From the Co-Chairs
Peter J. O'Dwyer, MD (left), and Mitchell D. Schnall, MD, PhD
June 2020

How odd not to be in Chicago as May rolls into June! And yet the presence of ECOG-ACRIN at ASCO was as strong virtually as it has been historically in person. We celebrate two Plenary presentations, delivered with confident grace by Drs. Seema Khan and Shaji Kumar, in breast cancer and myeloma respectively. Seema's presentation emphasizes the engagement of surgical oncologists in the activities of ECOG-ACRIN, while Shaji's underlined the need for careful assessment of purported advances in the treatment of myeloma. More on these two presentations later in this newsletter, but we would point out here that both of the trials were formally negative, yet each will have enormous impact both in the management of breast cancer and myeloma patients, as well as in defining productive directions for future research. We are fortunate to have these two rays of light at a time of great turmoil, sadness and anger in our society.

The horrific killing of George Floyd cannot pass into obscurity as the news cycle turns its focus elsewhere. We especially in ECOG-ACRIN, where health equity and diversity is one of our Specific Aims, and where our senior leadership includes colleagues of African-American heritage, cannot be complacent in the face of a global reassessment of race and bias. We have a responsibility to seize this moment, to assess where our contribution to justice may be, and that perhaps through that effort, society can begin to atone for the many, many predecessors who have met abuse or death in similar circumstances. Where do we look first in the quest to expunge racism? First, within ourselves, surely. This is a difficult task, to try to understand where what we might regard as simple preferences, can expand to the choices we make personally or professionally, choices that may deny access or equality of opportunity to those who may look different. For those interested in joining us in such self-assessment, we will make available an interactive session on unconscious bias. The details are being developed at the time of writing, and will be communicated soon.

Second, within our workplaces and institutions. There is no quantity of by-laws, regulations, or operating procedures that can establish equality if that concept is not embraced by the individuals who make up the institution. Indeed, we can state with some conviction that the top-down approach cannot work here, and that all of us who are the institution must work together if progress is to be made. To understand how others view the world, we use dialogue – our meetings with colleagues and even patients every day reflect that reality: we rarely have race and racism at the center of the discussion, and we hope that that can change. In ECOG-ACRIN, we will expand the focus of the Health Equity Committee, led by Drs. Simon and Mitchell, to look inward to our membership, in addition to its usual focus on patients. A New Testament verse says, "Physician, heal thyself" – we broaden that enjoinder to “Health Care Research Professionals, heal ourselves’ as a change first step to understanding. Through effort, we can advance understanding and empathy, from which we would collectively espouse ECOG-ACRIN change, not just a tolerant environment, but a specifically anti-racist culture.

Third, we must and will ramp up our quest to increase diversity and inclusion in this Group. In addition to our current partnership with the National Medical Association (and their Past-President Dr. Mitchell) to bring minority students, residents and fellows to our Group Meetings, we ask you our members to reach out and invite the participation of minority colleagues. Each of us is an agent of change, and in our (relatively) small organization, our quest for diversity can be a small step toward the greater goal of eliminating racism from society. We will welcome the responses and suggestions of our members at this important time. This cannot be a short-term commitment on the part of ECOG-ACRIN, and we are committed to long term engagement. However, we see this event and the public response to it as a potential inflection point in race relations and civil rights, one not to be wasted. Not only is this ethically the Right thing to do, but for ECOG-ACRIN, it is the Best thing to do.
Now Enrolling: **EA5181** – Randomized Phase III Trial of MEDI4736 (Durvalumab) as Concurrent and Consolidative Therapy or Consolidative Therapy Alone for Unresectable Stage 3 NSCLC

This study, led by Nathan Pennell, MD, PhD (Cleveland Clinic) and John Varlotto, MD (University of Massachusetts), is a randomized open label phase III trial for patients with unresectable stage III non-small cell lung cancer (NSCLC). **EA5181** aims to determine if concurrent MEDI4736 (durvalumab) with standard platinum doublet chemotherapy and radiation, followed by consolidative MEDI4736 (durvalumab), is a more effective treatment approach than the same concurrent chemoradiotherapy regimen alone followed by consolidative MEDI4736 (durvalumab). The primary objective is to evaluate whether there is an improvement in overall survival in the group that receives concurrent and consolidative therapy with MEDI4736 (durvalumab).

In 2018, the PACIFIC trial demonstrated that one year of consolidation MEDI4736 (durvalumab) after concurrent chemo/radiation was found to increase both overall survival and progression-free survival, establishing consolidation MEDI4736 (durvalumab) as the new standard of care. However, additional studies suggest immune checkpoint inhibitors such as MEDI4736 (durvalumab) may be even more effective when combined with cytotoxic therapy such as chemotherapy and/or radiation.

