Breadth of NRG Oncology Research to Be Highlighted
Presentations slated for the NRG Oncology Scientific Session, scheduled for Friday, July 11, from 8:00 AM to 10:00 AM, will review recent research results and the NRG Oncology trial, NSABP B-55/BIG 6-13 [OlympiA], preactivated on June 2 for patients with germline BRCA mutations and HER2-negative primary breast cancer.

Highlighted research will include (1) an investigation of whether there’s an association between institutional clinical trial accrual volume and the survival of study participants with lung cancer, (2) a study of the effectiveness and safety of adding the hypoxic cell sensitizer tirapazamine to standard chemoradiotherapy in locally advanced cervical cancer, and (3) the long-term follow-up results of a phase III study (RTOG 9802) evaluating radiotherapy with or without procarbazine, lomustine [CCNU], and vincristine (PCV) chemotherapy in patients with low-grade gliomas. The session will wrap up with an overview of the NCI Molecular Analysis for Therapy Choice (NCI Match) initiative that will serve as an umbrella protocol for multiple, single-arm phase II trials.

For the full scientific session and meeting agenda, visit July 2014 Semiannual Meeting.

Clinical Trials Enrollment Workshop to Provide Broad Perspective
Eighty percent of clinical trials experience difficulties in meeting their recruitment targets. The Clinical Trials Enrollment: Challenges and Opportunities workshop (Saturday, July 12, 8 AM to 10 AM) will examine this issue from the perspectives of (1) patient engagement, (2) NRG Oncology researchers—including a minority-based CCOP, (3) a population-based managed care model, and (4) the NCI. Specifically, recently completed cooperative group studies will be reviewed with a focus on patient and physician factors, the role of cultural competency and communication, Community Advisory Boards, and patient advocacy groups. The workshop will explore next steps and pose strategies for future effective and efficient trial enrollment interventions.

About Sandra E. Brooks, MD, MBA, Chair, Clinical Trials Enrollment Workshop
Dr. Brooks completed a residency in obstetrics and gynecology at the University of Pennsylvania in Philadelphia, a fellowship in gynecologic oncology at Brigham and Women’s Hospital in Boston, and an MBA at Johns Hopkins University in Baltimore. Most recently, she has led and developed population health-based prevention initiatives and held positions in research administration for a major health system. She currently holds a full professor appointment on the volunteer faculty of the University of Kentucky’s College of Public Health in Lexington. An author of 40 scholarly papers and book chapters, with a focus on health disparities and health outcomes, Dr. Brooks has served as the principal investigator on national clinical trials.

Immunomodulation Update
Learn what’s new in the field of immunomodulation research by attending the Translational Science Immunomodulation Subcommittee session scheduled for Friday, July 11, from...
Clinical Trial Updates

NRG Oncology Launches the Group’s Second Protocol

Preactivated on June 2, the Olaparib in Adjuvant breast cancer (OlympiA) is a double-blind, randomized, placebo-controlled, multicenter phase III study. It will assess the efficacy and safety of olaparib compared with placebo as adjuvant treatment in patients with both germline BRCA mutations and HER2-negative primary breast cancer who have undergone surgery and have been treated with neoadjuvant or adjuvant chemotherapy. Priya Rastogi, MD, Protocol Officer for the NSABP B-55 trial, stated, “This is an important trial, because olaparib could provide a new treatment option for women with a BRCA mutation.”

The OlympiA trial is a collaboration among the Breast International Group, NRG Oncology, and the Frontier Science & Technology Research Foundation. A total of 1,320 patients will be randomized in a 1:1 ratio to receive either olaparib (300 mg bid) or placebo and stratified by prior neoadjuvant compared with adjuvant chemotherapy and prior use of platinum-based treatment for breast cancer. Patients will receive study treatment for up to a maximum of 12 months. The primary end point of the study is invasive disease-free survival, with data analysis estimated at approximately 5.5 to 6 years after enrollment of the first subject.

For more information, the protocol is available on the Clinical Trials Support Unit website.

Phase II Component of RTOG 0912 Opens for Enrollment

With three run-in components having been completed to confirm the safety of a new treatment regimen (intensity-modulated radiotherapy, paclitaxel, and pazopanib suspension) for patients with anaplastic thyroid cancer (ATC), the phase II component of the RTOG 0912 trial is now open.

Affecting primarily adults 65 years and older, ATC accounts for only 1% to 2% of all thyroid cancer cases and is one of the most aggressive solid tumors, with a 1-year survival rate of approximately 10%. Although these factors make patient accrual challenging, site research teams were successful in meeting the accrual goals for the three run-in components.

