Cancer Prevention and Control Planning Grant Program
R34 or U34 (Clinical Trials Optional)

Brandy Heckman-Stoddard, PhD, MPH
Chief
Breast and Gynecologic Cancer Research Group
Division of Cancer Prevention
Current Types of Funding for Clinical Trials

- **R21**: Exploratory, Phase I, or non-randomized Phase II

- **R01**: All trials except Phase III clinical trials that test the efficacy of cancer-related medical (oncologic) interventions or Phase III clinical trials of cancer imaging (or other diagnostic) modalities

- **Network Funding**: Early Phase and Late Phase trials developed through network infrastructure
What is a R34 or U34?

From OER definition of grant mechanisms (R34 and U34):
To provide support for the initial development of a clinical trial or research project, including:

- establishment of the research team,
- development of tools for data management and research oversight
- development of a trial design or experimental research designs
- finalization of the protocol
- preparation of an operations/procedures manual
- collection of feasibility data for subsequent research projects

For clinical trials, the planning grant is designed to:

- permit early peer review of the rationale and concept for the proposed clinical trial;
- support development of essential elements of a clinical trial
- lead to an application for support of a full-scale trial, based on elements developed under the planning period
History of R34 and U34 at NIH

- R34 currently used by NIDA, NIDDK, NIAAA, NIMH, NIAID, NEI, NINDS, NCATS, and NHLBI
- U34 currently used by NCATS and NIDDK
- Not previously used by NCI
In non-cancer populations, SPRINT demonstrated that intensive systolic blood pressure (SBP) lowering to a target <120mmHg substantially reduces the rate of cardiovascular (CV) events and all-cause mortality.

Concerns about the tolerability of intensive SBP control that limited application of guidelines for aggressive SBP targets in clinical practice for oncology patients.

Designed to inform the design and execution of our Phase III RCT by:

- Perform a retrospective analysis to define the distributions of SBP, CV risk scores, incidence of CV events, and all-cause mortality rates in cancer patients

- Perform a 50-patient prospective pilot study using a site-based cluster randomization design amongst 4 ECOG-ACRIN sites comparing ‘Intensive SBP Control’ with ‘Usual Care.’ This will be facilitated by a centralized BP Advisory Core, and will inform the SBP trajectories, safety and tolerability of Intensive SBP control, and participant and site burden.
Endoscopic eradication therapy (EET) is the standard of care for patients with Barrett’s Esophagus (BE) and high-grade dysplasia (HGD) or mucosal esophageal adenocarcinoma.

Central unresolved issue is whether BE patients with low-grade dysplasia (LGD) benefit from EET.

Using a 1-year planning grant:

- Compare the two approaches using the primary endpoint of neoplastic progression rate (progression to HGD or mucosal or invasive EAC).
- Compare defined patient-centered outcomes such as health-related quality of life between the two treatment groups.
- Compare the performance of molecular (TissueCypher and p53 immunohistochemistry) and imaging (wide-area transepithelial sampling – WATS) biomarkers to conventional histologic assessment of dysplasia via forceps biopsy to improve risk-stratification in BE with LGD patients.
Why planning grants are needed for DCP and DCCPS late phase trials?

Cancer Prevention and Control trials:

▪ Often do not have pharmaceutical or industry support

▪ Involve multi-disciplinary teams that may not have worked together previously including primary care physicians and other specialists.

▪ Often challenging statistical issues about best study design, control group, endpoint, etc.

▪ Feasibility of recruitment and acceptance of randomization

▪ Design better trials that are more successful
Purpose

- Yield information that is both scientifically necessary and also sufficient to permit final decisions about the design or conduct of the large Phase II or beyond clinical trial.
- Application must include a summary of the future planned clinical trial
- Save time and cost by ensuring future trial success.
- Planning grant is not a prerequisite for an R01 funding clinical trial or a large trial through a network.
Examples of research needs include but are not limited to the following:

- Identify the appropriate control or comparison group to use in the subsequent clinical trial.
- Standardize and evaluate feasibility of the intervention or outcome across multiple sites.
- Feasibility and plan for development of a placebo.
- Validate survey instruments.
- Test effectiveness of training tools.
- Adapt and test an intervention or outcome instrument for a population that differs culturally from the population for which the instrument was originally designed.
- Modeling data to support trial assumptions in the study design.
- Statistical planning and design.
### Comparing and contrasting the R34 vs U34

<table>
<thead>
<tr>
<th>Investigator-initiated R34</th>
<th>Network facilitated U34</th>
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<tbody>
<tr>
<td>Preparatory to Phase II/III, but specific pathway undetermined</td>
<td>Preparatory to large Phase II/III within specified network</td>
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<tr>
<td>Necessary and sufficient</td>
<td>Required activities – stakeholder engagement, adhere to existing rules for concept and protocol review</td>
</tr>
<tr>
<td>R</td>
<td>U</td>
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<tr>
<td>1-3 Years</td>
<td>1-3 years</td>
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<tr>
<td>Followup study potentially funded through R01</td>
<td>Followup study potentially funded through CP-CTNet, ULACNet, NCORP, etc.</td>
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Justification for PAR

- **Review:**
  - NCI SEP requested with expertise focused on clinical trials design, implementation, and logistics. SEP should include patient advocates.
  - Special review criteria
    - 1) Define how the proposed work will generate the information scientifically necessary and sufficient to permit a decision about the design and conduct of the trial.
    - 2) Adequate statistical support
    - 3) Engagement of stakeholders.
    - For U mechanism applicants must have letter of support from research base or lead academic organization (LAO).

- **Receipt:** Two receipt dates per year are requested to accommodate 6 to 12 applications per round so that applications can be clustered for review
Budget

- No set aside
- Direct costs will be limited to $225,000 per year and total $450,000 over the 2-year project period.
- If the project includes a feasibility trial the budget can be up to 600,000 direct costs over 3 years.
- Potentially fund 4-6 per year across DCP and DCCPS
- For the U mechanism: work performed must be complimentary and not duplicative with work performed through the core infrastructure of the network
Evaluation Criteria for PAR

- **Short term metrics:**
  - number of R34 or U34 projects that identified issues needing correction
  - modifications in the subsequent trial that resulted from the knowledge gained
  - number that proceeded to a full clinical trial or definitively did not
  - number of clinical trial applications or protocols approved from R34 or U34 awardees
  - the publication of results, positive or negative.

- **Long term metrics:**
  - frequency of one or more major feasibility issues encountered in full clinical trials conducted by R34 or U34 awardees versus those conducted by non-R34 or U34 awardees
  - frequency of no-cost extensions or cost overruns, or insufficient accrual, in full clinical trials conducted by R34 or U34 awardees versus those conducted by non-R34 or U34 awardees.