Note From the Group Chairman

The first half of 2013 has been filled with many RTOG activities—foremost being the submission of the NRG Oncology grant application followed by the first meeting bringing together all three NRG Oncology legacy groups for the first time. Work continues towards conducting research as NRG Oncology and, for those attending the June Semiannual Meeting, Saturday’s Plenary Session will include updates about our progress. You also can keep up-to-date about NRG Oncology activities by visiting the group’s new Web site (www.NRGOncology.org) that displays group information and will continue to expand in the coming months.

RTOG’s science had a significant presence at the American Society of Clinical Oncology’s 2013 Annual Meeting, with 13 accepted abstracts. In particular, the selection of RTOG and GOG science for the ASCO plenary session presents an extremely positive outlook for NRG Oncology’s future research. In the past several weeks, we also have learned that RTOG research will be prominently featured at the American Society of Radiation Oncology Annual Meeting to be held this September in Atlanta, with at least 14 accepted abstracts, of which three will be part of the meeting’s plenary session. I congratulate our research teams on this extraordinary success!

I am also pleased to report that during this time of considerable change, site research teams continue to work hard on behalf of RTOG, as evidenced by the ongoing strong record of accrual. Study participant enrollment into CTEP-sponsored RTOG trials increased by 700 patients in 2012 compared with 2011 results, and overall accrual was up nearly 20%. Accrual results for the first half of 2013 are equally as impressive. The comments offered by RTOG investigators in this newsletter about successful accrual strategies provide insight into the group’s accrual success.

Finally, please join me in welcoming the new RTOG committee chairs—profiled herein and on the RTOG website; all of whom offer a strong vision for carrying out research as we transition to NRG Oncology.

RTOG Semiannual Meeting Highlights

Leading Genomics Experts to Present at RTOG Symposium

Presentations on the “Advances in Genomics for Cancer Clinical Trials” by an impressive roster of researchers are in store during the RTOG Symposium to be held on Friday, June 14 from 8:00 AM–11:00 AM. During the presentations, organized by RTOG Translational Research Program Vice Chair Adam Dicker, MD, PhD, a professor of radiation oncology and director of the Christine Baxter Research Laboratory for Experimental Cancer Therapies of Thomas Jefferson University in Philadelphia, leading experts in the field of precision oncology (the analysis of genetic changes in a patient’s tumor) will discuss how genomics technology will revolutionize cancer care.

Dr. Dicker emphasizes that the integration of genomics into our national and international clinical trials, and ultimately into clinical practice, remains to be fully understood. The symposium’s goal is to begin a focused dialogue about state-of-the-art sequencing technologies and the critical next steps for clinical research so as to effectively and expeditiously bridge the gap between the bench and the bedside.

For more information, go to: RTOG Symposium Agenda.

Scientific and Plenary Session Topics

Highlights of RTOG research results presented at the American Society of Clinical Oncology 2013 Annual Meeting will be featured at the RTOG Publications Scientific Session beginning at 1:00 on Saturday, June 15 to be followed by the Plenary Session with reports on RTOG and NRG Oncology progress, updates on NRG Oncology membership, and more insights about NRG Oncology’s research strategy.

For details, visit: Scientific and Plenary Agenda.

Mark Your Calendars!
The next NRG Oncology meeting is scheduled for:
February 6–9, 2014
Manchester Grand Hyatt
San Diego, CA

Visit www.RTOG.org for the latest group news
RTOG 0529 Results Show Patients With Anal Cancer Experience Fewer Acute Toxicities When Treated With Dose-Painted IMRT

The phase II trial results published in the International Journal of Radiation Oncology • Biology • Physics in May 2013 also highlight the importance of performing real-time quality assurance for trials of dose-painted intensity-modulated radiation therapy (DP-IMRT).

The vast majority of patients with non-metastatic anal cancer are successfully treated with RT with concurrent 5-fluorouracil (5-FU) and mitomycin-C (MMC); however, this standard treatment regimen often results in significant acute and long-term toxicities. The RTOG 0529 trial sought to determine if use of DP-IMRT with 5-FU and MMC would result in patients experiencing fewer gastrointestinal (GI) and genitourinary (GU) adverse events (AEs) as compared with AEs reported from the treatment arm (conventional RT with 5-FU and MMC) of the RTOG 9811 trial (A Phase III Randomized Study of 5-Fluorouracil, Mitomycin-C, and Radiotherapy Versus 5-Flourouracil, Cisplatin and Radiotherapy in Carcinoma of the Anal Canal). Fifty-two study participants were enrolled at 38 institutions between December 2006 and March 2008.

