Demystifying Clinical Trials
Bridging the Gap From Research to Patient Care

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Objectives

- Describe the different phases of clinical trials
- Identify the differences between clinical and research aspects of care including the importance of research assessment, data collection, and documentation
- Discuss implications for patients and families including ethical issues

National Institutes of Health (NIH)

Warren Grant Magnuson Clinical Center
The Mark O. Hatfield Clinical Research Center
Opening December 2004

Sponsors of Clinical Trials

- NIH Sponsored Programs
  - Intramural
  - Extramural
    - Cooperative groups
    - Comprehensive cancer centers
    - Community based research programs
  - Pharmaceutical companies

What Are Clinical Trials?

Clinical research designed to
- Answer a question
- Investigate a problem
- Determine the efficacy of an intervention

Types of Clinical Trials

- Preventative
- Screening & Early Detection
- Diagnostic
- Natural History
- Therapeutic
- Supportive
- Genetic and Family
Examples of Clinical Trials

- Prospective
- Retrospective
- Longitudinal
- Cross-sectional
- Psychosocial
- Behavioral

Obstacles to Conducting Clinical Trials

- Funding
- Inadequacies within the science of clinical trials
- Inadequate accession of clinical trials
- Ethical concerns
- Professional territorial issues

Elements of Clinical Trials

- High probability of generating useful knowledge
- Benefits
- Selection of subjects
- Informed consent
- Subject’s rights

Risks vs. Benefits
Protection of Research Participants

Guidelines and Regulations for Clinical Research

1947 Nuremberg Code
(http://ohsr.od.nih.gov/guidelines/nuremberg.html)

1964 Helsinki Declaration
(http://www.fda.gov/ohrms/dockets/ac/02/briefing/8021fnl1.html)

1974 National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research
(http://www.hhs.gov/ohrp/index.html)

1979 Belmont Report

Clinical Trial Development

“Ready, Fire, Aim!”

Phase I Clinical Trials

Establish maximum tolerated dose and dosing schedule
Determine drug pharmacology
Identify side effects & toxicities

Adult Phase I Clinical Trials

Small dose of drug arbitrarily chosen
Dose given to 15 - 80 subjects
Toxicity monitored & dose increased
Continue escalating until side effects are not tolerable (MTD)
Pediatric Phase I Clinical Trials

- Single agent
- Dose Escalation
  - Starting dose usually 50 - 80% of adult MTD
  - Dose increased by 20% increments
  - Usually pharmacologically guided

Phase II Clinical Trials

- Determine antitumor activity in specific cancers
- Determine effectiveness of drug for particular indication(s)
- Determine intervention effects
- Gather additional toxicity information to determine common short term effects

Phase III Clinical Trials

- Prospectively compare:
  - Investigational therapy against standard treatment
  - New intervention with standard intervention
  - Gather additional information about effectiveness & safety

Phase III Clinical Trials

- Stratification may be needed to assure balance

Phase IV Clinical Trials

- Delineates additional information about drug’s risk, benefits, and optional use
- Study of different doses and/or schedules of administration
- Integrate investigative treatment with other treatment modalities

Protocol Components

- Objectives
- Background & Rationale
- Inclusion Criteria
- Exclusion Criteria
- Treatment Plan
- Statistical Considerations
- Consent Form

http://ctep.cancer.gov/guidelines/templates.html
Toxicity Criteria

Toxicity Criteria for Myelosuppression

National Cancer Institute

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Grade 0</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
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<tbody>
<tr>
<td>WBC</td>
<td>&gt; 4000</td>
<td>3000 - 3900</td>
<td>2000 - 2900</td>
<td>1000 - 1900</td>
<td>&lt; 1000</td>
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<tr>
<td>Neutrophils</td>
<td>&gt; 2000</td>
<td>1500 - 1900</td>
<td>1000 - 1499</td>
<td>&lt; 500</td>
<td>&lt; 500</td>
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<tr>
<td>Lymphocytes</td>
<td>&gt; 2000</td>
<td>1500 - 1900</td>
<td>1000 - 1499</td>
<td>&lt; 500</td>
<td>&lt; 500</td>
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<tr>
<td>Hemoglobin</td>
<td>Normal</td>
<td>10.0 - 10.9</td>
<td>8.0 - 9.9</td>
<td>&lt; 6.5</td>
<td>&lt; 6.5</td>
</tr>
<tr>
<td>Platelets</td>
<td>Normal</td>
<td>75 K - 99.999 K</td>
<td>50 K - 74.999</td>
<td>25 K - 49.9 K</td>
<td>&lt; 25,000</td>
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http://ctep.cancer.gov/reporting/ctc.html

Informed Consent

- Purpose of study and expected study participation duration
- Description of drug, procedures, treatments and interventions
- Description of foreseeable risks or discomforts
- Description of benefits from study (subjects & others)
- Alternative procedures or treatment options
- Statement of confidentiality
- Compensation for injury
- Names and numbers of persons to contact
- Participation is voluntary

http://www.fda.gov/ohrpp/104000.htm
http://www.hhs.gov/ohrp/humansubjects/guidance/final423.html

Clinical Nurse Role

- Advocate
- Educator
- Liaison
- Patient Monitor
- Data Collector
- Communicator
- Follow-up

Nursing Role in Clinical Trials

Advocacy
- Promote open communication
- Encourage discussions
- Ensure adequate information is given
- Assist family in defining their goals and purpose for participation
- Assess patient’s understanding of risk vs. benefit
- Support family

