Message From Our NRG Oncology Group Chairs

Walter J. Curran, Jr., MD

Welcome to Atlanta for our semiannual meeting this month! Weather is projected to be mild with highs in the low 50’s and lows in the high 30’s. We expect that you will enjoy our Southern hospitality and the company of your friends and colleagues from around North America.

It is hard to believe that we are coming up on the second anniversary of the launch of NRG Oncology on March 1, 2014! Over the past two years, NRG has demonstrated its continued ability to develop and activate highly meaningful trials across its seven cancer disease sites, execute and complete significant translational science projects, and publish practice-defining and -redefining manuscripts. You will see several outstanding presentations of NRG Oncology research in the Publications Session on Friday morning, and you will also hear the most outstanding published manuscripts and abstracts from each of our protocol-generating committees identified in our NRG General Session on Saturday afternoon. Importantly, we have demonstrated to the world that three strong and highly productive cooperative groups can come together and succeed as a highly matrixed organization.

I want to give a special shout-out to all of the volunteer physicians, scientists, and professionals who dedicate your time and effort to support the mission of NRG Oncology. It is extremely gratifying to see the continued commitment of literally thousands of volunteers who made our research possible!

NRG Oncology Biospecimen Bank Program Progresses

The NRG Oncology Biospecimen Bank Program, formed from the three legacy biospecimen resources of RTOG, GOG, and NSABP, was launched on April 1 after its application for NCI funding received the highest rating of all cancer cooperative group proposals. Richard Jordan, DDS, PhD, FRCPath, is the contact principal investigator and recipient of the 5-year grant. Jordan, who is also the director of the San Francisco Bank, discusses the progress made and challenges ahead in meeting the proposal’s goals for furthering NRG Oncology’s increasingly important biospecimen banking program.

Biospecimen Banking in NRG Oncology Research

“In the era of targeted cancer therapy and personalized medicine, biobanking will be essential to identify potential targets and determine if the therapies we’re using to attack the targets work. Rather than collecting specimens for the sake of curiosity, we now have a structured and patient-tailored way to look at these markers. Testing the specimens is the only way we’ll know what works for a particular patient,” states Jordan. Examples of this already existing trend in legacy groups include head and neck cancer trials, in which patient tissue samples have been tested to identify the likelihood that antibodies used routinely will work, and NSABP trials, which have revolutionized breast cancer research with the introduction of the lumpectomy. As Sandy DeVries, MA, who is the San Francisco Laboratory Manager, adds, “This trend is also hugely beneficial for patients, because they don’t get treated unnecessarily or with a therapy that won’t work for them.”

SANDY DEVRIES
San Francisco Biospecimen Bank Laboratory Manager

“Plan to attend the NRG Oncology Semiannual Meeting Jan. 21–24, 2016

continued on page 10
Clinical Trial Highlights

NRG-GY004: A Phase III Study Comparing Single-Agent Olaparib or the Combination of Cediranib and Olaparib to Standard Platinum-Based Chemotherapy in Women With Recurrent Platinum-Sensitive Ovarian, Fallopian Tube, or Primary Peritoneal Cancer

Background
The standard of care for patients experiencing a recurrence of platinum-sensitive ovarian cancer is treatment with additional platinum-based doublet combinations of carboplatin, paclitaxel, gemcitabine, and pegylated liposomal doxorubicin. Although subsequent treatment with such regimens is associated with the risk of allergic reaction to platinum and worsening neuropathy and hematologic toxicities, few alternatives exist for the treatment of recurrent platinum-sensitive ovarian cancer. Ovarian cancer remains the leading cause of death from gynecologic malignancy in the United States.

Inhibitors of the enzyme poly ADP ribose polymerase (PARP), including olaparib, have demonstrated activity in platinum-sensitive disease, with or without germline or somatic breast cancer susceptibility gene (BRCA) mutations, and don’t jeopardize response to future platinum-containing drug regimens. Activity in ovarian cancer has also been demonstrated by cediranib, a small-molecule kinase inhibitor of vascular endothelial growth factor receptor (VEGFR), alone and in combination with platinum-based chemotherapy. In a multicenter, open-label randomized phase II trial of 90 patients with recurrent platinum-sensitive ovarian cancer, the combination of cediranib and olaparib extended progression-free-survival (PFS) and overall response rate (ORR) significantly compared with olaparib alone.