“The need for studies in this disease is significant, given the lack of prior trials and the poor prognosis for these patients. Due to the rarity and aggressiveness of this disease, I encourage investigators to open this trial at their institutions, even if they see only 1 or 2 affected patients per year,” says Walter J. Curran, Jr., MD, NRG Oncology Group Chairman and Executive Director of the Winship Cancer Institute of Emory University in Atlanta.

Study information is available at RTOG 0912. Congratulations to the protocol and site research teams for reaching this milestone.

July Semiannual Meeting (continued from page 1)

11:00 AM to 12:30 PM. Along with “Immunotherapy and Radiation Experience” and “Immunotherapy and Chemotherapy Experience” presentations, the session will include a panel discussion. The latter will allow for an interchange on critical immunomodulation issues and the translational barriers to and solutions for combining radiation or chemotherapy with emerging immunotherapeutics.

Head and Neck Cancer Workshop

Research personnel interested in participating in the NRG-HN001 trial (Randomized Phase II and Phase III Studies of Individualized Treatment for Nasopharyngeal Carcinoma Based on Biomarker Epstein Barr Virus DNA) should plan to attend the Head and Neck Cancer Workshop taking place Saturday, July 12, from 10 AM to 12:00 PM. Attendees will obtain updates on the trial’s conduct, other ongoing head and neck cancer trials, and research concepts in the clinical trials pipeline.
At ASCO 2014

More than 20 presentations reporting on NRG Oncology research were presented at the American Society of Clinical Oncology (ASCO) 2014 Annual Meeting, which took place May 30–June 3 at McCormick Place in Chicago. Highlights of several of the presentations are provided below.

Head and Neck Cancer

Results of a secondary RTOG 0522 study (A Randomized Phase III Trial of Concurrent Accelerated Radiation and Cisplatin versus Concurrent Accelerated Radiation, Cisplatin, and Cetuximab for Stage III and IV Head and Neck Carcinomas) found that patients with locally advanced head and neck squamous cell cancer with an inherited KRAS-variant gene mutation benefited significantly from a treatment regimen that included the drug cetuximab. The study results suggest that further investigation is warranted to enable the appropriate incorporation of the KRAS-variant marker into risk stratification to help direct personalized medicine for patients with head and neck cancer.

For the full abstract of the results reported by Joanne B. Weidhaas, MD, study investigator, along with a presentation video, podcast, and slides, visit the ASCO meeting library.

Gastrointestinal Cancer

Final results presented from NSABP R-04 (Neoadjuvant chemoradiation [RT] comparing continuous infusion [CIV] 5-FU with capecitabine [Cape] with or without oxaliplatin [Ox] in patients with stage II and III rectal cancer) establish Cape as the standard of care for treatment of rectal cancer in the preoperative setting. An analysis at 5 years after participant enrollment showed that CIV 5-FU or oral Cape combined with RT produced similar outcomes for local-regional (L-R) control, disease-free survival (DFS), and overall survival (OS). Additionally, Ox did not improve L-R failure rate, DFS, or OS for any patient risk group but did add significant toxicity.

For the full abstract and to view a presentation poster of the results reported by Carmen J. Allegra, MD, vice chair of the NSABP Colorectal Committee at the time NSABP R-04 was designed and implemented, visit the ASCO meeting library.

Carmen Allegra, an NRG Deputy Group Chair and Chief of Oncology and Hematology at the University of Florida provided a discussion of 3 randomized international trials in patients with early stage rectal cancer presented at ASCO. Each trial was designed to address the relevance of the addition of oxaliplatin (Ox) to fluoropyrimidine (FP) sensitized neoadjuvant radiation therapy as well as its role in combination with FPs in the adjuvant rectal setting. Allegra concluded that while Ox had no role as a radiation sensitizer in this setting, it clearly was associated with benefit in the adjuvant setting much the same as it has been shown to be of value in patients with early stage colon cancers when used in combination with FPs. Click here to view Allegra’s full presentation.

In a further report from the NSABP R-04 trial, results of a study validating the neoadjuvant rectal cancer (NAR) score were presented. 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.

For the full abstract of the results reported by Greg Yothers, PhD, trial biostatistician, visit the ASCO meeting library. Also, a report on study results Yothers presented at the January 2014 NRG Oncology Semiannual Meeting appears in the NRG Oncology Newsletter Vol. 1 2014.

