Accrual Activities in the National Clinical Trials Network (NCTN)

Andrea Denicoff, MS, RN, ANP
Holly Massett, PhD
Grace Mishkin, MPH, CHES

Presented to the Clinical Trials and Translational Research Advisory Committee (CTAC), March 4, 2015
Agenda

• Describe background for accrual activities

• Summarize the NCTN Accrual Meeting held Dec. 4-5\textsuperscript{th} at the NCI

• Describe key issues raised and steps to address them

• Gather CTAC input
Background – IOM Report

IOM Emphasized Critical Need for a Public Clinical Trials System

4 Consensus Goals for Modernization:

- Incorporate innovative science and trial design
- Improve speed & efficiency of trial development & activation
- Improve prioritization, support, and completion of trials
- Foster participation of patients and physicians
**Goal:** Adopt a multifaceted approach to mobilize entire research community to focus on improving accrual processes

**Improved Pre-Activation Timelines**

- Concept Development and Review
- Protocol Development and Review
- Activation
- Accrual
- Study Completion

**Now, Systematically Address Accrual**

Building on “NCI pilot intervention program to assist accrual for challenging late-phase clinical trials,” J Clin Oncol 32:5s, 2014 (suppl; abstr 6617).
Previous NCI-ASCO Accrual Meeting

Focus on Patient-Centered Solutions
1. Patient Decision-Making
2. Minority and Under-represented Populations
3. Community Outreach and Education

NCTN Meeting to Address Accrual Challenges in NCTN Clinical Trials in Adults and Adolescents and Young Adults (AYA)

• Co-sponsored with Foundation for the NIH (FNIH)
• Goals
  – Develop consensus around key operational accrual challenges in the NCTN and potential strategies to address those challenges
  – Lay the groundwork for a group devoted to NCTN accrual issues
• Scope
  – NCTN trial operations and administration at the NCI, Group, and site levels that impact accrual
• **NCTN Groups:** Rick Bangs, Mike Katz, Frank DeSanto, Sharon Hartson, Elise Horvath, Ruth Lambersky, Jamilah Owens

• **NCTN Lead Academic Participating Sites (LAPS):** Jordan Berlin, Miriam Bischoff, Anne Duli, Suresh Ramalingam, Wade Willams

• **NCI:** Andrea Denicoff, Holly Massett, Grace Mishkin
December 4 & 5 Meeting Participants

• 75 Group and LAPS participants
  – Group Operations and Communications
  – Group Patient Advocates
  – LAPS PIs
  – LAPS Operations

• Several NCI Divisions and Offices
Areas Explored

- Accrual strengths and challenges across stakeholders
- Trial accrual challenges - case studies
  - ALCHEMIST: early stage lung cancer precision medicine trial
  - ARST1321: AYA sarcoma trial
  - EA1131: triple negative breast cancer trial
  - Lung-MAP: advanced squamous cell lung cancer precision medicine trial
  - NRG-BN001: radiation trial for glioblastoma
- Next steps
  - Develop strategies to support accrual across the NCTN
  - Develop processes to build and maintain the implementation of such strategies
  - Continue to address challenging trials
Create a Network Accrual Core Team (ACT)

- **Objective:** Provide the NCTN and NCORP an inclusive forum to maximize accrual across the Networks through communication and collaboration

- **Goals:**
  - Give Groups, patient advocates and sites the opportunity to provide input and ideas for enhancing patient enrollment and site participation in NCTN and NCORP trials
  - Provide each Group an opportunity to present trials and receive Network input and accrual support
  - Work collaboratively to monitor accrual progress from Network efforts and refine processes as need to best support the Network
Network Accrual Core Team

NCTN Management Committee

- Meets regularly
- Reports to Management Committee
- Addresses issues in specific trials
- Develops and oversees Task Forces for more systemic issues as needed

Accrual Core Team

Topical Task Force e.g. Trial-Specific Templates

- Convened in response to issues identified by Core Team
- Meets regularly for a finite period of time to achieve specific outcomes
- Includes Core Team members and other participants

Topical Task Force e.g. Accrual Metrics

Topical Task Force e.g. CTSU Accrual Dashboards

NCTN NCI National Clinical Trials Network
Next Steps

• NCI internal retreat held Feb 6-7th to address NCI issues and develop plan of action
  – Communicated back to NCTN Groups and meeting participants
  – Continue to implement and report back to ACT

• Inviting representatives for ACT with plans to have quarterly calls / webinars and establish a working charter

