Clinical Trials in a Nutshell

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Disclosure

• Research contracts with Hologic, Inc., Koios Medical Inc., GE Healthcare
• Advisory Board: iCAD, Inc., MaiData Corp.
• Royalties: Hologic, Inc.
Overview of presentation

• Discuss concept of clinical trials
• Overview of components
• Goal is to give you a basic understanding of a clinical trial so that you can participate as an investigator without feeling completely lost
What is a clinical trial

• Clinical trial is a research study performed in people with the goal of evaluating a medical technology

• Designed to prove or disprove a hypothesis
  • This requires two different conditions (arms) that participants are subjected to
    • All participants could be subjected to both conditions
    • Participants are randomized in one of the two conditions
Study Design (in a nutshell)

1. Form an hypothesis (A is better than B)
2. Power the study (number of patients)
3. Recruit patients to the study
   - Record outcomes in the two study arms
     - Patient forms
   - Statistically test the hypothesis using the results
     - Biostatistician
1. Hypothesis versus Null Hypothesis

• Hypothesis: A is better than B
• Null hypothesis: There is no difference between A and B
• Want to disprove null hypothesis:
  \[|A-B| > 0\]
2. Trial Statistics (in one slide)

• Given a null hypothesis: $|A-B| > 0$
• Need to power the trial (# of patients) to have at least 80% confidence that we can disprove the null hypothesis
  • Type II error, accept null hypothesis when it is false (FN)
• Statistically, if we were to repeat the trial many times, then we want 95% of times $|A-B|>0$
  • Critical p-value, alpha = 0.05; want p-value < 0.05
  • Type I error, reject null hypothesis when it is true (FP)
3. Patient Recruitment

• Need to consent patients → IRB
  • Institutional Review Board
  • Approves all human subjects research
  • PI needs to submit a protocol for approval
What Does the IRB Do?

• They enforce the law: 45 CFR 46 (code of Federal Regulations)
• Protect the rights, privacy, and welfare of human participants in research
• Main responsibilities:
  • initial review
  • continuing review of research involving human subjects
Writing an IRB Protocol

• Similar to writing a grant (but less detail and less rigorous)

• Protocol contains:
  • Background
  • Hypothesis
  • Clinical significance
  • Method (outline only)
  • # of subjects
  • Statistical plan
  • Consent form

• Retrospective or Prospective study
Prospective study

• Patients will likely need to give consent
• A consent form will need to be written
Retrospective study

• De-identified data
  • Not human subjects research, if no research team member has access to patient identifiers

• Honest broker

• Will discuss in a few minutes
Types of Review by IRB Committee

(1) Exempt Review
   • not human subjects research
   • very low or no risk research

(2) Expedited Review
   • low-risk
   • don’t need to consent subjects

(3) Full Review
   • patient consent needed
Other (Important) Tidbits
Choose all that apply.

- [x] Responsible Conduct of Research
- [ ] COI PHS Regulated Course
- [x] Conflict of Interest
  This series consists of two basic tracks: COI PHS Regulated or COI Non-PHS Regulated.
  Courses for Human Subject Research

- [x] Human Subjects Protection
  This series consists of courses from two basic tracks: Biomedical or Social-Behavioral-Educational. The Biomedical course is required for all UPMC investigators.

- [ ] Good Clinical Practice
  This series consists of two basic tracks: Clinical Trials involving FDA regulated research or GCP - Social and Behavioral Research Best Practices for Clinical Research [Note: FDA regulated research GCP course is required for all UPMC investigators].

- [ ] Privacy & Information Security
  This series is required for any researchers who encounter protected health information. This course is required for all studies submitted to the UPMC OSPARS office.
HIPAA

• HIPAA = Health Insurance Portability & Accountability Act
• Provides data privacy and security
• PHI = protected health information
  • e.g., Name, medical record number, date of birth
Retrospective study

• De-identified data
  • Not human subjects research, if no research team member has access to patient identifiers
  • Cannot readily ascertain the identity of the individual(s) to whom the coded private information pertains

• Honest broker
  • Person not associated with the research project who de-identifies the data
Anonymize versus De-identify

• In practical terms:
  • Anonymize = remove or encode patient identifiers (PHI) so that patient cannot be identified based on identifiers
  • De-identify = modify patient data so that patient identification is not possible
    • e.g., AAPM member, diagnostic imaging, Full professor, 15213, Asian, male
Closing Thoughts

- Clinical trials are an essential component of medical research
- I encourage all AAPM members to participate in clinical trials
- You may still need to delve in deeper into these topics to fully participate in a clinical trial
- Education Council has identified several resources that you can use