“From a patient standpoint, the toxicities from the combined-modality treatment of anal cancer are very significant,” says study Principal Investigator (PI) Lisa Kachnic, MD, chair of the Department of Radiation Oncology at Boston University School of Medicine. She points out that breaks in treatment are much more likely to accompany severe toxicities and have been shown to have a higher risk of cancer recurrence and subsequent colostomy. “We hypothesized with the use of IMRT we could reduce acute toxicity, decrease the rate of treatment breaks, and, in turn, improve patient quality of life while at least maintaining the same outcome as with treatment using conventional RT,” explains Kachnic.

The trial’s initial results showed that the 15% reduction in grade >2+ combined GI and GU AEs established as the trial’s primary end point was not met; however, RTOG 0529 study participants experienced significantly fewer grade 3+ dermatologic and GI AEs and grade 2+ hematologic events than study participants receiving conventional RT in the prior RTOG 9811 trial. Additionally, treatment breaks due to toxicity were needed for 49% of the participants in RTOG 0529 compared with 62% in RTOG 9811, with median treatment duration of 43 days compared with 49 days, respectively. “These results provide evidence—albeit in a phase II trial—that IMRT performed across institutions lessens toxicity and that the increased cost for this technology is associated with an increased benefit for the patient,” says Kachnic.

RTOG 0529 was the first RTOG study to conduct real-time quality assurance (QA). “The protocol team thought there was a need for education to insure that the pelvic volumetric structures were drawn correctly, which turned out to be correct,” says Kachnic, who with her team reviewed treatment plans for target dose prescription and normal tissue constraint compliance. The authors report, of the 52 DP-IMRT cases, 81% required pretreatment planning revision on initial submission—emphasizing the importance of real-time radiation QA for IMRT trials. “We provided an atlas early on, reviewed plans, and connected with site investigators about how they could improve. We then reviewed resubmissions so that they were perfect,” says Kachnic of the QA process.

Review is now underway of the patterns of failure and patient outcome. “The early clinical complete response is encouraging, but we need to look at our 2-year end points to validate this approach,” says Kachnic.

“There’s strong potential for IMRT with 5-FU and MMC to become the standard arm for future RTOG anal cancer trials and to become the future standard of care practice. I look forward to follow-up studies and publications.”

—Walter J. Curran, Jr., MD, RTOG Chairman and Executive Director, Winship Cancer Institute of Emory University, Atlanta
High-Profile RTOG Research Presented at ASCO

Participants at the American Society of Clinical Oncology (ASCO) 2013 Annual Meeting received updates on scientific questions investigated by RTOG-sponsored research involving advances in the science underlying radiation oncology. Among the 13 total RTOG invited presentations was a plenary session report of the highly anticipated primary aim results of RTOG 0825. Three additional oral presentations of RTOG 0825 analyses were also presented.

Bevacizumab for Initial GBM Treatment Found Not to Improve Patient Survival

RTOG 0825: A phase III double-blind placebo-controlled trial evaluating bevacizumab in patients with newly diagnosed glioblastoma was designed to test the primary hypothesis that “anti-angiogenic targeted therapies would normalize the tumor’s rapidly forming and underdeveloped blood vessels, resulting in improved oxygen and chemotherapy delivery to the tumor and potentially enhancing radiotherapy and chemotherapy treatment,” according to Mark Gilbert, MD, professor of neuro- oncology at The University of Texas MD Anderson Cancer Center in Houston, who led the trial.

Data analysis of 637 study participants found no statistical difference in overall survival (OS) between the experimental and standard study arms (16.1 months versus 15.7 months, respectively). Although there was a difference in progression-free survival (PFS) between the experimental and standard arms (10.7 months versus 7.3 months, respectively), the established level of benefit for PFS was not reached. In clarifying the relevant result, Gilbert states, “The upfront use of bevacizumab does not prolong survival. We now know that by administering bevacizumab later rather than earlier in treatment, you avoid the risk of toxicity, and that may be relevant.” Visit RTOG.org for the full press release.

