In this second issue of the ECOG-ACRIN Newsletter, we broach a major topic in cancer research: which is more important, prevention or cure? Long viewed as a hypothetical question, to be deliberated over in an armchair, coffee shop, or bar, the answer may not have much mattered, since not much of the nation’s resources were going to either. We are in a different world: research dollars for cancer are now close to six billion from US government sources alone; however, while over 50 cents of every dollar goes toward understanding cancer biology and cancer treatment, only 2 cents are available for prevention.

This issue was highlighted at a recent meeting in Santa Monica by Dr. David Crosby, of Cancer Research UK, who pointed out that the imbalance is even greater in pharmaceutical industry spending. There seems little incentive to develop drugs to prevent cancer. Some of this is justified by the response to prior efforts to define useful interventions. The seminal studies of the late Dr. Waun Ki Hong of MD Anderson showed that cis-retinoic acid could prevent second primaries in head and neck cancer, yet the uptake on the part of head and neck specialists and patients has been sparse. Similarly, the evidence that antiestrogens can protect women from breast cancer has been met with low interest. This might be seen as disappointing in light of the resources required to perform these trials in some 90,000 women, but in both cases the response of the patients is understandable: the agents can have side effects, often with an impact on quality of life.

Clearly in the area of chemoprevention, we need less toxic interventions, and better characterization of the patients at risk, such that the incremental benefit could be maximized. Further, interventions such as nutritional strategies (can that field ever be wrested back from charlatans?!), exercise, weight control, and other behavioral modifications may have even greater population effects. But, just as early cancers are more amenable to treatment than more advanced versions, a complementary approach focuses on early detection and intervention.

Led by Drs. Barry Kramer (recently retired) and Worta McCaskill-Stevens at the NCI's Division of Cancer Prevention, several large-scale trials aimed at early detection of cancer have been developed. We will discuss in a future issue some of the trials in people at risk for specific cancer types, but our focus today is on breast cancer detection, and the TMIST trial of mammography that is our major commitment in this arena. “Nearly 50 million screening mammograms occur each year in the United States, yet it has been decades since a large-scale randomized trial of mammography has been done,” said Dr. McCaskill-Stevens. “The evolution of mammography technology provides us with an opportunity to fill in the gaps in our knowledge about two available breast cancer screening tests.” There is an opportunity to add more sites to accrue this trial, and resources are available to assist in its implementation locally.

In another section of this issue, we introduce a member institution, and highlight some of the investigators and research staff who together define the institution’s contribution to EA. This section of the newsletter will be a regular feature, so we urge you to self-nominate, send pictures, bios, and anecdotes, and we will respond! One of the newest members of EA is the University of Texas Southwestern, or UTSW, the most important academic institution in Dallas, and a basic and translational science powerhouse. The PI for UTSW is Dr. David Gerber, a leader in the Thoracic Committee and someone with broad interests in medicine. The Cancer Center Director, Dr. Carlos Arteaga, is a translational scientist in breast cancer, who has been a co-investigator with us on the MATCH trial, and an enthusiastic supporter of collaborative translational research. Take a look at how they are thinking about how we actually do this research! We are delighted to recognize and applaud the contributions of UTSW to EA, and their continued success.
LANDMARK TMIST BREAST CANCER SCREENING TRIAL TO INFORM SCREENING POLICY
A CONVERSATION WITH STUDY CHAIR ETTA D. PISCANO, MD

The Tomosynthesis Mammographic Imaging Screening Trial (TMIST) is the first randomized controlled trial to compare two types of digital mammography for breast cancer screening, digital breast tomosynthesis (DBT), or 3D mammography, and conventional (2D) mammography. The 165,000 planned participants will help researchers identify women for whom DBT may outperform 2D mammography in reducing advanced breast cancer development. TMIST is currently enrolling healthy women ages 45 to 74 at 58 sites throughout North America and more sites are welcome. The study was developed by ECOG-ACRIN and the NCI, and is recruiting patients through both the National Clinical Trials Network (NCTN) and the National Community Oncology Research Program (NCORP).