The NRG-GY004 trial proposes to assess the efficacy and tolerability of single-agent olaparib versus the combination of cediranib and olaparib versus platinum-based chemotherapy. Powered to allow comparison of both experimental arms to the reference platinum-based chemotherapy for assessment of PFS, the trial will not be blinded or placebo controlled due to the variations in route of drug administration, schedules, and anticipated drug-related toxicities.

Primary Objective
- To assess the efficacy of either single-agent olaparib or the combination of cediranib and olaparib, as measured by PFS, as compared with standard platinum-based chemotherapy in the setting of recurrent platinum-sensitive ovarian, fallopian tube, or primary peritoneal cancer

Secondary Objectives
- To assess the efficacy of single-agent olaparib or the combination of cediranib and olaparib, as measured by response rate, overall survival, time to next chemotherapy or surgery, and PFS as compared with standard platinum-based chemotherapy in the setting of recurrent platinum-sensitive ovarian, fallopian tube, or primary peritoneal cancer
- To assess the effect on quality of life, as assessed through disease-related symptoms as measured by the Disease-Related Symptoms Subscale (DRS)-related items of National Comprehensive Cancer Network-Functional Assessment of Cancer Therapy (NCCN-FACT) Ovarian Symptom Index-18 (NFOSI-18), of single-agent olaparib or the combination of cediranib and olaparib, compared with standard platinum-based chemotherapy in the setting of recurrent platinum-sensitive ovarian, fallopian tube, or primary peritoneal cancer

Patient Population
- Patients with platinum-sensitive recurrent high-grade serous or high-grade endometrioid ovarian, fallopian tube, or primary peritoneal cancer
- Patients with known deleterious or suspected deleterious germline BRCA1 or BRCA2 mutation on a clinical assay with an ovarian, fallopian tube, or primary peritoneal cancer of the following other Mullerian histologies: clear cell, mixed epithelial, undifferentiated carcinoma, or transitional cell carcinoma
- Patients with evaluable disease, defined as Response Evaluation Criteria in Solid Tumors (RESIST) 1.1 measurable disease or as solid and/or cystic abnormalities on radiographic imaging that do not meet RECIST 1.1 definitions for target lesions OR ascites and/or pleural effusion that has been demonstrated pathologically to be disease-related in the setting of a cancer antigen 125 (CA125) >2 times the upper limit of normal (ULN)
- Patients whose prior chemotherapy included a first-line platinum-based regimen
- Patients who have not previously received a PARP inhibitor

continued
Clinical Trial Highlights (continued)

Target Accrual
- 450 eligible patients (including some of the 238 patients accrued per year to the GOG-0213 trial)

Schema

NRG-GY006: A Randomized Phase II Trial of Radiation Therapy and Cisplatin Alone or in Combination With Intravenous Triapine in Women With Newly Diagnosed Bulky Stage IB2, Stage II, IIIB, or IVA Cancer of the Uterine Cervix or Stage II-IVA Vaginal Cancer

Background
Patients with cervical cancer who undergo standard-of-care cisplatin-based radiochemotherapy have a progression-free survival (PFS) rate of 64.5% and a metabolic complete response (mCR) rate of 60% to 85%, according to previous trial results. The unmet therapeutic need for a biologic agent to improve PFS and mCR in women receiving standard treatment for uterine cervix cancers has led researchers to study ribonucleotide reductase overactivity—a molecular pathway that acts preferentially on these cancers. The combination of ribonucleotide reductase inhibitors, such as triapine, and cisplatin-based radiochemotherapy suggests a disease-free survival rate of 82%. Preclinical studies of triapine alone, combined with cisplatin, and combined with cisplatin plus radiation, have demonstrated cytotoxic rates of 20%, 60%, and 90%, respectively. Three-year overall and disease-free survival estimates for patients with advanced-stage cervical and vaginal cancer who were treated with triapine in phase I and phase II trials were 82% and 80%, respectively.

