In this issue of the ECOG-ACRIN Newsletter, we highlight the work of the Cancer Research Advocates Committee, ably led by Mary Lou Smith, co-founder of the Research Advocacy Network (RAN) and herself a cancer survivor. We bring the activities of this group to your attention to highlight its importance to our scientific mission. This committee is a vital link between our cancer research efforts and our patients. Its members are embedded in all of our committees, to bring the patient voice to our proposed studies, to participate in deliberations during committee meetings, to inform and assess feasibility and community opinions, and to lead in the education of patients considering participation in trials. Patient review and comment is ingrained in all processes up to and including the Executive Committee. We are fortunate to have this direct link to patients, and would point out that the influence is bi-directional – several committees have projects being co-developed with the help of advocacy foundations, collaborations that can harmonize the goals of both patients and researchers to accelerate progress. The interactions focus also on the value of our work, and assessing its impact on patients, as reflected perhaps by our increasing focus on patient-reported outcomes. The patient and advocate contribution to ECOG-ACRIN research has been productive, and has changed approaches to therapy (as with Mike Katz’s proposal that dexamethasone dose be addressed in myeloma). We are planning additional partnerships with the Cancer Research Advocates Committee to expand the bi-directional dialogue, to work together to influence stakeholders and funders of our research, and for us to provide additional clinical research resources to implement specific advocacy goals. Please feel free to invite participation of patients and advocates in these activities as we expand this work.

We look forward to discussing advocacy in future issues, but an immediate example is provided by the GU committee’s patient representative Deb Maskens, co-founder of Kidney Cancer Canada and vice-chair of the International Kidney Cancer Coalition, who has been a tireless advocate for the PROSPER trial. This trial is outlined on page three of this newsletter, and is presented to increase awareness and uptake, even as we have cracked the accrual of 30 patients per month, almost at the target rate of 31 per month. The scientific underpinning of the trial is novel and exciting: it asks the question if pre-operative immunotherapy, effective in the management of metastatic disease, has the potential to cure more patients with resectable kidney cancer, the first and currently the only randomized trial to address this question. The successful implementation of this study is the result of the commitment of all involved with this trial. Let us take this opportunity also to dispel a myth in regard to the impact of pretreatment doses of nivolumab on resectability of the primary: there are no published data to this effect. One of the surgeons whose initial data on neoadjuvant immunotherapy underpinned the PROSPER trial, Mo Allaf, remarks: “Pre-operative dosing with nivolumab did not result in a significant delay to surgery nor did it cause any adverse events that affected the surgical course. In fact, in our smaller trial none of the surgical complications were attributable to nivolumab. As a result, we are excited about neoadjuvant immunotherapy therapy and await the results of the PROSPER trial with great optimism.” We look forward to seeing this trial reach its full accrual, and to the results changing the practice of medicine.

Finally, we want to announce, well in advance of the Fall 2019 Group Meeting, that as part of a reorganization of the schedule, we will begin each meeting with the Robert L. Comis Translational Science Symposium, which will replace the Scientific Planning Committee (SPC) Symposium, and which will be open to all Group members. We urge all committee members especially to make travel plans to allow for attending the Symposium, beginning at noon on the first day (Thursday, October 24 for our upcoming meeting). As has been the case with the SPC activities, the topics chosen as a focus for this symposium will be those most important to the scientific goals of the Group, and the presentations will be designed to outline research opportunities that can be further developed by the individual committees. The first topic to be addressed is Big Data – itself a large and complex subject. The agenda (which we will post in advance on the website and meeting app) is in three parts: a general introduction to the potential and structures of Big Data as currently being implemented in health care; a session on the “toolbox” available to interrogate the databases we currently have, or can develop; and third, a set of use cases in various disciplines that provide examples of applications that can maximize the value of the data we collect. This symposium can help us to think in this “meta” plane, even as we plan very focused clinical trials in specific diseases. We trust that the expertise and imagination of our investigators will reveal opportunities and value that we may not currently envisage.
What are some significant ways advocates can help advance cancer research?

