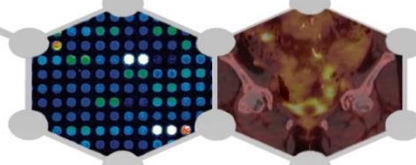
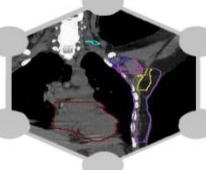


NRG ONCOLOGY

Advancing Research. Improving Lives.™



Gynecologic Cancer Committee Clinical Trial Development

Gynecologic Cancer Committee

Chair: Carol Aghajanian, MD

Co Chairs: Paul DiSilvestro, MD & William Small, MD

Translational Science Co-Chair: Heather Lankes, PhD

GYN Developmental Therapeutics Committee

Chair: Roisin O'Cearbhaill, MD

Co-Chair: Floortje Backes, MD

TS Co-Chair: Panagiotis Konstantinopoulos, MD, PhD

GYN Phase I Subcommittee

Chair: Russell Schilder, MD

Co-Chair: Stephanie Gaillard, MD, PhD

Translational Science
Michael Birrer, MD, PhD

Cervix/Vulvar Cancer Subcommittee

Chair: Charles Leath, MD

Co-Chair: Jyoti Mayadev, MD

TS Co-Chair: Dmitriy Zamarin, MD, PhD

Ovarian Cancer Subcommittee

Chair: Kathleen Moore, MD

Co-Chair: Robert Burger, MD

TS Co-Chairs: Elizabeth Swisher, MD & Rebecca Arend, MD

Rare Tumor Subcommittee

Chair: Allan Covens, MD

Co-Chair: Jubilee Brown, MD

Uterine Corpus Cancer Subcommittee

Chair: Matthew Powell, MD

Co-Chair: Ann Klopp, MD

TS Co-Chair: Douglas Levine, MD

Submitting LOIs/Concepts to NRG Oncology

Request for proposals broadcast prior to Semi-Annual Meetings

"Proposals are to be submitted on the ***CTEP LOI submission form*** for any proposal targeting 97 patients or less **or** the ***CTEP concept submission form*** if targeting 98 or more patients. Current versions of CTEP LOI submission form and concept submission form can be found at: https://ctep.cancer.gov/protocolDevelopment/lois_concepts.htm. Submit completed proposals to GYNconcepts@nrgoncology.org by *."

Review of Submitted LOIs/Concepts

LOI (≤ 97 patients)

NRG Oncology
- Subcommittee
- GYN Cancer Committee
- NRG Oncology Research Strategy Committee

CTEP
- LOI to PIO
- ⓾ Protocol Review Committee (PRC)
- ⓾ Industry Partner

Concepts (≥ 98 patients)

NRG Oncology
- Subcommittee
- GYN Cancer Committee
- NRG Oncology Research Strategy Committee

Scientific Steering Committee (SSC)*
- Concept to PIO
- ⓾ Task Force
- ⓾ Gynecologic Cancer Steering Committee (GCSC)
- ⓾ Industry Partner

*https://www.cancer.gov/about-nci/organization/ccct/steering-committees

Types of Trials

CTEP Supported NCTN Intervention Trials

1. CTEP IND Agents (https://ctep.cancer.gov/protocolDevelopment/agents_drugs.htm)
   - Study team prepares LOI (for trials with 97 or less patients) or concept submission form (for trials with 98 or more patients) https://ctep.cancer.gov/protocolDevelopment/lois_concepts.htm
   - Protocol Administrator (PA) submits LOI or concept submission form to PIO
   - CTEP holds the IND
   - CTEP (PMB) supplies and distributes experimental agent(s)
2. Non-CTEP IND Agents
   - Either the pharmaceutical company or NRG Oncology can hold the IND. If NRG Oncology holds the IND, they cross file on the pharmaceutical company's IND.
   - The pharmaceutical company is responsible for supply and distribution of the experimental agent(s). They can supply/distribute themselves or contract with a 3rd party. NRG Oncology does NOT have the infrastructure to distribute drugs.
   - CTEP has to scientifically approve these studies. This requires submission of LOI or concept submission form and **IB** for the agent(s). Review of LOI or concept is the same as process for #1 above.