NRG-GY006 is a phase II trial of daily radiation therapy and once-weekly intravenous cisplatin chemotherapy alone (Arm 1) or with coadministered ribonucleotide reductase inhibition by intravenous triapine (Arm 2) in women with uterine cervix and vaginal cancer. This trial will evaluate the 3-month posttherapy 18F-FDG PET/CT mCR as an early surrogate end point for PFS and overall survival (OS). In addition, the trial allows the use of image-guided intensity-modulated radiation therapy (IG-IMRT) as a randomization stratification variable, a factor that is expected to facilitate patient accrual. The trial provides an opportunity to study simultaneously the effects of concurrent chemotherapy intensification and radiotherapy deintensification on quality of life/patient-reported outcomes for patients with locoregionally advanced cervical cancer.

Primary Objective
- To evaluate the efficacy of the experimental regimen of triapine, cisplatin, and radiation to increase PFS relative to the standard/control regimen of cisplatin and radiation in women with uterine cervix and vaginal cancer

Secondary Objectives
- To determine the posttherapy 3-month 18F-FDG PET/CT mCR rate in the uterine cervix and vagina by treatment arm
- To determine the OS after triapine-cisplatin radiochemotherapy and cisplatin radiochemotherapy

Platinum-based chemotherapy options may include carboplatin and paclitaxel, carboplatin and gemcitabine, or carboplatin and pegylated liposomal doxorubicin.

“Although chemoradiation has been the standard of care for nearly 20 years for locally advanced cervical cancer, agents or therapeutic approaches that may improve upon the current treatment backbone are critically needed for this disease process. Building upon the pivotal work by Dr. Charles Kunos and colleagues with the novel agent triapine (a ribonucleotide reductase inhibitor), GY006 is the next trial in a series from the Gynecology Oncology Group/NRG Oncology designed to improve outcomes for women with locally advanced cervical cancer.”

CHARLES A. LEATH III, MD, MSPH
NRG-GY006 Co-Principal Investigator
Clinical Trial Highlights (continued)

- To test the hypothesis that IG-IMRT reduces hematologic (as assessed by clinical laboratory and positron emission tomography tests) and gastrointestinal toxicity compared with conventional pelvic radiotherapy
- To test the hypothesis that IG-IMRT increases quality of life, with equal or superior PFS and OS, compared with conventional pelvic radiotherapy
- To summarize and compare differences in acute adverse events (CTCAE, v4.0) by treatment arm and radiation modality
- To summarize and compare differences in chronic or late (≥30 days from off study treatment date) adverse events (CTCAE, v4.0) by treatment arm and radiation modality

Patient Population

- Patients with pathologic diagnosis of stage IB2 (>5 cm), II, IIIB, or IVA squamous, adenocarcinoma, or adenosquamous carcinoma of the uterine cervix or stage II-IVA squamous, adenocarcinoma, or adenosquamous carcinoma of the vagina not amenable to curative surgical resection alone
- Patients without para-aortic lymph node metastasis, based on pretherapy 18F-FDG PET/CT
- Patients without another concurrent active invasive malignancy
- Patients without a prior invasive malignancy diagnosed within the previous 3 years (except nonmelanoma skin cancer or in situ carcinoma of the cervix)
- Patients who have not received prior pelvic radiotherapy that would contribute radiation dose that would exceed tolerance of normal tissues

Target Accrual

- 172 to 188 patients, at a rate of 8 to 10 patients per month and for a period of 18 to 24 months (based on experience and anticipated intergroup collaboration on GOG-0219 trial)
New Protocol Support Committee Column

Welcome to the inaugural Protocol Support Committee (PSC) column of the NRG Oncology Newsletter. This column is dedicated to informing, educating, and clarifying topics of interest to the Clinical Trials Nurse (CTN) and Clinical Research Associate (CRA) roles in the conduct of NRG Oncology clinical research trials.