Molecular Predictors of Outcome and Response

A secondary objective of the trial was to determine whether the tumor molecular profile would be associated with increased OS or PFS from the addition of bevacizumab. Toward that end, study participants were stratified equally across study arms by prognostic molecular markers of tumor O6-methylguanine–DNA methyltransferase (MGMT) methylation status and a tumor-based 9-gene assay. Erick P. Sulman, MD, PhD, from the University of Texas MD Anderson Cancer Center reported on the analysis of tests of verbal learning and memory, processing speed and executive function, and verbal fluency completed by participants at baseline and at weeks 10, 22, and 34. Mean test performance at baseline was equivalent between study arms, and there were no statistically significant between-arm differences in frequency of improvement through week 34. NCF test performances at baseline and from baseline to week 10 were prognostic for OS and PFS.

Neurocognitive Function Outcomes

Jeffrey S. Wefel, PhD, ABPP, from the University of Texas MD Anderson Cancer Center reported on the analysis of tests of verbal learning and memory, processing speed and executive function, and verbal fluency completed by participants at baseline and at weeks 10, 22, and 34. Mean test performance at baseline was equivalent between study arms, and there were no statistically significant between-arm differences in frequency of improvement through week 34. NCF test performances at baseline and from baseline to week 10 were prognostic for OS and PFS.

Patient-Reported Outcomes

Terri S. Armstrong, PhD, ANP-BC, from the University of Texas Health Science Center, and co-PI for the trial’s quality of life (QOL) component, presented the analysis on the impact of treatment on patient-reported outcomes (PROs) in the trial’s two arms. Analysis of QOL and brain tumor symptom questionnaires completed at baseline and at weeks 10, 22, and 34 by randomized participants with continued PFS revealed more deterioration in symptoms and QOL in the bevacizumab arm compared with the placebo arm, with persistent significant differences in treatment-associated symptoms. Questionnaire-identified symptoms occurring at baseline and from baseline to week 10 were prognostic for OS and PFS.

Fine-Tuning the RT Dose

RTOG 0617: A randomized phase III comparison of standard-dose vs. high-dose conformal chemoradiotherapy +/- cetuximab for stage III non-small cell lung cancer sought to identify the optimal RT dose for the treatment of advanced NSCLC. The trial randomized 464 patients with pathologically diagnosed unresectable stage IIIA or IIIB NSCLC to standard-dose (SD) (60 Gy) or high-dose (HD) (74 Gy) RT arms.

Median follow-up of the trial’s 419 evaluable patients was 17.2 months, with a median survival of 28.7 versus 19.5 months and 18-month overall survival rates of 66.9% versus 53.9% for the SD and HD arms, respectively. Local failure rates at 18 months similarly favored the SD arm. “In the setting of concurrent chemotherapy with daily radiation therapy for stage III lung cancer, these results definitively confirm that 60 gray is superior to 74 gray, with a clear detriment associated with the higher radiation dose,” concludes trial PI Jeffrey D. Bradley, MD, a professor in radiation oncology at Washington University School of Medicine in St. Louis, MO. Visit RTOG.org for the full press release.
Select Studies Offered Enhanced Case Payment Through CTEP Initiative

Select phase II studies will receive an additional $3,000 (over the $2,000 standard case reimbursement) per eligible study participant enrolled onto a trial for a total case reimbursement of $5,000. The additional funding is made available through a Cancer Therapy Evaluation Program (CTEP)-sponsored initiative for studies that met specific complexity requirements and has since closed to any additional trials.

Protocols included in the enhanced case payment initiative include:

- **RTOG 1106**, Randomized Phase II Trial of Individualized Adaptive Radiotherapy Using During-Treatment FDG-PET/CT and Modern Technology in Locally Advanced NSCLC
- **RTOG 1114**, Phase II Randomized Study of Rituximab, Methotrexate, Procarbazine, Vincristine, and Cytarabine With and Without Low-Dose Whole-Brain Radiotherapy for Primary CNS Lymphoma
- **RTOG 1119**, Phase II Randomized Study of Whole Brain Radiotherapy in Combination With Concurrent Lapatinib in Patients With Brain Metastasis From HER2-Positive Breast Cancer
- **RTOG 1122**, Phase II Double-Blinded Placebo-Controlled Study of Bevacizumab With or Without AMG 386 in Patients With Recurrent Glioblastoma or Gliosarcoma
- **RTOG 1205**, Randomized Phase II Trial of Concurrent Bevacizumab and Re-Irradiation Versus Bevacizumab Alone as Treatment for Recurrent Glioblastoma

Did You Know?

