LIKE WHAT YOU’RE READING?
This marks the sixth issue of News from ECOG-ACRIN. Now that we’re halfway through the year, we want to hear from you! Send us feedback to let us know what you’ve enjoyed reading, topics you’d like to see covered, or ways we could improve. Complete this short survey or send us an email at support@ecog-acrin.org.

FROM THE CO-CHAIRS
PETER J. O’DWYER, MD (LEFT), AND MITCHELL D. SCHNALL, MD, PhD
JUNE 2019

As summer brings us long days and outdoor activities, there is no room for torpor among the oncology community. The annual lead-in to summer consists of two big events: the ECOG-ACRIN Spring Group Meeting in May, and the ASCO Annual Meeting in June. Both have reported results – detailed in this issue – that will keep us busy over the next several months. As you heard at the EA General Session, Dr. April Salama presented the results of Arm H of MATCH – a trial of dabrafenib (a RAF inhibitor) and trametinib (a MEK inhibitor) in patients whose tumors harbor a V600 mutation. The results were markedly positive across a range of different histologies. Our goal is to expand accrual to this trial, in the hope that with a larger number of patients, these results across tumor types will be confirmed – and if so, support a broad regulatory approval for this combination. Though MATCH was designed as a screening trial, the opportunity to bring effective drugs and regimens to genomically-defined patient populations, no matter how rare their tumor, must be availed of. We believe that there is the will on the part of all involved to help make this happen, and we will certainly keep you updated. The observation and the drive to carry MATCH forward for maximum impact emphasizes further the value of this initial precision medicine approach in oncology. Of the eleven treatment arms of MATCH reported to this point, three have been positive so far, and will help to define standards of care. So it is with some confidence that we work with our colleagues at NCI and in the other cooperative groups to develop the next generation of such trials.

Since March, planning has been underway to branch out the current EA-led NCI-MATCH trial to three trials based on the same model: ComboMATCH to be led by EA, an AML trial led by the NCI, and an immunological trial, I-MATCH, to be led by SWOG. Following preliminary meetings in Rockville, both pharma and interested investigators from across the groups were invited to meet at ASCO, where the plans were outlined and ideas invited for arms of the ComboMATCH trial. The ideas can come from companies or from investigators, and each group is tasked with organizing and prioritizing a set of trial proposals. This effort in EA is being chaired by Dr. James Ford, Stanford, who also serves as Co-PI of the trial. The therapeutic trial protocols in ComboMATCH are being proposed now, and discussions will continue over several months. We detail in this issue the process for submitting proposals, and encourage all investigators to participate.

Significant advances in randomized trials from ECOG-ACRIN are also discussed in this issue. Refinement of recurrence risk in young women with breast cancer by the addition of tumor size and grade was presented by Dr. Joseph Sparano. These features have long been known to determine recurrence risk, and their identification as independent variables provides context (as do the results of MATCH) to the incorporation of genomic data into treatment decisions. Dr. Ahmad Tarhini’s presentation showing that ipilimumab is superior to high-dose interferon in adjuvant therapy of high-risk melanoma in E1609 is an important milestone in this disease, and provides solid underpinning of the emerging role of checkpoint inhibitors. Dr. Len Appleman’s presentation of the results of E2810, showing that adjuvant pazopanib has no benefit in unselected patients with resected high-risk kidney cancer adds to the weight of evidence that the oral anti-angiogenic agents are inactive in this setting, and emphasizes the importance of our current IO trial in this area, EA8143. Finally, Dr. Sagar Lonial presented data that early treatment of smoldering myeloma with lenalidomide can prevent progression, a finding that will change practice in the management of this disease.

Lastly, we salute the awardees of LAPS grants in this cycle, and the new ECOG-ACRIN institutions in the Program. The scientific contributions, proficiencies in the careful conduct of ground-breaking clinical research, and accrual to trials across the groups are all recognized in these awards, and we add our congratulations.
LAPS PLAY VITAL ROLE IN EA’S SCIENTIFIC LEADERSHIP AND NCTN TRIAL ACCRUAL

Lead Academic Participating Sites (LAPS) represent an integral part of EA’s member network, providing scientific leadership in the design and conduct of clinical trials and contributing substantially to accrual across the NCTN.