PSC Structure
With the formation of NRG Oncology, the PSC resulted from the synergistic union of the legacy Clinical Trial Nursing and Clinical Research Coordinator committees. Its structure consists of an Executive Committee (a chair and two co-chairs), two subcommittees (each with a chair and two co-chairs), and four working groups led by the PSC and subcommittee leadership (see sidebar for leadership specifics).

PSC Purpose
The fundamental purpose of the PSC is to support the CTNs and CRAs working within NRG Oncology. The PSC facilitates quality control of protocol-related activities, provides education and training, mentors new CRAs/CTNs, and ensures that CTNs/CRAs have a voice as voting members of the disease site and scientific core committees. The members of this multidisciplinary committee include nurses, research associates, International Members, Headquarters Office staff, physicians, and patient advocates.

The CTN and CRA Subcommittees provide global oversight of protocol development and implementation. Each subcommittee provides a unique viewpoint and fosters dialogue that NRG Oncology recognizes as distinct. Together, the subcommittees fulfill the missions of the PSC and NRG Oncology to ensure rigor in protocol development, implementation, patient care and compliance, data collection, and ongoing education.

The following four Working Groups focus on implementation of the goals of the PSC, including protocol review, educational and training programs, promotion of best practices and protocol compliance, and mentorship:
1. Protocol Review Working Group
2. Education and Training Working Group
3. Quality Control Working Group
4. Mentorship Working Group

PSC Activities at the NRG Oncology Semiannual Meeting
The PSC hosts many hours of educational sessions during the three-day NRG Oncology Semiannual Meeting. In January, the PSC will conduct an annual full-day orientation session (Introduction to Clinical Trials: Principles of Clinical Trial Management) for new-to-practice CTNs and CRAs, who will gain invaluable practice, policy, and procedural information as well as a comprehensive introduction to the scope of NRG Oncology research. CTNs and CRAs who attend the NRG Oncology Semiannual meeting in Atlanta, Georgia, from January 21–24, 2016 will be certain to leave with the expanded understanding and skills required to conduct NRG Oncology research effectively.

The PSC leadership wants to hear from NRG Oncology CTNs and CRAs about suggested topics, challenges, or opportunities you would like to see featured in this column in future issues of the newsletter. Forward those ideas to appropriate members of the PSC leadership at the email addresses included in the sidebar.

“The PSC is an integral component of NRG Oncology. The CTNs and CRAs are valued members of NRG Oncology whose participation and feedback in committee activities and educational programs is welcome and encouraged. CTNs and CRAs are essential to the success of clinical trials because of their expertise, hard work in meeting protocol guidelines and as advocates for patients and their families.”

SUSAN NOLTE, PSC CHAIR; NANCY KNUDSEN, PSC CO-CHAIR; TERRY THOMAS, PSC CO-CHAIR

continued
New Protocol Support Committee Column (continued)

PSC Leadership

**PSC:** Chair: Susan Nolte, PhD, CRNP, snolte@ahmh.org
Co-Chairs: Nancy Knudsen, RN, BSN, wlnnk@msn.com; Terry Thomas, MS, CCRC, Terry.Thomas@DignityHealth.org

**CTN Subcommittee:** Chair: Cindy Licavoli, RN, BSN, MA, cmi2392@bjc.org
Co-Chair: Nancy Fusco, RN, BSN, Nancy.Fusco@Uhhospitals.org

**CRA Subcommittee:** Chair: Sharon Stockman, BA, CCRP, sharon-stockman@uiowa.edu
Co-Chairs: Sally Brown, RN, BSN, MGA, sally.brown@medstar.net; Joyce Neading, RHIT, CTR, joyce.neading@gmail.com

ASTRO Research Presentations

The results of NRG Oncology research studies were represented majorly at the American Society for Radiation Oncology (ASTRO) 57th Annual Meeting, held October 18–21 in San Antonio. Of the 23 total NRG Oncology presentations, two were presented during plenary sessions and one was selected for inclusion in the Best of ASTRO meeting, which highlights the top-ranked and most influential abstracts of the Annual Meeting. Disease sites represented in these presentations included brain tumors (5), breast cancer (3), cervical cancer (1), head and neck cancer (1), lung cancer (4), pancreatic cancer (1), and prostate cancer (8).

