How we perceive these days of COVID-19 depends very much on where we sit. Most of us have curtailed patient contact, have embraced telehealth, and are acclimating to this new reality while confined largely to home. Many others have barely diminished clinical responsibilities that may overlap with the care of COVID-afflicted patients, especially in community settings. Maintaining clinical services safely on the part of our imaging members is a daily challenge. Many, including our nursing committee membership, may have been assigned responsibilities quite different from usual oncology care. For all we wish good health, a safe environment, and successful treatment of all patients under our care.

We can report that through this time, we have been occupied with assuring the seamless management of our patients on trials, together with ongoing and continuing assessment of the impact of changes in approach on the scientific endpoints of the trials. Safety is clearly paramount, and ensuring that we address prospectively the effects of delays in treatment or scans on the primary endpoints is a serious consideration. We have reached out to community sites in a town hall that explored the impact of the virus on cancer patients, and on research approaches. The proceedings are available on our website. With the pace of emerging information, we expect that an information exchange will be useful in another couple of weeks – please let us know if additional resources would be useful by emailing TownHall@ecog-acrin.org.

The majority of our therapeutic trials are active, and though accrual has been down, are available for patients in whom a trial may represent the best approach to their cancer. In this regard, we have been especially concerned about the information gap surrounding COVID-19 infection in patients who are on immunotherapy. Early data seem inconclusive, but a danger signal has not emerged at this time of writing (from a series of AACR presentations). Part of the re-institution of usual cancer care (standard or research) will be data-driven, and we ask the Group's continued focus on reporting events in virus-infected patients. A slightly greater decrease in accrual, understandably, has occurred in screening studies, but these are poised to resume activity as normal routines are re-established. The support from both CTEP and DCP through this time has been exemplary. And although most studies have significant reductions as expected during April, it is encouraging to see EA4151 and EA5163 retain modest accrual rates and EA1131 and EA3161 increase from the previous month.

And with sadness, in this March/April issue we remember Dr. Uma Rao, a pathologist of great accomplishment, whose ECOG-ACRIN contributions are celebrated by Drs. Kirkwood and Michalopoulos. Dr. Rao was among the leaders in bringing together pathologists and clinical researchers in solid tumors, a collaboration that has defined ECOG-ACRIN research for more than 20 years. We also recognize the participation of the minority/underserved NCORP site at John H. Stroger, Jr. Hospital of Cook County (SHCC), and the leadership of Dr. Thomas Lad, whose broad participation in EA activities reflects the very positive impact of this member site. And we discuss the EROS trial (E1011) co-led by Dr. Ashlesha Patel from SHCC, and bring it to your attention for participation. We will follow this issue in a few weeks with the May issue, in which, among other plans, we will outline changes to our Community Cancer Committee structure that will allow for greater participation and new roles for our community oncologists.
Now Enrolling: CompassHER2 pCR (EA1181) – Testing the Ability to Decrease Chemotherapy in Patients with HER2 Positive Breast Cancer Who Have No Remaining Cancer at Surgery after Limited Pre-Operative Chemotherapy and HER2 Targeted Therapy

This study is a neoadjuvant trial for patients with clinical stage II or III HER2 positive breast cancer. It is asking if adjuvant therapy after surgery can safely be omitted for patients with pathologic complete response (pCR) after 12 weeks of pre-operative THP (single agent taxane plus trastuzumab and pertuzumab). The primary endpoint of the study for patients with pCR is 3-year recurrence-free survival.

Neoadjuvant therapy is now standard for newly diagnosed HER2 positive disease above Stage I. It offers the potential to optimize systemic therapy by decreasing unnecessary chemotherapy (and toxicities) in those with pCR. A more intensive HER2 targeted regimen with the antibody-drug conjugate T-DM1, and possibly more chemotherapy, is then reserved for patients with residual disease (RD).

