Clinical Trial Protocols and Protocol Review From the Advocate/Patient Perspective

I-SPY2 Advocate Webinar
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Barbara K. LeStage
Jan Butts
Webinar Objectives

Advocates Will Learn:

- Where to find templates and instructions about clinical trial protocols
- What the purpose of a protocol is
- What the elements of a clinical trial protocol are
- How to review a protocol from the patient perspective
Purpose of Clinical Trial Protocols

- Describes purpose of trial
- Describes exactly how trial is to be conducted
- Sets uniform standards for the way each patient is treated to allow researchers to combine data and reach valid conclusions
- Ensures the comparison of apples to apples
Basic Elements of a Clinical Trial Protocol

- Why study is being done
- How many people will be in the study
- Who can participate
Basic Elements of a Clinical Trial Protocol

- What procedures will be done/how often
- What tests will be done/how often
- What information will be gathered
Basic Elements of a Clinical Trial Protocol

- What are the study endpoints
- What is the “Informed Consent” process
Additional Elements of a Clinical Trial Protocol

- Title Page
  - Name
  - Principle Investigator [ PI ]
  - Statistician, etc

- Schema
- Hypothesis
- Objectives
- Background and Rationale
I-SPY2 Cover Page

COVER PAGE

NCI Protocol #: This number will be assigned by NCI and may be the same as or different from the local protocol number. The NCI protocol number must appear on all protocol document versions and all communication to NCI.

Local Protocol #: Insert your local protocol # for this study. If a local protocol number has not been assigned, indicate 'pending'. DEFINITION: The local protocol number is assigned by the organization according to local institutional conventions.

Protocol Title: I-SPY 2 Trial (Investigation of Serial Studies to Predict Your Therapeutic Response with Imaging And Molecular Analysis)

Organization Name:
University of California, San Francisco

Protocol Principal Investigator:
Laura Esserman, MD, MBA
Dept of Surgery, MC Box 1610
San Francisco, CA 94143
Tel: (415) 885-7891 Fax: (415) 353-3973
laura.esserman@ucsfmedctr.org

Co-Investigator(s):

Organizations:

University of Texas, MDACC
Dendal Berry, PhD
1315 Holcombe Ave
Houston, TX 77030-4009
Tel: (713) 743-5500 Fax: (713) 792-4272
dberry@mdanderson.org

NOTE: If this is a multi-institution study:
1. The protocol title page(s) must include the name and address of each participating institution and any affiliate participating in the study.
2. The protocol title page(s) must include the names of all investigators at each institution; their telephone, Fax, and e-mail address.
3. Indicate the protocol lead investigator responsible for the study at each institution; his/her telephone, Fax, and e-mail address.
I-SPY2 Schema

I-SPY 2 TRIAL Schema

Patient with ≥3cm measurable invasive breast cancer → REGISTER

MRI Core Biopsy → Patients with MammaPrint High risk, or MammaPrint Low risk & ER negative, or MammaPrint Low risk & ER positive & HER2 positive

RANDOMIZATION

HER2+

Taxane + Trastuzumab

Taxane + Trastuzumab + Novel Agent

AC (4 cycles)

SURGERY

Follow for 10 years, Adjuvant therapy at discretion of Physician

HER2–

Taxane

Taxane + Novel Agent
Additional Elements of a Clinical Trial Protocol

- Eligibility Criteria
- Exclusion Criteria
- Study Plan
- Study Calendar
# Study Plan: PICO Summary

<table>
<thead>
<tr>
<th>Design Component</th>
<th>I-SPY-2</th>
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| **P** atients    | • Breast Cancer patients at high risk of recurrence  
|                  | • MammaPrint High (~30% chance of metastases within 10 years) |
| **I** nvestigational Intervention | • Investigational agents that have adequate safety data when paired with a Taxane,  
|                  | • Plus all control interventions |
| **C** ontrol     | • Taxane (12 weekly cycles) with Herceptin if HER2+  
|                  | • Followed by Anthracycline (4 cycles)  
|                  | • Followed by surgery (lumpectomy or mastectomy)  
|                  | • Core biopsies (3)  
|                  | • MRIs (4) |
| **O** utcome     | • Primary: pathological complete response (pCR)  
|                  | • Secondary: DFS, MRIs, biomarkers |
I-SPY2 Study Calendar

Taxane +/- Investigational Agent (12 weekly cycles)

Anthacycline (AC) (4 cycles)

Eligible? → Register & On Study → MRI → MRI → Biopsy, MRI Blood, Tissue → Surgery
Additional Elements of a Clinical Trial Protocol