One of the plenary presentations was given by William U. Shipley, MD, FACR, FASTRO, who is the Andres Soriano Distinguished Professor of Radiation Oncology at the Massachusetts General Hospital and the Harvard Medical School, both in Boston. He reported that the long-term results of NRG Oncology/RTOG 9601 demonstrate that for men with prostate cancer recurrence following radical prostatectomy, adding 24 months of antiandrogen therapy with bicalutamide during and after salvage radiotherapy (RT) improved survival statistically compared with treating them with salvage RT alone and reduced prostate cancer death and the development of metastatic disease without increasing radiation toxicity. See full press release here.

The study results suggest strongly that low BRCA1 protein expression in the GBM tumor, and the consequent low DNA repair, causes the cancer cells to be more susceptible to DNA-damaging cancer treatment.**

MARIA VASILAKOPOULOU, MD, PhD
RT0G 0126 Lead Author

In another featured research presentation, Andrea Bezjak, MD, MSc, FRCP, a professor of radiation oncology at the University of Toronto in Ontario, Canada, reported toxicity data for the use of stereotactic body RT (SBRT) in the treatment of patients with early-stage, inoperable, and centrally located non-small cell lung cancer (NSCLC). NRG Oncology/RTOG 0813 is the first trial to implement a phase I/II continuous reassessment design to collect toxicity and efficacy data in the evaluation of dose-escalating SBRT, which is widely used currently in the treatment of patients with NSCLC tumors located in the periphery of the lung. Bezjak reported that overall the treatment was well tolerated and that the highest dose level allowed by the protocol (12 Gy delivered in 5 fractions over 1.5–2 weeks, total dose 60 Gy) was associated with a 7.2% probability of dose-limiting toxicity. See full press release here.

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“Our results show that salvage RT plus peripheral androgen blockade (AAT with bicalutamide), when compared with RT plus a placebo, improved long-term overall survival and reduced death from prostate cancer without adding significantly to radiation toxicity.”

WILLIAM U. SHIPLEY, MD, FACC, FASTRO
NRG 9601 Protocol Principal Investigator and Lead Author

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NRG NCORP Receives Funding Award to Carry Out a Cost-Effectiveness Analysis for the NRG-CC003 Trial

NRG Oncology has received funding from the NCI’s Biomarker, Imaging and Quality of Life Studies Funding Program (BIQSFP) to conduct a cost-effectiveness analysis (CEA) alongside the phase III portion of NRG-CC003 (A Randomized Phase II/III Trial of Prophylactic Cranial Irradiation With or Without Hippocampal Avoidance for Small Cell Lung Cancer). This grant represents the first CEA funded by the BIQSFP in its 5-year history. The work will be led by Andre Konski, MD, MBA, who is medical director of the Department of Radiation Oncology at Chester County Hospital and professor of clinical radiation oncology in the Department of Radiation Oncology in the Perelman School of Medicine at the University of Pennsylvania.

The NRG-CC003 trial’s phase II results demonstrated noninferiority of the 12-month intracranial relapse rate following hippocampal avoidance (HA) during prophylactic cranial irradiation (PCI) compared with the rate following PCI without HA for patients with small cell lung cancer (SCLC). In the phase III portion of the trial, investigators will assess whether sparing the hippocampus through the use of intensity-modulated radiotherapy (IMRT) techniques reduces the likelihood of cognitive deficits.

RTOG 0933, a phase II study, tested IMRT in the use of HA whole brain radiation therapy (WBRT) in the treatment of patients with brain metastases. The memory preservation benefit of HA in this trial was maintained at 6 months, and HA-WBRT was also associated with preservation of patient-reported quality of life. Given these results and the ability of community oncology programs to perform the IMRT techniques involved in HA-PCI effectively and safely in past trials, investigators predict the adoption of this treatment technique as the standard of care for the treatment of patients with SCLC within the United States and internationally.

