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

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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

Example R34 - R34HL146927(Bonnie Ky)

- 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.

Example U34- U34DK124174-01(Sachin Wani)

- 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

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

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.

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