Education
- Clinical trial
- Protocol requirements
- Medication administration
- Side effects and symptom management
- Self-care measures
- Resources available
Nursing Role in Clinical Trials

Patient Monitoring
- Assessment
- Identification of side effects
- Response to intervention
- Data Collection
  - Specimen collection
  - Documentation

Patient Diary

Filgrastim/Research Drug

<table>
<thead>
<tr>
<th>Name</th>
<th>Dose</th>
<th>Cycle Number</th>
<th>Cycle Start Date</th>
<th>Drug Start Date</th>
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<tbody>
<tr>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>Date</th>
<th>Time dose given</th>
<th>Indications or missed dose?</th>
<th>Daily temperature</th>
<th>Side Effects</th>
<th>Bone or joint pain</th>
<th>Muscle aches</th>
<th>Headaches</th>
<th>Fever</th>
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* If you missed a dose write “M” in the box.
Follow-up

Comparison of Clinical and Research Aspects of Care

Interventions
- Management and effectiveness
- Response to therapy or treatment

Pharmacokinetics

Studies performed to determine the absorption, distribution, metabolism, and excretion of investigational agents as well as their effects on the body

Pharmacokinetics

Nursing Considerations in Pharmacokinetics/Serial Bloods
- IV access
- Sampling site
- Medication administration
- Documentation
- Sampling time
- Transporting specimens

Comparison of Clinical and Research Aspects of Care

Laboratory and Diagnostic Studies
- Routine labs and diagnostic studies
- Research specimens
- Blood limits
- Drug levels
- Pharmacokinetics and serial blood tests

Pharmacokinetics

Nursing Considerations in Pharmacokinetics/Serial Bloods

- IV access
- Sampling site
- Medication administration
- Documentation
- Sampling time
- Transporting specimens
PK Worksheet

Filgrastim/Research Drug Pharmacokinetic Worksheet

Patient Name: ____________________  Study ID#: __________________
Height (cm): ________  Weight (kg): __________  BSA: ____________

<table>
<thead>
<tr>
<th>Filgrastim/Research Dose (mcg)</th>
<th>Date</th>
<th>Time</th>
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<tbody>
<tr>
<td>Pre dose</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 hr post</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 hr post</td>
<td></td>
<td></td>
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<tr>
<td>3 hr post</td>
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<tr>
<td>4 hr post</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 hr post</td>
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R115777 Biologic Effects

Inhibition of Farnesyltransferase

Pre Steady State

FTase Activity (cpm)

165 mg/m²
200 mg/m²
275 mg/m²
375 mg/m²

PK Studies

Drug Concentration

Time

Pharmacokinetic Sampling

- Labeling
- Transportation
- Processing
- Documentation

Comparison of Clinical and Research Aspects of Care

Medications
- Verification
- Documentation
- Side effects

Comparison of Clinical and Research Aspects of Care

Care Conferences
- Guided by clinical or research aspects
**Comparison of Clinical and Research Aspects of Care**

**Teaching**
- Disease process and symptom management
- Medications
- Monitoring
- Self Care
- Notification

**Coordination of Services**
- Communication
- Medication preparation and delivery

**Case Scenarios**

**Adult Case Study**
Ms. T. G. is a semi-retired R.N. newly diagnosed with stage IV pancreatic cancer.
Eager to join phase II vaccine study because she heard it makes a difference and she doesn’t want to die.
Disease progression ……continues on study

**Ethical Issues**
- Respect for persons
- Autonomy
- Self-determination
- Privacy

**Potential Research Candidate**
Mrs. D. P.
- 57 year old widow with 2 adult children
- Newly diagnosed with multiple myeloma
- Interested in a phase I vaccine research study

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The Ethical Issues

The Belmont Report

- Respect for person
- Beneficence
- Justice


The Next Visit

Mrs. D. P., her daughter, and 3 grandchildren

Illiteracy does not equal incompetence.

Comprehension is relative.

Factors associated with a greater knowledge

- College education
- Speak only English at home
- Read consent carefully
- Time to consider
- Nurse present
- Received simplified consent


Consent Guidelines

Be clear and concise.

Check reading level…

usually 8th grade is okay.

Check for understanding frequently.

Pediatric Case Scenario

Kaitlyn is a preschooler who has refractory stage IV neuroblastoma. She has been referred to your institution for the phase II protocol of Temacide. Her parents have been searching everywhere for treatment options and are desperate to be entered into this study.

Twenty subjects are to be accrued on the Temacide study. Kaitlyn would be subject #7 if she meets eligibility criteria.

- Three of the six patients have died of disease progression
- One patient is experiencing severe complications of the treatment regimen
- The remaining two subjects have stable disease and are experiencing minimal to moderate side effects.
Pediatric Case Scenario

- Based on your knowledge of the research findings, should the study continue to accrue subjects?
- How should the findings be shared with the family during the informed consent process if at all?
- How will the parents' motives for participation influence their decision?
- Do you believe this family can give an informed consent that is in the best interest of their child?

Adolescent Case Scenario

Michael is a 16 year old who presents to your clinical setting to rule out Sarcoma.

He is accompanied by his parents. His family informs you they do not want him to know his potential diagnosis.

After completing diagnostic work up, he is eligible for the Sarcoma research protocol.

- Is it acceptable to enter a teenager who does not know their diagnosis on a research study?
- How do you obtain an informed assent or do you?
- How do you respect the parent's wishes but maintain honesty with Michael?
- What do you do if Michael asks you why the other children in the clinical setting are bald?
- How would you teach him about treatment side effects and management?
Questions

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