Despite the increased total direct medical cost of HA-PCI compared with PCI, which results from the use of IMRT instead of 3-dimensional (3D) conformal radiotherapy, the investigators expect the increase to be justified by a decrease in chronic morbidity and an improvement in quality of life in the patients treated with HA-PCI. They cite study results demonstrating high rates of cognitive toxicity associated with even standard-dose PCI and the appearance of these deficits preceding decline in other quality of life domains. The CEA will collect cost data related to caregiving needs, work loss, and direct medical services during the trial to improve their accuracy and to prevent loss of data if collection were delayed.

In order to include indirect costs, including missed time from work, transportation costs, and nursing home or assisted living costs, the CEA will be based on a societal rather than payer or patient perspective. “Currently, IMRT is not routinely covered in the treatment of patients with brain metastases,” explains Konski. “However, if NRG-CC003 finds its use to be cost effective and insurance coverage is forthcoming, the trial would change the practice of radiation oncology in SCLC significantly by encouraging more patients and physicians to accept this therapy.” Using data on the total costs associated with treating dementia, the investigators predict that a 14 million dollar savings could be realized through reducing the indirect cost of cancer care with the use of IMRT.

The CEA requires the development of a health resource utilization diary to measure the services consumed by the patient and the use of the Work Productivity and Activity Impairment Questionnaire to assess work and productivity and to assess patient and caregiver lost wages and productivity. The BIQSFP funding will be used to support additional personnel needed to collect diary data and monitor completion and submission by the research sites.

“The application process for BIQSFP funding is rigorously competitive, and NRG Oncology is proud to be leading this CEA research effort,” states Deborah W. Bruner, RN, PHDr, FAAN, who is the Deputy Group Chair of the NRG Oncology Scientific Publications Committee and the contact principal investigator of the NRG Oncology NCORP.
Featured Publications

From the Cancer Prevention and Control Committee
Cartographic Mapping and Travel Burden to Assess and Develop Strategies to Improve Minority Access to National Cancer Clinical Trials

The results of a study assessing how accrual to cancer clinical trials is related to US minority population density relative to clinical trial site location and distance traveled by patients enrolled in Radiation Therapy Oncology Group (RTOG) trials were published online in the July 10 issue of the International Journal of Radiation Oncology • Biology • Physics. Complete data collected for 4913 patients enrolled from 2006 to 2009 included the RTOG member site address and ZIP codes, patient accrual, and patient race or ethnicity and ZIP code. Geographic Information System (GIS) maps were developed for overall, Latino (see map), and African American accrual to trials by population density.

Investigators found that distribution of the RTOG US sites is in concordance with overall population density. No clustering of sites with the highest accrual rates was demonstrated, nor did the highest minority accrual cluster in areas of highest US minority population density. Minority accrual in cancer clinical trials versus US population representation by minority was 4.3% versus 15.1% for Latinos and 11.2% versus 12.4% for African Americans, respectively. Patients traveled a median of 11.6 miles to participate in clinical trials, with whites traveling statistically longer distances (12.9 miles), Latinos traveling 8.22 miles, and African Americans traveling 5.85 miles. Patients also traveled significantly further to academic sites than to community sites.

The use of visual maps was found to help identify gaps in patient accrual that were not as readily recognized through tables and graphs, such as the fact that sites that accrue well overall seem to accrue minorities better than sites located in higher-density minority population areas. With many sites remaining with poor accrual regardless of state socioeconomic status, the study points to the need for identifying the best practices among the highest-accruing sites.

“These results show that geographic location of treatment sites relative to minority population density and travel distance to sites represent important components to equal access.”

DEBORAH W. BRUNER, RN, PHD, FAAN
Contact Principal Investigator of the NRG Oncology NCORP

Bruner, PhD, RN, FAAN, who is the NRG Oncology Deputy Group Chair for Scientific Publications and the contact principal investigator of the NRG Oncology NCORP. Bruner is also the Associate Director for Outcomes Research at the Winship Cancer Institute of Emory University in Atlanta.

From the Gastrointestinal Cancer Committee
Neoadjuvant 5-FU or Capecitabine Plus Radiation With or Without Oxaliplatin in Rectal Patients: A Phase III Randomized Clinical Trial

Patients with rectal cancer who receive oral capecitabine combined with preoperative radiotherapy have outcomes for locoregional control, disease-free survival (DFS), and overall survival (OS) that are similar to those of patients receiving continuous infusion 5-FU, regardless of whether they also received oxaliplatin, according to results published online in the September 14 issue of the Journal of the National Cancer Institute.

