

NCTN Working Group Interim Report

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



NCTN WG Charge

Initial Focus

- 1) **Assess the strength and balance of the active NCTN clinical trials portfolio**
 - 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

Portfolio Assessment Overview

- **4 meetings held to assess the NCTN trial portfolio**
 - Assessed strength and balance of the NCTN portfolio
 - Recommended strategic priorities and directions
- **Portfolios from 14 Steering Committees assessed**

Meeting Date	Portfolios Assessed
July 2012 (pilot)	Colorectal cancer from GI portfolio
Dec. 2012	Breast, GI (minus colorectal), GU, leukemia, lymphoma
Mar. 2013	Myeloma, thoracic, brain (adult and pediatric), pediatric (solid tumor and leukemia and lymphoma)
July 2013	Gynecologic, clinical imaging, symptom management/quality of life, head and neck



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**

Unique Suitability for NCTN Program

- **Understudied/rare diseases or understudied populations**
- **Radiotherapy/surgery/imaging techniques**
- **Combination trials**
- **Therapy optimization trials (e.g., alternative regimens)**
- **Unlikely to be performed by industry**
- **Provides important tissue or data resources for public use**

Cross-Portfolio Recommendations

- Aimed at improving the portfolios and are directed jointly to the NCTN Groups, Scientific Steering Committees and the NCI
- Fall into 5 major categories
 - Emphasize Innovative Science Driven Trials
 - Consider Reallocation of NCTN Resources
 - Enhance Coordinated Strategic Planning
 - Strengthen Evaluation Criteria
 - Optimize Steering Committee Processes

Emphasize Innovative Science Driven Trials

- NCTN Groups and Steering Committees 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.
- NCTN Groups and Steering Committees 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.

Consider Reallocation of NCTN Resources

- NCI should conduct an analysis of resource allocation across diseases, taking into account current survival rates and likely cost/benefit from additional advances.
- 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.

Enhance Coordinated Strategic Planning

- Steering Committees should increase their involvement in strategic planning and guidance for future trials in collaboration with the NCTN Groups.
- Greater emphasis should be placed on sharing strategic and tactical best practices across diseases in terms of trial design, accrual, preliminary data requirements, etc.

Strengthen Evaluation Criteria

- 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.
- 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.
- Steering Committees should develop standardized guidelines for the level and types of preliminary data required for trial concepts.



Optimize Steering Committee Processes

- Steering Committees should optimize their use of Task Forces, Working Groups and Clinical Trial Planning Meetings.

CTAC Reporting on Portfolio Assessment

Meeting Date	Portfolios Assessed	Presented to CTAC?
July 2012 (pilot)	Colorectal cancer from GI portfolio	Previously presented
Dec. 2012	Breast, GI (minus colorectal), GU, leukemia, lymphoma	
Mar. 2013	Myeloma, thoracic, brain (adult and pediatric), pediatric (solid tumor and leukemia and lymphoma)	Bold presented today, remainder presented at a future meeting
July 2013	Gynecologic , clinical imaging, symptom management/quality of life, head and neck	



Thoracic Portfolio

- **Summary conclusions**

- Strength of concepts submitted to the Steering Committee has improved over time
- Excellent job carving out NCTN niche and not directly competing with industry
- Recent trials incorporate local treatment modality approaches and biomarkers, in addition to testing new agents
- Master screening protocols linked with testing of multiple therapies viewed as an important advance, including the collaboration with TCGA to sequence specimens from the ALCHEMIST screening protocol

- **Key recommendations**

- Find ways to accrue a larger proportion of screened patients to NCTN trials
- Form closer collaborations with industry so that screened patients ineligible for NCTN studies can be referred to industry protocols
- Ensure that screened patients are representative of national population

The Steering Committee has done a good job working together and should consider ways to examine and mitigate barriers to accrual.



