

Activities to Enhance Accrual to NCTN Trials


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Presentation to the 35th meeting of the
Clinical Trials and Translational Research Advisory Committee
March 7, 2018

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1. *Review goals and work of the Network Accrual Core Team (ACT)*
 2. *Provide update on trials reviewed and strategies recommended to enhance accrual*
 3. *Describe task force efforts*
 4. *Discuss lessons learned*

PROTOCOL ACCRUAL LIFECYCLE



How to support trial accrual across the NCTN?

- Held a 2-day strategy meeting in December 2014
 - National Clinical Trials Network (NCTN) Meeting to Address Accrual Challenges in NCTN Clinical Trials in Adults and Adolescents and Young Adults
 - Meeting goals:
 1. Develop consensus around key accrual challenges
 2. Identify potential strategies
 - Attendees:
 - Representatives from Groups, LAPS, & NCORP (operations, PIs, research staff, patient advocates)
 - NCI offices (DCTD, DCP, OD, DCCPS)

Outcome: Organize a cross-network committee to meet on a regular basis



Network Accrual Core Team (ACT)

Network ACT

- Provide the NCTN and NCORP an inclusive forum to maximize accrual through communication and collaboration
 - Representatives from:
 - NCI/CTSU
 - Network Operations Offices
 - Main Member Sites
 - LAPS Sites
 - NCORP Sites
 - Patient Advocates
- Reps have varying expertise in disciplines, cancers, treatment focus, diversity, setting
- Approximately 30 members meet monthly via WebEx
 - Rotating membership every 2-3 years
 - Collaboration portal via the CTSU website

Network ACT Structure

1. Protocol discussions of trials with challenging accrual
2. Task force meetings
 - Address key concerns identified and within a finite timeline
 - Currently:
 - Eligibility Task Force
 - Data Inventory Task Force
3. National webinars
 - via NCI's Cancer Trials Support Unit (CTSU)

Protocol Discussions

- Identify protocols & concepts that have challenging or slow accrual
 - Protocols typically recommended by:
 - Lead Network (Operations office, Disease Chair, Study PI, Patient Advocate)
 - NCI, Clinical Investigations Branch (CIB)
- ‘Roundtable’ format via WebEx with Study Chair
 - Overview of trial design
 - Accrual update
 - Anticipated/unanticipated issues
 - Strategies employed to date
 - Cross-Network opportunities for increasing accrual

Protocols Discussed to Date

- 28 protocols discussed since September 2015
 - By Network Group:
 - Alliance: 9
 - COG: 3
 - ECOG-ACRIN: 5
 - NRG: 6
 - SWOG: 6
 - By disease:
 - Bladder: 3
 - Bone: 2
 - Breast: 4
 - Germ Cell: 1
 - GI: 3
 - Female Reproductive System: 1
 - Leukemia: 1
 - Lung: 4
 - Lymphoma: 1
 - Melanoma: 2
 - Myeloma: 2
 - Salivary: 1
 - Sarcoma: 1
 - Thyroid: 1

