

NCTN Working Group Interim Report

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**NCI Clinical Trials and Translational
Research Advisory Committee**

NCTN Working Group Update Topics

- **Recap of NCTN WG charge and initial focus**
- **December 2012 meeting summary**
- **Interim report and recommendations**
- **Proposed plan for implementation of disease-specific recommendations**
 - Communication with Steering Committee leadership
 - Communication with NCTN Group Disease Committee Chairs
- **Future plans**

NCTN WG Charge

Initial Focus

- 1) **Assess the strength and balance of the active NCTN clinical trials portfolio (Cross-Disease Portfolio Management)**
 - Within each *disease*
 - Across all *diseases*

- 2) **Recommend new strategic priorities and directions for the NCTN based on:**
 - Current trial portfolio and gaps
 - Evolving clinical needs
 - Emerging scientific opportunities

- 3) **Review and assess the CTWG Evaluation process and results**
 - Quality of completed trial outcomes
 - Operational performance of Scientific Steering Committees
 - Efficiency of clinical trial conduct

- 4) **Provide strategic advice to enhance NCTN clinical trial operations**
 - E.g. Collaboration and timeliness

Criteria for Evaluating Trials

- **Feasibility**
 - Accrual difficulty
 - Time and cost to implement at sites
- **Clinical Importance**
 - Importance of study question relative to state of the science in the disease
 - Benefit per patient and for population (e.g. life years saved)
 - Benefit in light of disease context
- **Scientific Contribution**
 - Tests important scientific or clinical proof of principle question
 - Importance of integral or integrated correlative study questions
- **Relative cost/resources**
 - Total number of patients required
 - Length of study (accrual and follow-up)
- **Appropriateness for NCTN Program**



Summary of December 2012 NCTN WG Meeting

- **Evaluated the Breast, Leukemia, Lymphoma, Gastrointestinal and Genitourinary portfolios**
- **Cross-disease comments and recommendations highlight that some disease portfolios have more scientific opportunities than others resulting in more highly rated trials.**
- **Some common concerns emerged:**
 - A tension between selection of more nimble, biology driven, randomized phase 2 trials versus larger, more resource-intensive phase 3 trials;
 - Lack of drug availability due to pharma/biotech unwillingness to collaborate in certain areas; and
 - Difficulties of predicting accrual feasibility in advance.
- **Recommendations focused on how to best advance cutting-edge science in the genomic era in a time of fiscal constraint**

Interim Cross-Disease Recommendations

(slide 1)

1. NCI should conduct an analysis of resource allocation across diseases, taking into account current survival rates and likely cost/benefit from additional advances.
2. NCTN Groups and DS SSCs should work together to achieve the appropriate balance of innovative, biology-driven randomized phase 2 trials and larger, more resource intensive phase 3 trials in each disease portfolio.
3. NCTN Groups and DS SSCs should emphasize biology-driven (e.g., molecularly-driven, pathway-driven) trials that advance the science by incorporating genomics, biomarker tests and correlative science into study designs.
4. To empower innovative, biology-driven trials, additional NCI funding should be provided for correlative science studies, biomarker validation and the development of molecular classification algorithms.

Interim Cross-Disease Recommendations

(slide 2)

5. Accrual challenges should be taken more seriously in proposing and approving trial concepts, balancing the importance of the clinical question with the perceived difficulty of accrual.
6. More consideration should be given to competing European and industry trials in proposing and approving trial concepts as well as to the potential for collaboration with European and industry partners.
7. DS SSCs should increase their involvement in strategic planning and guidance for future trials in collaboration with the NCTN Groups.
8. DS SSCs should develop standardized guidelines for the level and types of preliminary data required for trial concepts.
9. DS SSCs should optimize their use of Task Forces (TFs), Working Groups (WGs) and Clinical Trial Planning Meetings (CTPMs).
10. Greater emphasis should be placed on sharing strategic and tactical best practices across diseases in terms of trial design, accrual, preliminary data requirements, etc.

Breast Cancer Portfolio

- **Summary conclusions**

- addresses several key clinically important questions
- studies are multidisciplinary
- good balance of systemic and local-regional trials

- **Key recommendations**

- incorporate smaller, nimble randomized phase II trials of newer approaches to balance large adjuvant studies
- priority should be given to molecularly-driven trials, marker validation, correlative science
- incorporate studies on limiting toxicity, improving QoL, and assessing survivorship

The BCSC can facilitate change by providing strategic guidance for concept selection, developing standards for trial design, and optimizing the use of TFs, WGs, and CTPMs.