Letter of Intent (LOI) Types

- Project Team Member Applications (PTMA)

-CrD PTMA

-Replaced mass solicitation in March 2014

- Unsolicited LOI

-CrDL LOI

CrDL = Career Development LOI

Career Development LOI (CrDL)*

- Eligibility
  - Study chair (PI) should have a major interest in clinical research and the intention to develop a career in that field
  - He/she should be within 7 years of completion of fellowship training
  - He/she must be a faculty member (fellows may not serve as PIs on studies) at an institution with a successful track record in conducting cancer clinical trials
- Requirements
  - Letter of commitment – NRG Oncology Group Chairs
  - Letter of commitment from mentor
  - Biosketch mentee (study chair/PI) AND mentor

CrDL is for LOI only (NOT concepts)

PTMA replaces Mass Solicitation March 2014

PTMA	Mass Solicitation
Application by **individuals** for membership to project team	LOI
Drug development plan by project team occurs during CRADA negotiations	Mass solicitation issued after CRADA negotiations completed
Career Development PTMA (CrD PTMA) •Applicant's and Mentor's NIH Biosketch •Mentor Letter of Commitment •NRG Oncology Letter of Commitment (Group Chair Letter)	

CRADA – Cooperative Research and Development Agreement

Request for PTMA

Team members – Apply as

Trials conducted in the ETCTN, CTEP brain tumor consortia, CITN or NCTN

- Clinical Scientist (Part A)
- Translational Scientist (biomarker development expert) (Part B)
- Basic Scientist (expert in mechanism of action of agent) (Part C)

Project Team

- 8-12 weeks
- Intramural and extramural co-chairs
- WebEx (no in person meetings)
- Attendance mandatory
  - Non-participating members will be dropped
    - for CrD applicants this includes your mentor
  - Non-participating clinicians should not expect to have leadership roles in studies

NRG Oncology PTMA Process

- Project Team Announcements are broadcasted electronically by NCI CTEP PIO
- NRG Oncology (Protocol Development) in turn electronically broadcasts Project Team Announcements to entire membership
- Interested applicants should notify NRG Oncology leadership
  - Research Strategy Committee Chair
  - Disease Site Committee Chair and/or Non-Disease Site Scientific Committee Chair (DT and/or Translational Science)
  - Copy Protocol Development Office (Francy Fonzi, Kia Neff, Nancy Soto)
- PTMA for **individuals** planning on conducting trials in NRG Oncology must be submitted by NRG Oncology
- Application is for individual (not LOI or concept submission form), so the usual Research Strategy Committee requirement of concept approval is not applicable
  - Project team members leave process with requirement to submit LOI or Concept Submission Form (triggers OEWG deadline) and generate protocol
  - LOI/Concept and protocol development is per usual NRG Oncology processes
  - All correspondence with NCI must be submitted by NRG Oncology Protocol Development Office (LOI/Concept submission, protocol submission, etc.)

Unsolicited LOIs

- Before submitting unsolicited LOI (including CrDL), contact the IDB monitor(s) for the intended CTEP agent(s) to schedule a preliminary teleconference (TC)
  - TC must be set up by NRG Oncology Protocol Administrator (PA)
  - Sub-Committee/Committee Chair contact Kia Neff to set up TC (NeffK@nrgoncology.org)
- For CrDL LOI, both the mentor and mentee MUST participate in TC
- TC attendees:
  - Study Chair/PI (mentee)
  - Mentor
  - Sub-Committee/Committee Chair +/- Co-Chair(s) +/- Translational Science representative(s)
  - Representative from Protocol Administration (PA)

  NOTE: Statistician/SDC should NOT be included (statistician gets involved once go ahead is given by CTEP to develop and submit LOI)
- Unsolicited LOIs without a preliminary teleconference will be refused by CTEP