RTOG CCOP Announces Request for Proposal Opportunity

The RTOG Community Clinical Oncology Program (CCOP) is soliciting for project applications centered on pilot studies designed to lead to a phase II or phase III CCOP symptom management intervention trial or to CCOP studies that improve the understanding of the biological mechanism of RT-related symptoms. Funding can be requested for up to $75,000. Applications are due by July 15, 2013. For full details, see Request for Proposal.

Submit Applications by July 15, 2013 to:

Karan Boparai, BS, RT (R)(M)
Assistant Director, Clinical Trials Administration
kboparai@acr.org
Tel: 215-717-2758

NCI Revised Model Consent Template

The NCI has revised the NCI Model Informed Consent Template. Implementation began on May 15, 2013. RTOG has begun using the new template on all developing trials. To view the new NCI informed consent template, visit [http://ctep.cancer.gov](http://ctep.cancer.gov), click on the “Protocol Development” tab, and select “Informed Consent” from the drop-down menu.

Submission of Digital Data in DICOM (RT) Format Required

DICOM (Digital Imaging and COmmunication in Medicine) format has been widely adopted in the medical field with DICOM (RT) adopted by radiation oncology. The DICOM (RT) standard ensures interoperability between digital data processing programs.

Starting July 1, 2013, all digital RT data submission will require DICOM (RT) format. At that time, the RTOG format will no longer be accepted or supported. For questions, please contact:

Tammy McGlade | RTQA Data Assistant & Credentialing | (215) 574-3219 | tmcglade@acr.org

Visit the NRG Oncology Web site

The Web site now offers the latest news on NRG Oncology research plans, upcoming meetings, membership, and more.

www.nrgoncology.org
Introducing New RTOG Leadership

RTOG is pleased to welcome the following investigators as they assume new group leadership roles.

David Raben, MD, Establishes RTOG Developmental Therapeutics Committee

David Raben, MD, a professor of radiation oncology at the University of Colorado Cancer Center in Aurora has been appointed the chair of the newly established RTOG Developmental Therapeutics Committee (DTC). Known for his work in prostate, lung, and head and neck cancer research, Dr. Raben has special enthusiasm for the latter, evidenced by his active role as an RTOG Head and Neck Cancer Committee member, a previous PI of an RTOG head and neck cancer trial, and, most recently, as a co-author of an oral abstract presented at the American Association of Clinical Oncology 2013 Annual Meeting (p16 expression as a human papillomavirus [HPV]-independent prognostic biomarker of non- oropharyngeal squamous cell carcinoma). Additionally, he is the PI of an investigator-initiated clinical trial combining a PARP inhibitor with cetuximab and IMRT for heavy smoker patients with locally advanced head and neck cancer, as well as a strong promoter of the University of Colorado Cancer Center’s active participation in RTOG clinical trials.

Dr. Raben stresses the importance of interaction with a wide variety of stakeholders as a key component for the DTC’s success. “It really comes down to building relationships with NCI-affiliated investigators, industry collaborators, members of the Translational Science Committee, liaisons from the disease site committees, and biostatisticians, among others. I look forward to devising a committee structure that actively promotes communication to ensure that we move the science forward quickly and effectively,” says Raben. Visit RTOG.org to read the full announcement.

Doctors Xiao and Fox Lead the RTOG Medical Physics Committee

Physicists Ying Xiao, PhD, FAAPM, and Tim Fox, PhD, offer in-depth and unique expertise for guiding the Medical Physics Committee’s integration into NRG Oncology and undertaking the challenges associated with RT’s advancing technologies.

Dr. Xiao, whose research interests include optimization of IMRT treatment planning, image-guided RT (IGRT), and RT quality assurance, is excited about the expanded medical physics research opportunities of two future initiatives: (1) NRG Oncology’s Center for Innovation in Radiation Oncology (CIRO), designed to accelerate the development and testing of innovative advanced radiation oncology technology across the entire National Clinical Trials Network (NCTN), and (2) the Imaging and Radiation Oncology Core (IROC) Group, established to manage imaging and RT quality assurance for the NCTN.

