National Cancer Institute

NCTN NCI National Clinical Trials Network
Research Driving Progress

Accrual Activities in the National Clinical Trials Network (NCTN)

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

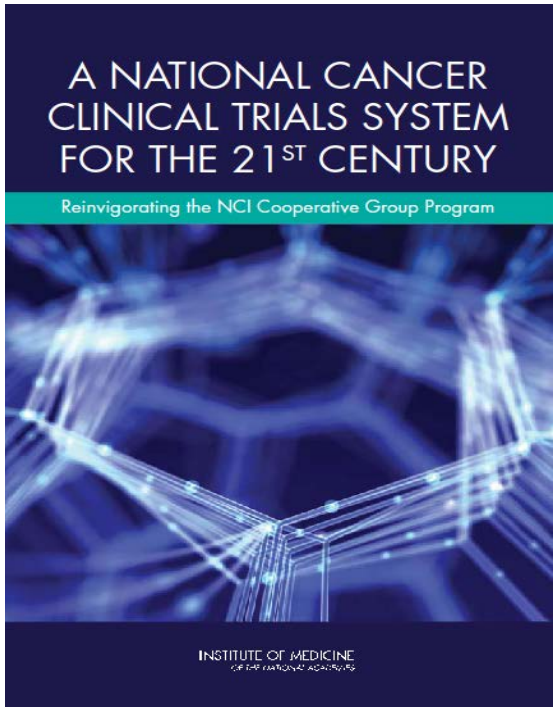
U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health

Agenda

- **Describe background for accrual activities**
- **Summarize the NCTN Accrual Meeting held Dec. 4-5th 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



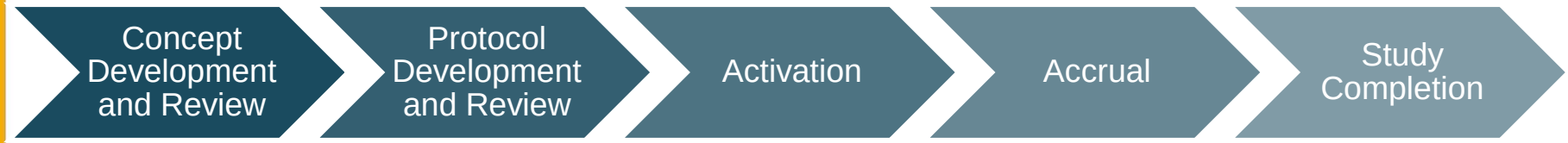
4 Consensus Goals for Modernization:

- ✓ 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

OEWG – Moving Forward

Goal: Adopt a multifaceted approach to mobilize entire research community to focus on improving accrual processes

Improved Pre-Activation Timelines



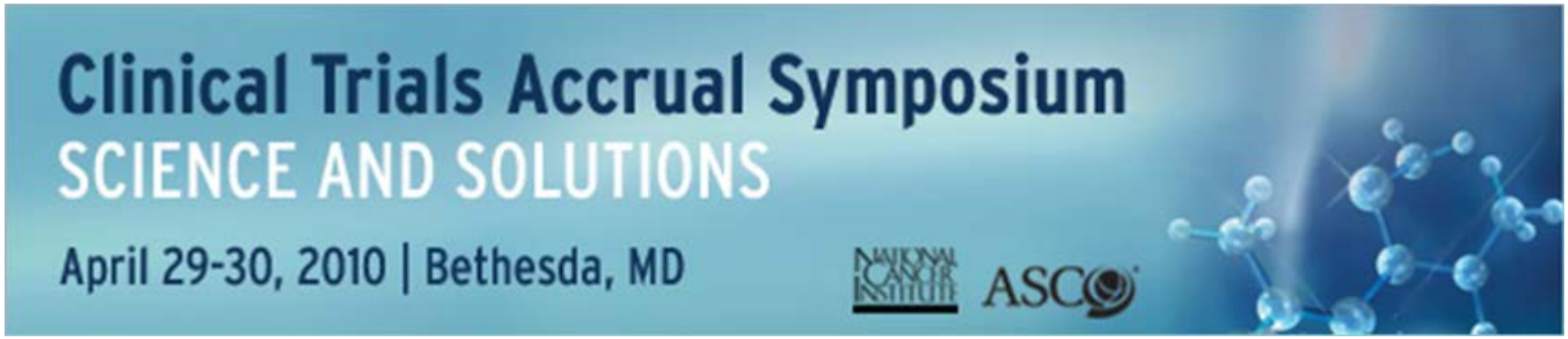
Now, Systematically Address Accrual

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**



"The National Cancer Institute-American Society of Clinical Oncology Cancer Trial Accrual Symposium: summary and recommendations." J Oncol Pract. 2013 Nov;9(6):267-76. doi: 10.1200/JOP.2013.001119. Epub 2013 Oct 15.