TMIST is led by Etta D. Pisano, MD, of Beth Israel Deaconess Medical Center, Harvard Medical School, and the American College of Radiology. Learn more from our Q&A with her below, or visit ACR.org/TMIST.

Can you provide some background on the TMIST trial?

TMIST is really a study about screening, not about the technologies per se. There hasn't been a big screening trial since the 1980s and a lot has changed since then. The technologies have improved, and we are finding abnormalities much smaller, and earlier. Chemotherapy has improved, and so has our understanding of the different kinds of breast cancer. There is a lot more nuance to the diagnosis of breast cancer than there once was.

Now, people are asking questions like, "Does very early detection actually benefit women or are we just pushing back the diagnosis?" I believe there is a benefit to finding things as early as possible, because that often means less aggressive surgery or treatment. The real question is: Can we state with certainty that tomosynthesis improves patient care? We need to provide evidence that the more refined technologies actually do improve a woman's probability of living longer.

What do you hope the study's impact will be?

The other piece of this trial that's really important, and will be integral in terms of changing screening, is that we are collecting blood and buccal smears for as many patients as we can. We will study the genomes of these patients, their demographic information, and pathology specimens – both benign and malignant. With all that information, we'll be able to create models for how breast cancer screening should be accomplished with newer tools. In other words, we're heading toward more individualized screening strategies for breast cancer. That's something we haven't studied well up until now. We have individualized therapies for breast cancer; we need to develop individualized screening strategies, too.

What are some challenges TMIST has faced and how have they been addressed?

We would like to have had more rapid site activation and recruitment, such that accrual is going more slowly than we'd hoped. We have learned that women are enthusiastic about participating, and we are working tirelessly to make the study available as broadly as possible.

That's something we're focusing on right now. If you're reading this and want to participate we'd love to have you. Don't wait to hear from us – get in touch at TMIST@acr.org, or visit ACR.org/TMIST.
LANDMARK TMIST BREAST CANCER SCREENING TRIAL TO INFORM SCREENING POLICY (CONT'D)

We've also learned some of the sites are only putting a part-time research associate on the study; that has to change. The volume that needs to be recruited at each site is so great, it really requires a full-time RA. We're working with sites to address this issue. The study easily pays for itself if recruitment is up to the right level.

What would you say to a site that's considering taking part in TMIST about why they should join the study?

Participating sites are all really interested in answering the basic questions we're raising in this study. The sites, and the women, want to help develop the next screening strategy. Right now, we have one-size-fits-all screening, based primarily on age. Everybody goes through the same procedure regardless of how low risk they are. That's extremely costly and inefficient.

There are other reasons to join as well. Sites that serve large numbers of uninsured women can benefit because we have a fund to reimburse those women for mammograms, potentially at a greater level than other sources of charity reimbursement. Additionally, this trial is well-funded by the NCI. Sites that want to participate can easily afford to do so, and will be compensated for their work.

What will the results of this trial mean for patient care?

When we devised our current screening strategies we didn't have the genetic information we have now. We couldn't sequence people's genomes, and the way we looked at breast cancer was much less sophisticated. So much basic science has occurred since we last had a screening trial. The revolution in our understanding of the molecular biology of breast cancer and genetics needs to be applied to our screening strategies.

"Wouldn't it be better if we could adapt based on all this new knowledge and provide individualized [screening] recommendations?"

We could keep things the same for the next 50 years and women would benefit from screening, but wouldn't it be better if we could adapt based on all this new knowledge and provide individualized recommendations? Women with lower risk could get screened less frequently and women with higher risk more intensively. We could develop a tool that allows us to tell individual women, “Given your risk factors, your particular circumstances, and your genetics, here is what we recommend.” Doctors will have better, more comprehensive information to advise patients as to what they, as individuals, will need. Improving breast cancer screening in this way is an important scientific and public health goal.