Review of LOIs/Concepts

- LOIs
  - Reviewed by CTEP Protocol Review Committee (PRC)*
  - CTEP approved LOIs are sent to the pharmaceutical collaborator for review and agent commitment (if applicable)
- Concepts
  - Reviewed by NCI Scientific Steering Committee (Gynecologic Cancer Steering Committee [GCSC]**)
  - GCSC approved concepts are sent to the pharmaceutical collaborator (if applicable) for review and agent commitment

*Reviewed by Biomarker Review Committee (BRC) if applicable
**Review by Task force (Cervical Cancer, Ovarian Cancer, Uterine Cancer) prior to GCSC submission is recommended (although not required)

Integral & Integrated Biomarkers

- Integral Studies
  - Assays/tests that must be performed in order for the trial to proceed or to support the primary analysis. Integral studies are inherent to the design of the trial and must be performed on all participants, usually in real time. The assay/test must support one of the trial's primary hypotheses.
  - This includes:
    - Tests to establish eligibility, randomization, stratification, or treatment assignment in a treatment, imaging, prevention or symptom science trial
    - Functional imaging or molecular characterization linked to execution of primary analysis, such as non-reimbursable PET scans or biomarker evaluation
- Integrated Studies
  - Intended to validate markers, imaging tests or tools, or QOL/PRO instruments for possible use as an integral biomarker in future trials or in clinical practice. Integrated studies should test a specific hypothesis with a preplanned statistical design, and are not hypothesis generating or exploratory. Integrated studies must be included in the protocol as a secondary objective.
    - Real time (RT) integrated studies
    - Non-real time (NRT) integrated studies

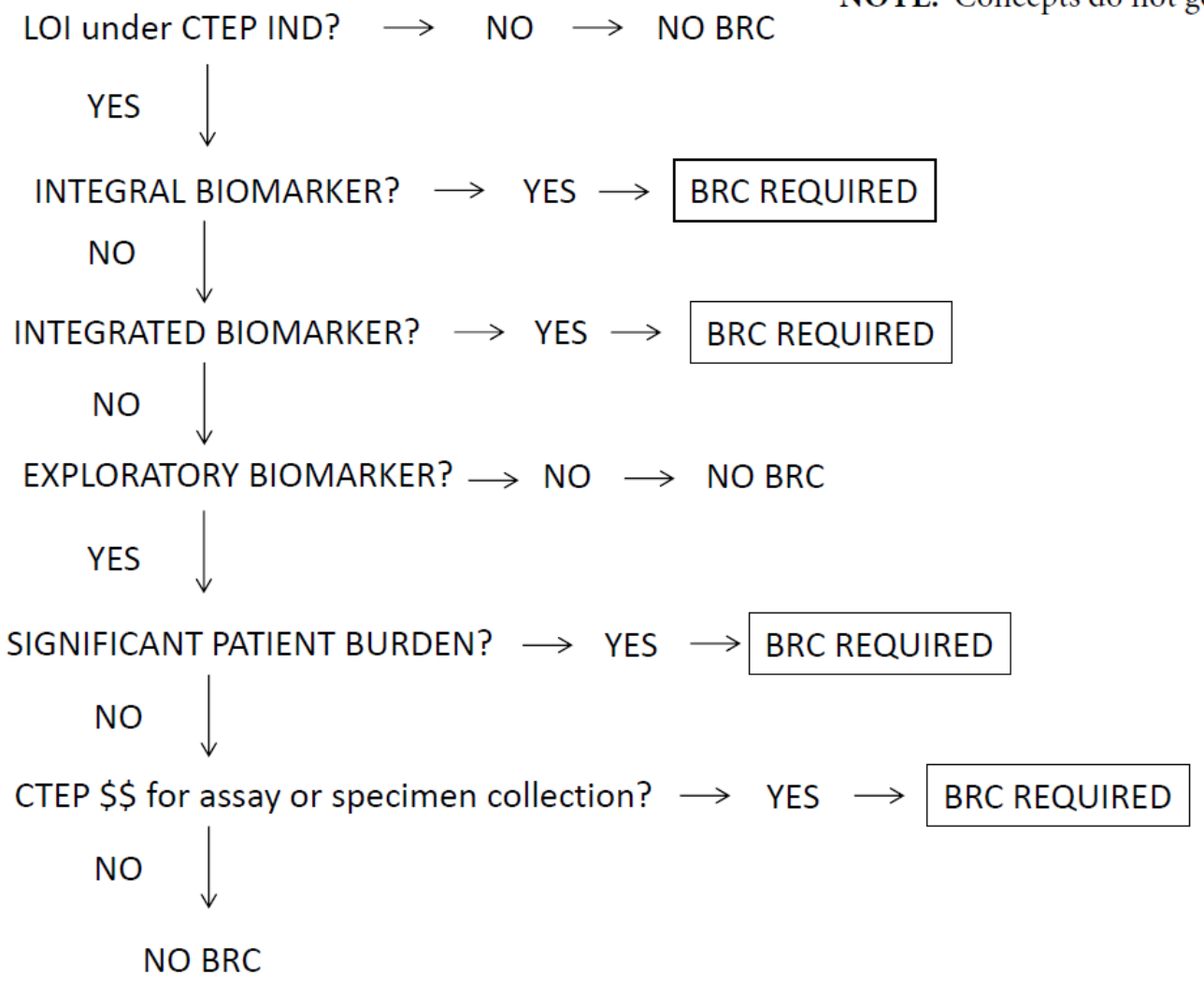
Biomarker Review Committee (BRC)