Accrual Meeting: December 4 - 5, 2014

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

December 4 & 5 Meeting Planning Group

- **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**

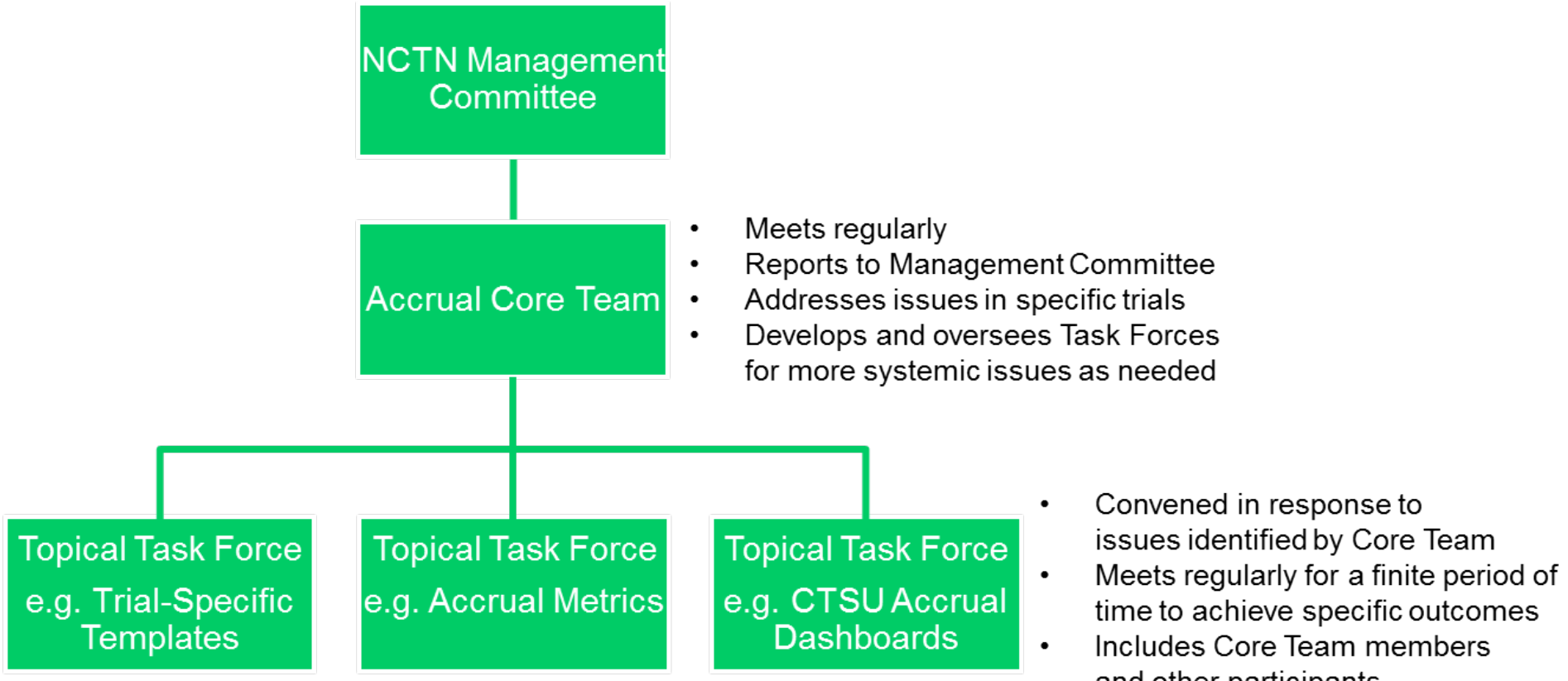
Areas Explored

- **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



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

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NCTN
NCI National Clinical Trials Network
Research driving progress.

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

Funding Source and Study Component		Mandatory/ Mandatory Request or Event/ Optional	Study Specific Notes	Enter Collect Date in OPEN?	NCTN Funding Amount per Patient (a) Standard/ LAPS	NCORP Funding Amount per Patient (b) Std/HP
Federal	Base Intervention (Standard/LAPS)	Mandatory	1	No	$1750 / $3500	$2000/ $3500
Federal	Biospecimen - Peripheral Blood	Mandatory Request	2	Yes	$100	$100
Federal	Biospecimen (Tissue) collection at time of progression	Mandatory Request	2, 4	Yes	$300	$300
Total Potential Federal Funds					**$2150/ $3900**	**$2400/ $3900**
Non-Federal	Additional capitation resources from industry partners (Standard/LAPS)	Mandatory	3	No	$2640 / $890	$2390 / $890
Total Non-Federal Funds (c)					**$2640 / $890**	**$2390 / $890**
Total Potential Funds (d)					**$4790/ $4790**	**$4790/ $4790**

Funding for intervention and biospecimens

BIOPSY: EITHER CT Image Guided OR Bronchoscopy at progression with response to Arm 1						
Non-Federal	**CT image guided biopsy**	Mandatory Event	4	No	**$3000**	**$3000**
Non-Federal	**Bronchoscopy biopsy**	Mandatory	4	No	**$6000**	**$6000**