Leukemia Portfolio

- **Summary conclusions**

- includes many innovative, biologically-based, and scientifically important trials
- addresses several key clinically important questions
- strong CLL trial in older adults

- **Key recommendations**

- priority should be given to molecularly-driven trials, marker validation, correlative science, and imaging technologies
- prioritize biospecimen collection
- develop molecular classification algorithms for patient stratification

The LKSC should build on its strengths in strategic planning, collaboration, and refining trial ideas by working collaboratively with the NCTN Groups to make these improvements and work to enhance accrual.

Gastrointestinal Cancer Portfolio

- **Summary conclusions**

- addresses several key clinically important questions
- addresses questions industry would not
- includes rare cancers

- **Key recommendations**

- greater focus on scientific innovation, biology, and genomics
- promote studies that incorporate pathways, biomarker screening, and targeted therapies
- promote use of molecular classification for treatment selection

The GISC should leverage its strengths in organization, efficiency, use of TFs and intergroup and global collaboration to work collaboratively with the NCTN Groups to make these improvements and improve the process for assessing accrual feasibility.

Lymphoma Portfolio

- **Summary conclusions**

- concern that competition from industry and Europe has resulted in the best new agents in lymphoma not being developed through the NCTN

- **Key recommendations**

- focus on innovative, correlative and translational science
- incorporate integral biomarkers and molecular characterization into trial concepts
- develop a niche in applying molecular science to trial concepts
- work on data standardization and address accrual issues

The LYSC should continue its strategic planning and guidance of early concept development and work with the NCTN Groups to promote development of phase II trials that inform or lead to phase III trials.

Genitourinary Cancer Portfolio

- **Summary conclusions**

- recent and ongoing trials are likely to have only moderate scientific and clinical impact
- addresses questions industry would not

- **Key recommendations**

- in addition to the focus on prostate cancer, include trials in diseases with poorer outcomes such as renal and bladder
- focus on scientifically important, molecularly-driven, multidisciplinary trials with greater clinical impact
- leverage new drugs, and move toward smaller phase II studies
- incorporate more molecular correlates and biomarkers, technology assessment, QOL and patient reported outcomes into concept designs

The GUSC and the NCTN Groups should develop a strategic plan to guide concept development and decision-making processes, and balance prostate and large phase III trials with other diseases and trial types.

Summary of the December 2012 NCTN WG Meeting

- **Completed comprehensive and critical review of the five disease-specific portfolios**
- **Allowed for critical assessment of the strengths and weaknesses of the portfolios presented**
- **Developed interim recommendations to improve clinical cancer research portfolios supported by the NCI**
- **Recommendations will be further refined based on the review of the trial portfolios for the remaining diseases**

NCTN Current Status & Future Plans

- **Anticipate a total of 3 meetings needed to complete the assessment of the strength and balance of the active phase 3 and large phase 2 clinical trials currently conducted by the NCTN Program:**
 - **December 2012:**
 - Analyzed the breast, GI, GU, leukemia, and lymphoma portfolios
 - **March 2013**
 - Analyze the myeloma, brain, thoracic, and pediatric portfolios
 - **Summer 2013**
 - Review remainder of the portfolio including symptom management trials
- **Cross-disease portfolio assessment activities to follow the individual disease portfolio assessments.**

Proposed Implementation of Disease-specific Recommendations

- **Communication with Steering Committee Leadership**
- **Communication with NCTN Group Disease Committee Chairs**
- **Achieving recommended goals will require collaboration between NCI, NCTN Groups, and SSC**
- **Series of disease specific conference calls with NCTN WG Chairs, SSC Chairs, and NCTN Disease Committee Chairs**

Discussion Topics

- **Strength and Weakness of Process**
 - Comments from NCTN WG members
 - Comments from Strategic Planning Subcommittee
- **NCI Pipeline**
 - How to integrate information on NCI's early clinical trials programs, i.e., SPORE, IDB, CTSU Flex, etc into portfolio development
- **Implementation of disease-specific versus cross-disease recommendations**