Observations on Two ASCO Lung Cancer Presentations

At ASCO 2014 the results presented from a European and a Japanese study underscore the importance of an NRG Oncology clinical trial (RTOG 0937) underway for contributing additional information to aid treatment decision making for patients with extensive-disease small cell lung cancer (ED-SCLC). Here, Elizabeth Gore, MD, principal investigator of RTOG 0937 (Randomized Phase II Study Comparing Prophylactic Cranial Irradiation [PCI] Alone to PCI and Consolidative Extra-Cranial Irradiation for ED-SCLC), provides observations on the two trials’ results and their significance with regard to the RTOG 0937 trial.

Consolidative Thoracic Radiation Therapy

In the European study presented by Ben J. Slotman, MD, PhD (abstract 7502), patients (World Health Organization performance status 0–2) with confirmed ED-SCLC who had a response after 4 to 6 cycles of standard chemotherapy were randomized to receive thoracic radiation therapy (TRT) (30 Gy/10 fractions) or no TRT. Slotman reported that TRT improved progression-free survival. Although TRT did not influence the risk of death in the first year, it led to a significant increase in 2-year survival rates.

Dr. Gore’s comments: “It’s encouraging that consolidative chest irradiation, when added to PCI, may improve overall survival. However, the primary end point of the study was not met, as a survival benefit wasn’t realized until after the defined end point. RTOG 0937 is evaluating a patient...
population with low-volume metastatic disease (up to 4 metastatic lesions) and includes consolidative radiation therapy (30–45 Gy) to the chest (TRT) and metastatic lesions. Data from this study will assist in clarifying the role of consolidative TRT in patients with ED-SCLC.”

**Prophylactic Cranial Irradiation**

In the study from Japan presented by Takashi Seto, MD, PhD (abstract 7503), patients with ED-SCLC who had any response to first-line platinum-based doublet chemotherapy were randomized to prophylactic cranial irradiation (PCI) (25 Gy/10 fractions) or observation (Obs).

A preplanned interim analysis was conducted of the survival data for 163 patients. The study was terminated because of futility (unlikely to show a survival advantage with PCI); with a median follow-up of 9.4 months and 111 observed deaths, the median overall survival was 10.1 and 15.1 months for PCI (n = 84) and Obs (n = 79), respectively. Bayesian predictive probability of showing superiority of PCI over Obs was 0.01%. PCI significantly reduced the risk of brain metastases as compared with Obs (32.4% vs 58.0% at 12 months; Gray’s test, P < 0.001).

**Dr. Gore’s Comments:** “Although the patients randomized to PCI in this study had a shorter median survival at the interim analysis, there is no evidence that PCI influenced this outcome. In fact, PCI decreased brain metastases risk from 58% to 32.4% at 12 months. The lack of a survival benefit shown in this underpowered randomized trial shouldn’t change the interpretation of a larger randomized European Organisation for Research and Treatment of Cancer (EORTC) trial that showed a 27% versus 13% OS benefit for PCI.” A criticism of the EORTC study is that it did not require restaging MRI before PCI, which might have identified patients with subclinical brain metastases. A planned dedicated peer-review process for the Japanese study may help us better understand the trial data. Practice standards are not expected to be influenced in the interim.”

**Walter J. Curran, Jr., MD,** an NRG Oncology Group Chair and Executive Director of the Winship Cancer Institute of Emory University in Atlanta, provided an overview of the two ED-SCLC studies presented at ASCO and the Slotman study published in 2007 in *New England Journal of Medicine.* In his presentation, Curran also pointed to the positive results of the RTOG 0933 study (A Phase II Trial of Hippocampal Avoidance During Whole Brain Radiotherapy for Brain Metastases—an RTOG CCOP study), presented at the 2013 ASTRO Annual Meeting (Plenary Session), and the potential impact of this technique on the benefits of PCI. With NCORP support, NRG Oncology will test this technique in the setting of limited-stage SCLC. Click here to view Curran’s presentation.


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**Investigator in the Spotlight**

An article by NRG Oncology’s Translational Science Committee Co-chair Adam Dicker, MD, PhD, “Potential Opportunities for Integrating Molecular Signatures and Genomic Classifiers in Radiation Oncology,” was featured in the summer 2014 issue of ASTRONews, ASTRO’s quarterly news magazine. In the article, Dicker considers Mayo Clinic’s Breast Cancer Genome-Guided Therapy (BEAUTY) study, the potential of comparative effectiveness research for advancing personalized medicine, and the prospect of molecular or genetic signatures developed for a specific purpose—such as determining an individual’s risk for cancer recurrence—being used to determine which patients with cancer should be considered for radiotherapy.

To view the article, provided as a courtesy by ASTRO, see ASTRONews.