Cooperative Groups Session
Transforming the NCI Clinical Trials System

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Cancer Therapy Evaluation Program
National Cancer Institute

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Carlsbad, CA
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I have no disclosures
Emphasized need for public clinical trials system

Consensus achieved on 4 goals for transforming the system:
- Improve speed/efficiency of development & conduct
- Incorporate innovative science and trial design
- Improve trial prioritization, support, & completion
- Incentivize participation of patients & physicians

In response, NCI is transforming its clinical trial system to create a highly integrated network to address rapid advances in cancer biology based on:
- Recommendations from the IOM Report
- Previous reports (CTWG & Operational Efficiency)
- Current stakeholder input
Recent ASCO Recommendations

• Enhance inclusion of innovative and clinically meaningful science & decrease duplication across all NCI-supported clinical trials
  – Improve connections between NCI translational and early-phase clinical trial mechanisms
  – National Clinical Trials Network (NCTN) (revised Cooperative Group Program) should be open to scientific concepts from outside the Groups or other NCI-supported mechanism
Recent ASCO Recommendations

- Prioritize Trials that are Practice-changing with Meaningful Clinical Benefit
  - Federal system should focus on multi-modality treatments, adjuvant therapy, combinations of novel agents, screening and prevention strategies and therapies for rare diseases

- Improve Timelines of Trial Development

- Promote Efficiency across the Network
  - Standards for protocol development & trial conduct, Central IRB, emphasis on collaboration

- Increase Funding for Clinical Trials

- Ensure National Infrastructure Enables Physician Participation
GROUP CONSOLIDATION & CREATING A NETWORK

• Ability to prioritize molecular characterization resources & develop molecularly-driven trial designs is critical for success of multisite clinical trials: these trials often require screening of large populations.

• Need to improve prioritization of phase 3 portfolio across disease entities as trial costs (due to size and/or complexity) increase with limited resources.

• Removes disincentives to study less common diseases because of accrual risks.
Scientific Rationale for Transforming Current System

- **Shared IT infrastructure** for clinical data & tissue resource management & **harmonized procedures** for oversight for therapeutic trials & QOL/cancer control studies more feasible with fewer groups

- **Scientific interactions around imaging** facilitated by integrating American College of Radiology Imaging Network (ACRIN) into collaborative network

- **Optimal use of biospecimens** by creating integrated national banking resource

- **Open access to national network** for clinical/ translational investigators not currently involved in Groups
NCI Recommendations

• Integration into not more than 4 Adult and 1 Pediatric Group with multi-modality capacity in a broad range of diseases all fully committed to a national clinical trials network

• Potential strategies to assist integration:
  — NIH grants now permits multiple PIs which may help with leadership transition
  — Incentivize transition with additional resources
  — Allow distributed data mgt & operations to avoid disruptions of ongoing trials
  — Combine (rather than disband) overlapping disease committees to include all current participants

• Re-configure NCI review of the clinical trials program with emphasis on incentives for a national system
Proposed New Organizational Structure for the NCI’s Clinical Trials Program

Across Disease/Trials Oversight Panel

NCI Disease Steering Committees: Evaluation/Prioritization of Trials

Common Clinical Trials Mgt System

NCI DEA Review

Consolidation to 4 Adult Groups; 1 Pediatric Group

NCI Clinical Trials Network

Central Access to NCI Clinical Trials Portfolio (Cancer Trials Support Unit)

Cancer Centers

Other Academic Ctrs

CCOPS & MB-CCOPs

Community Practices

International Members

NCI Central IRB

CTSU
NCI’s Response to Recommendations

Progress:

- Engaged in discussion with Group Chairs about potential consolidation activities & incentivize the transition with provision of additional resources
  
  1st steps to consolidation/transition: RTOG-NSABP; ACOSOG-CALGB-NCCTG; ECOG-ACRIN

- Consideration of modified site U10 program and proposed new funding model based on increased per case reimbursement for high-accruing sites

- Planning NCI external peer-review of Groups in same review cycle & new review criteria on collaboration/evaluation as partners in National Clinical Trials Network; use of NIH/NCI multiple PI construct for program grants
NCI’s Response to Recommendations

Progress:

- Instituted comprehensive, central 24/7 patient registration for all adult Group trials, w/ regulatory & site verification of participation by Cancer Trials Support Unit (CTSU);
  - incorporation of COG into system in near future

- Implemented OEWG timelines for concept evaluation, protocol development, trial activation