Advocates can help during the design stage of a trial, identifying questions for researchers that are meaningful to patients. We can share the patient experience, which is important in trial design, but also in activation and recruitment. Advocates can describe what it is like to undergo a particular therapy or to live with a certain disease or side effect. We can also suggest ways to communicate effectively with patients. Since researchers have such an in-depth understanding of the science, sometimes they overlook when the person they are speaking to is not getting the full picture.

How can principal investigators and study teams utilize the advocacy community to build awareness and understanding of trials?

Advocates are great at making connections, so one way we can help is by introducing researchers to individuals at organizations that focus on specific cancer types and serve specific patient communities. PI’s and study teams should consider the ECOG-ACRIN Cancer Research Advocates Committee a valuable resource for this. I would also encourage researchers to simply remain open to advocate feedback. Communication between physicians and patients can sometimes be a challenge. We can help with this, and translate information into lay language so patients can feel informed when making decisions.

What projects or initiatives is the Cancer Research Advocates Committee focused on right now?

We’re focused on a couple of things. One of them is shared research – or community-based participatory research – and applying that framework to our efforts. It involves a patient population identifying problems within their own group, and then working on solutions together with the researchers.

We’re also investigating how to better incorporate the community voice into our committee discussions. Attendance at the Group Meetings is limited among community oncology professionals and advocates, so we’re trying to identify other ways to gather community input, especially from the NCI Community Oncology Research Program (NCORP) sites.

What else would you like EA members to know about advocacy or the Cancer Research Advocates Committee?

We are a resource for them, and we want to help make their research as good as it can be. Our committee is really varied: we have different races, ethnicities, genders – and of course different cancers – represented. We include advocates from all the major cancers that are part of ECOG-ACRIN’s research agenda. We can do things as simple as send a letter of support for a trial when it goes to a steering committee, or find a patient willing to attend a call and provide input. These are not huge things, but they can have a big impact.

BRINGING MAMMOGRAMS, AND TMIST, TO UNDERSERVED COMMUNITIES

Edith Mitchell, MD, who serves on ECOG-ACRIN's Executive, Principal Investigator, and Health Equity Committees, has been partnering with Alpha Kappa Alpha Sorority, Inc. (AKA) to raise awareness in underserved communities about the importance of breast cancer screening – and about EA's TMIST trial, the first randomized study to compare two types of digital mammography. Dr. Mitchell is director of Jefferson University's Center to Eliminate Cancer Disparities; AKA is an international service organization, and the oldest Greek-letter organization established by African American college-educated women. In 2018, as part of the sorority's breast cancer initiative, it debuted the AKA Mobile Mammography Unit to provide free mammograms to women with limited or no access.

This summer, Dr. Mitchell traveled to events in Nashville (2019 AKA Leadership Seminar) and New Orleans (Essence Festival) where the unit was present. In Nashville, 100 free mammograms were provided to underserved women while 102 were provided to women in New Orleans. At both events, educational materials were distributed broadly, including information about the TMIST trial and instructions for participation. The AKA Mobile Mammography Unit team received support in New Orleans from Augusto Ochoa, MD, director of the Louisiana State University Stanley S. Scott Cancer Center, and his staff.
**TRIAL SPOTLIGHT: A PHASE 3 RANDOMIZED STUDY COMPARING PERIOPERATIVE NIVOLUMAB VS. OBSERVATION IN PATIENTS WITH RENAL CELL CARCINOMA UNDERGOING NEPHRECTOMY (EA8143/PROSPER RCC)**

LAUREN C. HArSHMAN, MD

PROSPER RCC is an innovative phase 3 randomized study poised to transform how we treat advanced high risk renal cell cancer planned for nephrectomy. In 2019, there remains no proven adjuvant systemic therapy that can increase overall survival over surgery alone for non-metastatic renal cell carcinoma (RCC). The checkpoint inhibitors are broadly effective for RCC, proven to increase overall survival in both the first and second line metastatic setting. Nivolumab, the anti-PD-1 antibody, has the longest track record and is generally tolerable.