LOIs require BRC review/approval if they include any of the following:

- Integral and/or integrated markers
- Requests for NCI funding for biomarker assays
- Requests for NCI funding for sample acquisition

NOTE: Exploratory biomarkers that will not be funded by NCI will not undergo BRC review

NOTE: Concepts do not go to BRC.



Biomarker, Imaging and Quality of Life Studies Funding Program
BIQSFP

BIQSFP Funding (NCTN/NCORP)

Eligible trials are those conducted by NCTN Groups and NCORP Research Bases AND reviewed by NCI Steering committees:

1. **Randomized Phase 2 and Phase 3 NCTN treatment trials**
2. **Randomized Phase 2 and Phase 3 NCORP cancer prevention clinical trials**
3. **Randomized symptom science/supportive care clinical trials with efficacy endpoints**
4. **Cost effectiveness analysis (CEA) proposals (if part of randomized phase III trial)**

Application materials and instructions can be found at:
https://www.cancer.gov/about-nci/organization/ccct/funding/biqsfp

Biomarker, Imaging and Quality of Life Studies Funding Program
BIQSFP

BIQSFP Funding (NCTN/NCORP)

- Integral Studies
  - Submit with concept (review is concurrent)
- Real Time (RT) Integrated Studies
  - Submit after concept approval
- Non-Real Time (NRT) Integrated Studies
  - Submit between ≥ 75% accrual to ≤ 6 months after publication (abstract or manuscript) of primary endpoint (whichever occurs first)

Application materials and instructions can be found at:

https://www.cancer.gov/about-nci/organization/ccct/funding/biqsfp

Abbreviations

AOH- Approval on Hold
BIQSFP – Biomarker, Imaging, Quality of Life Studies Funding Program
BRC – CTEP Biomarker Review Committee
CIRB – NCI Central Investigational Review Board
CRM – CTEP Concept Review Meeting
CRR – Consensus Review Response
CTEP – NCI Cancer Therapy Evaluation Program
DCP – NCI Division of Cancer Prevention
GCSC – Gynecologic Cancer Steering Committee
HRC – Human Research Committee
IDB – CTEP Investigational Drug Branch
LOI – Letter of Intent
NCI – National Cancer Institute
NCORP – NCI Community Oncology Research Program
NCTN – NCI National Clinical Trials Network
OEWG – Operational Efficiency Working Group
PIO – CTEP Protocol and Information Office
PRC – CTEP Protocol Review Committee
PRO – Patient Reported Outcomes/Quality of Life
PSC – NRG Oncology Protocol Support Committee
PTMA – Project Team Member Application
RSC – NRG Oncology Research Strategy Committee
Task Forces – Cervical Cancer (CTF), Ovarian Cancer (OTF), Uterine Cancer (UTF)
TC – Teleconference
TS –Translational Science