Dr. Xiao also emphasizes the exceptional potential the future holds for collecting expansive RT data with the new systems envisioned for CIRO and IROC—a topic of particular interest to Fox, director of medical physics and associate professor for the Department of Radiation Oncology at Emory University School of Medicine in Atlanta. “To me, data are the new currency in health care, and clinical trials have a tremendous amount of value by being able to collect multi-institutional data,” says Fox, whose strong information technology background has led to a research focus on data integration. “There’s so much technology being used in radiation therapy—both for planning and delivery—and it is important that we collect technical data and have the capability to integrate, for example, diagnostic imaging and RT treatment data, so that investigators have a complete picture of how to create a more successful outcome for our patients,” he explains. Visit RTOG.org to read the full announcement.

Dr. John A. Ridge Appointed RTOG Surgical Oncology Committee Chair

John A. “Drew” Ridge, MD, PhD, FACS, chief of head and neck surgery at Fox Chase Cancer Center in Philadelphia, PA, is the new chair of the RTOG Surgical Oncology Committee. Ridge, who also serves on RTOG’s Head and Neck Cancer Committee, has been enrolling patients onto RTOG trials for many years and considers his RTOG involvement to be an important element of his rewarding academic career. Although Ridge’s research specialization is head and neck cancer, he notes that his general surgical oncology background and experience allow him to place things within the context of other cancer disease sites.

Continued
Ridge is motivated to assume the chair’s role by his ardent belief in the role of clinical trials to improve patient care and his keen interest in trial design. “It’s what I do,” says Ridge, “and I have enthusiasm about NRG Oncology’s potential for producing tremendous advances in clinical research.” He also reflects that this is a particularly exciting time to be involved in clinical research as the field brings greater computing power to bear for surgical robotics, advances in radiotherapy, and new targeted therapies—all with significant potential to extend patients’ lives and limit treatment morbidity. Visit RTOG.org to read the full announcement.

Kathryn Yeager to Lead Special Populations Committee
Kate Yeager, RN, PhD, brings broad insight to her new role as chair of the RTOG Special Populations Committee. She understands intimately the day-to-day challenges of enrolling patients onto clinical trials, having worked for 15 years as a clinical research project manager. Most recently, through her doctoral studies, she’s gained extensive insight about the systemic causes of health disparities—many, which directly impact clinical trial participation. “As an oncology nurse, I was certainly cognizant of disparities among my patients. However, when delving into this topic, I found the extent of disparities in our country dismaying,” says Yeager, “with the impact of cancer incidence, survival, and the overall burden of cancer being significantly different among underserved populations.”

A research assistant professor at Emory University in Atlanta, Yeager is engaged in research on symptom management with an emphasis on pain management and a focus on underserved communities. Most recently, she submitted a grant for an investigation exploring how African Americans manage pain and take pain medication when they have advanced cancer.

With regard to the future direction of the Special Populations Committee, Yeager points out the different levels of opportunities that potentially can be pursued—from supporting site research teams with tools to aid recruitment of special populations to analyzing patterns of patient enrollment across RTOG institutions. Visit RTOG.org to read the full announcement.

Marka Crittenden, MD, PhD, to Co-Lead Translational Research Program’s Immunomodulation Subcommittee
Radiation oncologist Marka Crittenden, MD, PhD, director of translational radiation research at the Earle A. Chiles Research Institute of Providence Cancer Center in Portland, OR, joins James Hodge, PhD, MBA, as a liaison of the RTOG Translational Research Program’s (TRP’s) Immunomodulation Subcommittee. Hodge held the subcommittee’s inaugural meeting at the June 2012 RTOG Semiannual Meeting. Crittenden and Hodge will work together to carry out the subcommittee’s goals to contribute to the design and analysis of prospective clinical trials incorporating immunotherapy with radiation across disease sites and to carry out retrospective analyses of archival biopsies to focus on immune correlates of antitumor activity. “Dr. Crittenden brings significant research and authorship experience to this role,” says RTOG TRP Chair Adam Dicker, MD, PhD, professor and chair of the Department of Radiation Oncology at Thomas Jefferson University in Philadelphia. “I’m extremely enthusiastic about her and Dr. Hodge’s combined and complementary expertise, high energy, and results-oriented leadership for guiding this important research area.”

