We're looking forward to meeting in Boston in the first week of May. With almost 1,000 advance registrants, this will be our largest meeting ever, bringing together researchers from all disciplines of clinical cancer research, the nurses and CRAs who both conduct and design the research, and our patient advocates who have made such an impact on the way we now plan and conduct our studies. Highlights of the meeting will include an initial Scientific Planning Committee meeting that will bring novel imaging approaches and metabolomics to the attention of the membership. Expansion of this meeting to a new format, will be announced during the meeting.

In the past weeks, we have also received word of our very positive priority score from the NCORP grant. Together with that from the NCTN grant, we can now move forward, funding and stability assured. The first year of the new NCTN grant began on March 1, though the awards were not made public until the last week of April. In addition, both the Leukemia and Thoracic Malignancies Translational Centers of Excellence (led by Ross Levine and Suresh Ramalingam, respectively) were funded for an additional six years, much to the credit of both of these highly-productive programs. The stability implied by these reviews puts ECOG-ACRIN in an excellent position to grow and develop in these next funding periods.

At this meeting too, we celebrate the NCI-MATCH trial. Since the end of the 6,000-patient screening portion of the trial in May 2017, accrual to treatment arms has continued through a network of commercial and academic laboratories, to the point that 982 patients have been enrolled to substudies to date. Eleven of the 39 substudies have already been reported, and the results of several will be discussed at the meeting. We will describe this progress to date in the General Session on Friday evening, and we are delighted that this will be attended by Dr. Jim Doroshow, Deputy Director of the NCI, who was a motive force in securing the support and funding for a trial of this magnitude at the Institute. We will have a presentation of one of the successful arms, which provides strong evidence of the value of such trials.

**NCI-MATCH Timeline**

A MATCH session will also be conducted on Saturday morning, at which some of the current MATCH activities will be described. At this meeting, in addition, we will look forward to the “daughters of MATCH,” which have been in the planning for the past few months. The figure here shows the evolution of the NCI-MATCH trial over the past six years. While the Designated Labs accrual continues, and new arms are being activated, the next generation of targeted trials has begun planning. ECOG-ACRIN will coordinate Combo-MATCH, which will investigate combinations of treatments in genomically-defined subsets, and we will participate in trials of I-MATCH, an immunologically targeted study to be coordinated by SWOG. In both studies there will be research opportunities for our investigators and institutions. We look forward to seeing you there.
THE VALUE OF PATIENT-REPORTED OUTCOMES AS A CLINICAL TRIAL ENDPOINT: BRINGING THE PATIENT'S VOICE TO THE CLINICAL ENCOUNTER

LYNNE I. WAGNER, PhD

This common clinical scenario may seem familiar: You enter the exam room and inquire, “How are you?” Your patient responds, “I’m fine,” and the clinical encounter proceeds. While extremely brief, this common exchange of social pleasantries conveys much more than the words spoken. Your take away from this conversation is that since your patient says they are fine, their quality of life remains intact, therefore they must be adequately managing any symptoms and tolerating treatment well. On the other side of the desk, your patient adheres to social expectations by replying they’re “fine.” Issues with symptoms are not raised, because they assume if their fatigue, mucositis, hair loss, neuropathy, sexual function, or any of the other domains affected by their treatment were relevant, you would inquire directly.

The communication dynamics are complex. Clinicians understandably assume patients will initiate a discussion about problematic symptoms. Patients assume if these symptoms were relevant to their care, the clinician would initiate a discussion. This leads to the perfect storm, in that symptoms that can significantly impact quality of life are not addressed. More subjective domains (e.g. fatigue) and more sensitive domains (e.g. sexual function, drug and alcohol use) are at the greatest risk for under-reporting and under-detection. Additionally, patients know that difficulties tolerating treatment will result in dose reductions, delays, or treatment discontinuation. Patients have an inherent disincentive to minimize their symptoms in the clinical encounter to avoid treatment disruption, so as not to distract their team from treating their cancer. Patients frequently arrive to appointments with cookies, gifts, treats – they want to stay in their team’s good graces; they do not want to be perceived as a complainer. This familiar scenario routinely contributes to the under-recognition of symptoms and concerns which may compromise patients’ quality of life. Imagine how this scenario would play out differently if the patient had completed a questionnaire ahead of time, rating the severity of their symptoms. The precision of the discussion would be greatly enhanced. “How are you?” could be quickly followed by “Let’s do something about your fatigue.”