TMIST RECRUITMENT AND RETENTION RESOURCES

A variety of materials are available to help support recruitment and retention efforts at TMIST sites, including:

- Clinic Poster
- Letter to a Woman Scheduled for a Mammogram
- Participant Recruitment Email Template
- Phone Script
- Reminder Card
- Thank You Card

All materials are Central Institutional Review Board (CIRB)-approved, and can be downloaded from the Clinical Trials Support Unit website.
With 6 Nobel laureates and 22 members of the National Academy of Sciences, the University of Texas Southwestern Medical Center in Dallas has a longstanding history of excellence in the basic sciences. Over the past two decades, UT Southwestern and its Harold C. Simmons Comprehensive Cancer Center have also made major advances in, and contributions to, clinical investigation. In addition to enrolling an increasing number of patients on National Clinical Trials Network (NCTN) studies, faculty at UT Southwestern have systematically examined factors that influence clinical trial accrual. A recent analysis demonstrating ongoing increase in the number and complexity of eligibility criteria and study procedures in ECOG-ACRIN thoracic trials was featured in the Washington Post, evidence that these issues are concerning not only to clinicians and investigators, but also to patients, their families, and the general public. A series of publications examining prior cancer diagnosis-related exclusion criteria in thoracic trials found that the practice was widespread (>80% of EA thoracic trials), resulting in exclusion of more than 15% of otherwise eligible patients, and may not be justified. This work, covered in the New York Times, eventually resulted in modification of these exclusion criteria in EA and other lung cancer trials globally.

Beyond trial design, UT Southwestern researchers have also investigated the trial consent process, finding that a consenter’s protocol-specific experience had a major effect on patient interest in clinical research.

Another major area of interest in the Simmons Comprehensive Cancer Center is underrepresented minority access to cancer clinical trials. While many cancer centers have reduced clinical research activity in public hospitals, at Parkland Health and Hospital System—the safety-net medical provider for Dallas County—Simmons investigators are enrolling an increasing number of patients on an increasing number of EA and other cooperative group clinical trials through the NCTN, with 21% African American and 15% Hispanic enrollment on adult cooperative group trials in 2018. As part of this effort, Simmons faculty have studied trial availability in safety-net settings, finding that industry sponsors are decreasingly likely to support protocol activation at these satellite sites, rendering NCTN trials critical to bringing trial opportunities to these underserved populations. To extend these findings, Simmons Cancer Research Office (CRO) leadership and faculty have partnered with the LIVESTRONG Cancer Institute on a project to bridge the gaps between cancer patients and clinical trials, and have worked with Sustainable Healthy Communities to identify notable practices facilitating racial and ethnic minority group participation in cancer clinical trials.

Looking beyond trial eligibility and enrollment on-study activities, Simmons investigators have partnered with scientists from Purdue University to study the interface and interactions between clinical research personnel and clinic staff. Because clinical research represents a highly dynamic entity—with studies frequently opening, closing, and undergoing modifications—concerted efforts of multiple teams are needed to respond to these changes while continuing to provide consistent, high-level care and timely, accurate clinical data. Through surveys of more than 100 staff, the investigators identified and characterized challenges faced by clinical research teams including: alignment of goals, communication, rivalries among teams, lack of cooperation and cohesion, and more. To address these issues, Simmons CRO staff now shadow clinic staff as part of the onboarding process, and infusion nurses attend tailored clinical research staff training. Early feedback from both CRO and clinic personnel suggests that these efforts have improved mutual understanding, communication, and collaboration.

**CLINICAL TRIAL LEADERSHIP AT UTSW**

Left to right: Carlos Arteaga, MD, Director, Simmons Comprehensive Cancer Center & Associate Dean, Oncology Programs at UTSW Medical Center; Shalaan Beg, MD, Assistant Professor of Hematology/Medical Oncology & Medical Director, Clinical Research Office; Erin Williams, MBA, Associate Director, Clinical Research Operations
NEWS IN BRIEF
Is something new or noteworthy happening at your institution? Send your updates to support@ecog-acrin.org and we will do our best to include them in an upcoming issue.