In the NRG Oncology/National Surgical Adjuvant Breast and Bowel Project (NSABP) R-04 trial, 1608 patients with stage II or III rectal cancer were randomized in a 2x2 factorial design to one of four chemotherapy regimens: continuous infusion 5-FU or oral capecitabine with or without oxaliplatin. No statistically significant differences were seen between the 5-FU and capecitabine groups in the rates of 3-year locoregional events (11.2% vs 11.8%), 5-year DFS (66.4% vs 67.7%), or 5-year OS (79.9% vs 80.8%). Although rates of these end points for patients who received or did not...
receive oxaliplatin similarly showed no statistically significant differences (11.2% vs 12.1%, 69.2% vs 64.2%, and 81.3% vs 79.0%, respectively), patients receiving the drug experienced statistically significantly more overall and grade 3 and 4 diarrhea. Investigators observed a numerically greater number of deaths while on or within 45 days of treatment with capecitabine compared with 5-FU (1.3%–1.6% and 0.3%, respectively), however, this increase did not reach statistical significance.

“We already knew from the early end point results of R-04 that the use of 5-FU and capecitabine use were associated with similar rates of pathologic complete response and of sphincter-sparing surgery and surgical downstaging. The trial’s recently published mature data support the use of either oral capecitabine or 5-FU infusion as a standard of care for treatment of patients with rectal cancer in the neoadjuvant setting. Our hope that the addition of oxaliplatin would further enhance the activity of fluoropyrimidine-sensitized radiation was not demonstrated. Based on this lack of additional benefit, along with the substantial toxicity associated with its use, the use of oxaliplatin in the rectal neoadjuvant setting is not recommended,” says Carmen J. Allegra, MD, the lead author of the study article, who is chief of the Division of Hematology and Oncology and the associate director for clinical and translational research at the University of Florida Health Cancer Center in Gainesville.

From the Gynecologic Cancer Committee

Relationships of Tubal Ligation to Endometrial Cancer Stage and Mortality in the NRG Oncology/Gynecologic Oncology Group 210 Trial

A history of tubal ligation (TL) was associated with lower cancer stage and lower endometrial cancer-specific mortality in a study of 4489 patients with aggressive endometrial carcinoma types in which investigators examined patient-completed risk factor questionnaires and pathology data derived from clinical reports and central review. The results of NRG Oncology/Gynecologic Oncology Group 210 Trial were published online in the June 18 issue of the Journal of the National Cancer Institute.

Of the study participants, 27.6% (n=1238) reported a previous TL at a median age of 32 years (range=18–59 years). TL was associated with younger age at diagnosis, aggressive tumor subtypes, absence of myometrial invasion, lower stage, negative peritoneal cytology, and negative peritoneal biopsies. Overall and among individual tumor subtypes, TL was inversely associated with stage III (OR=0.63) and stage IV (OR=0.14) carcinomas compared with stage I. TL was also inversely related to peritoneal metastasis overall (OR=0.39) and among serous carcinomas (OR=0.28). Although TL was associated with lower endometrial carcinoma-specific mortality (HR=0.74) in multivariate analysis, adjustment for stage eliminated the survival advantage.

“We sought to examine patterns of endometrial carcinoma tumor spread that affect staging, which has served as the basis for treatment planning. These results provide evidence that the passage of endometrial carcinoma cells through the fallopian tubes into the peritoneum is an important mechanism of metastasis for aggressive tumor subtypes. Moreover, they indicate that tubal ligation can inhibit this avenue of metastatic spread,” says the lead author of the study article, Ashley S. Felix, PhD, MPH, researcher in the Hormonal and Reproductive Epidemiology Branch of the Division of Cancer Epidemiology and Genetics at the National Cancer Institute in Bethesda, Maryland.