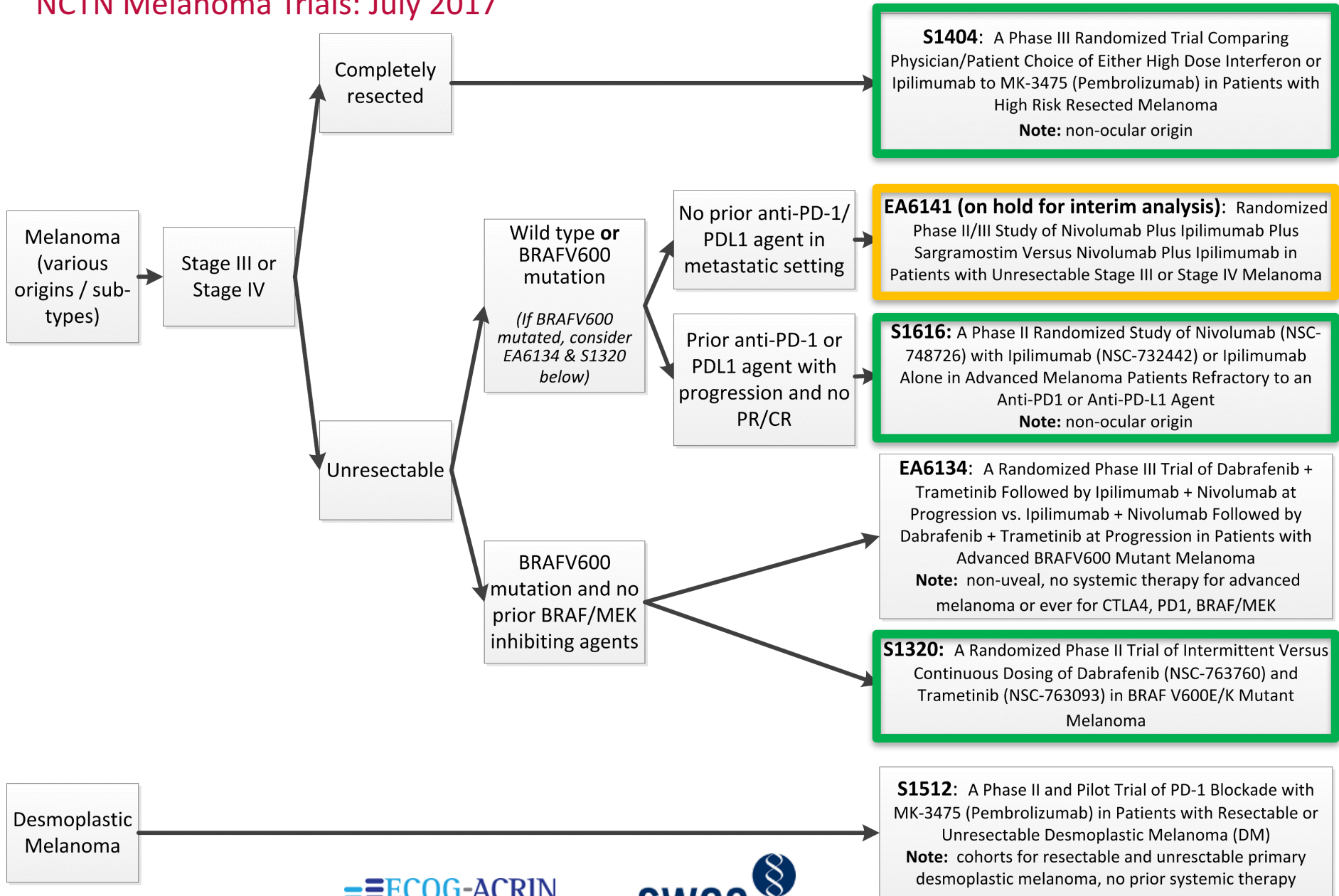
CTSU Webinars

- Hour-long WebEx sessions with PI presentations and Q&A
 - Open to NCTN/NCORP sites and promoted through CTSU, Network Operations offices, and other groups
- Ideas for webinars raised on ACT calls and discussed with CIB
- Registered participants:
 - Median of ~450 registrants/webinar (Range: 156-1012 registrants)
- Multiple trials presented per webinar:
 - AYA Trials
 - Lung Trials
 - Breast ('Sister' and Triple Negative Trials)
 - GU Trials
 - Melanoma Trials
 - Myeloma Trials
 - Colorectal Trials
 - Lymphoma Trials (upcoming)

Network ACT Recommendations

- Protocol “champions” identified
 - PI from each Network group who promotes trial internally
- Networking suggestions
 - Provide contacts for patient advocates, special committees (e.g. aging), survivorship clinics, etc.
- Request for PI to provide clarity to the field around:
 - Regulatory
 - Eligibility criteria
 - Toxicity levels of the investigational arm
 - Amendments
 - Funding
 - Drug supply
- Educational recommendations and/or materials
 - Protocol fact sheets, video tutorials, training webinars

NCTN Melanoma Trials: July 2017



One-page Handouts

Have you been newly diagnosed with multiple myeloma?