LAPS grants have been awarded to 32 US academic research institutions (four new this year: Northwestern University, Medical College of Wisconsin, Thomas Jefferson University, and University of Rochester). Sites receiving these grants have fellowship training programs, and most are NCI-Designated Cancer Centers. Successful applicants demonstrated an ability to enroll high numbers of patients onto NCTN trials, including those for rare cancers, as well as a commitment to recruiting special and traditionally underserved populations.

Importantly, LAPS grants provide funding for the research staff needed to manage a robust clinical trial enterprise, recognizing the increased workload and sustained level of data management work required over several years to achieve desired higher enrollment levels. These awards also include funding for site-based scientific and administrative leadership, so that LAPS PIs can prioritize educating and training clinical research staff—including the mentorship of junior investigators—and develop strategies to promote patient enrollment.

LEAD ACADEMIC PARTICIPATING SITE GRANTEES

CASE WESTERN RESERVE UNIVERSITY
DANA-FARBER CANCER INSTITUTE
DARTMOUTH COLLEGE
DUKE UNIVERSITY
EMORY UNIVERSITY
FRED HUTCHINSON CANCER RESEARCH CENTER
JOHNS HOPKINS UNIVERSITY
MAYO CLINIC ROCHESTER
MEDICAL COLLEGE OF WISCONSIN
NORTHERN UNIVERSITY AT CHICAGO
OHIO STATE UNIVERSITY
ROSWELL PARK CANCER INSTITUTE
SLOAN KETTERING INSTITUTE FOR CANCER RESEARCH
THOMAS JEFFERSON UNIVERSITY
UNIVERSITY OF NORTH CAROLINA CHAPEL HILL
UNIVERSITY OF ALABAMA AT BIRMINGHAM
UNIVERSITY OF CALIFORNIA DAVIS*
UNIVERSITY OF CHICAGO
UNIVERSITY OF COLORADO DENVER
UNIVERSITY OF MICHIGAN
UNIVERSITY OF OKLAHOMA HEALTH SCIENCES CENTER
UNIVERSITY OF PITTSBURGH AT PITTSBURGH
UNIVERSITY OF ROCHESTER*
UNIVERSITY OF SOUTHERN CALIFORNIA
UNIVERSITY OF UTAH*
UNIVERSITY OF WISCONSIN-MADISON
UT MD ANDERSON CANCER CENTER
UT SOUTHWESTERN MEDICAL CENTER
VANDERBILT UNIVERSITY MEDICAL CENTER
WASHINGTON UNIVERSITY
WAYNE STATE UNIVERSITY
YALE UNIVERSITY

* Institutions marked * are unaffiliated with ECOG-ACRIN, but are members of other NCTN Network Groups.
HIGHLIGHTS FROM THE 2019 ASCO ANNUAL MEETING

New results from the NCI-MATCH (EAY131) and TAILORx trials were among the EA research highlights at the 2019 annual meeting of the American Society of Clinical Oncology (ASCO). EA researchers also presented final results from four large randomized phase III studies and reported discovery of a biomarker in prostate cancer.

NCI-MATCH Arm H Results

Among 35 patients representing 17 distinct tumor types—several rare—with BRAF mutations, the dabrafenib–trametinib combination showed promising activity outside of currently approved FDA indications (Abstract 3002). “Arm H met its primary endpoint with an overall objective response rate of 33 percent,” said study chair April Salama, MD (Duke U). “These results are especially relevant given that this was a heterogeneous cohort of heavily pre-treated patients who had meaningful clinical benefit.” Press Release

New TAILORx Data on Younger Women

An assessment of recurrence risk based on classic clinical features—tumor size and histologic grade—adds prognostic information that is complementary to the 21-gene Recurrence Score (RS) test (Abstract 503). The new data guides adjuvant therapy in younger breast cancer patients with even greater precision than the original findings. “With this new analysis, it is clear that women ages 50 or younger with a Recurrence Score result between 16 and 20 and at low risk, clinically, do not need chemotherapy,” said study chair Joe Sparano, MD (Montefiore/Albert Einstein). “Furthermore, the integration of the RS with clinical risk information could identify premenopausal women with higher clinical risk who may benefit from ovarian function suppression and more aggressive anti-estrogen therapy.”