Despite over 40 years of clinical trials testing various forms of cytokine based immunotherapy, chemotherapy, vaccines, and most recently targeted therapy, we still have no effective regimen that increases survival over surgery alone. To break this losing streak in kidney cancer and by considering the biology of how PD-1 blockade works, i.e., that it requires tumor antigen to work and build the T cell army, PROSPER is shifting from the usual surgery first/adjuvant only paradigm and priming the immune system with one dose of nivolumab prior to nephrectomy. This strategy makes sense when you think about the biology of PD-1 blockade and is backed up from mouse solid tumor models that have revealed a benefit with a short course of neoadjuvant PD-1 blockade compared to adjuvant only therapy. In humans, we have seen encouraging rates of significant pathologic response in several other cancers such as bladder, breast and lung with neoadjuvant PD-1 blockade. Two ongoing phase 2 studies of perioperative nivolumab in RCC patients have shown preliminary feasibility and safety with no surgical delays or complications.

Ultimately, the PROSPER RCC trial strives to test whether the addition of perioperative nivolumab to radical or partial nephrectomy can improve clinical outcomes in patients with high risk localized and oligometastatic disease. Specifically, we aim to increase cures and recurrence-free survival (RFS) rates by executing a three-pronged, multidisciplinary approach of presurgical priming with nivolumab followed by nephrectomy and further engagement of the immune system with 9 months of adjuvant PD-1 blockade. We plan to enroll 805 patients with clinical stage T2 or node positive M0 RCC of any histology (clear cell or non-clear cell) in this global, randomized, unblinded, phase 3 National Clinical Trials Network study. Oligometastatic disease is allowed if <3 metastases (no brain, liver or bone) that can be resected or thermally ablated within a 12 week period. The investigational arm will receive 1 dose of nivolumab 480mg IV prior to surgery followed by adjuvant nivolumab monthly for 9 months. The control arm will undergo the current standard of care: partial or radical nephrectomy followed by observation. Key safety, feasibility, and quality of life endpoints are incorporated. PROSPER RCC exemplifies team science with a host of planned correliative work to investigate the impact of the baseline immune milieu and changes after neoadjuvant priming on clinical outcomes with room for more collaborations.

PROSPER is one-third of the way accrued to our 805 patient goal, so we are calling on all NCTN sites to join us in our fight for the cure in RCC! If interested, learn more on ClinicalTrials.gov or get in touch via email at: EA8143_PROSPER@ecog-acrin.org or LaurenC_Harshman@dfci.harvard.edu.

Why should you be a PROSPER Champion?

- **Surgical monotherapy does not cure a significant number of high risk M0 RCC patients**
- **Learn from the past:** Why continue to pursue unsuccessful strategies just because it is more feasible/easier? No purely adjuvant systemic therapy has been proven to increase overall survival as of 2019
- **There is strong preclinical evidence** that the mechanism behind PD-1 blockade relies on antigen—so it makes sense to **prime the immune system** when there is a greater burden of tumor antigen (primary tumor) present
- **Mounting clinical evidence** in other cancers, such as breast, lung and bladder, support efficacy of pre-surgical PD-1 blockade
- **The possible science and potential for biomarker discovery with neoadjuvant priming is priceless** with the ability to interrogate the impact on tissue and sera
- **No randomization to placebo** (patients do care about this!)
- **Change is good**—pausing for systemic therapy prior to surgery may mean a significant difference in cure rates and overall survival.
NEWS IN BRIEF

Is something new or noteworthy happening at your institution? Send your updates to support@ecog-acrin.org.