The ramifications of the under-detection of symptoms are magnified in the context of clinical trials, where novel therapies have toxicities yet to be identified and understood. When this systematic under-detection of cancer- and treatment-related symptoms occurs in the clinical trials context, valuable opportunities to understand aspects of the patient’s experience with treatment are missed. As a powerful illustration, aromatase inhibitors (AIs) were initially assumed to be well tolerated with few side effects. Patient advocates first alerted us to AI-arthralgias and warned us that over 30% of breast cancer survivors were discontinuing therapy within the first few months of treatment. These observations underscored the need for a systematic approach to measure treatment-related symptoms, and this recognition occurred in tandem with mounting evidence demonstrating discrepancies between clinician-rated toxicities and patient-rated toxicities. Patient-reported outcome (PRO) measures provide a methodologically rigorous strategy to quantify symptoms, toxicities, and health-related quality of life.

ECOG-ACRIN embraced the value of collecting PROs among clinical trial participants long ago, establishing our group as a leader in the field. ECOG-ACRIN PRO initiatives intersect with our scientific priorities in several areas. The quantitation of symptomatic benefit and preserved functional status is essential for trials seeking to maintain therapeutic benefit with de-intensified approaches. Among E1308 participants, the preservation of swallow function in patients receiving de-intensified
THE VALUE OF PATIENT-REPORTED OUTCOMES AS A CLINICAL TRIAL ENDPOINT: BRINGING THE PATIENT’S VOICE TO THE CLINICAL ENCOUNTER (CONT’D)

treatment compared to those receiving standard care was quantified using PRO measures. Among TAILORx participants, PROs demonstrated that while more cognitive impairments were observed acutely during chemotherapy in women randomized to the chemoendocrine arm, women receiving endocrine therapy alone reported comparable impairments at 12 months and beyond, challenging the colloquialism “chemo-brain” and signifying the need to better understand endocrine therapy-related symptoms. In the RESORT lymphoma trial (E4402), participants randomized to scheduled rituximab versus treatment at progression reported comparable health-related anxiety, providing clinicians with assurance that holding treatment until recurrence would not impose undue anxiety among their patients.

In the metastatic setting, PROs quantify symptom palliation, and thus can be used as a proxy for treatment response. The E3805 trial evaluated chemohormonal therapy versus androgen deprivation alone among men with metastatic prostate cancer. Higher symptom burden during chemotherapy compared to androgen therapy alone was balanced by fewer prostate-related symptoms at follow-up, potentially due to superior control of disease.

“PROs provide tremendous value in identifying emerging toxicities from novel therapeutic approaches.”

PROs provide tremendous value in identifying emerging toxicities from novel therapeutic approaches. The NCI developed PRO-CTCAE items, to obtain patient-reported scores on symptomatic adverse events to complement clinician-rated CTCAE items. ECOG-ACRIN’s early adoption of PRO-CTCAE items on melanoma and breast cancer trials has led to the systematic documentation of patient-rated toxicities associated with immuno-oncology therapy and novel therapeutic strategies. On these trials, PROs will quantify the effects of toxicities on health-related quality of life and adherence.

Additionally, treatment tolerability is an increasingly salient construct given the growing use of anti-cancer oral therapies, which are vulnerable to elective patient discontinuation. The ECOG trial E1Z03 found that patient-reported bother by treatment side effects (FACT-G item GPS) at initiation of AI therapy was highly predictive of women at risk for discontinuing therapy early. Through Cancer Moonshot funding, our team of biostatisticians, PRO experts, and clinical trialists have begun to examine PRO, PRO-CTCAE, and CTCAE data from 12 ECOG-ACRIN trials to replicate this finding in other cancer types and with other treatment regimens, and more broadly to improve our understanding of treatment tolerability.

