Clinical Trials 101

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&

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Overview

- What are Clinical Trials?
- How to review a Clinical Trial Protocol
- How to review a Consent Form
What are Clinical Trials

- Definition
- Why they are Important
- Phases of Clinical Trials
- Barriers
- Benefits
- Risks
- Protections
- Resources
What are Cancer Clinical Trials?

- Research studies involving people
- They try to answer scientific questions and find better ways to prevent, diagnose, or treat cancer
Why Are Cancer Clinical Trials Important?

- Cancer affects all of us

- Each year in the U.S.A:
  - 1,500 people die each day
  - 1 of 4 deaths is from cancer
  - The more people that take part, the faster we can:
    - Answer critical research questions
    - Find better treatments and ways to prevent cancer
Clinical Trial Phases

- **Phase I**
  - What dose is safe
  - A few people in one or two centers

- **Phase II**
  - Safety and effectiveness
  - <100 people in a few centers

- **Phase III**
  - Compare it against standard of care
  - Large numbers of people, around the Country

- **Phase IV**
  - After drug is approved, further safety and effectiveness
Barriers to Participation in Clinical Trials

Physicians & other providers may:

- Be unwilling to lose control of patient’s care
- Believe that standard therapy is best
- Believe that clinical trials are more work
- Worry about the patient’s care or how the person will react to suggestion of clinical trial participation
Barriers to Participation in Clinical Trials

Patients may:
- Be unaware of clinical trials
- Lack access to trials
- Fear or be suspicious of research
- Have practical or personal obstacles
- Face insurance or cost problems
- Be unwilling to go against their physicians’ wishes
Benefits of Participation

Possible benefits:

- Subjects may receive, at a minimum, the best standard treatment

- If the new treatment or intervention is proven to work, subjects may be among the first to benefit

- Subjects have a chance to help others and improve cancer care
Risks of Participation

Possible risks:

- New treatments or interventions under study are not always better than, or even as good as, standard care.

- Even if a new treatment has benefits, it may not work for every subject.

- Health insurance and managed care providers do not always cover clinical trials.
Protection of Participants

- Nuremberg
- National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research
- Belmont Report
- National Research Act
Protecting Participants Before a Trial

- Scientific review by sponsoring organization
- Institutional review board approval
- Informed consent
Protecting Participants During a Clinical Trial

- **Institutional review boards (IRBs)**
- **Data & safety monitoring boards (DSMBs)**
  - Minimize risks
  - Ensure integrity of data
  - Can stop study if necessary
Questions: Ask & Answered

- What is the study about?
- Who put the study together?
- Where is the trial being conducted?
- What will the I get out of the study?
- What are the risks?
- How long will the study last?
- What tests are involved?
More Questions: Ask & Answered

- How will I be protected from harm?
- Do I have to pay for any part of the trial?
- Who should be contacted for problems or questions?
- What do I have to do in this study?
- What are my other options?
Subject’s Decision & Rights

- The decision to participate is the subject’s
- Informed Consent is more than a signature - it is a process
  - All the facts about a study must be given before the patient decides to participate
  - Including details about all treatments and test(s) and the benefits and risks
  - Rights should be fully explained
How to Find Clinical Trials

- The Internet
  - National Library of Medicine
  - Centerwatch Clinical Trials
    - http://www.centerwatch.com
  - NCI/CancerNet
    - www.cancer.gov

- Your healthcare provider
- 1-800-4-CANCER (1-800-422-6237)
Today’s Standard Treatment Was Yesterday’s Clinical Trial
How to Review a Clinical Trial Protocol

- Use ACRIN’s project IMPACT template
- Why our review is important
- Basic
Project IMPACT

- [www.ACRIN.org](http://www.ACRIN.org) / project IMPACT

- A template designed by advocates FOR advocates
Why our Review is Important

- Scientists focus on what they care about
- We provide a reality check: what is doable
- Paper Trail:
  - Comments on conference calls may not be captured
  - No record of advocate concerns/support
  - No way to track if our concerns where incorporated into protocol
  - No way to capture our accountability to process
Structure of all Protocols

- Background / Introduction
- Study Hypothesis
- Study Design
- Rationale / Objective
- Eligibility
- Statistical Design
- Schema / Flowchart
- Informed Consent Process
- Accrual / Communication Plan
Background / Introduction

- What is the question?
- What is the value to patients?
- Will the study help patients live longer?
- How long will it take to complete the trial?
- Will the answer be relevant when the trial is over?
Study Hypothesis

- Define the Hypothesis: *so you understand it*

- Indicate what kind of study it is
  - Treatment
  - QOL
  - Surgery
  - Imaging
  - Prevention
  - New dosing
  - New order drugs are given
Study Design

- How does the study design compare to standard of care
- Do you feel that demands on patients are reasonable compared to standard of care? (Yes/No)
- Are correlative studies included? Encourage
- Will this study be conducted in the community? (Yes/No)
Rationale / Study Objective

- What are the formal trial endpoints?
- Do they compare to the hypothesis goals?
  - For example, if the hypothesis states that the trial will increase survival, but the endpoints don’t measure survival, why not?
Eligibility

- Who’s included - excluded

- Do you think that the trial population is representative of the patient population?

- Will the study be open in sites with diverse populations?
Preliminary Statistical Design

- If the trial examines more than one treatment, are participants randomized to a single treatment?