Brain Portfolio

- **Summary conclusion**

- Pediatric brain cancer generally viewed as a strong portfolio of trials

- **Key recommendations**

- Focus on developing more biology-based, genomics-based, and pathway-directed trials involving biomarkers
- Integrate genomics and correlative science into future protocols whenever possible perhaps through collaboration with the adult brain SPOREs
- More consideration should be given as to whether studies should be designed as phase 2 or phase 3
- Explore combination therapies as single agents are often not optimally effective
- Broaden scope of adult brain portfolio beyond bevacizumab and try to develop some late phase trials

The Steering Committee should strive for better collaboration with the NCTN Groups and should consider reviewing all phase 2 protocols for adult brain cancer, as they do for pediatric brain cancer.



Gynecologic Portfolio

- **Summary conclusions**

- Recent increase in randomized phase 2 and phase 3 trials over single arm phase 2 trials
- Strong international collaborations and generally strong accrual record

- **Key recommendations**

- Work to achieve better balance between innovative, science-driven trials and incremental/ confirmatory trials
- Focus on translational science with clear endpoints and goals including greater collaboration with SPOREs and other translational investigators
- Pursue more systematic design of trials based on past positive or negative results
- For ovarian trials, include endpoints other than PFS and expand beyond the current focus on bevacizumab
- The cervical portfolio should focus more on detection, prevention and radiation therapy trials

The Steering Committee and GOG along with NCI should work together more closely in developing future strategic directions.



Symptom Management/Quality of Life Portfolio

- **Summary conclusions**

- Addresses wide variety of symptoms across many disease sites
- Good accrual record and uniquely suited to the NCTN program

- **Key recommendations**

- Emphasize trials of new interventions over trials that disprove or confirm current interventions
- Strengthen the basic science and preclinical foundation for trials, collaborate with symptom management scientists working in other fields to leverage synergies
- Conduct fewer, but more in depth, trials based on strong biological evidence, exploring innovative agents, comparing interventions against one another rather than placebo, and employing multi-agent therapies
- Pursue more systematic design of trials based on past positive or negative results

The Steering Committee, the CCOP Research Bases, and NCI should collaborate in developing strategic directions and standard data definitions, endpoints, etc. so trials can more easily be compared.



Head & Neck Portfolio

- **Summary conclusions**

- Strong portfolio , potentially practice-changing trials, endpoints aggressive and seek major increases in benefit instead of incremental progress
- Uniquely suited to the NCTN program
- Successfully employs biomarker stratification for understanding subpopulations
- Good collection of tissue samples given access issues
- Effective pursuit of international collaborations

- **Key recommendations**

- Improve incorporation of biological and translational advances such as next-generation sequencing and understanding of disease mechanisms into trial designs
- Place more emphasis on designing strong translational science studies to make optimal use of collected tissues
- Pursue more interaction with SPOREs to address the lack of translational science
- Pursue more interaction with investigators performing single arm phase 2 trials outside the NCTN Program to identify emerging opportunities

The Steering Committee has achieved appropriate balance of review and collaborative development of concepts.

Communication of NCTN WG Findings & Recommendations

- Series of portfolio specific conference calls with appropriate stakeholders, i.e., NCTN WG Chairs, Steering Committee Chairs, NCTN Disease Committee Chairs, NCI staff, CCOP Research Base PIs, etc. (10 of 13 complete)
- Final report to be presented to CTAC after the NCTN WG meeting on December 19, 2013

December 19, 2013 NCTN WG Meeting

- Review stakeholder feedback and finalize Portfolio Assessment Report
- Discuss implementation of NCTN WG recommendations
- Discuss cross-portfolio prioritization process
- Review Gynecologic and Gastrointestinal Steering Committee pilot evaluation findings



Discussion Topics

- **Strengths and Weaknesses of the NCTN WG Process**
- **Feedback on Cross-Disease Recommendations**

Extra Slides

Scoring Rubric for the Five Criteria and Overall

Scoring Category	December 2012 Meeting	March and July 2013 Meetings
Individual criteria <i>(Stayed the same)</i>	<ul style="list-style-type: none"> • High • Medium • Low 	<ul style="list-style-type: none"> • High • Medium • Low
Overall <i>(Changed)</i>	<ul style="list-style-type: none"> • High • Medium • Low 	<ul style="list-style-type: none"> • 1 – Exceptional • 2 – Excellent • 3 – Good • 4 – Fair • 5 – Poor