Reviewing Clinical Trial Concepts

Overview, Worksheet, and Checklist for Advocates

Overview of Concept Scoring categories | Overview of Ethical Guidelines for Clinical Research

A non-official Concept Review Worksheet | A Checklist for Advocate Review

Evaluator Name:

Date of Evaluation:

Concept ID #/Title:

OVERVIEW OF SCORING CATEGORIES:

Clinical Impact ( )
Would a positive study change standard of care or lead to new and significant biological Insights to guide subsequent research?

Overall feasibility ( )
What is expected ease of accrual. Are there adequate resources for level of difficulty? (e.g., will be acceptable to referring physicians and patients as a therapeutic decision?)

Level of innovation ( )
Does this study introduce something really new
(e.g., not testing a me-too drug)?

Group Relevance ( )
Is the proposed study best done in cooperative group setting?
(e.g., is it a study that could be done by an industry sponsor?)

Study Design ( )
Is the design of the study likely to answer the study questions with optimal use of resources? Might tests used to measure outcomes apply to future studies making subsequent studies more efficient?

OVERVIEW OF ETHICAL PRINCIPLES FOR CLINICAL RESEARCH:

Principles of Clinical research based on the Belmont Report

Respect for persons (to insure self-determination)
Autonomy, informed choice, voluntary, non-coercive, protect vulnerable, privacy and confidentiality

Beneficence (to protect well-being of subjects)
Appropriate risk/benefit -- do not harm; maximize possible benefits and minimize possible harms

Justice (distribution of risk should be borne equally)
Examine the characteristics of study population, ease of availability to participation, not exclude classes of individual

Related resources:

Online book:
http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.html

Excellent hard cover book - Institutional Review Board Member Handbook
Recommended book - Amazon.com http://www.amazon.com/Institutional-Review-Board-Member-Handbook/dp/1449647448

Worksheet for Review

WORKSHEET

Scientific, Design, Feasibility, Clinical Significance, General Relevance and other Issues

1. **Adequacy of Background and Preliminary Data**

   (Does the preclinical or clinical data adequately support the proposed study questions? Make use of citations in concept protocol if necessary.)

   Concept strengths:

   Concept weaknesses:

2. **Strength of Study Design,**
   Including Statistical Design / Correlative Science / QOL / Imaging / Biomarker, etc.

   (Typically this section is the domain of statisticians and clinical experts. The focus is on appropriateness of the primary and secondary endpoints, adequacy of sample size to meet study objectives.

   Advocates may inquire about: optimal use of the resources; safeguards and monitoring for patient protection; hw eligible participants are selected? Is it the right control group in a randomized trial? Is patient selection appropriate – representing the population in need? Is it based on a biomarker, and/ or by clinical factors: age, treatment history, type of cancer, subtype of cancer?

   Concept strengths:

   Concept weaknesses:

3. **Study Feasibility**
   (What is the likelihood of achieving stated accrual rates and proposed study duration and of collecting and testing tissues as specified in the Concept Proposal? How is study treatment different from usual care for eligible participants (use citations and literature search)? Are there competing studies that may be more attractive to eligible patients? Search: www.clinicaltrials.gov

   Concept strengths:

Concept weaknesses:

4. <u>Importance of the Research Question</u> in Contributing to the Overall Management of the Disease

(In view of the current treatment approaches for the disease, is the study likely to make a meaningful contribution to patient care if positive (meets primary endpoint); or will it just make treatment more expensive without a clear measure of its effect on overall survival?)

Concept strengths:

Concept weaknesses:

5. Potential <u>General Relevance</u> to Cancer Therapy

(Do overarching treatment approaches and techniques being tested have relevance for other tumor types? Does it include tests that may make other trials more efficient, or help to other to select patients for future trials with more precision?)

Concept strengths:

Concept weaknesses:

6. Is special attention needed as the model <u>informed consent document</u> is prepared?

- Do you anticipate that special attention needs to be paid to particular populations (such as older patients – particularly if the condition primarily affects older patients)?
- How long will the patients be on the study treatment and how does this compare to regular treatments for the condition?
- Do you feel that the patients need to be made aware of any particular treatment alternatives?
- Are number and type of <u>extra</u> tests / biopsies appropriate?
- Are biopsies mandated in order to participate in the study?
  Is this appropriate (integral to the study)? Is study on this tissue exploratory?

a. Are there <u>other patient-related issues</u> that should be considered at the Concept Evaluation Meeting?