- Working with Groups on a single, harmonized approach to clinical trial management, including protocol authoring, case report forms, standardized data collection & management

- Working on establishing ongoing collaborative management team to manage program as a national program
Components of New Review Process for Transformed System

Re-configure NCI external peer-review of trials program grants w/ emphasis on incentives for a national system – all trials open to all sites & sites can credit any Group to which they belong

- Components of review for the national system
  - Disease-specific SCs evaluate/prioritize specific trials
  - Reconfigures NCI/NIH external peer review of new system
    - Criteria for scientific evaluation will no longer focus on trials put forward by disease committees; emphasis will shift to evaluating role of Group in national clinical trials network & overall scientific direction/quality

- Operational Efficiency
- Review criteria for collaborative management of the system
  - Coordination with other NCI-funded programs CCOPs, Tumor Banks, Cancer Centers, SPORES, N01s/U01s, P01s
<table>
<thead>
<tr>
<th>Date Range</th>
<th>Event Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dec 2010 – Jul 2011</td>
<td>Gather information/input from stakeholders &amp; community for New FOA &amp; Guidelines; develop Concept</td>
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<td>Aug 2011</td>
<td>NCI Divisional/CTROC Concept Review</td>
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<td>Sept 2011</td>
<td>NCI Scientific Program Leadership Concept Review</td>
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<tr>
<td>Nov 2011</td>
<td><strong>BSA Concept Review</strong></td>
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<tr>
<td>Nov 2011 – July 2012</td>
<td>NCI DEA &amp; NIH Review of FOA &amp; Guidelines</td>
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<tr>
<td>July 2012</td>
<td><strong>New FOA Released/Published</strong></td>
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<tr>
<td>Nov 2012</td>
<td>Receipt of Competing Applications for New FOA</td>
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<tr>
<td>Feb 2013</td>
<td>Review of Competing Applications by DEA</td>
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<tr>
<td>May 2013</td>
<td>NCAB Review</td>
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<td>After Oct 2013</td>
<td>Rollout of Awards in FY2014</td>
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NCI has re-evaluated & changed its role in clinical trials system

- Initiated Clinical Trials and Translational Research Advisory Committee: First federally-chartered NCI advisory group in a decade; in operation for >3 years with specific responsibilities for NCI’s clinical trials programs; currently engaged in evaluation of implementation of CTWG recommendations

- Revamped prioritization process for large phase 2 and phase 3 treatment and control trials by creating disease- and modality-specific Steering Committees to ensure that most important trials are given highest priority
  - Steering Committees convene clinical trials planning meetings to identify critical clinical trial issues for future studies
  - While NCI has voice on the Steering Committees, its role is to facilitate trial implementation, rather than to direct primary review
Clinical Trials Planning Meetings (CTPMs)

2006
- Endometrial Cancer (GCSC)

2007
- Cervical Cancer (GCSC)
- Pancreas Cancer (GISC)

2008
- Gastrointestinal Stromal Tumors (GISC)
- Squamous Cell Head & Neck Cancer & HPV (HNSC)
- Hepatocellular Carcinoma HCC (GISC)

2009
- Chemotherapy Induced Peripheral Neuropathy (SxQOL)
- Ovarian Cancer (GCSC)
- Neuroendocrine Tumors (GISC)

2010
- Cancer-related Fatigue (SxQOL)
- Androgen Receptor (AR) & AR Signaling in Prostate Cancer (GUSC)

2011
- Rectal & Colon Cancer (GISC)
- Next Generation Trials for HER-2-positive Breast Cancer (BCSC)
- Building Bridges: the Identification of Core Symptom & HRQOL Domains for use in Cancer Research (SxQOL)

2011 / 2012
- Transoral Resection of Pharynx Cancer (HNSC)
- Strategies for Integrating Biomarkers into Clinical Therapies for Lung Cancer (TMSC)
- Ovarian Cancer (GCSC)
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Central IRB

CTSU

Disease Committees

5 Ops, Stats & Data Mgt Centers

Tumor Banks

Adult Group #1

COG

Adult Group #2

Adult Group #3

Adult Group #4
Scientific Steering Committees are disease or modality focused.

NCI, Group Chairs and CCOP Research Base PIs need feedback and assistance in assessing cross-disease and modality priorities.

This feedback should be provided by thought leaders from within and outside the Groups, and should be part of CTAC.

This is NOT another level of protocol-specific review.

