RT) for Men With Localized Prostate Cancer
  Presenter: Jeff Michalski, MD, MBA – Washington University School of Medicine (St. Louis, MO)

Oral Presentations
• RTOG 0524: Phase II/II Trial of a Combination of Paclitaxel and Trastuzumab With Daily Irradiation or Paclitaxel Alone With Daily Irradiation Following Transurethral Surgery for Noncystectomy Candidates With Muscle-Invasive Bladder Cancer
  Presenter: Huong T. Pham, MD – Virginia Mason Medical Center (Seattle)
• RTOG 1012: Randomized Phase II Trial of Best Supportive Care, Manuka Honey Liquid and Manuka Honey Lozenges for Prevention of Radiation Esophagitis During Chemotherapy and Radiotherapy for Lung Cancer
  Presenter: Lawrence B. Berk, MD, PhD – Tampa General Hospital of the University of South Florida
• RTOG 0621: Adjuvant Radiation Therapy, Androgen Deprivation, and Docetaxel for High-Risk Prostate Cancer Post-Prostatectomy
  Presenter: Mark Hurwitz, MD – Thomas Jefferson University and Hospitals (Philadelphia)

In addition, Minesh Mehta, MD, FASTRO (University of Maryland School of Medicine, Baltimore) will present the long-term results of RTOG 9802 (A Phase III Study of Radiation Therapy With or Without PCV Chemotherapy in Unfavorable Low-Grade Glioma), which provide new treatment insights.

For the full schedule of presentations, visit NRG Oncology at ASTRO

Shout Out to Sites
Collecting information and preparing the extensive documentation required for submission of a protocol to an institutional review board (IRB) requires significant collaboration on the part of site research teams. Obtaining expeditious IRB approval is critical for a study to meet accrual milestones and to obtain the research data necessary to answer important questions related to improving patient care.

We are pleased to recognize the research sites first to provide notice of IRB approval that allowed for activation of the following NRG Oncology clinical trials:

NRG-HN001
• Stanford University
• University of Oklahoma Health Sciences Center
COG-NRG ARST1321
• Maine Children’s Cancer Program
NSABP B-55
• Cancer Research for the Ozarks CCOP, Springfield, MO
NRG-BR001
• Nevada Cancer Research Foundation NCORP

NCTN Panel Session
The panel session “Radiation Oncology in the New National Cancer Institute National Clinical Trials Network” will take place on Wednesday, September 17 from 3:00 – 4:30
Daniel Low, PhD and Jeff Michalski, MD, MBA, FASTRO moderate the session with panelists Walter Curran Jr., MD, James Dignam, PhD, and David Scott Followill, PhD.

NRG Oncology NEWSLETTER

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

Group Chairs | Walter J. Curran, Jr., MD; Philip J. DiSaia, MD; and Norman Wolmark, MD
Editors and Contributors | Julie Catagnus, MSW, ELS; Cathy Galoppo; Barbara C. Good, PhD; and Nancy Fredericks, MBA
Executive Directors | Joan “Kip” Goldberg, MPH; Sharon Hartson Stine, BA; and Laura L. Reese, JD
Design | Biddle Design

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