CONSIDER THE E1A11 ENDURANCE STUDY.



What is the ENDURANCE study?

The E1A11 ENDURANCE study is a clinical trial sponsored by the U.S. National Cancer Institute. A clinical trial is a research study that involves patient volunteers -- these studies help doctors test new treatments that might benefit patients. The ENDURANCE study is looking to see how a new combination of drugs, or different amounts of an approved drug, compares to the usual care for patients with multiple myeloma. There is no placebo in the ENDURANCE study -- all patients receive treatment for their cancer.

What is the usual care for patients with multiple myeloma?

People with newly diagnosed multiple myeloma usually take a combination of three drugs (bortezomib, lenalidomide and dexamethasone) over the course of 6 to 12 months (also called "induction treatment"). After the induction treatment, patients usually continue to receive one drug (lenalidomide) as maintenance until their disease comes back, or they may undergo a stem cell transplant. The decision is based on a patient's health and the doctor's recommendation.

What is the purpose of the ENDURANCE study?

Doctors are always looking to find new treatments to better control multiple myeloma. The ENDURANCE study is helping to find out two questions for patients:

1. How does a different combination of drugs (carfilzomib, lenalidomide and dexamethasone) compare to the usual care in treating multiple myeloma? Carfilzomib is a new drug for treating myeloma that has been very effective in trial.
2. How does stopping lenalidomide after 2 years of maintenance compare to giving patients lenalidomide until the cancer returns?

What will happen if I choose to participate in the ENDURANCE study?

The ENDURANCE study has two steps. The picture on the next page describes these two steps. Both steps follow the usual care choices available to patients with newly diagnosed multiple myeloma.

Step 1: The first step is during your induction treatment. You will receive either the usual care (combination of bortezomib, lenalidomide and dexamethasone) or a different combination of drugs (carfilzomib, lenalidomide and dexamethasone) that has also been shown to be effective in treating multiple myeloma. A computer will decide which group you are in. You will have an equal chance of being in either group.

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S1400 Lung-MAP Study: Patient Questions and Answers

WHAT IS LUNG-MAP?

Lung-MAP is a large clinical trial, or research study, testing several new treatments for patients who have advanced-stage squamous cell lung cancer and whose cancer has continued to grow even after being treated with standard therapy. Lung-MAP is focused on squamous cell lung cancer because it is common and hard to treat. There are few effective treatments for squamous patients, particularly those who don't respond to chemotherapy.

Squamous cell lung cancer accounts for about 25 to 30 percent of non-small-cell lung cancer. Squamous cells are thin, flat cells that line the airways of the lungs. In advanced stage patients, the cancer has usually spread to other organs in their body.

While squamous cell lung cancer starts in a single group of cells, it is not a single disease. There are many different changes to a person's cancer genes that can cause squamous cells to grow out of control and become cancerous. Recently, researchers have developed new drugs that might "target" these genetic changes better and with fewer side effects.

With Lung-MAP, researchers test DNA from each patient's tumor to see if the patient has a genetic change in the cancer cells that may be causing the cancer to grow. If a change is detected in a patient's tumor, and if they meet other requirements, the patient will be eligible to get the drug that targets that specific genetic change. They will not get a placebo.

WHAT IF I DON'T HAVE A GENETIC CHANGE?

For some patients, their tumor will not match the genetic changes that are being tested in the trial. However, these patients may be able to join the "non-match" sub-study in Lung-MAP.

This sub-study tests drugs that may help the immune system fight the cancer cells. Patients will be randomly assigned to one of two groups. Both offer a drug, nivolumab, which is approved for safety and effectiveness by the U.S. Food and Drug Administration for patients with advanced squamous cell lung cancer. One group of patients will be treated with nivolumab alone; the other will receive nivolumab plus another drug, ipilimumab.

