With this issue, we salute the end of a busy year. We can reflect on some remarkable progress, the most striking being the ramp-up of the Tomosynthesis Mammographic Imaging Screening Trial (TMIST/EA1151) to a level of recruitment unprecedented in oncology trials. In 2019, the number of patients enrolled increased 400 percent, and the study, now open globally, is approaching its target accrual rate. The NCORP grant, under which TMIST is funded, was also renewed in 2019. Within the subject areas involved in this research, we are making substantial progress in screening, symptom control, and cancer care delivery research.

With the renewed funding, and the endorsement of the research plans we put forward, we are adding resources to help develop these efforts beyond even the goals we outlined. The broad experience of Al B. Benson, MD, recently appointed Deputy Chair, Policy and Implementation, will connect our research to national standards of cancer care and implementation. Linking advances in our disease committees to those in cancer care delivery represents our commitment to accelerating progress, and evaluating its impact on global standards. A salient example of this progress is the chronic lymphocytic leukemia (CLL) trial E1912, led by Tait Shanafelt, MD of Stanford University. The results, first presented as a late-breaking abstract at the 2018 American Society of Hematology (ASH) Annual Meeting and published in the New England Journal of Medicine in August 2019, revealed that the combination of ibrutinib plus rituximab was superior to standard treatment for patients age 70 and younger with previously untreated CLL. These practice-changing findings immediately established a new standard of care for the initial treatment of CLL in patients age 70 and younger. Follow-up data presented at the 2019 ASH Annual Meeting in December showed that the combination treatment continued to provide superior progression-free survival and overall survival compared to standard chemoimmunotherapy for this patient population.

Another high point of the year was the initiation, also across ECOG-ACRIN domains, of a new working group to address Social Determinants of Health, led by Otis W. Brawley, MD. We expect that the work of this group, with goals magnificently outlined by Dr. Brawley at the General Session of our Fall Group Meeting, will explore new fields, expanding upon and complementing our current efforts.

Finally, the Inaugural Robert L. Comis, MD Translational Science Symposium, which also occurred at the Fall Group Meeting, has resulted in great interest among our therapeutic committees for future analysis of clinical and correlative data. Collaborations on genomic and radiomic studies are in progress, and multiple opportunities exist for analysis of existing clinical data from ECOG-ACRIN trials. An irony of considering Big Data and AI in the context of cooperative group trials is that we have in recent years sought to minimize the data we collect, to maximize efficiency. To change this practice, while not overburdening our standard case report forms, will require new approaches. Under the guidance of our biostatistical group, and with the participation of patient advocates, we will develop pilots to guide our future development. In addition, we are in the process of developing working groups across the domains that may be relevant to Big Data investigations: clinical data, genomics, radiomics, pathomics, and PROs, and will seed individual projects in those spaces. We will welcome the participation especially of early-career investigators in these groups. Please be in touch with either of us to get involved.
RECENTLY ACTIVATED: EA2182/DECREASE TRIAL FOR EARLY-STAGE ANAL SQUAMOUS CELL CARCINOMA

The DECREASE study, led by Jennifer A. Dorth, MD (Case Western, pictured right), hypothesizes that lower chemoradiation (CRT) doses will be able to effectively treat early-stage anal squamous cell carcinoma while improving patient-reported health-related quality of life (HRQOL) related to anorectal dysfunction, erectile dysfunction, dyspareunia and vaginal stenosis. Currently, there is not an established treatment standard that is individualized for patients with early-stage anal cancer, defined as T1-2N0. Across many studies utilizing very different doses of CRT, local control is excellent at around 90%. DECREASE is a phase II study that will randomize patients 2:1 to lower dose versus standard dose CRT. Novel secondary endpoints are to validate imaging features of low-risk lymph nodes, measure changes in serum testosterone, correlate vaginal dilator use during RT with sexual function, determine the incidence and predictors for cardiovascular toxicity, and to determine if an online 3D contouring atlas can improve radiation treatment planning. Learn more.