Eligible patients with stage II-IIIa (T2-3; N0-2) HER2 positive breast cancer will receive 4 cycles (12 weeks) of neoadjuvant THP (physician's choice of weekly paclitaxel or every 3-week docetaxel) then surgery. If pCR, patients will complete a year of trastuzumab and pertuzumab plus hormonal therapy and radiation if indicated. If RD, patients will receive standard post-operative adjuvant therapy and may enroll on other clinical trials, such as the upcoming companion trial A011801 (CompassHER2 RD), that Alliance will activate in mid-2020 to test the addition of tucatinib to standard T-DM1. Blood samples for the correlative aims will be collected at 5 time points (before, during, and after treatment), and tumor samples will be collected from the clinical biopsy and surgical specimen. Correlative objectives will assess whether any biomarkers can predict which patients are most likely to attain pCR with this approach. All patients will be followed for recurrence and survival.

The ECOG-ACRIN Breast Committee and Study Chair Dr. Nadine Tung (pictured above) are looking forward to ECOG-ACRIN membership participation in this important study! Additional information can be obtained from the EA1181 Study Team, the ECOG-ACRIN website, the CTSU and ClinicalTrials.gov (NCT04266249).

Now Enrolling: EA6183 – A Phase II Neoadjuvant Study of Encorafenib with Binimetinib in Patients with Resectable Locoregional Metastases from Cutaneous or Unknown Primary Melanoma (Stages III NIB/C/D)

This study, led by Dr. Leslie Fecher (University of Michigan), is a single arm phase II trial that aims to determine how well encorafenib, a selective BRAF inhibitor, and binimetinib, a MEK inhibitor, work before surgery in treating patients with BRAF V600-mutated stage IIIIB-D melanoma that has spread to the lymph nodes. The trial is also assessing how well 18F-FLT positron emission tomography (PET)/computed tomography (CT) works in predicting the response of melanoma to encorafenib and binimetinib.

The primary endpoint is pathologic complete response (pCR) as determined by local assessment of surgical pathologic specimens and radiology studies. Additionally, the trial will include a radiologic key secondary endpoint with a molecular imaging marker FLT PET, designed to test an early response indicator that could be used to guide BRAF/MEK targeted therapy. FLT-PET scans will be evaluated at two time points (baseline and eight weeks after therapy initiation) and correlated with pCR.

Additional information about EA6183 can be obtained from the EA6183 Study Team, the ECOG-ACRIN website, the CTSU and ClinicalTrials.gov (NCT04221438).
Trial Results

Journal of Clinical Oncology Publishes Patient-Reported Data From TAILORx

The Journal of Clinical Oncology published patient-reported data from TAILORx, the largest ever breast cancer treatment trial. The sub-study, led by Lynne I. Wagner, PhD (Wake Forest), found that the cognitive decline from chemotherapy was early and abrupt but no worse over time. Cognition was also impaired in the group on hormone therapy alone. Read the full press release.

Journal of the American Medical Association Publishes Results From EA1141 Abbreviated Breast MRI Study

The Journal of the American Medical Association published the results from EA1141: Abbreviated Breast MRI and Digital Tomosynthesis Mammography in Screening Women With Dense breasts. The study, led by Christopher E. Comstock, MD (Memorial Sloan Kettering), revealed that abbreviated breast MRI detected significantly more cancers than digital breast tomosynthesis in average-risk women with dense breast tissue. Read the full press release.

In Memorial: Uma Rao, MD

Uma Rao, MD was a cornerstone member of the University of Pittsburgh Cancer Institute (or UPCI, now the UPMC Hillman Cancer Center). Within a few years of the founding of UPCI by Ronald Herberman in 1986, she joined the Melanoma Program with John M. Kirkwood, MD. Together, they instituted weekly pathology reviews that rapidly became a focus of education and quality control for multiple studies of the Melanoma Program at UPCI, and for ECOG’s (now ECOG-ACRIN’s) Melanoma Committee after 1989.