WHY IS THIS STUDY BEING DONE?

The purpose of the Lung-MAP study is to learn if the drugs that target the genetic changes in the cancer cells will slow or stop the squamous cell lung cancer from growing. For the non-match sub-study,



ACT Task Forces

Eligibility Task Force

- Goal: Promote the use of thoughtful, less restrictive eligibility criteria in NCTN & NCORP trials
- Network Groups share current processes
- ASCO-Friends of Cancer Research (Friends) manuscripts on broadening eligibility criteria in JCO 2017
 - <http://ascopubs.org/jco/specialseries/2017/broadening-eligibility-criteria-clinical-oncology-trials>
- NCI and Groups are reviewing ASCO-Friends template language with internal committees and protocol operations to incorporate into protocol templates and review processes.

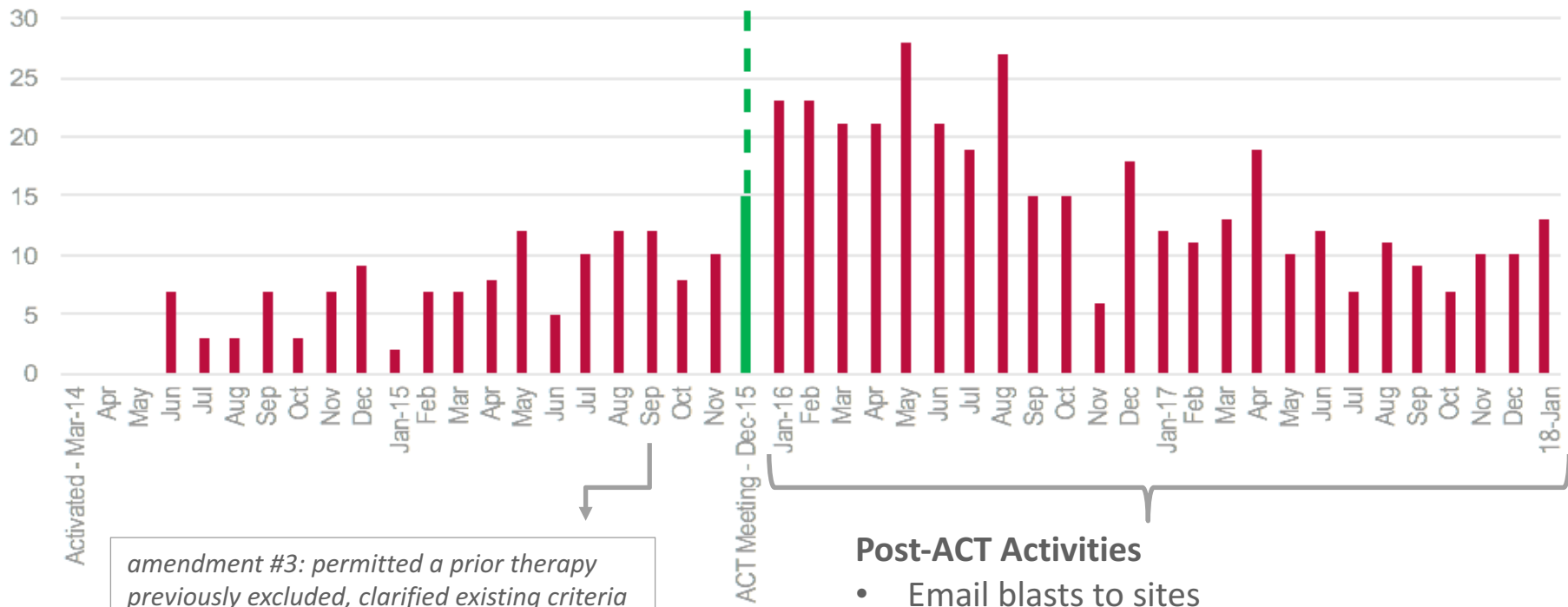
Data Inventory Task Force