- Is crossover allowed whereby participants may receive some or all of the treatments being studied?
  - Why or why not
  - Do you agree with the trial design?
Feasibility

- Do you think patients will be interested in enrolling? (Yes/No)

- Do you think the numbers expected to enroll are reasonable? (Yes/No)

- Are there aspects of the trial that you think will make accrual more difficult? (Yes/No)

- Diversity:
  - Is there a plan to include a diverse population? (Yes/No)
  - Will the trial be at sites with diverse populations? (Yes/No)
Is the schema designed in a patient-friendly form? (Yes/No)

Reading left to right, not top to bottom? (Yes/No)

Other specific comments on how to make it as patient-friendly as possible?
Informed Consent Process

- Does the protocol describe the informed consent process (Yes/No)
  - Are there Follow-up materials? (Yes/No)

- Is the informed consent based on the new NCI template? (Yes/No)

- What happens in the event of an injury:

- Any correlative studies (i.e. tissue)
  - Use patient’s tissue for future studies? (Yes/No)
How to review a Consent Form

- From an Advocate Perspective
The Consent Form

- 6-8 Grade Reading Level
- Formatting
- Study Requirements clear
- Other Options Clear
The Consent Form: Readability

- **6th-8th Grade level**: 14-17 words/sentence; 139-147 syllables/100 words

- **Does “readability” = “understanding”**
  - Concept words; category words; value judgment word

- **Clear Writing Tips**

- **Word Substitution Lists**

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2. Kripalani, S., Texas Medicine, 91(8), 40-45
Techniques to use:
- Use font size of 12 or greater
- Use fonts with “tails”, like GRAMMOND, CENTURY or COPPER PLATE LIGHT
- Bullet all:
  - study requirements, headings, and risks
- Use short paragraphs
- Lots of white space

¹ courtesy of Ralph Kennedy
The Consent Form: What is required

- Techniques to use:
  - List all Treatments
  - List all Tests
  - List extra visits
  - How does that fit into daily life
    - Graphic flowchart

¹ CISN
The Consent Form: Options Are Clear

**Techniques to use**
- List other options
- Not just standard of care
- Compare clinical trial & standard of care
- Better distinction between risks and benefits
  - side by side comparison chart

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² CISN
Need: Educational Materials

- **Too many elements to process**¹
  - 14 required, 6 optional + 5 HIPPA
  - Decision to participate may be based on what patient is able to process and understand

- **Omission neglect:** You can’t use what you don’t see¹,²
  - Compare standard vs. study

¹ Hochhauser, M., “Applying Consumer Psychology to Subject Recruitment”, actmagazine.com

² F.R. Kardes and D.M. Sanbonmatsu, ”Ommision Neglect, the importance of Missing Information,” Skeptical Inquierer, 27(2) 42-46 (2003)
Need: Educational Materials

- Learning Styles Matter

- Patients learn best when there is a match between their preferred learning style and the presentation style:
  - Visual Learner
  - Auditory Learner
  - Sensory Learner
  - Kinesthetic Learner

¹ Adapted from: Teachers Make The Difference by Susan Kovalik
Need: Educational Materials

- **Study Schema** *(graphic) ¹, ²*
  - Calendar Format
  - Clear / color coded

- **Study Brochure** ², ³
  - Address possible hurdles
    - Randomization
    - Placebo

¹ CISN
² Hochhauser, M., “Applying Consumer Psychology to Subject Recruitment”, actmagazine.com
FNA, core biopsy, or diagnostic mamogram

MRI at 2 weeks post start of chemo

Anthracycline based chemo

Core Biopsies x 4
(2 Frozen, 2 Parrafin), serum drawn, 2-4 days post start of chemo

Taxane therapy

Core Biopsies x 4
(2 Frozen, 2 Parrafin)
2-4 days post start of taxane therapy

Tissue taken at time of surgery and MRI

MRI

Surgery

Surgery

Core Biopsies x 4
(2 Frozen, 2 Parrafin), serum drawn, and MRI

Register
CISN Version of Study Schema

Neoadjuvant MRI Correlative Science Trial Procedure Time Line

Date
Date
Date
Date
Date

1
2
3
4
5

Advocate Call
1/2/03

AC Chemo dates

Mammogram
MRI #1
Core Biopsy #1
Serum sample

Mammogram
MRI #2
Core Biopsy #2

Mammogram
MRI #3

Cycle 1
Start AC
Cycle 2
Cycle 3
End AC
Cycle 4

48 hrs after AC starts (24-96 hrs)
2 weeks after AC starts

Patient

SURGERY Date
O.R. Tissue Specimens

Start TAXANE see page 2

Study timeline developed for UCSF by Peggy Devine
MRI of the Contralateral Breast

ACRIN Research Study 6667

An ACRIN Research Study for Women with a Recent Diagnosis of Breast Cancer

Information for Participants

Breast MRI Study
Imaging your cancer-free breast

Are you a breast cancer patient with concerns about your healthy breast?
Summary

- Advocates Can Make a Difference
  - When reviewing protocols
  - Helping write the consent form
Thank You

- Summit Series on Clinic Trials
- Coalition of Cancer Cooperative Groups
- Funders
- ACOSOG and ACRIN
- CISN