Patients assigned to the concurrent and consolidative therapy group will receive platinum doublet chemotherapy and concurrent thoracic radiotherapy, as well as MEDI4736 (durvalumab). Patients assigned to the consolidative therapy alone group will receive platinum doublet chemotherapy and concurrent thoracic radiotherapy only. Patients from both groups will then proceed to Step 2, consolidative MEDI4736 (durvalumab) every four weeks for up to one year.

Learn more about EA5181 on [ECOG-ACRIN.org](http://ECOG-ACRIN.org), the [CTSU website](http://www.ctsu.chest.org), or [ClinicalTrials.gov](http://www.clinicaltrials.gov).

Now Enrolling: **PrE0905** – Gilteritinib vs. Midostaurin for FLT3-Mutated Acute Myeloid Leukemia

![PrECOG](https://praco.gov/)

Approximately one-third of patients with acute myeloid leukemia (AML) have a FLT3 mutation, and their relapse and survival rates are much worse than patients with AML whose leukemia cells don’t harbor this mutation. **PrE0905**, an open-label phase II study led by Selina Luger, MD (University of Pennsylvania), is exploring a new treatment approach for this group: the potent FLT3 inhibitor gilteritinib.

Untreated adult patients with FLT3 AML are eligible for this trial and enrollees will be randomized to receive gilteritinib or midostaurin during the induction and consolidation phases of treatment. Patients will also receive standard chemotherapy of daunorubicin and cytarabine during induction and high-dose cytarabine during consolidation. AML patients with known core binding factor and patients with acute promyelocytic leukemia (with or without a FLT3 mutation) are not eligible for this study.

In the last year, gilteritinib was approved for patients with relapsed/refractory FLT3-mutated AML, having demonstrated its effectiveness in improving survival as a single agent in this setting. The FLT3 inhibitor has not yet been approved in the upfront setting, and thus, Dr. Luger notes, PrE0905 is the only trial that will allow participating sites to potentially get gilteritinib added to induction therapy for AML.

Learn more about the trial on [ClinicalTrials.gov](http://www.clinicaltrials.gov). Dr. Luger also has recorded a brief, informational video for physicians and site staff that includes details on the patient screening process and procedures for submitting samples for FLT3 testing.

PrE0905 is currently open at approximately 20 sites across the US. Any site that is interested in participating should contact PrECOG.
**Trial Results: E2112 Finds No Significant Overall Survival (OS) Benefit With Entinostat/Exemestane in Advanced Breast Cancer**

Final results reported last month from E2112, the phase III trial evaluating the addition of entinostat to endocrine therapy in over 600 patients with hormone receptor (HR)-positive, HER2-negative advanced breast cancer, revealed that the investigational agent did not demonstrate a statistically significant OS benefit over endocrine therapy with placebo.

Although E2112’s primary endpoint was not met, the findings provided critical insight into whether adding entinostat to exemestane might improve outcomes for this difficult-to-treat population. Entinostat is a class I histone deacetylase (HDAC) inhibitor developed by Syndax.

“We are very grateful to you, the study team, for all of your efforts over the last few years and especially in these last few months,” noted E2112 Study Chair Roisin M. Connolly, MBCh, MD. “Your hard work and diligence have helped us answer an extremely important question.” Dr. Connolly is formerly of Johns Hopkins University and now the Cancer Research Chair at University College Cork in Ireland; she was named ECOG-ACRIN’s Young Investigator of the Year in 2019.

E2112 was developed based on promising preclinical data, and results from the phase II ENCORE301 trial which found that the entinostat/exemestane combination demonstrated activity in a similar patient population.

“E2112 was an FDA registration trial that EA was able to complete due to significant collaboration involving patients, patient advocates, academic and community sites across the NCT’s National Clinical Trials Network, industry, and regulatory agencies,” Dr. Connolly continued. “These results highlight the importance of conducting well-designed randomized controlled trials to confirm or refute phase II clinical trial findings and investigate new treatment options for patients with advanced cancer.”

The study results as well as correlative analyses will be reported in an upcoming meeting.

**The Value of TMIST Compared to Other Breast Cancer Screening Studies**

There have been multiple published retrospective case series demonstrating that digital breast tomosynthesis (DBT) detects more breast cancer than planar digital mammography (DM). Among the largest series, the Population-Based Research to Optimize the Screening Process (PROSPR) consortium demonstrated (Conant et al JAMA ONCOL 2019) a cancer detection rate of 5.8/1,000 screens for DBT vs 4.4/1,000 for DM. In addition, the cancers detected by DBT were smaller and less likely to be associated with nodal metastasis.

Do these results impact the importance of TMIST? Although this and other series clearly demonstrate that DBT will detect more early cancer, they do not relate the detection of these early cancers to better outcomes for the screening population. TMIST is a multi-year randomized study of DBT and DM that will assess the impact of this early detection on reducing the incidence of life-threatening cancer over the five year study timeline. This unique study design will provide critical data to relate the increased detection rate to clinical outcomes. So, the answer to the above question is a clear “no.” If anything, these previous results highlight the importance of TMIST.