- Goal: Identify best practices to enhance accrual; collect existing accrual support tools; develop new templates where needed
 1. Accrual Planning Checklist for Study Teams
 - Purpose: to identify potential accrual barriers so appropriate actions can be taken early to enhance accrual
 - Assess site, patient, scheduling, timing, biospecimen issues
 - Currently being tested for feasibility
 2. Communication Plan Template for Study Teams
 - Utilize information from the new accrual plan checklist to connect to a checklist of communication strategies
 - Site and public focused communication



Data from Selected Trials

E2112: A Randomized Phase III Trial of Endocrine Therapy Plus Entinostat/Placebo in Patients with Hormone Receptor–Positive Advanced Breast Cancer



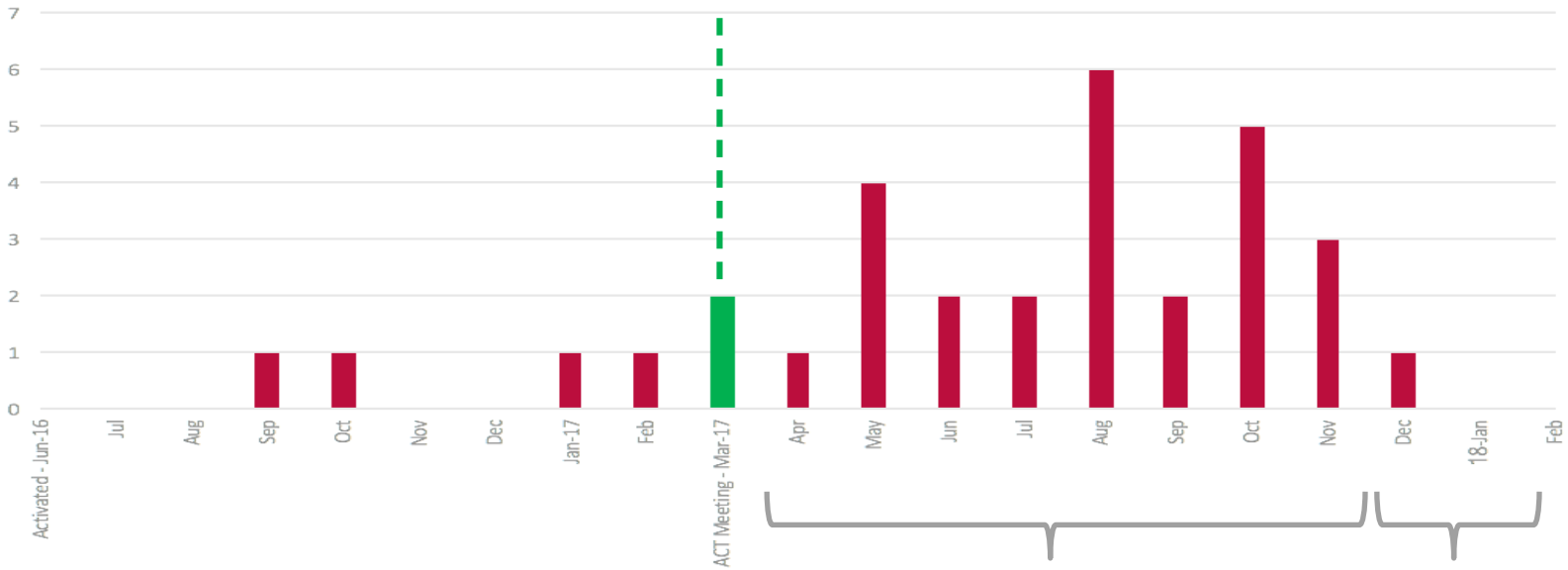
amendment #3: permitted a prior therapy previously excluded, clarified existing criteria