RECENTLY ACTIVATED: EAZ171 TRIAL FOR PERIPHERAL NEUROPATHY IN AFRICAN AMERICAN WOMEN WITH BREAST CANCER

Recent research shows patients of African ancestry have a much higher risk of experiencing side effects from chemotherapy, especially neuropathy, and thus have a higher risk of discontinuing treatment. This results in increased recurrence and worse survival rates in Black patients compared with White patients. EAZ171, led by Bryan P. Schneider, MD (Indiana University, pictured right), aims to improve outcomes for Black women with breast cancer by:

1. Determining which women are most at risk for neuropathy based on their DNA, and
2. Determining which regularly prescribed chemotherapy treatment, docetaxel or paclitaxel, will result in less neuropathy

Through this work, researchers hope to definitively conclude which treatment is better, and less likely to cause neuropathy, for women of African ancestry. They also hope to learn more about why Black women, specifically, are more susceptible to neuropathy. Learn more.

NCI-MATCH/EAY131 TRIAL UPDATE

A series of changes were recently incorporated in NCI-MATCH/EAY131 addendum #24. First, two new correlative proposals, CS-MATCH-0014ctR and CS-MATCH-0015ctR, were adapted into appendices for the master protocol. Revisions were implemented for multiple pre-existing sub-protocols (approximately 17 arms), including the following: modifications to improve slow accruing arms — aMOI additions; expansion of arms EAY131-C1 (15), H (50), M (14), and Z1C (14) with justification; modifications to affected sub-protocols to account for the copy number amplification threshold; adaptation of new correlative proposal CS-MATCH-0012 into appendices for sub-protocol EAY131-Q; revisions to the IHC enrollment process, affecting sub-protocols EAY131-Z1G and Z1H; and RRA's for trametinib, dabrafenib, and palbociclib affecting arms EAY131-H, R, S1, S2, Z1C.

Additionally, both orthogonal assay language and nucleic acid language were added to the master screening document, as well as revised novel inclusionary and exclusionary aMOI language. Finally, minor administrative edits were made throughout the master and screening consent documents. For questions or more information, email eamatchpm@ecog-acrin.org.

The Journal of Clinical Oncology reports results for Arm Z1D of NCI-MATCH, investigating the activity of nivolumab in 18 different cancer types, mostly rare and none colorectal, with DNA repair defects. The 36% response rate across a range of cancers compares well with a previous 31% response in colon cancer. Read more.
CANCER RESEARCH ADVOCATES CORNER: LATE EFFECTS OF CANCER

A CONVERSATION WITH GERALD GREEN
MEMBER, EA CANCER RESEARCH ADVOCATES COMMITTEE

Gerald Green (pictured right) was diagnosed with tongue cancer in 1995, when he was in his mid-forties. Physicians did not expect him to live beyond 50. Today, nearly 25 years later, he has survived two additional cancer diagnoses (neck cancer in 1997 and prostate cancer in 2008), and serves as an active member of ECOG-ACRIN’s Cancer Research Advocates Committee.

Stories like Gerald’s are becoming more common – a fact worth celebrating. Yet, as people begin living longer after cancer treatment, they are experiencing side effects they did not anticipate; symptoms and conditions that do not appear until months or years after treatment has ended. These long-term side effects, or late effects, can greatly affect a person’s quality of life. Managing them successfully is an essential component of survivorship care.

“We need to stop talking about 5-year and 10-year survival,” Gerald explained. “People are now living 15, 20, even 25 years past their diagnosis, which is great, but they’re not the same people they were when they were first treated.”

Over the years, Gerald encountered a variety of late effects. He noticed changes to the sound of his voice, likely caused by radiation to his vocal chords. Radiation also affected his teeth, resulting in the loss of several of them, and the inability to receive implants. His throat is constricted, so he has to eat small portions – though fortunately he does not have trouble swallowing like many head and neck cancer survivors. Additionally, Gerald has neuropathy in his mouth and lips, which causes burning and tingling sensations. Medication helps with his neuropathy, but it is unlikely the condition will improve.

“We need to stop talking about 5-year and 10-year survival; people are now living 15, 20, even 25 years past their diagnosis, which is great, but they’re not the same people they were when they were first treated.”

“I knew there would be side effects from the radiation,” Gerald said, “but every year, as life progressed for me, things changed.”

The EA Cancer Research Advocates Committee (CRAC) is now working to bring awareness to this important survivorship issue, and has established a Late Effects of Cancer Working Group. The working group was formed after several members of the CRAC discovered they had a similar experience: upon hitting the 5-year survival mark, they transitioned from their oncologist back to their primary care provider – who knew very little about the late effects of cancer or how to treat them. Several projects are currently underway, including a late effects webinar series for NCI Community Oncology Research Program (NCORP) site staff.

