

Investigator Responsibilities in Clinical Research

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Topics to be Discussed

- Overview of Clinical Trials
- Good Clinical Practice
- The “Research Team”
- The Role and Responsibilities of the Principal Investigator

Overview of Clinical Trials

■ Definition

- Research studies involving patients or populations at risk for disease
- May be directed at questions of causation, prevention, early detection or treatment
- Designed in a scientific manner and conform to ethical standards

Importance of Clinical Trials

- To increase knowledge
- To provide “evidence-based” patient care or prevention of disease
- To improve the quality of care
 - Patients participating in a trial tend to receive better care
 - Quality of care for other patients who are not participating in a trial can also be improved (i.e., supportive care)

Why the Emphasis on Evidence?

- To reverse the following problems:
 - Assumptions that are not based upon facts continue to be made
 - Doctors work largely independently without incentives to update their knowledge – often “behind the times”
 - Traditional or professors’ approaches generally used – may be ineffective
 - “Eminence based” medicine

Who Conducts Clinical Trials?

- Academic centers
- Groups of academic centers – cooperative groups
- Government agencies or institutions
- Corporations (pharmaceutical companies, biotechnology companies)
 - Usually done via academic or private institutions

The Conduct of Clinical Trials

- Frame a hypothesis based upon present knowledge
 - Is the study question important and relevant?
- Design a study to test the hypothesis
- Write a detailed plan of the study (protocol)
- Obtain ethical review and approval
- Conduct study, adhering closely to the protocol
- Collect relevant, pre-determined data elements
- Ensure that the data is of the highest quality possible
- Analyze the data and draw conclusions

The Protocol Document

- Detailed plan and instructions for the conduct of the trial
- Guidebook for those involved in the day-to-day care of the patient enrolled on the trial

Elements of the Protocol Document

- Title Page
- Objectives (primary and secondary)
- Background and rationale
- Eligibility Criteria (inclusion and exclusion criteria)
- Evaluation parameters – baseline and those that support and confirm eligibility
- Treatment plan
 - Modifications
 - Supportive care
 - Concurrent therapies (including contraindications)

Elements of the Protocol Document

- Treatment Plan (con't)
 - Surgical guidelines
 - Radiation therapy guidelines
- Off-study criteria
- Post-study evaluation (what tests should be done and how often)
- Data collection and reporting procedures
- Statistical section
 - Sample size, study duration, relevant endpoints

Elements of the Protocol Document

- Statistical section
 - How endpoints will be evaluated (e.g., response, adverse events)
- Multi-institutional guidelines (if applicable)

Elements of the Protocol Document

- Ethical Considerations
 - Discussion of rationale for risks
 - Are risks reasonable in relation to the anticipated benefits?
 - Are risks reasonable in relation to the importance of the knowledge to be gained?



Elements of the Protocol Document

- Ethical Considerations (con't)
 - Informed consent procedures
 - Conflicts of interest
- Pharmaceutical Section
 - Information about the study drug(s)
- Publication Policy
 - Who will be involved, registration of the trial
- References

Good Clinical Practice (GCP)

- International and scientific *quality standard* for:

- Designing
- Conducting
- Recording
- Reporting

Trials that involve the participation of human subjects

Compliance with GCP

- Provides *public assurance* that the:
 - Rights, safety and well-being of patients are protected and consistent with the Declaration of Helsinki
- Ensures that *clinical trial data* and *reported results* are:
 - Accurate
 - Credible

Do We Really Need GCP?



Why We Need GCP

- International concern for the protection of human subjects involved in research has increased
 - Historical influences (WWII, vulnerable populations)
 - Need for research to advance medical knowledge
- Unified to facilitate mutual acceptance of clinical data by regulatory authorities

The Research Team

- Definition

- A group of people working together in a systematic and scientific manner to establish facts
- Committed to applying the principles of GCP in the conduct of clinical research that may have an impact on the
 - Safety and well-being of human subjects

Members of the Research Team

- Principal Investigator
- Co-investigators or associate investigators
- Clinical research coordinator
- Data manager
- Clinical pharmacist
- Statistician

Members of the Research Team

- Patient(s)
- Institutional Review Board (IRB)
- Regulatory Bodies

The Principal Investigator

- The individual who actually conducts the clinical trial or research study (usually referred to as the PI)
- The leader of the research team at the site