Post-ACT Activities

- Email blasts to sites
- Meeting with SWOG Breast Committee
- Newsletter announcements
- Group Meeting Talks
- ASCO Breakfast for trial
- Summer NRG Meeting
- Spring SWOG Meeting
- MBCN Advocacy Network Webcast

Accrual goal: 600
 Accrual (as of 3/1/18): 531

A091404: A Phase II Study of Enzalutamide (NSC# 766085) for Patients with Androgen Receptor Positive Salivary Cancers



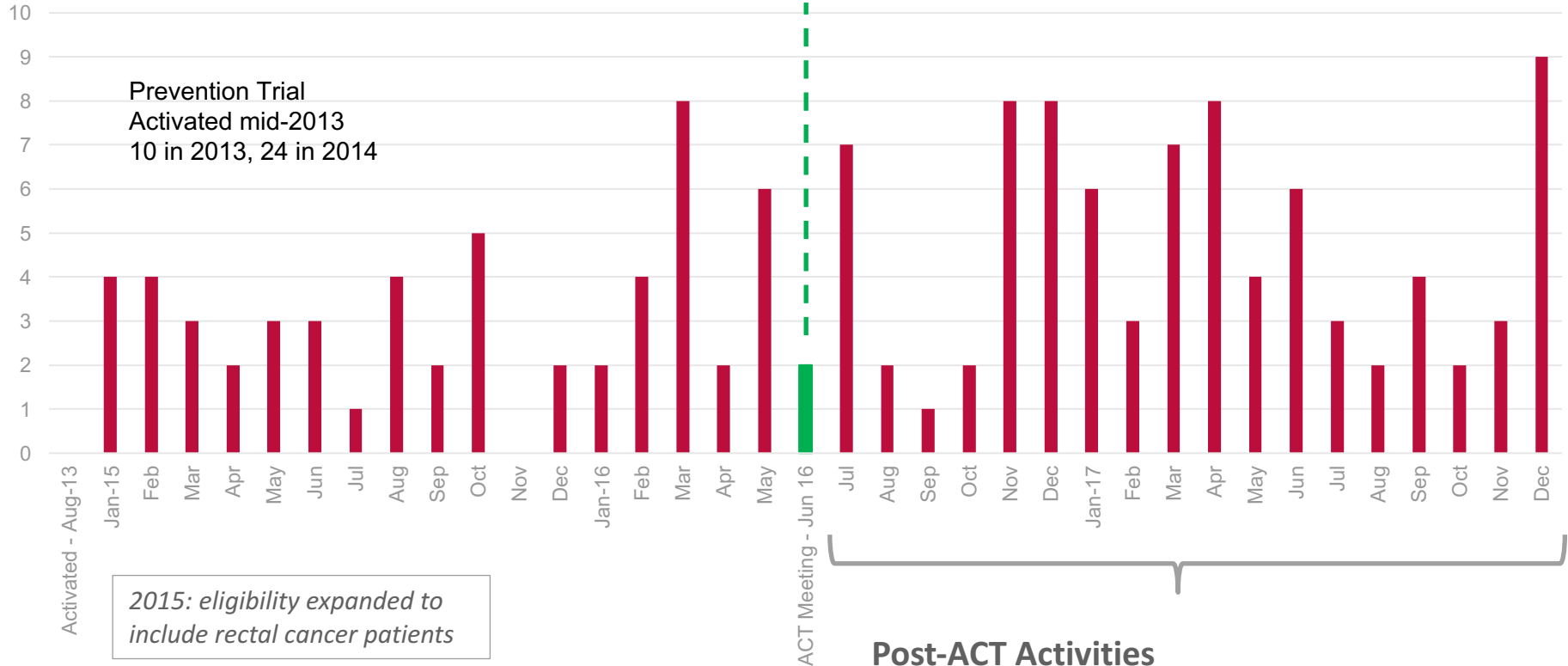
Post-ACT Activities

- Addition of NRG, ECOG, SWOG Physician Champions

Suspended to new patient pre-registration for interim analysis (patients pre-registered allowed to proceed to registration)

