Principals of Basic Research & Initiating a Research Trial

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THE CONSORTIUM OF MULTIPLE SCLEROSIS CENTERS

Faculty Affiliation and Disclosure

- Retired Clinical Nurse Coordinator, University of Alabama at Birmingham (2014)
- Disclosures

  Speakers Bureau: Biogen Idec, Genzyme, Pfizer

  Consultant: Biogen Idec, Genzyme, Questcor

Learning Objectives

- Review the drug development process and clinical trial design terms
- Examine select components of a clinical study protocol
- Identify resources to identify current research studies and for the conduct of research trials

WHAT IS RESEARCH?

"Diligent, systematic inquiry or investigation to validate old knowledge and generate new knowledge"

WHY DO WE NEED CLINICAL TRIALS?

- Definitive answers
- Safety
- Opinion leaders not impartial
- Most ethical method

Clinical Trials: Secondary Benefits

- Standard measurements
- Documented record of activity
- Qualification of adverse events
- Generation of new hypotheses
- Ancillary studies
- Cost-effectiveness & outcomes

Drug Development Process

- Preclinical: Animal Tests
- Phase I: Human Tests of Toxicity & Dosage
- Phase II: Human Tests of Effectiveness/Safety
- Phase III: Large-Scale, “Double-Blind” Human Tests
- FDA Approval
- Phase IV: Additional Studies

Pre-clinical Testing

- Efficacy in tissue culture/animal models
- Biologic and pharmacologic studies
- Toxicity testing
- Consideration of efficacy/toxicity to determine if clinical trials should be attempted

Initial FDA Application for IND (Investigational New Drug)

- Describes development/testing in tissue and animal models
- Provides results of preclinical testing
- Describes compound & how it may work

Phase I

- Small study – few subjects
- Healthy volunteers
- Safety/Tolerance
- Dose/Route of administration/Schedule of delivery
- Usually no control group
- Short study – Less than one year

Phase II

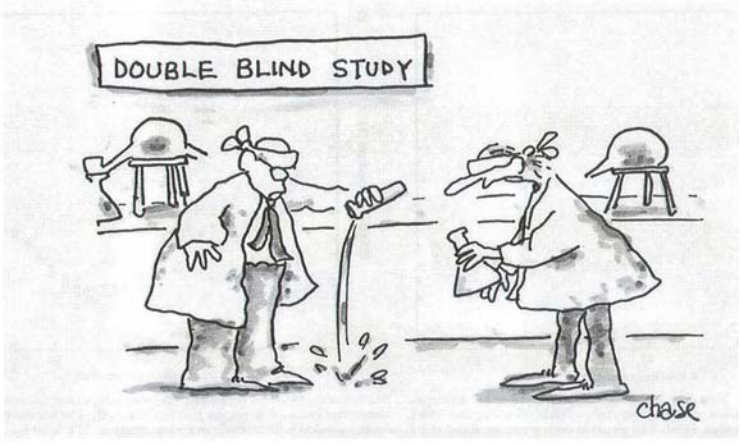
- Acceptable toxicity profile in Phase I
- Effectiveness for agent in a specific treatment group
- Controlled pilot study – small number, carefully selected patients
- Test real agent vs. placebo
- Narrow the dosage
- Continue to look at effectiveness & safety profile

Phase III

- Carefully designed
- Strict guidelines from FDA
- Multicenter
- Usually randomized with assignment to and treatment on two or more arms of the study
- Safety profile and effectiveness

Phase IV

- Follows FDA approval & licensing
- Additional safety and efficacy data
- Track adverse events



Clinical Trial Design Terms

- Prospective
- Controlled
- Randomized
- Open-Label
- Double-blind
- Cross-over

Trial Designs

- Open Label: the investigator and patients are aware of what drug or device is being tested
- Single-blinded Study: the patient is blinded to the treatment, but the investigator is aware of what is being tested

Trial Designs

- Double-blinded study
  - Neither the investigator nor the patient know who has been randomly assigned the treatment or placebo. This design provides the most reliable and scientific data. It involves a large sample at multiple sites.

Trial Designs

- Crossover study
  - Participants receive either placebo or commercial therapy for a specific time and then the investigational drug for the remainder. This type is usually double-blind, randomized, and allows for periods when treatment is not given (“wash out”) so as not to blur data from one phase to another.

Clinical Study Protocol

- Sponsor/study site selection
- Contract
- Institutional Review Board
- Inclusion/Exclusion criteria
- Informed consent
- Visit-specific examinations
- Sub-studies
- Study documentation

COMMONLY USED OUTCOME MEASURES

Relapse
- Relapse Rate
- Severity
- Treatment Required

Progression of Disease
- EDSS
- Ambulation Index
- MS Functional Composite

MRI
- T1
- T2
- Gad

Quality of Life
- Health Status Questionnaire
- Mental Health Inventory
- Modified Fatigue Impact Scale

National MS Society website, section for Researchers: Clinical Study Measures

The Role of the FDA

- Oversees all clinical trials from design to completion
- Must give the stamp of approval before the product can be used and marketed
- Continues to monitor after the drug is approved
- It is a cumbersome, tedious, lengthy process but is necessary for consumer protection

FDA Audit

- Good nursing practice is key to surviving an audit
- Honesty and simplicity
- Proper documentation
- Well-organized and complete regulatory file

Common Deficiencies Found in FDA Audits

- Problems with consent forms
- Nonadherence to the protocol
- Inadequate drug accountability
- Inaccurate or incomplete records
- IRB problems
- Inappropriate delegation of authority
- Nonavailability of records
- Failure to obtain consent

Lisook AB. *J Clin Pharmacol*. 1990;30:296-302.

What's in it for me?

"Pros and Cons of Participation"

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Resources for Current Research Studies

- National MS Society:
  1-800-FIGHT-MS
  website: www.nationalmssociety.org
- Inside MS – National MS Society publication
- Local MS Society Chapter publications/mail-outs
- Local neurologist
- Multiple sclerosis centers
- MEDLINE plus
  website: www.nim.nih.gov/medlineplus

Resources on the Web

- Association of Rehabilitation Nurses (ARN)
  www.rehabnurse.org
- Consortium of Multiple Sclerosis Centers (CMSC)
  www.mscare.org
- International Journal of MS Care
  www.mscare.com
- International Organization of MS Nurses (IOMSN)
  www.iomsn.org
- Nursing Center
  www.nursingcenter.com

Nursing Text

- Nursing Practice in Multiple Sclerosis – A Core Curriculum. 3rd Edition (Halper, , Harris).
  - Section 19 – A Nurse's Role in MS Research
- Advanced Concepts in Multiple Sclerosis Nursing Care. 2nd Edition June Halper, MSN, ANP, FAAN – Editor.
  - Section 9 – Research Coordinator: Another Dimension of Multiple Sclerosis Nursing– Linda Morgante