This analysis reports that the modest chemotherapy benefit originally observed in younger women with RS 16-25 may be due to a castration effect associated with cytotoxic therapy. The New England Journal of Medicine simultaneously published the data along with an invited editorial. Press Release

Randomized Phase III Trial Results

Renal Cell Carcinoma – Final results from study E2810 showed no benefit from pazopanib in advanced kidney cancer, after surgery to remove metastases (Abstract 4502). “Pazopanib treatment for one year did not improve the chance of survival without disease recurrence,” said study chair Len Appleman, MD, PhD (U Pittsburgh). “This finding is important because these patients are at particularly high risk of recurrence, and treatments shown to benefit metastatic disease in place have been attractive to study after surgery to completely remove all visible sites of cancer.” Press Release

Melanoma – Study E1609 evaluated the relative safety and efficacy of ipilimumab at 3 and 10 mg/kg compared to high-dose interferon-α2b (HDI), the adjuvant standard for resected high-risk melanoma until recently. Study chair Ahmad Tarhini, MD (U Pittsburgh) presented the results (Abstract 9504). “For the first time in the history of melanoma adjuvant therapy... E1609 has demonstrated a significant improvement in the primary endpoint of OS against an active control regimen previously shown to have OS and RFS benefits, supporting early systemic adjuvant therapy for high-risk melanoma,” he said.

Myeloma – Final results from study E3A06 show that lenalidomide significantly reduces the risk of smoldering multiple myeloma from progressing to overt multiple myeloma in individuals at moderate or high risk. Observation is the current standard of care. The significance of these findings led ASCO to highlight this presentation on its press program. Press Release
**HIGHLIGHTS FROM THE 2019 ASCO ANNUAL MEETING (CONT’D)**

*Lung Cancer* – E5508 was conducted to determine the optimal maintenance therapy for advanced non-squamous NSCLC. While maintenance therapy is a standard approach, pemetrexed or bevacizumab are considered evidence-based options. The combination of bevacizumab and pemetrexed has been shown to improve progression-free survival. E5508 found that single-agent bevacizumab or pemetrexed is the optimal maintenance therapy. Study chair *Suresh Ramalingam, MD* (Emory U) concluded that the combination of bevacizumab and pemetrexed cannot be recommended due to the lack of survival benefit in this definitive study. (Abstract 9002).

**Biomarker Discovery**

*Prostate Cancer* – *Jason Hearn, MD* (U Michigan) revealed a discovery from a recent analysis of data from the E3805 (CHAARTED) trial (Abstract 5020). Inheritance of the *HSD3B1*(1245C) variant allele that augments dihydrotestosterone (DHT) synthesis may be associated with lower overall survival in men treated with androgen deprivation therapy (ADT) with or without docetaxel for low-volume newly metastatic disease.

**EA NOW ACCEPTING SCIENTIFIC CONCEPTS FOR COMBOMATCH, A SUCCESSOR PRECISION MEDICINE TRIAL TO NCI-MATCH**

ECOG-ACRIN Cancer Research Group, in collaboration with the National Cancer Institute (NCI) and the National Clinical Trials Network (NCTN), is developing the successor precision medicine trial to NCI-MATCH. The trial, called *ComboMATCH*, will concentrate on targeted drug combination signal-seeking studies supported by preclinical *in vivo* evidence.

The hypothesis behind this trial is that *in vivo* evidence, in particular PDX and cell line derived xenograft data, can be used to predict the benefit of drug combination therapy in multiple specified patient subgroups. Like MATCH, ComboMATCH is conceived as a signal-seeking study. To distinguish this trial from the original MATCH trial, this trial will focus on rational combinations of agents supported by preclinical *in vivo* evidence.