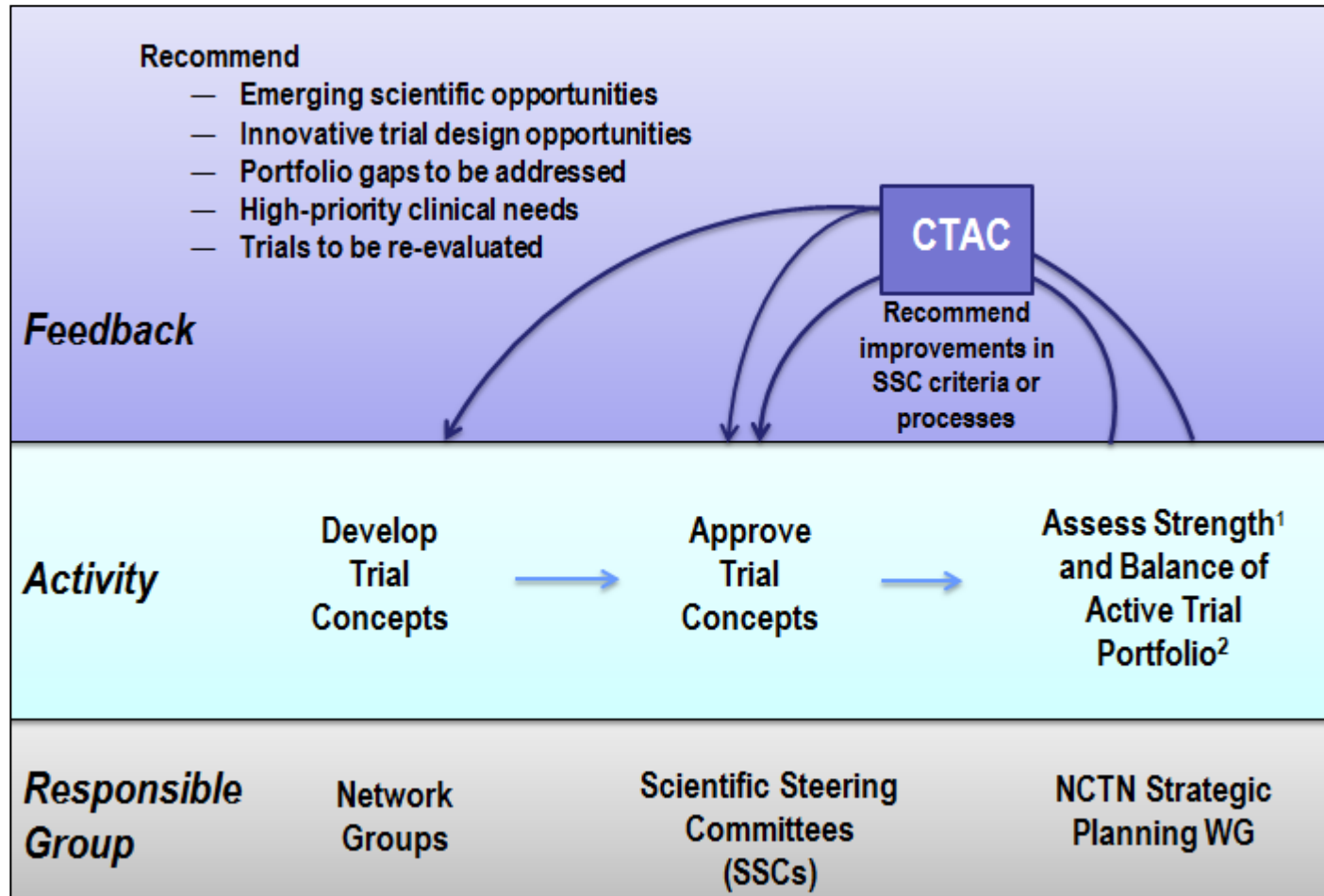
Extra Slides

NCTN Clinical Trials Portfolio

Prioritization Process

- **3 groups assist NCI in managing & prioritizing the portfolio:**
 - **Network Groups (Cooperative Groups)** develop trial concepts and conduct trials.
 - **Scientific Steering Committees (SSCs)** evaluate trial concepts and approve those judged scientifically and clinically meritorious and worthy of the expenditure of NCI resources.
 - **NCTN WG of CTAC** assesses the strength and balance of the active trial portfolio and recommends improvements through the Clinical Trials Strategic Planning Subcommittee of CTAC.
- **Continuous collaboration and feedback through CTAC and its Clinical Trials Strategic Planning Subcommittee**
 - Identify emerging scientific opportunities
 - Assess portfolio strengths and gaps
 - Respond to high priority clinical needs

Collaborative NCTN Clinical Trials Prioritization Model



¹Trial "strength" is the potential for generating high quality trial outcomes.

²Includes active phase 3 and large randomized phase 2 trials and concepts approved by an SSC but not yet activated.

Summary of First NCTN WG Meeting

July 2012

- **Piloted the process to assess the strength and balance of the NCTN trials utilizing the colorectal cancer clinical trials portfolio as the test case.**
- **Concluded review of individual trials within a disease is appropriate and feasible.**
- **Refined criteria for evaluating trials.**
- **Recommended assigning each trial an overall score based on individual trial evaluation criteria.**
- **Concluded presentations of clinical trial portfolio and strategy in disease area by CTEP Medical Officer and Steering Committee Chair is valuable for putting trials in context and understanding the basis for Steering Committee decisions.**
- **Recommended summary information on other major ongoing trials outside of NCTN (e.g., industry, international) in disease area be provided.**
- **Recommended that WG members be assigned to disease based subgroups to take the lead in the review of each disease area.**