INTRODUCING EA’S NEW DIRECTOR, AUDIT AND QUALITY CONTROL

Joshua Schoppe, MPH, CCRP is now serving as Director, Audit and Quality Control at ECOG-ACRIN. With over 15 years of experience in clinical research, most recently at the Sidney Kimmel Cancer Center at Thomas Jefferson University Hospital, Josh is dedicated to ensuring quality and excellence in clinical research.

At Jefferson, Josh oversaw initiatives to improve the management of research conducted within the Sidney Kimmel Cancer Network. As a clinical research champion, he worked to expand clinical trial access to community partners throughout the Delaware Valley. He also managed an educational program promoting quality assurance and professional development for clinical research staff. Prior to joining ECOG-ACRIN, Josh was involved with the Group as both Chair of the Clinical Research Associates Core Committee and a member of the Audit Committee.

"Josh is a great addition to the EA leadership team and brings site experience to inform discussions," said Donna Marinucci, BSMT, Executive Director of ECOG-ACRIN. "I recently asked him to represent EA at the ASCO Research Community Forum Stakeholder Meeting in December of 2018."

MEMBERSHIP AND USE

As of March 1, 2019, all US sites, hospitals, clinics, and institutions that wish to participate in the National Cancer Institute’s NCTN and NCORP clinical trials MUST BECOME A MEMBER OF THE CIRB. On this date, sites that are not CIRB members will be put in a “Suspended” status on the NCTN and NCORP membership rosters and will not be able to enroll new patients to NCTN and NCORP trials. If a site is otherwise in good standing and becomes a CIRB member, the site status will return to "Active" and the site may begin enrolling patients again.

All NCTN and NCORP trials activated on or after March 1, 2019 will be reviewed by the CIRB. For NCTN and NCORP trials that have an activation date on or after March 1, 2019, sites must open the trials using the CIRB as the IRB of record. Use of a local IRB as the IRB of record for these trials will not be allowed. However, sites will not be required to transition CIRB studies approved using a local IRB as the IRB of record that were activated at the site prior to March 1, 2019.

If your site has any questions please contact us at EA_CIRB_HELP@ecog-acrin.org.

SAVE THE DATE: ECOG-ACRIN SPRING GROUP MEETING IS MAY 2 – 4 IN BOSTON

Mark your calendar for the ECOG-ACRIN Spring Group Meeting, May 2 – 4 at the Boston Marriott Copley Place in Boston, Massachusetts. Connect with colleagues and learn the latest in basic, clinical, and translational research. Visit the meeting website for preliminary details: bit.ly/EA_Spring2019 or watch for an email from the Group Meeting Planners when registration opens in mid-March. Upon registering, a confirmation email will be sent with a link to reserve your hotel room online. Rooms can also be reserved over the phone at (800) 228-9290. Be sure to request the ECOG-ACRIN room block.

For those planning further ahead, the Fall Group Meeting will take place October 24 – 26 at the Marriott Harbor Beach Hotel in Fort Lauderdale, Florida. Questions? Contact the Group Meeting Planners at gmp@ecog-acrin.org or (215) 399-0440.

REMINDER: DEADLINE APPROACHING FOR EA YOUNG INVESTIGATOR AWARD NOMINATIONS, PAUL CARBONE, MD FELLOWSHIP APPLICATIONS

All nominations for the ECOG-ACRIN Young Investigator Award, as well as applications for the Paul Carbone, MD Fellowship Award, must be submitted by Friday, March 1, 2019. The Young Investigator Award is a professional honor that aims to recognize scientific achievements made by investigators during the early years of their careers; the Paul Carbone, MD Fellowship Award is a research grant that aims to develop and promote excellence in clinical trials leading to improvements in cancer care. Learn more at ecog-acrin.org/research-support/mentorship

IMPLICATIONS OF THE NEW REQUIREMENTS FOR CENTRAL INSTITUTIONAL REVIEW BOARD (CIRB)