Uma had boundless enthusiasm for melanoma and sarcoma pathology, teaching, and mentorship – serving as ECOG’s Melanoma Committee Pathology Liaison for trials E1684, E1690, E1694, E1697, and E2696, documenting the benefits of IFNalpha-2b alone and then in comparison or combination with the GMK vaccine in a series of pivotal adjuvant trials, including the recently published anti-CTLA4 checkpoint blockade trial E1609. Uma taught multiple generations of faculty, fellows, residents, and students at the 14-headed microscope and was indefatigable in her pursuit of molecular and anatomic pathology of melanoma and sarcoma. She collaborated widely with the leadership of the field, where her studies of ECOG tissue samples with Martin Mihm, Jr., MD established the role of micrometastases in primary melanoma using samples from E1690.

Uma Rao joined the Department of Pathology at the University of Pittsburgh in 1993 and worked as faculty until 2019. She was highly respected as an academic colleague. Her work in pathobiology and genomics of sarcomas and melanoma gained her respect nationally and internationally. She trained a large number of pathologists as residents and also through the Bone and Soft Tissue subspecialty clinical fellowship. Most of her clinical fellow trainees are now in faculty positions of their own. As faculty, she always had the courage of her convictions and clearly stated constructive solutions to solve academic and diagnostic delivery problems. She maintained a profile of courage and creativity, despite experiencing some very serious health problems.

In 2019, she transitioned to join the Gynecologic Cancer Center of Excellence (GYN-COE), one of three intramural Department of Defense-funded cancer centers, where she led the Research Pathology Center in the affiliated Women’s Health Integrated Research Center at Inova Health System – a key resource for the US Federal Cancer Moonshot’s Applied Proteogenomics Organizational Learning and Outcomes (APOLLO) research network. She died suddenly on April 7, 2020 and leaves behind her sister Jamuna Benjamin. She will be missed by all of her colleagues at the University of Pittsburgh and at ECOG-ACRIN, with which she continued an active dialogue in email through March of 2020.
Institution Spotlight: John H. Stroger, Jr. Hospital of Cook County (SHCC) Minority Underserved NCI Community Oncology Program (MU-NCORP)

Thomas E. Lad, MD

Together with my colleague Urjeet Patel, MD, I lead the John H. Stroger, Jr. Hospital of Cook County (SHCC) Minority Underserved NCI Community Oncology Program (MU-NCORP). SHCC is the safety net hospital for uninsured patients in Chicago, Illinois and the surrounding suburbs. The program was established in 2002, initially as a Minority-Based Community Clinical Oncology Program (MBCCOP) and subsequently as a MU NCORP since 2014. SHCC remains one of the only single-site NCORP organizations with no affiliates or sub-affiliates. The program has received over $17 million in support for clinical research from the National Cancer Institute (NCI) during this time. In August 2019, the NCI renewed funding in the amount of $5 million over six years. This funding continues to support the research follow-up care for over 2,100 patients currently enrolled in clinical trials and cancer care delivery studies; credit for 582 accruals was given to ECOG-ACRIN Cancer Research Group (EA). SHCC is one of the highest accruing sites to the TrACER study, contributing 148 patients and crediting EA.

Members of the SHCC team have participated in several ECOG-ACRIN committees which include: Cancer Care Delivery Research, Health Disparities, Healthy Equity, NCORP Community Advisory, Cancer Control and Survivorship, Patient-Reported Outcomes, and Clinical Research Associates Core Committee. Our Physician Assistant/Clinical Research Associate, Wendy Rogowski, and I have both served as auditors for ECOG-ACRIN member audits.