Accrual goal: 45
 Accrual (as of 3/1/18): 32

S0820: A Double Blind Placebo-Controlled Trial of Eflornithine and Sulindac to Prevent Recurrence of High Risk Adenomas and Second Primary Colorectal Cancers in Patients with Stage 0-III Colon Cancer, Phase III - Preventing Adenomas of the Colon with Eflornithine and Sulindac (PACES)



Post-ACT Activities

- Added NRG, ECOG-ACRIN Champions
- Promoted study redesign through website, social media, newsletters
- FAQs, protocol cards, materials, updated and promoted
- 2017: study redesign (4-arm to 2-arm)

Accrual goal: 480
Accrual (as of 3/1/18): 186



Lessons Learned

Feedback from PIs/Study Teams

- *We have implemented your suggestions...and we believe the suggestions certainly help!*
- *The most critical component is keeping the study on people's radars so that they offer it to patients*
- *I had attempted to secure a PI from other groups without success...it was really helpful to re-approach with this Network ACT recommendation...now we have PI's in each NCTN helping to keep this trial on everyone's radar*
- *I think our study is doing much better now in terms of accrual*
- *I would recommend (Network ACT) to other PIs - it was a good experience*

Limitations of ACT

- Large membership ensures inclusivity, but can be difficult to fully engage
- Monthly meetings work well for the demands of members' schedules, but can slow desired progress on task force goals
- Coordination of Study Chairs' schedules for CTSU Webinars is challenging, leading to delays or last minute changes
- Assessing direct impact of ACT's recommendations on accrual is not feasible:
 - Many confounding variables would interfere with any claim of causality
 - Difficult to track timing and implementation of strategies adopted by PIs
 - No strategy will be able to overcome the challenges and pressures at the sites that are out of our control

Value of Network ACT

Network ACT provides a regular forum for NCTN stakeholders to:

- Share knowledge and experiences related to clinical trial accrual
- Seek cross-Network support and generate ideas for specific trials that face accrual challenges
- Engage Study PIs to develop and implement accrual strategies for their trials, and encourage them to proactively plan before activation
- Develop and disseminate accrual tools across the NCTN
- Identify areas, and bring in additional expertise and support to address accrual barriers that affect all clinical trials (e.g., eligibility criteria)

Network ACT Members

- NCTN Operations Representatives: Trini Ajazi/Michael Kelly/Priya Kumthekar (Alliance), Deborah Crabtree (COG), Karen Padilla/Liz Roben/Lauren Green (ECOG-ACRIN), Anna Sadura (CCTG), Sharon Hartson Stine (NRG), Dana Sparks/Wendy Lawton/Jennifer Maeser (SWOG), Betty O'Meara (IROC)
- NCTN Patient Advocate Representatives: Patty Spears (Alliance), Caroline Berberich/Kristy Sharif/Melissa Martin (COG), Mary Lou Smith (ECOG-ACRIN), Judy Needham (CCTG), Mary Jackson-Scroggins (NRG), Rick Bangs (SWOG)
- NCTN Main Member Representatives: David Freyer (COG), Renee Webb (ECOG-ACRIN), Susan Goodin (ECOG-ACRIN), Paul Hesketh (SWOG)
- NCTN LAPS Representatives: Wendy Bloomer (Alliance), Marilyn Leitch (Alliance), Mitch Machtay (NRG), Annette Betley (SWOG)
- NCORP Representatives: Anthony Jaslowski (Alliance), Audrey Haas (ECOG-ACRIN), Nancy Paris (NRG), Sharad Ghamande (NRG)
- NCI Representatives: Andrea Denicoff, Holly Massett, Marge Good, Rhonda DeJoice, Laurie Cynkin, Grace Mishkin
- CTSU Representatives: Vinita Gotting, Demetrius Williams, Lena Muwakki, Carl Riley, Martha Hering



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