Recognition of Past Leadership
RTOG gratefully recognizes the following individuals for their past contribution as committee leaders.

Peter W. T. Pisters, MD, FACS
Chair, Surgical Oncology Committee
Michael T. Gillin, PhD, FAAPM, FACMP, FACR, FASTRO
Co-Chair, Medical Physics Committee
James M. Galvin, DSc
Co-Chair, Medical Physics Committee
Dwight E. Heron, MD
Chair, Special Populations Committee
Mary Lou Smith
Co-Chair, Patient Advocacy Committee

“Volunteerism is at the core of what makes a cooperative research group work. On behalf of the RTOG, I extend a sincere thank you to these individuals for their role in advancing RTOG’s research.”

-Walter J. Curran, Jr., MD
Research Participation Invigorates Private Practice Radiation Oncologists

RTOG site PIs Christopher U. Jones, MD, FACR, (Radiological Associates of Sacramento [RAS]), and Adam Raben, MD (Christiana Care Health System), are champions of clinical research participation within their respective private practices and health care networks. An article published in the June 2013 issue of the ACR Bulletin features a discussion with Jones and Raben about their motivations for active involvement in RTOG research. The following are excerpts of the article, which can be read in its entirety in the June issue of the ACR Bulletin.

With a team of 15 physicians and five clinical research staff, RAS has 21 trials open and 860 patients in follow-up as a result of its affiliation with RTOG. Jones reports benefits of the group’s clinical research participation have included the opportunity to keep up-to-date on practice standards for the numerous types of cancer and disease sites, as well as on the appropriate implementation of technological advances for delivering RT, particularly IGRT, IMRT, and brachytherapy. “Carrying out trials has been especially helpful in determining when and how to use any new technology we acquire,” says Jones. “The prestige of maintaining the updated standards required for research participation also assures the hospitals in which we practice of high-quality care.”

Regarding his personal motivation to assume RTOG leadership responsibilities, Jones notes, “Making even a small contribution to the advancement of clinical oncological medical care by offering cutting-edge treatment and helping the field move to the next standard of care is satisfying.” Attending RTOG meetings helps Jones keep current in his specialty of head and neck cancer—a field in which the advanced scientific questions outnumber the patients available for study enrollment. “It’s exhilarating to talk with colleagues specializing in different areas and to hear their thought processes about cancer management,” he adds. “It keeps the field fresh and fun for me.”

Adam Raben, MD, credits his practice’s leadership roles in cooperative group, including RTOG, clinical research, with laying the groundwork for more cohesive interaction among the disciplines at Christiana’s Helen F. Graham Cancer Center. “Over the last decade, our cancer center has moved from performing assembly line oncology to a multidisciplinary approach that fully integrates nursing staff into the process,” elaborates Raben. “We are currently the second-highest–accruing CCOP member in the United States and the highest-accruing single institution.”

Karen Sites, BSN, RN, OCN, nurse coordinator, and RTOG research associate at Christiana, believes the center’s enrollment success is related to the research department being embedded in the radiation department office space. “We are accessible to inform the physicians, nurses, and dosimeter therapists of potential research patients as well as to complete enrollment and follow patients throughout treatment,” notes Sites. “Research is a high priority, and the buy-in of everyone involved is important.”

Raben expresses concern about the lag time between the publishing of a landmark radiation oncology trial’s results and their adoption into clinical practice. “Governmental and private insurers may be unaware that physicians are still using or offering patients treatment modalities and regimens that have been proven ineffective. Our practice is committed to quickly carrying out new standards of care,” Raben says. “It comes down to whether you’re advancing cancer management or not, and we wanted to be part of the RTOG research mission that is committed to enhancing and improving patient outcomes.”

“People in the News”

Adam Raben, MD, and Karen Sites, BSN, RN, OCN

Christopher U. Jones, MD, FACR

“The prestige of maintaining the updated standards required for research participation also assures the hospitals in which we practice of high-quality care.”

— Christopher U. Jones, MD, FACR, Radiological Associates of Sacramento

“It comes down to whether you’re advancing cancer management or not, and we wanted to be part of the RTOG research mission that is committed to enhancing and improving patient outcomes.”

— Adam Raben, MD, Christiana Care Health System
**Trial Updates**

**RTOG 1201 Soon to Activate**
Be sure to watch for the announcement of group activation for RTOG 1201: A Phase II Randomized Trial of High vs. Standard Intensity Local or Systemic Therapy for Unresectable Pancreatic Cancer.