**EA Research at #ASCO20: How Twitter Helped Fill the Virtual Void**

This year’s ASCO Annual Meeting was a significant one for ECOG-ACRIN. EA investigators shared a wide range of research results, presenting findings from eight different clinical trials, including late-breaking data in two plenary presentations. The meeting was also significant in another key way – not just for EA, but for all attendees. It took place entirely online.

This new virtual format, developed out of necessity, yielded some interesting effects. One, in particular, was an increase in social media activity, likely resulting from the loss of face-to-face interactions. According to an article in Medscape, this year’s meeting generated almost 18K tweets compared to approximately 15K tweets last year, and this despite 300 or so fewer users contributing to the conversation.

What did some of these conversations look like? Consider those sparked by the two ECOG-ACRIN plenary presentations. In LBA2, lead investigator Seema A Khan, MD (Northwestern University) shared the results of E2108, which found that surgery
and radiation after initial systemic therapy do not improve overall survival for women who first present with metastatic breast cancer. In LBA3, lead investigator Shaji K. Kumar, MD (Mayo Clinic) presented data from the ENDURANCE/E1A11 trial, showing that the drug carfilzomib does not improve outcomes in newly diagnosed myeloma compared to bortezomib.

**E2108**

Tatiana Prowell, MD @tmpowell - May 31

Agree. E2108 reminds us that 1) OS is an important endpt 2) it’s not the only important endpt 3) neg RCTs can be just as practice-changing as positive ones. & that’s why you’re seeing it in the Plenary (same for ANNOUNCE trial in sarcoma in ASCO19 Plenary).

Vinay Prasad @VPrasadMDmph - May 31

One of the great virtues of ECOG ACRIN is to measure quality of life alongside surrogates like local regional control

This should be the norm

#ASCO2020 #asco20

**ENDURANCE/E1A11**

Rafael Fonseca MD @Rfonsei1 - May 31

Congratulations to @myelomaMD, @VincentRK as well as @e african group for a crisp plenary presentation. This very important study builds on our fund of knowledge to better treat MM.

TBH I wish Shaji could have done in person but instead join me in a virtual applause

#mm

Mayo Clinic Cancer Center @MayoCancerCare - May 31

Check out the ASCO20 Plenary Session today, May 31 at 1 pm ET for Dr. Shaji Kumar’s abstract on results of the ENDURANCE (E1A11) phase III trial: bit.ly/2TP2WA @mms #MultipleMyeloma @MayoClinic

Sergio Giralt @sgiraltbmtmdoc - May 31

And please let’s not call this a flawed study design No study is perfect and all of them require an enormous time and effort to complete. Let’s respect patients and investigators who dedicated themselves to this study. With the data we can make our own conclusions

Vincent Rajkumar @VincentRK - May 31

Thanks Rafael. Thanks Sergio.

Neelima Denduril @ndenduril1 - May 31

Appreciated the discussion by Dr. White mentioning the low utilization of HER2 targeted therapy in pts treated in India - we need to improve #access for all - another place #asco is leading with resource stratified #guidelines @jgiralong @mdmanishshah @aakonc

Saroj Nairaula MD MSc @sarojniiraula - May 31

Agree. We have looked at this specific issue (HER2) in a meta-analysis. Selective shorter duration of herceptin might be a consideration as a trade-off with resource constraints.

Navneet Majhail, MD @BldCancerDoc - May 31

Replying to @VincentRK @sgiraltbmtmdoc and 3 others

Second that @Rfonsei1 and @sgiraltbmtmdoc - important triplet vs triplet study that shows no clear benefit of KRd over VRd - congrats to @myelomaMD @VincentRK and all study investigators/patients for this important practice defining #myeloma trial #ASCO20

One could argue that, this year, social media played a more critical role than usual, fostering discussions and debates that simply could not happen in person. However, most seemed to feel that social media was an imperfect substitute. The sentiment behind Dr. Fonseca’s statement above, “TBH I wish Shaji could have done in person...” was echoed by many others.

At least, as Dr. Hamilton notes above, “there was no sacrifice of science,” and the oncology community found a way forward through challenging circumstances. That in itself was no small feat, and all those affected by cancer will be better for it. In addition to the two plenary presentations, EA also shared findings from two TAILORx sub-studies, head and neck cancer trial E3311, lung cancer trial EA5161, arm Z1F of the NCI-MATCH trial, and the cancer care delivery study COMET. Learn more about the results of these trials.

Also of note, PrECOG, LLC reported positive results from mesothelioma trial PrE0505. Led by Patrick Forde, MD (Johns Hopkins), the study found that adding durvalumab to standard chemotherapy improved overall survival in mesothelioma. PrECOG is a cancer research group formed in 2006 by the ECOG Research and Education Foundation, Inc. Learn more about PrE0505.