Phase 1 and 2 Studies

* safety first...

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FDA/CDER/DMIP
Overview

➢ Background
  • FDA Mission
  • Drug Development Basics

➢ Phase 1 Studies

➢ Phase 2 Studies

➢ Take Away Points
What We Do

“The FDA is responsible for **protecting the public health** by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation’s food supply, cosmetics, and products that emit radiation.’

“The FDA is also responsible for **advancing the public health** by helping to speed innovations that make medicines and foods more effective, safer, and more affordable; and **helping the public get the accurate, science-based information** they need to use medicines and foods to improve their health.”

Reference: www.fda.gov/aboutfda/whatwedo/default.htm
FDA
Evaluates risks/benefits for a population

Provider
Evaluates risks/benefits for a patient

Patient
Evaluates risks/benefits for himself/herself
FDA Roles in Drug Development

- Assuring the **safety** and **effectiveness** of drugs
- **Safety** of study participants
  - Human subject protection
    (consent, GCP, safety monitoring)
- “**Speed innovations**”
  - Helping in the development of more effective, safer and more affordable drugs – *promoting good science*
    - Involvement throughout all phases of drug development
    - Providing advise on the design of well controlled, safe investigations
Milestone Meetings with FDA

Sponsor submits IND application

Non-Clinical Phase 1 Phase 2 Phase 3 NDA/BLA

Active IND

Sponsor conducts Clinical Studies

Pre-IND Meeting EOP 2 Meeting Pre-NDA Meeting

Patient Access to New Drug (Post-Marketing)
Phase 1 and 2

- From a regulatory perspective: Investigational diagnostic tests offer no advantage to study subjects: drug and associated cameras/devices must have acceptable safety threshold.

- Studies should collect sufficient data to allow for refinements at next step of develop pathway

- Begin thinking about clinical use early in order to develop indication statement and appropriately designed studies to test the proposed use.
Phase 1

Initial introduction of investigational drug into humans

- Designed to collect safety data, determine metabolism, PK & early dosing information.

- Closely monitored for safety
  - Small numbers of subjects, sequential dose evaluation
  - Adverse event collection during imaging and follow up
  - Vital signs, EKG, clinical labs baseline and after imaging
  - Pregnancy testing prior to enrollment
Phase 1

Initial introduction of investigational drug into humans

- Should collect sufficient information to design a well controlled hypothesis generating study
  - Early safety/tolerance issues
  - Imaging uptake characteristics
  - Best imaging time points

- Imaging characteristics at different dosing
  - Begin thinking about optimal dose early
    - Although not typically determined until phase 2 or 3 studies.
Phase 2

- Controlled clinical study to collect early effectiveness data and generate hypotheses.
  - Refine dosing based on phase 1 safety/bio-distribution data
  - Further develop:
    - Imaging time points/procedures
    - Image interpretation standards
    - Hypotheses and reference standards

- Aids in early understanding of AE profile.
  - Well controlled, closely monitored
  - Relatively small numbers
  - Appropriate clinical laboratory and vital sign assessments
Phase 2 Example

- Optical imaging agent X given via IV injection.

- Objectives: Safety & early efficacy

- Population: Stage 4 cancer scheduled to undergo surgery

- Efficacy Endpoints: Imaging results as compared to reference standard (histology)
Phase 2 Example

Procedures: Standard of care (SOC) surgical resection/de-bulking with additional imaging using agent X and camera device

- Sponsor should ensure SOC will be maintained and protect subjects from false imaging results/unwarranted surgical procedures

Safety Monitoring: adverse events, vital signs, EKG, clinical labs at multiple time points; pregnancy testing at baseline.
Take Away Points

- Investigational imaging agents offer no therapeutic advantage: high safety threshold should be supported by non-clinical studies to support clinical studies.
- Early studies should ensure SOC treatment.
- Appropriate monitoring and laboratory assessments should begin in phase 1 to allow for adjustments in phase 2.
- Collect sufficient information to refine at next step in development.
Thank you!