In the Spotlight

Doctor Norman Wolmark Receives Lecture Award at 2015 San Antonio Breast Cancer Symposium

Norman Wolmark, MD, presented the William L. McGuire Memorial Lecture, “The Contribution of NSABP Clinical Trials to the Management of Early Breast Cancer,” on December 9, 2015, at the 38th Annual San Antonio Breast Cancer Symposium (SABCS). Dr. Wolmark was selected to present this year’s lecture by the SABCS Executive Committee and Program Planning Committee from nominations by distinguished researchers in the field of breast cancer. Established in 1992, the William L. McGuire Memorial Lectureship commemorates the significant contributions to oncology medicine of the late William L. McGuire, who co-founded the SABCS in 1977.
The role played by biospecimen banking in primary trials has expanded greatly over the last decade. In the past, biospecimens were accrued mainly to be used in spinoff translational research studies conducted after a primary trial had closed. The thrust of such continuing studies has changed to focus more on immunotherapies and targeted therapies. However, as Jordan states, “With biospecimens now being collected as part of the primary trial, it is more common to test tissue samples even before patients are enrolled in the trial, a practice that was nonexistent in the past.”

**Biospecimen Bank Accomplishments**

Jordan emphasizes the progress already made in harmonizing the procedures and data management across the three legacy biospecimen bank sites. “Establishing a unified inventory and tracking system—the STARS database—has been a significant achievement,” states Jordan. “We’ve learned that biospecimens without data regarding the patient, including demographics, condition, and genetics, are of limited value. The intimate connection between the tissue samples and the data about how the patient did on the trial is of utmost importance.”

Strategies for meeting the increased demand for biospecimen banking, especially given the 34% reduction in the NCI funding grant, include outsourcing some technical aspects of the testing procedures and using digital imaging to review biospecimens online. “Although the costs of obtaining biospecimens that are integral to randomization in the primary trial are paid by the cooperative group or through mechanisms like the Biomarker, Imaging and Quality Life Studies Funding Program (BIQSFP), the costs of obtaining biospecimens for translational research studies are increasingly falling on the backs of investigators or industry, with fees being harmonized across cancer cooperative groups,” states Jordan.

**Changes on the Horizon for Site Personnel**

Site research personnel enrolling patients on NRG Oncology trials can expect, in the short term, to be encouraged to batch ship patient tissue samples, and in the long term, to anticipate longer turnaround times for return requests, as the Biospecimen Banks are doing more with less. They will also be asked to provide more data associated with the biospecimens being submitted. “It is important for sites to submit the right data,” states DeVries. “The actual information, rather than an ‘unknown’ status, is now required on the transmittal forms.” In addition, Jordan sees a need to better integrate the data sent to the statistical centers with those submitted to the Biospecimen Bank, so that a two-way exchange of data is achieved. “It is in everyone’s best interests that biospecimen data be linked intimately with statistical data,” states Jordan. “This leads to better treatment for patients and better outcomes and results.”

Jordan points to a misconception on the part of pathologists that legal requirements prohibit them from sending tissue blocks to the Biospecimen Bank. “If the patient consents to the use of his or her biospecimens in the research, then it’s acceptable and legal for the pathologist to release them,” states Jordan. The use of a punch to take a biopsy of a tissue block has been helpful in resolving this issue.

**Expectations Down the Road**

Looking to the future, the NRG Oncology Biospecimen Bank expects to have standard operating procedures (SOPs) and protocol-specific instructions systematized across the legacy cooperative groups within the next 12 to 18 months. “Developing a handout for use during presentations to CRAs at NRG Oncology meetings has helped groups begin to process tissue samples in a uniform way,” states DeVries. “Monthly conference calls among the biospecimen bank leaders and among the bank operations managers have also enhanced information sharing.” “The most important reason for harmonizing SOPs,” states Jordan, “is to produce more consistent and reliable biospecimens for use in research studies. Investigators will know and be able to count on that what they’re receiving is the same across all the groups and that tissue samples are being submitted and retrieved in the same manner.” See sidebar for a list of the biospecimen facilities and leadership.

Site research personnel can obtain more information at https://www.nrgoncology.org/Nurses-CRAs.