**Overview**
Pancreatic cancer is a common and lethal disease, with most cases presenting as either locally advanced or metastatic disease not treatable with resection. The RTOG 1201 trial seeks to determine if intensifying local therapy or systematic therapy can extend the survival of patients diagnosed with unresectable pancreatic cancer. Specifically, the trial will evaluate whether (1) high-dose (63.0 Gy) radiotherapy using IMRT and standard chemotherapy or (2) FOLFIRINOX chemotherapy—not previously tested in nonmetastatic, unresectable pancreatic cancer—can improve local control and survival.

Recent data suggest that pancreatic cancers encompass distinct genetic subtypes that result in different patterns of treatment failure and causes of death. In particular, several small studies suggest that the loss of SMAD4 immunolabeling was highly correlated with death due to pancreatic cancer metastasis while intact SMAD4 was highly correlated with a locally destructive phenotype. To test whether SMAD4 status might serve as a biomarker to guide therapy in future trials, RTOG 1201 investigators will conduct subgroup analyses to determine if intensified systemic therapy improved survival in patients with SMAD4-lost and intensified radiochemotherapy improved survival in patients with SMAD4-intact status.

Further advances in unresectable pancreatic cancer will require an improved understanding of tumor biology. The investigations to be carried out in this trial will provide the data required to determine if SMAD4 status could be used to drive treatment allocation in future trials and, if so, will provide a more robust assessment of this biomarker’s performance characteristics within the collaborative group setting.

**Patient Population**: patients with histopathological or cytological diagnosis of adenocarcinoma of the pancreas; tumor diameter ≤7 cm, unresectable by radiographic criteria (pancreas protocol CT or MRI) or exploration, no distant metastases

**Target Accrual**: 288 study participants

**Objectives**

**Primary**
- To determine if intensified radiochemotherapy in patients with unresectable pancreatic cancer will show a signal for improved 2-year OS from 10% to 22.5%
- To determine if intensified systemic therapy in patients with unresectable pancreatic cancer will show a signal for improved 2-year OS from 10% to 22.5%

**Secondary**
- To evaluate patterns of failure (local and systemic progression) by SMAD4 status and intensity of therapy
- To evaluate the impact of intensified radiotherapy on OS for the subset of SMAD4-intact patients
- To evaluate the impact of intensified chemotherapy on OS for the subset of SMAD4-lost patients
- To evaluate adverse events associated with the treatments
- To evaluate the correlation between SMAD4 status determined by immunohistochemistry and genetic SMAD4 status

**Trial Schema**

RTOG 1201 investigators will conduct a subgroup analyses to determine if intensified systemic therapy improved survival in patients with SMAD4-lost and intensified radiochemotherapy improved survival in patients with SMAD4-intact status.
Strategies of Top Accruing RTOG Sites

Investigators and research associates at top performing sites for the enrollment of study participants onto particularly challenging RTOG clinical trials were asked to provide insight about their strategies for success. Themes of constant communication and teamwork across specialties resonate throughout the responses presented below. Thank you to the individuals who took the time to share their thoughts and experiences with the RTOG Newsletter readership.

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RTOG 0839—A Randomized Phase II Study of Pre-Operative Chemoradiotherapy +/- Panitumumab Followed by Consolidation Chemotherapy in Potentially Operable Locally Advanced Non-Small Cell Lung Cancer

All the specialists involved in conducting this tri-modality trial must believe in the role of surgery following pre-operative chemoradiotherapy for the target patient population, which is the case here at Jefferson. Our thoracic surgeons are very supportive of the trial and, in fact, surgeon Nathaniel Evans, MD, is the RTOG 0839 institutional principal investigator for the trial supported by his surgical colleague Scott Cowan, MD.

Having a multidisciplinary team approach in place to identify potential study participants is another key aspect of successful accrual. We have an extremely collegial atmosphere at Jefferson with a multidisciplinary thoracic clinic and conference that has been in existence for 18 years. Every week the thoracic surgeons, medical oncologists, radiation oncologists, pulmonologists and others meet to discuss all new patients and which trials might be appropriate.