• Gather input from CTAC
KEY MEETING TAKEAWAYS
Funding and Resource Concerns

• Sites incur activation costs before a study even opens
  – Formulating trial budget
  – Obtaining IRB approval
  – Preparing Medicare / Insurance Coverage Analysis
  – Entering protocol in Electronic Medical Record (EMR) software
  – Obtaining departmental sign-off (e.g. interventional radiology)
  – Training and informing study staff

Funding and resource concerns were ranked the top challenge by LAPS and Groups in meeting prioritization activity
Continue to Build on Network Efficiencies

• Moving away from different systems for each group
  – Oncology Patient Enrollment Network (OPEN) for all enrollments to NCTN clinical trials
  – Medidata Rave clinical data management system for all NCTN trials
  – Cancer Trials Support Unit (CTSU) website posts all trial-specific materials for all NCTN trials
  – NCI Central IRB (CIRB) independent review model with over 70% of sites participating

• Highlight availability of additional funds
  – New funding sheets for each NCTN trial
**PROTOCOL S1400D:**
A Phase II/III Randomized Study of AZD4547 Versus Docetaxel as Second Line Therapy for Biomarker Selected Patients with Stage IV Squamous Cell Lung Cancer

(S1400D is a treatment companion trial to S1400: Phase II/III Biomarker-Driven Master Protocol for Second Line Therapy of Squamous Cell Lung Cancer: Lung-Map)

**Study Activation: 06/15/2014**

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<th>Funding Source and Study Component</th>
<th>Mandatory/ Mandatory Request or Event/ Optional</th>
<th>Study Specific Notes</th>
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<th>NCTN Funding Amount per Patient (a) Standard/LAPS</th>
<th>NCORP Funding Amount per Patient (b) Std/HP</th>
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**Total Potential Federal Funds**

$2150 / $3900

$2400 / $3900

**Non-Federal**

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Funding for intervention and biospecimens
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<th>Funding Source</th>
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<th>Non-NCORP Amount per Patient</th>
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**Total Potential Funds Per Patient for S1400D**

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<th>Non-NCORP Amount per Patient</th>
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Additional biopsy funding

Additional support
Enhancing Investigator Buy-In

- **Assess investigator interest early and often**
  - Ensure accrual projections are feasible based on interest across the investigator community (e.g. using NCI surveys)
- **Promote trials succinctly to specific investigators**
  - Send notifications from key leaders (e.g. disease chairs)
  - Target communications by specialty or interest area
  - Clearly communicate trial rationale and advantages of participation
- **Make it easy for investigators (and administrators) to find and search trials**
  - Provide clinical decision trees for trials in similar disease settings (e.g. three neoadjuvant breast cancer trials from different groups)
New CTSU Dashboard for Sites
New CTSU Dashboard for Sites

- Portals in the dashboard show:
  - Site accrual
  - In-progress enrollments
  - Multi-step enrollments
  - Protocol updates
  - Newly posted protocols
  - Expiring IRB approvals
CRISP

(CTSU Report Information and Subscription Portal)

• Single location for site users and investigators to subscribe to CTSU email notifications and reports
  – E.g. posting of new protocol documents, expiration of IRB approvals
  – Subscriptions can be chosen by users based on disease type, areas of research interest, site preferences
Enhancing Trial Engagement

- Increase awareness of trials for adolescent and young adults (AYA)

- Engage patient advocate input early on feasibility and patient education issues

- Consider underserved and minority patient issues in trials with expected larger accrual
  - E.g. increase awareness of Spanish-language consent forms
Enhancing Investigator Buy-In

• **NCI Cancer Centers prioritize investigator-initiated trials over NCTN trials**
  – Harmonize grant objectives across NCI

• **Raise the value of NCTN trials at sites and centers**
  – Create a recognizable NCTN brand

• **Engage their competitive instincts**
  – Promote top accruers and encourage high-accruing sites to share expertise
Precision Medicine & Rare Disease Trials

• New emphasis on rare disease trials means new and different accrual challenges
  – Common diseases are being dissected into “rare” subgroups
  – Accrual from sites across the network is needed for these trials to be successful

• Funding and investigator interest issues are enhanced when there is low expected site accrual
  – Significant investment of resources in trial activation
  – Sites avoid opening trials they may never accrue to
  – Some cancer centers will not open trials expected to accrue fewer than 1 or 2 patients per year
  – Possible alternative: “Just In Time” activation
Questions for CTAC

• What new or additional efforts may be needed to support accrual to rare disease trials?

• What new or additional efforts may be needed to support accrual to precision medicine trials?

• Other suggestions?