EA TRIAL RESULTS PUBLISHED IN HIGH-ImpACT Journals

Final results from trial E1912, led by Tait Shanafelt, MD (Stanford), appeared in the New England Journal of Medicine in early August. The findings were first presented as a late-breaking abstract at the American Society of Hematology (ASH) Annual Meeting in December 2018. The trial found the combination of ibrutinib plus rituximab superior to standard treatment for patients age 70 and younger with previously untreated chronic lymphocytic leukemia (CLL). Learn more.

Results from trial ACRIN 6685, led by Val Lowe, MD (Mayo Clinic), were published in the Journal of Clinical Oncology in July. The study was the largest prospective multicenter trial conducted of FDG-PET/CT in head and neck cancer, and it demonstrated that FDG-PET/CT may help clinicians decide on the best therapy for the clinically node-negative neck in patients with head and neck squamous cell carcinoma. Learn more.

ECOG-ACRIN LEADERS ON THE MOVE

Joseph A. Sparano, MD (Montefiore), EA’s Vice Chair, will receive the William L. McGuire Memorial Lecture Award at the 2019 San Antonio Breast Cancer Symposium (SABCS), taking place December 10-14. He is being recognized for a career distinguished by leadership, collaboration, and practice-changing achievements in clinical and translational breast cancer research.

Heather A. Wakelee, MD (Stanford), who serves on several EA leadership committees and co-chairs the Thoracic Cancer Committee, was recently named President-Elect of the International Association for the Study of Lung Cancer (IASLC) where she is currently a board member.

Kim L. Sandler, MD (Vanderbilt-Ingram) was appointed Imaging Chair for the Thoracic Cancer Committee, effective July 2019. She replaces Caroline Chiles, MD (Wake Forest) in this role.

Jonathan E. McConathy, MD, PhD (University of Alabama), was appointed Chair of the Experimental Imaging Working Group, effective May 2019. He replaces David A. Mankoff, MD, PhD (University of Pennsylvania) in this role.

Two EA Member Sites Earn NCI RECOgnition

Recently, The Indiana University Melvin and Bren Simon Cancer Center, an EA member since 1986, achieved the highest recognition from the National Cancer Institute: Comprehensive Cancer Center. This designation reflects research excellence and a commitment to delivering cutting-edge cancer care. At the same time, NCI named The University of Miami Sylvester Comprehensive Cancer Center, an EA member since 2005, its 71st NCI-Designated Cancer Center. EA’s current Principal Investigator at Miami U is Chukwuemeka V. Ikpeazu, Sr., MD, PhD, MBA while Kathy D. Miller, MD is the current EA Principal Investigator at Indiana U.

TMIST IN THE NEWS

The TMIST breast cancer screening trial was highlighted in the July edition of The Bmj as part of an article exploring the value of 3D mammography. Learn more (Please note: you must have a paid subscription to access the full article).

TMIST was also featured in The Cancer Letter in July. In the piece, Amy Curtis, MD (Spartanburg Medical Center) shares her perspective as a community oncologist on why TMIST is so important. Read the full article.

CALL FOR ABSTRACTS: Young Investigator Symposium AT THE FALL GROUP MEETING

ECOG-ACRIN is currently accepting research abstracts from young investigators interested in presenting your research at the upcoming Fall Group Meeting (October 24 – 26 in Fort Lauderdale, FL). You may be eligible to apply if you are engaged in clinical, translational, imaging, or basic cancer research or in non-cancer related research that has application to cancer biology, prevention, screening, diagnosis, imaging, or treatment. The submission deadline is Thursday, September 12 at 11:59 PM (EDT). View full eligibility criteria and the abstract submission form.

SAMPLE TRACKING SYSTEM (STS) USER GUIDE: Version 7 NOW AVAILABLE

Version 7 of the Sample Tracking System (STS) User Guide went into effect on July 23, 2019. With V7, the Translational Science Team made significant updates to describe current procedures since V6 in 2014. The document lives at a stable link on ecog-acrin.org for use across the EA webapps portal, and within the STS itself.