MARIA WERNER-WASKIK, MD
Radiation Oncologist
Thomas Jefferson University Hospital

•••

RTOG 1115—A Phase III Trial of Dose Escalated Radiation Therapy and Standard Androgen Deprivation Therapy (ADT) with a GnRH Agonist vs. Dose Escalated Radiation Therapy and Enhanced ADT with a GnRH Agonist and TAK-700 for Men with High Risk Prostate Cancer

We have not found it difficult to enroll patients due to our positive working relationship with referring physicians. They are equally interested to learn if this new drug can help improve outcomes in this patient population that currently experiences a 40% to 60% treatment failure rate. My day-to-day routine provides opportunities to have an ongoing dialogue with the urologists and medical oncologists about the trial and to keep it top-of-mind for them.

UCSF’s multi-disciplinary approach to care provides opportunities to remind clinicians about the trial. Discussions with urologists and medical oncologists have even led to the prospect of establishing a special clinic for patients at high risk for prostate cancer recurrence. I take extra time to walk patients through the consent form and have found them very receptive to trial participation—both for the opportunity to potentially receive a drug that could better treat their cancer and to advance care for future patients.

ALBERT CHANG, MD, PhD
Radiation Oncologist
University of California San Francisco

The RTOG 0631 Research Team at the University of Utah Health Science Center.

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RTOG 0631—A Phase II/III Study of Image-Guided Radiosurgery/SBRT for Localized Spine Metastasis—RTOG CCOP Study

Vertebral metastases are a very common cancer complication, and most patients present with back pain or have neurologic symptoms. Rapid and durable symptom control is important to improve patients’ quality of life and function recovery.

Our group has participated in RTOG 0631 since it opened as a phase II study, and our faculty fully supports the trial. During the weekly chart rounds, we try to keep in mind identifying eligible patients. We also have monthly RTOG study review, a brief presentation lead by our faculty, to discuss and remind the group of study criteria and enrollment status. All faculty physicians are participating in RTOG 0631 and our medical physicists have provided strong technical and quality assurance support. We will continue to contribute our effect and hope image-guided radiosurgery/SBRT will demonstrate improved pain control with a rapid and durable result for patients with spine metastases.

YING HITCHCOCK, MD
Radiation Oncologist
University of Utah Health Science Center

Continued
We believe evidence is needed to determine the best treatment for patients with spine metastases [image-guided radiosurgery/SBRT in a single fraction dose of 16 or 18 Gy vs. conventional external beam radiotherapy (EBRT) in a single dose of 8 Gy]. Therefore, we are committed to the trial and use the following approach to identify and enroll potential study participants:

- Screen every patient with bone metastasis for eligibility
- Request referring physicians help document the pain scale
- Pay close attention to the revised eligibility criteria that allows multiple small metastatic lesions when these are <20% of the volume of the vertebral body
- Remain cognizant that radioresistant tumors are allowed.
- Discuss with patients the role of palliative EBRT for pain management and introduce the RTOG 0631 study to those who are interested, including the key points:
  - Randomization to the experimental arm is twice as high as to the conventional arm
  - EBRT also uses highly advanced technology
  - “Cross-over” treatment is possible if pain recurs
  - Pain, clinical status, and quality of life are closely monitored
  - The patient’s time and careful consideration of study participation is appreciated.

ELEANOR WALKER, MD
Radiation Oncologist
Henry Ford Hospital

RTOG 1119—A Phase II Randomized Study of Whole Brain Radiotherapy in Combination With Concurrent Lapatinib in Patients With Brain Metastasis From HER2-Positive Breast Cancer: A Collaborative Study of RTOG and Korean Radiation Oncology Group (KROG)

Before opening the trial I presented it several times to my breast medical oncology colleagues at breast tumor board. I have also mentioned it almost every time a breast cancer patient has been found to have brain metastases. Since this trial is only available to patients with HER-amplified disease, I try to emphasize to my colleagues: “if they had HER-amplified disease they would have been eligible for the RTOG trial.” I think this helps raise awareness and is a contributing factor to Washington University becoming a top accrual site for this trial.

IMRAN ZOBERI, MD
Radiation Oncologist
Washington University

I also presented the trial to the medical oncology breast team. We discussed the eligibility criteria and the highlights of the trial. The doctors and residents have done a great job identifying patients for us in a timely fashion. This has provided me with enough time to register the patients on trial.

PAM SLOAN
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