The trial is envisioned as having an overall Master Control document managed by EA that will coordinate separate NCTN group-specific treatment “cassettes” that each have 4-6 sub-protocols. Each cassette of 4-6 sub-protocols will be administratively managed by each of the Networks in coordination with EA.

Sub-protocol proposals will be reviewed by the ComboMATCH Agents and Genes Working Group (C-AGWG). This will consist of four members from each NCTN along with additional members with developmental therapeutics and precision oncology expertise. Accepted sub-protocols will be assembled into the different cassettes by this committee in coordination with each of the Networks.

**View more information** on ComboMATCH and ECOG-ACRIN’s ComboMATCH RFP.

ECOG–ACRIN is soliciting ideas for possible ComboMATCH sub-protocols. Proposals may be general and are not required to be fully designed at this time. To submit a proposal, email a completed ComboMATCH Concept Sheet with any additional desired supporting material to Erin Mendelsohn at emendelsohn@ecog-acrin.org.
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.

NEW TAILORx DATA TO BE FEATURED AT THE 2019 BEST OF ASCO® MEETINGS

Global exposure to the TAILORx data presented at the 2019 ASCO Annual Meeting will increase greatly this summer, now that the abstract is hand-selected for the 2019 Best of ASCO® program. In addition to meetings in Seattle, Austin, and Baltimore, the data will be featured in 30 international programs. See page three of this newsletter for a summary of the data.

ECOG-ACRIN LEADERS ON THE MOVE

Congratulations to a number of EA committee chairs for being named a 2019 Fellow of the American Society of Clinical Oncology. These individuals include Suresh S. Ramalingam, MD and Heather A. Wakelee, MD (Thoracic Committee); Mary Lou Smith, JD, MBA (Cancer Research Advocates Committee); and David Cell, PhD (Cancer Control and Survivorship Committee).

Lymphoma Committee Chair Brad S. Kahl, MD (Washington U in St. Louis) has been named program chair for the 2019 North American Educational Forum on Lymphoma, occurring October 18 – 20 in Chicago.

NCI CIRB OPEN CALL FOR NEW BOARD MEMBERS

The NCI CIRB is currently seeking new board members. In particular, they are looking for medical oncologists, medical oncologists with immunotherapy experience, pharmacists, ethicists, statisticians, and a cancer care delivery expert. Applications must be submitted by Wednesday, July 31. View the application and additional information on the NCI CIRB website.

The new 2019 board members will be appointed in October, oriented in November, and will join the boards in January 2020.

EA8143/PROSPER RCC KIDNEY CANCER TRIAL OPENS IN CANADA

EA8143/PROSPER RCC opened at its first site in Canada, Princess Margaret Cancer Center (Toronto), in mid-June. The study, led by Lauren C. Harshman, MD of Dana-Farber Cancer Institute, aims to determine whether treatment with an immunotherapy agent plus surgery is more effective than surgery alone for patients with renal cell carcinoma.

“This is a biologically interesting trial with strong leadership,” said Michael Jewett, MD (pictured above), Professor of Surgery (Urology) at the University of Toronto and urologic oncologist at Princess Margaret Cancer Center. “It deserves our support.”

PLAN AHEAD FOR THE ECOG-ACRIN FALL 2019 GROUP MEETING

Save the date for the ECOG-ACRIN Fall 2019 Group Meeting, taking place October 24 – 26 at the Fort Lauderdale Marriott Harbor Beach Hotel in Fort Lauderdale, Florida. Sessions begin at 8:00 AM on Thursday and end at 1:00 PM on Saturday (subject to change). Registration will open approximately 10 weeks prior to the meeting, in mid-August.

REMINDER: GET IN TOUCH WITH THE EA AUDIT TEAM

The ECOG-ACRIN Audit Program is a key component of the Group’s Quality Assurance efforts. Yet, the process can be at times confusing and challenging. The ECOG-ACRIN Audit group has created an email address to provide an easy way for EA sites to ask audit-related questions.

Please use the AskEAAudit@ecog-acrin.org email address to ask questions related to the EA audit process, the Clinical Trial Management Branch (CTMB) audit guidelines, or EA Audit work practices.