Qualifications of the PI

- An appropriately qualified person in the relevant field of health care (MD, PhD, Pharm D, nurse)
- Trained and experienced in clinical research
- Familiar with the study background and requirements

Responsibilities of the PI

- Familiar with the background of the study (e.g., disease, management of the disease, side effects of treatment)
- Familiar with the study – the protocol document and study procedures
- Remember – READING IS FUNDAMENTAL *if you want to be an effective PI*

Some Things to Think About

- How many errors could be avoided by taking the time to read the protocol?
- If short-cuts in reading the protocol (schema only) are taken
 - Are you prepared to conduct the protocol?
 - Will you be effective as a leader?
 - Don't set a bad example!
- What if you or your institution is unable to carry out some protocol related procedures or tests?
 - Should you agree to participate?

Responsibilities of the PI

- Obtain IRB approval of the protocol and informed consent *prior* to the initiation of the study (i.e., patient enrollment)
- Be familiar with any national laws that may impact the study design or participation
 - Drug approval
 - Importation of drugs (where, how, costs)
 - Human tissues (storage, use, transfer to another institution or other country)
 - Funding policies or rules

Responsibilities of the PI

- Obtain informed consent from patients or parents of minor patients
 - *Prior* to starting protocol treatment
 - *Prior* to randomizing patients if the study is a randomized trial

Informed Consent

- Informed consent is a “process” – it does not end with the signature of the patient on a piece of paper
- On-going and interactive process between the research team and the patient
 - To ensure patient understands the study
 - To ensure patient understands what is required to participate in the study

Informed Consent – PI Responsibilities

- Provide the necessary information to the patient or parent of a minor child about the study
- Obtain the informed consent (documentation that the process took place)
- May “delegate” to other members of the research team if they are knowledgeable about the informed consent process

Informed Consent – Information to be Conveyed

- Participation is voluntary
- Information about the patient's disease
- Rationale for specific therapy planned in the trial
- Description of the "research" objectives
- Differentiation between "research" elements and "standard care"

Informed Consent – Information to be Conveyed

- Patient's "required involvement"
 - Duration of participation
 - Frequency of hospitalizations, out patient visits during treatment
 - Frequency of visits after treatment
- Alternative approaches to treatment
 - Standard treatment
 - No treatment if no alternatives exist
- Risks or discomforts (side effects of treatment and procedures)

Informed Consent – Information to be Conveyed

- State how patient's confidentiality will be maintained
- Provisions for research-related injuries and compensation for disability or death
- Costs to the patient as a result of participation
- Contact details for problems or questions
 - PI
 - Patient advocate

Responsibilities of the PI

- Enroll only eligible patients
- Observe, evaluate, manage and document all effects of treatment
 - Response
 - Other study end-points
 - Adverse events
 - Deaths
- Report adverse events and deaths as specified within the protocol
 - IRB
 - Sponsor (if study sponsored)

Responsibilities of the PI

- Notify IRB and/or Sponsor of any issues that pose a threat to the *safety* and *well-being* of the patients in the study
- Submit any changes (amendments) made to the protocol to the IRB for approval
- Provide information about protocol progress to the IRB on an annual basis (annual continuing reviews)

Responsibilities of the PI

- Record all data pertinent to the study
- Maintain all study documentation
- Perform data verification
 - Match case report forms with source data
- Make data available for external monitors (if applicable)

Responsibilities of the PI

- Comply with all procedures specified in the protocol in accordance with GCP

Responsibilities of the PI

- May delegate responsibilities to other members of the research team
 - Associate or Co-Investigators
 - Data manager

Delegation ≠ Abdication of Responsibilities

- Supervision of the delegated work is essential
 - Informed consent process and procedures
 - Quality and accuracy of the data recorded on study case report forms
- Supervision of the care delivered by the staff responsible for the patient is essential
 - Adherence to the protocol treatment plan
 - Appropriate supportive care
 - Intervention when adverse events occur

Being the “PI” is not a title only, it implies assumption of responsibilities



Conclusions

- Clinical trials imply a disciplined approach to the care of the patients enrolled on the studies
- A “research team” approach is ideal
- The PI is ultimately accountable and responsible for the conduct of the clinical trial

Conclusions

- The PI should strive to meet the high standards of GCP in order to provide public assurance that the
 - Rights, safety and well-being of patients are PROTECTED
 - Data is ACCURATE
 - Reported results are CREDIBLE

Thank You