- Strategy as opposed to tactics
- Longer-term planning as opposed to short-term objectives
Responsibilities of the Strategic Working Group

- Monitor and assess scientific effectiveness of individual Steering Committees as well as balance & appropriateness of NCI’s overall late stage clinical trials portfolio

- Recommend improvements, including new strategic priorities and directions for late stage clinical trials based on the current portfolio of trials, evolving clinical needs & emerging scientific opportunities

- Anticipated membership to include Group Chairs & Biostatisticians, Cancer Center Directors, CCOP PIs, Patient Advocates, Translational Scientists (SPORE/P01), Cancer Control PIs, Steering Committee Chairs, CTAC members, NCI
Vision of Transformed Network

- System provides essential infrastructure for Group trials in treatment, control, screening, diagnosis, & prevention; and is major enabler of efforts for definitive confirmation of cutting-edge discoveries across all of NCI’s clinical research programs

- Trials approved by Steering Committees are rapidly opened and complete accrual according to defined guidelines by leveraging an integrated national network of performance sites

- User-friendly system with harmonized processes is available to the extramural cancer community: investigators, patients, advocates, and industry

- New system provides an optimal platform to perform large scale testing of increasingly smaller subsets of molecularly-defined cancers, and efficiently answers critical questions not well supported in a commercial environment
THANK YOU!
Back-up slides
# Disease-Specific Steering Committees: Prioritizing Clinical Trials

<table>
<thead>
<tr>
<th>Steering Committee</th>
<th>Year Established</th>
<th>Co-Chairs</th>
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<tbody>
<tr>
<td>GI</td>
<td>2006</td>
<td>Dan Haller, MD &amp; Joel Tepper, MD</td>
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<tr>
<td>Gyne</td>
<td>2006</td>
<td>David M. Gershenson, MD, Gillian Thomas, MD, &amp; Michael Birrer, MD</td>
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<tr>
<td>Head &amp; Neck</td>
<td>2007</td>
<td>David Adelstein, MD, David Brizel, MD, &amp; David Schuller, MD</td>
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<td>GU</td>
<td>2008</td>
<td>Eric Klein, MD, George Wilding, MD*, &amp; Anthony Zietman, MD</td>
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<tr>
<td>Breast</td>
<td>2008</td>
<td>Charles Geyer, MD &amp; Nancy Davidson, MD*</td>
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<tr>
<td>Thoracic</td>
<td>2008</td>
<td>David Harpole, MD, William Sause, MD, &amp; Mark Socinski, MD</td>
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<td>Leukemia</td>
<td>2009</td>
<td>Wendy Stock, MD &amp; Jerry Radich, MD</td>
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<td>Lymphoma</td>
<td>2009</td>
<td>Oliver Press, MD &amp; Julie Vose, MD</td>
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<tr>
<td>Myeloma</td>
<td>2009</td>
<td>Morie Gertz, MD &amp; Nikhil Munshi, MD</td>
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<tr>
<td>Brain</td>
<td>2010</td>
<td>Ian Pollack, MD &amp; Al Yung, MD</td>
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<tr>
<td>Pediatrics</td>
<td>2011</td>
<td>David Poplack, MD (Leukemia &amp; Lymphoma) Mark Bernstein, MD (Solid Tumors)</td>
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*Over 185 Concepts evaluated since inception of SCs

*Cancer Center Directors
Other Related Steering Committees:
(Non-disease Focus)

- Investigational Drug Steering Committee
  - Co-Chairs: Pat LoRusso, DO, & Dan Sullivan, MD

- Clinical Imaging Steering Committee
  - Co-Chairs: Steven Larson, MD and Etta Pisano, MD

- Symptom Management & Health-Related Quality of Life Steering Committee
  - Co-Chairs: Deborah Bruner, RN, PhD & Michael J. Fisch, MD, MPH

- Patient Advocate Steering Committee
  - Co-Chairs: Regina Vidaver & Nancy Roach
Dual Function of Steering Committees

- Steering Committees evaluate and prioritize trial concepts received from Group and non-Group investigators for large phase 2 and phase 3 trials
  - Some SC’s have divided into Task Forces to help with this evaluation

- Steering Committees strategize regarding needs of clinical research in their domain and may form Task Forces, Working Groups and/or hold Clinical Trials Planning Meetings to encourage/develop trials to respond to unmet needs
### NCI Thoracic Malignancies Steering Committee - Concepts

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<tr>
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<tr>
<td><strong>Total</strong></td>
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<td>5</td>
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RPh2: 13 Ph3 or 2/3: 5  
1 RPh2 received, not reviewed yet