The primary goal of the Late Effects Working Group is to support the development of studies that contribute to the understanding of late effects of cancer and its treatment. Two such studies are featured in this issue, both recently activated. EAS182/DECREASE has several secondary endpoints, including determining the incidence and predictors for cardiovascular toxicity in patients receiving chemoradiation for anal cancer; EAZ171 aims to address the issue of neuropathy in African American women with breast cancer. As knowledge and awareness of late effects improves, so too may quality of life for survivors.

“What I would tell anyone who survived cancer is that it is going to be a journey,” said Gerald. “Your side effects may vary depending on the type of treatment you received, or the timing – but you are going to have side effects, and it is up to you and the people surrounding you to develop a strategy to mitigate their impact on your life.”
INSTITUTION SPOTLIGHT: 
FOX CHASE CANCER CENTER

MARTIN EDELMAN, MD
CHAIR, DEPARTMENT OF HEMATOLOGY/ONCOLOGY

Since its founding in Philadelphia in 1904 as one of the first cancer hospitals and research institutes in the United States, Fox Chase Cancer Center has been a leader in advancing cancer care in both the clinic and the lab. In 1974, Fox Chase became one of the first institutions to receive the NCI’s elite designation as a Comprehensive Cancer Center.

Fox Chase prides itself on its major and continuing contributions to the three domains of cancer research: basic, clinical, and prevention. Two of the center’s researchers have been awarded a Nobel Prize. Baruch S. Blumberg, MD, PhD, was awarded the Nobel Prize in physiology or medicine in 1976 for his work in identifying the hepatitis B virus and developing a vaccine for it. In 2004, Irwin A. Rose, PhD, was one of the recipients of the Nobel Prize in chemistry for his work studying the breakdown and recycling of proteins.

In 1960, David A. Hungerford, a graduate student at Fox Chase, and Peter C. Nowell, MD, of the University of Pennsylvania, discovered the Philadelphia chromosome, which established cancer as a genetic disorder. Alfred G. Knudson Jr., MD, PhD, developed the two-hit theory of cancer causation, which explained the relationship between hereditary and nonhereditary forms of cancer and predicted the existence of tumor-suppressor genes.

Fox Chase has contributed substantially to the development of novel therapeutics for the treatment of cancer. Robert F. Ozols, MD, PhD, Corey Langer, MD, and the late Robert Comis, MD, (former ECOG-ACRIN chair) led efforts that developed paclitaxel for the treatment of gynecologic and thoracic malignancies.

Hossein Borghaei, DO, MS, has been a leader in the development of immunotherapy, including as principal investigator for a study that led to the approval of nivolumab for the treatment of lung cancer. He currently leads EA5163, which will define the optimal approach to immunotherapy and chemoinmunotherapy for advanced non-small cell lung cancer.

Lori Goldstein, MD, FASCO, is the institutional principal investigator for ECOG-ACRIN at Fox Chase and has led several major trials for drugs to treat breast cancer.

Efrat Dotan, MD, is a leader in researching and developing protocols for the treatment of elderly cancer patients, which is particularly pressing work given that older adults are the fastest growing group of cancer patients in the United States. She has developed and will chair EA2186, which will attempt to define a standard therapy for patients over the age of 70 with newly diagnosed metastatic pancreatic cancer. It will also evaluate the association between geriatric risk factors and outcomes, as well as various biomarkers of aging.

David Weinberg, MD, a gastroenterologist and chair of the Department of Medicine, is leading a unique study that anticipates enrolling over 4,500 patients to evaluate strategies for the surveillance of pancreatic cysts.

Margaret von Mehren, MD, is exploring the problem of resistance with a study looking at combination therapies for gastrointestinal stromal tumors to overcome resistance found in clinical studies. Elizabeth Plimack, MD, is a leader in the field of genitourinary malignancies and is investigating approaches to reverse the resistance of some bladder cancers to any prior immunotherapy checkpoint inhibitors.

In the fields of prevention and population science, Mary Daly, MD, PhD, created one of the first programs in the world to identify genetic risk factors associated with the development of cancer and provide appropriate counseling. Paul Engstrom, MD, former chair of Hematology/Oncology at Fox Chase, led some of the first trials of chemoprevention.

Fox Chase is a high accruing site for ECOG-ACRIN, a feat that could not be accomplished without the support of the over 100 staff members of the Office of Clinical Research, as well as the staff of the investigational pharmacy and the overall institutional commitment to clinical and translational research.