SHCC is also heavily involved in protocol development and support at ECOG-ACRIN. Erika Radeke, MPS, the SHCC MU NCORP Administrator, and Ashlesha Patel, MD, MPH are chairs of the ECOG-ACRIN study E1Q11: Engendering Reproductive Health in Oncologic Survivorship (EROS) which is currently open and accruing. The study has reached 54% of its accrual goal of 668 females between the ages of 15 and 55. I participated in the study design and development of EAQ161CD, a biomarker testing survey to assess the level of precision medicine practice in the community. Additionally, I provide scientific direction and mentorship activities concerning new study implementation involving minority and underserved populations to the EA Health Equity Committee. I also contribute insight, advice, and thoughts regarding feasibility and interest during concept development to the Community Advisory Committee.

Further, in collaboration with Northwestern University and Wake Forest University, our team participated in the planning and development of a concept proposal to ECOG-ACRIN titled Preparatory work for evaluation of a PROMIS-based and eHealth-Enhanced Psychosocial Distress Screening and Monitoring in Oncology Settings to Improve Care and PROs and Reduce Health Disparities. However, this concept did not transition to a full protocol.

Lastly, our contributions to clinical trial accrual have led to continuous renewal of SHCCs accreditation through the American College of Surgeons’ Commission on Cancer (CoC). Our research activity has met CoC standards with commendations at each review since 2002.
Trial Spotlight: EROS (E1Q11) – Engendering Reproductive Health Within Oncologic Survivorship

The E1Q11 / EROS trial is a behavioral intervention study in premenopausal females of reproductive age (15-55) with cancer. Its primary aim is to evaluate the ability of an educational program for health care providers to improve patients' understanding of their reproductive risks and receipt of appropriate treatment to achieve their reproductive health goals. The NCI is funding EROS through its NCORP grant mechanism. EROS opened in September of 2015 and is at 54% of enrollment (364/668).

EROS is the only trial of its kind. The NCI cites it as exemplary cancer care delivery research for its potential to offer every young woman with cancer an assessment of her goals for fertility and family planning to make the most of cancer treatment and preserve her future reproductive health.

The EROS study team is implementing three novel strategies to boost accrual to this trial.

Shorter Follow-up: A January protocol amendment slashed the follow-up period from five to two years. This change should make participation in the trial more attractive and less burdensome for patients and clinicians alike, and thus, increase the pace of accrual. Participants meet the primary endpoint at three months after baseline and the secondary endpoints at six months. These evaluate females' attitudes, functioning, and practice related to sexuality during the two years after a cancer diagnosis.

The EROS Trial Challenge: Participating NCORPs are being asked to enroll three patients per month per NCORP for five months. If each of the 21 participating NCORPs (with a total of nearly 80 affiliate sites) takes the pledge, study leaders are confident that they can complete accrual within months.

Focus on Pediatrics: The EROS leadership is reaching out to currently participating NCORP sites who have access to pediatric patients or have pediatric components and asking them to invite their pediatric colleagues to join the study as an affiliate. They are also welcoming new NCORP sites that serve pediatric patients.

Many eligible women in the NCORP programs have been missed, according to the study team. The omission is due mainly to personnel not feeling comfortable talking to women about contraception and reproductive health. Also, some clinicians did not want to be study participants themselves.

Chairing the trial is Ashlesha Patel, MD, MPH (Stroger Hospital of Cook County Minority Underserved NCORP). The co-chairs are Howard Zaren, MD (Georgia NCORP), and Erika Radeke, MPS (also at Cook County).

Currently, providers have minimal information available to help guide discussions with their patients about such issues as fertility and sexuality during cancer care. This study concerns all stages of female reproductive health, which early on pertain to the ability to become pregnant and carry a child to term. Later stages are early menopause or ending of menstruation, pain or discomfort from sexual intercourse, or lack of intimacy from anxiety or distress due to early menopause.

As a quality-of-life objective, all subjects are part of a longitudinal study using the PROMIS sexual function survey. The first 200 registered patients who agreed to participate are part of a study following endocrine markers of fertility (reproductive health, fertility status, and endocrine disruption).

Learn more about E1Q11 / EROS.