Looking forward, ECOG-ACRIN will continue to employ PROs in tandem with de-intensified therapeutic strategies to quantify symptom and functional benefit. We will continue to utilize PROs to quantify cancer- and treatment-related symptoms to indicate treatment response, as well as treatment-related toxicities. The use of hypothesis-driven, methodologically robust PRO measurement strategies increases our confidence that we have accurately captured patients’ experiences with cancer and treatment. As we continue to understand emerging toxicities and treatment tolerability-related issues, we will pivot from PROs as descriptive to PROs as actionable. We will use PROs as a biomarker, signifying risk for suboptimal treatment outcomes by identifying patients vulnerable to early discontinuation. Conceptualizing PROs like a biomarker, we will explore strategies to integrate clinical actionability of PROs through advancing a scientific agenda related to ePRO symptom monitoring.

ECOG-ACRIN is uniquely suited to lead trials that integrate molecular profiling and imaging. With greater personalization of therapy, understanding the decision-making process will become increasingly important. PROs to assess patient values with regard to the tradeoff between potential treatment benefit versus toxicities, decision-making, and decisional satisfaction will contribute a critical patient-centered perspective to precision treatment. In doing so, ECOG-ACRIN will lead the way in shaping precision patient-centered treatment.
INSTITUTION SPOTLIGHT
DAVID M. KING, MD
PRINCIPAL INVESTIGATOR COMMITTEE MEMBER

The Metro-Minnesota Community Oncology Research Consortium (MMCORC) is a nonprofit research program sponsored by the National Cancer Institute Community Oncology Research Program (NCORP) and participating hospitals and clinics. MMCORC provides people in the Minneapolis-St. Paul area access to the newest therapies available for cancer treatment, management of treatment side effects and disease symptoms, and cancer prevention and care delivery research.

The MMCORC consortium represents an established community program that began in 1979 through an NCI-funded Community Hospital Cancer Program (CHCP) Award. In 1983, MMCORC received one of the initial Community Clinical Oncology Program (CCOP) Grant awards. In 2018, the consortium was awarded a NCORP grant to continue its research efforts. Since its founding, MMCORC has enrolled more than 15,000 patients into clinical trials.

Currently, the consortium represents 25 hospitals and clinics in Minneapolis-St. Paul and the surrounding suburbs, as well as Cambridge, Monticello, New Ulm, Princeton, Stillwater, Willmar, and New Richmond, Wisconsin. Twenty sites are registered with NCORP to implement Cancer Care Delivery Research (CCDR) with more than 160 physician investigators participating, representing medical oncology, radiation oncology, surgical oncology, neuro-oncology, thoracic surgery, gynecologic oncology and pulmonology.

MMCORC has been involved with ECOG-ACRIN since 1983; since 1985, it has had three principal investigators — Patrick J. Flynn, MD, Joseph Leach, MD, and me — all of whom have served on EA’s Principal Investigator Committee. A number of other staff are currently engaged with EA in various capacities: Michele Lacy, director of MMCORC, Audrey Haas, RN, and I all volunteer to audit for ECOG-ACRIN. Audrey Haas also serves as the community representative on the Network Accrual Core team (ACT).

Today, MMCORC is playing a key role in supporting accrual for several EA studies, including EA1151/TMIST, EAQ162CD, and E1Q11. TMIST was activated at one of the consortium’s minority centers in July 2018; 160 patients have been enrolled to date and two additional TMIST sites are planned to open in 2019 thanks to the efforts of Pam Felix, RN and Heather Schlemme, CRA. For EAQ162CD and E1Q11, MMCORC is demonstrating high accrual. These studies are led by Heather Kehn, RN, MPH and Jessica Miller, CCRP respectively. Due to the consortium’s long and successful history with ECOG-ACRIN, staff are often asked for feedback or to participate in pilot studies. MMCORC has also acknowledged the importance of the patient voice by establishing relationships with patient advocates in the Minneapolis-St. Paul community who also serve on the EA Cancer Research Advocates Committee. These are just a few of the key ways MMCORC is helping to move patient care forward.