Additional biopsy funding

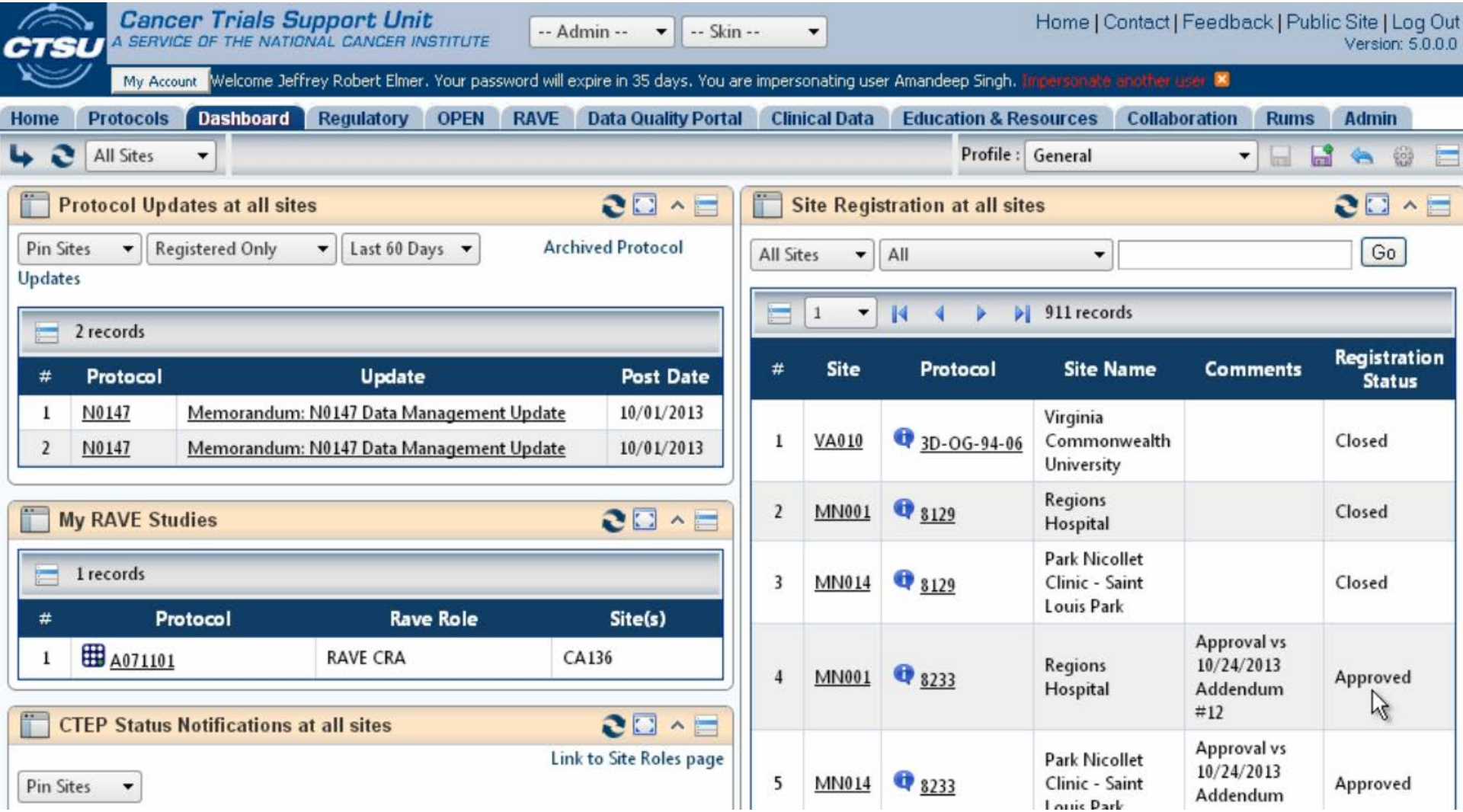
Additional Support for S1400D						
Sites will be reimbursed for the following procedures for S1400D (FGFR-AZD4547 versus Docetaxel)						
Funding Source	**Study Component**	**Mandatory/ Mandatory Request or Event/ Optional**	**Study Specific Notes**	**Enter Collect Date in OPEN?**	**Non-NCORP Amount per Patient**	**NCORP Amount per Patient**
Non-Federal	OCT exam performed ($315 x 4 timepoints estimated)	Mandatory	5	No	$1,260	$1,260
Non-Federal	Ophthalmic Assessment ($625 x 6 timepoints estimated)	Mandatory	5	No	$3,750	$3,750
Non-Federal	ECHO/MUGA exam performed ($1,100 x 3 timepoints estimated)	Mandatory	5	No	$3,300	$3,300
Non-Federal	Phosphate ($40 x 8 timepoints estimated)	Mandatory	5	No	$320	$320
Non-Federal	Urinalysis ($15 x 8 timepoints estimated)	Mandatory	5	No	$120	$120
Non-Federal	Troponin ($45 x 8 timepoints estimated)	Mandatory	5	No	$360	$360
Total Potential Funds Per Patient for S1400D					**$9,110**	**$9,110**

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

In the Works

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

NCI CCC®

A Comprehensive Cancer Center Designated by the National Cancer Institute

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?**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