7. How well does the concept relate to NCI National Clinical Trials Network (NCTN) Working Group Final Report recommendations for the disease?

See NCI National Clinical Trials Network Working Group (NCTN WG) Final Report (2014) http://deainfo.nci.nih.gov/advisory/ctac/0714/NCTNwgFinalReport.pdf

8. List any key questions that the <u>Study Principal Investigator</u> could address which might change your recommendation regarding the proposed concept

(This step is optional but highly recommended in some situations. Be sure to carefully review the concept to make sure the answer is not already provided … and review citations that may answer your question).

CHECK LIST FOR ADVOCATE REVIEWERS

Meeting preparations:

- ☐ Review materials and citations
    - Make notes in the worksheet and make use of checklist as you review materials
- ☐ Prepare questions and comments in advance of meeting in writing
    - Anticipate a fast-paced discussion among many experts in field and that it can be challenging to make verbal comments or questions.
    - Listen carefully. Be flexible. Ask questions and provide comments in concise way. (Usually it's best to focus on questions and avoid opinion in oral part of review.)
    - Make note that you are layperson when commenting on scientific aspects of concept
- ☐ Even if optional, provide your final comment, score, and questions in writing.
- ☐ When you have pre-meeting questions submit to NCI and indicate your desire to submit the question to the study chair ahead of the oral meeting.

General:

- ☐ How might this study protocol be better than what currently exists?
- ☐ Why is this trial important to patients?
- ☐ What are the possible trade-offs with the study
    - Are these measured in the study?
    - Are there ways to tie in quality of life (QOL) and other patient considerations?
- ☐ How is study protocol different than regular treatment?
    - How does the duration of study treatment compare to regular treatment?
    - What might patients / referring physicians consider or shy away from?
- ☐ What questions are investigators looking to answer by this trial?
  (See Objectives and Endpoints in concept protocol)
    - How important are these goals from a patient perspective?
    - What is the clinical significance?
- ☐ Does the concept include steps to include vulnerable populations or diverse populations?

Study design

- ☐ Is standard of care changing rapidly?
    - Are findings likely to be relevant when completed? To doctors? To patients?
- ☐ What is the competition for this trial with this patient population
  (i.e., other trials, regular therapies)?
- ☐ What else can we learn in this trial with this group of people?

- ☐ What is the appropriate control and type of allocation to study groups?
    - Might a historical control be appropriate in this population?
    - Does it have to be randomized? If so, why? How will the allocation method affect feasibility – referral to the trial?
- ☐ Can we learn more from the correlative science component (i.e., tissue collection and testing)?

Study design - eligibility and exclusion criteria

- ☐ Are there any criteria that are unnecessary to the conduct of the trial and protection of patient safety?
    - Are they too restrictive? Not restrictive enough?
    - What about other health problems (i.e., diabetes) and how are they handled?
    - Is life expectancy criterion used? Is it necessary for this study?
- ☐ Are all of the exclusion criteria appropriate or necessary? Why?
- ☐ What about other populations? Are there health disparities that need to be addressed?

ADDITIONAL RESOURCES / BACKGROUND READING

Background disease information

- ☐ PubMed http://www.ncbi.nlm.nih.gov/ to search for published articles on disease
- ☐ NCI Web site www.cancer.gov then select the type of cancer for general information.
- ☐ NCI Web site http://www.cancer.gov/clinicaltrials/findtrials

Informed consent and human protection

- ☐ Human Research protection: http://cme.cancer.gov/clinicaltrials/learning/humanparticipant-protections.asp take the online course on "Human Participant Protections Education for Research Teams."
- ☐ Review the NCI Simplified Informed Consent Form at http://ctep.cancer.gov/guidelines/consent.html and http://www.cancer.gov/clinicaltrials/understanding/simplification-of-informed-consent-docs
- ☐ Learn about Federal Regulations: the Common Rule at http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm
- ☐ And http://www.hhs.gov/ohrp/ for additional information.