- Monitoring of Patients
- Response Assessment
- Dose Modification
- Adverse Events
- Off Study Criteria
Additional Elements of a Clinical Trial Protocol

- Statistical Considerations
- Correlative Studies
Reviewing a Protocol from the Advocate/Patient Perspective

- Why is this study important i.e. will it help patients live longer or with a better quality of life?
- How many patients have this disease at this stage? How many will die from it?
- How long will it take to complete?
- Will the answer still be relevant?
Reviewing a Protocol from the Advocate/Patient Perspective

- What are the study hypotheses i.e. what does the PI expect will happen?
- What kind of trial is it (screening, diagnostic, staging, treatment response)?
Reviewing a Protocol from the Advocate/Patient Perspective

- What are the formal trial endpoints?
- How do endpoints compare to the goals in the hypotheses i.e.
  - if hypothesis is that the treatment will increase survival, is one of the endpoints to measure length of survival?
Reviewing a Protocol from the Advocate/Patient Perspective

- How does the study design compare to standard treatment of care?
- Are the demands on the patient reasonable compared to standard treatment?
- Do experimental interventions sound promising without too many side effects?
- What is the expected impact on “quality of life”?
- How will non-standard procedures be paid for?
Reviewing a Protocol from the Advocate/Patient Perspective

- Where will the study be conducted:
  - in community settings or
  - only large medical centers?
Reviewing a Protocol from the Advocate/Patient Perspective

- Who’s included and excluded from the trial?

- Are the patients who are eligible representative of the patient population described?
Reviewing a Protocol from the Advocate/Patient Perspective

- Has the PI provided information on how this trial fits into an appropriate organization’s strategic plan, e.g. NCI Scientific Steering Committee?

- Are there other trials which may be trying to recruit the same patients?
Reviewing a Protocol from the Advocate/Patient Perspective

- Will patients be interested in enrolling?
- Is the accrual goal reasonable?
- Are there aspects of the trial which you think will make accrual difficult?
Reviewing a Protocol from the Advocate/Patient Perspective

- Has a patient recruitment plan been written?
- Have needed recruitment materials been identified?
- Does the protocol include a section about:
  - monitoring accrual
  - taking corrective action should accrual fall short of target goal?
Reviewing a Protocol from the Advocate/Patient Perspective

- Does the protocol include a section regarding accrual of diverse population?
- Will any of the eligibility requirements make it difficult for diverse populations to accrue?
- Will the trial be open (accessible) where diverse populations receive care?
Reviewing a Protocol from the Advocate/Patient Perspective

- Does the protocol describe the informed consent PROCESS to be used (not just an Informed Consent form)?

- Does the Informed Consent form have a schema clearly showing what will happen to the patient?
Reviewing a Protocol from the Advocate/Patient Perspective

- Are all procedures clearly explained?

- Can a *calendar* be overlaid, so it will be clear not only WHAT will happen, but WHEN procedures will occur?
Reviewing a Protocol from the Advocate/Patient Perspective

- At what grade level is the Informed Consent written?

- Are there provisions for people with limited reading ability?
Reviewing a Protocol from the Advocate/Patient Perspective

- What happens if a patient is injured?
- Who has to pay for any treatment necessary in case of an injury?
Reviewing a Protocol from the Advocate/Patient Perspective

- How will patient confidentiality be maintained?
Are there any correlative studies planned?

If so, does the Informed Consent have a separate section asking the patient to consent to:

- donate tissue/fluids for this study?
- donate tissue/fluids for other or future studies?
- be contacted in the future about other studies?
- enroll in a Quality of Life study?
Reviewing a Protocol from the Advocate/Patient Perspective

- Will correlative study specimens be read in a central lab assuring uniform interpretation?
- Will correlative study imaging scans be read in a central lab assuring uniform interpretation?
Reviewing a Protocol from the Advocate/Patient Perspective

- Is there a plan to:
  - disseminate results to patients when trial is complete?
  - notify patients if trial is discontinued?
Additional Resources

- NCI Cancer Clinical Trial Basic Workbook
  http://www.cancer.gov/clinicaltrials/resources/basicworkbook

  Section 3.1 describes Components of a Protocol Document.
  http://ctep.cancer.gov/protocolDevelopment.docs/protocol_authoring_handbook.doc

- NCI Cancer Therapy Evaluation Program Phase II Protocol Template
  http://ctep.cancer.gov/forms/default.htm
Additional Resources - 2

- ACRIN Project Impact Review Form
- CALGB Hints on Reviewing Protocols

Copies available at I_SPY2 Advocate Website