Appreciation of the Drug Development Process through Understanding Clinical Trials

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FARA Friedreich's Ataxia Research Alliance

Learning Objectives

- Summarize clinical trials.
- Describe different types and phases of trials.
- Construct questions and assessments related to clinical trials.
- Identify what you can do.

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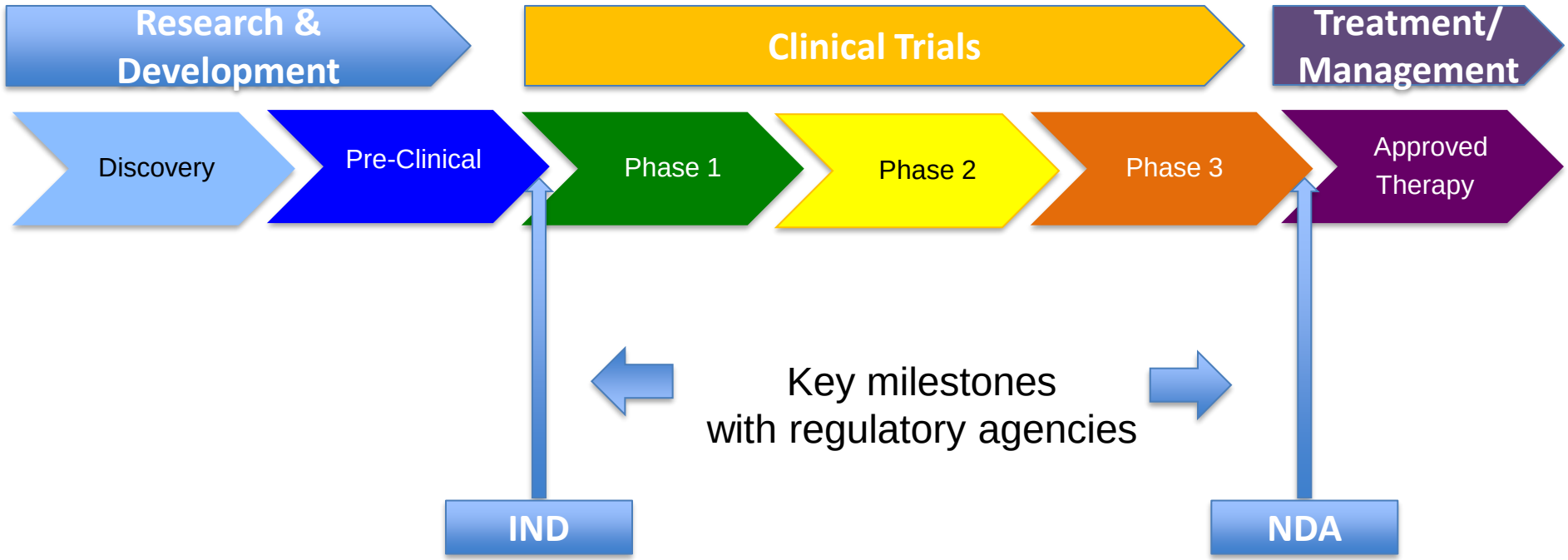
Drug Development and Clinical Trials Process



Investigational **N**ew **D**rug:
application to FDA (U.S.) to obtain permission to start human clinical trials and to ship an experimental drug to clinical investigators.

New **D**rug **A**pplication:
industry sponsor formally proposes that FDA approve new drug for prescription use; the application must establish the complete investigational history of the candidate drug.

The time and effort at each stage can vary. For example, pre-clinical data can take many years to collect while each phase of a trial might be completed over a 12-month period; ability to manufacture drug might slow down progression between phases of a clinical trial; the FDA might request additional data at the IND or NDA stages before approval is granted to move forward.

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What is a clinical trial?

- A clinical trial is a biomedical or health-related INVESTIGATIONAL RESEARCH study in HUMANS that follows a pre-defined STUDY PROTOCOL.

- A clinical trial is an EXPERIMENT. The trial outcome either implicates proceeding with further study (e.g., Phase 1 > Phase 2) or proceeding to working with regulatory agencies for approval. Possible outcomes could also include terminating the study for safety issues and/or no apparent benefits.

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What are the different types of clinical trials?

Treatment trials test investigational treatments, new combinations of drugs, or new approaches to surgery or radiation therapy.

Prevention trials look for better ways to prevent disease in people who have never had the disease or to prevent a disease from returning. These approaches may include medicines, vaccines, vitamins, minerals, or lifestyle changes.

Diagnostic trials are conducted to find better tests or procedures for diagnosing a particular disease or condition.

Screening trials test the best way to detect certain diseases or health conditions.

Quality of Life trials (or Supportive Care trials) explore ways to improve comfort and the quality of life for individuals with a chronic illness.

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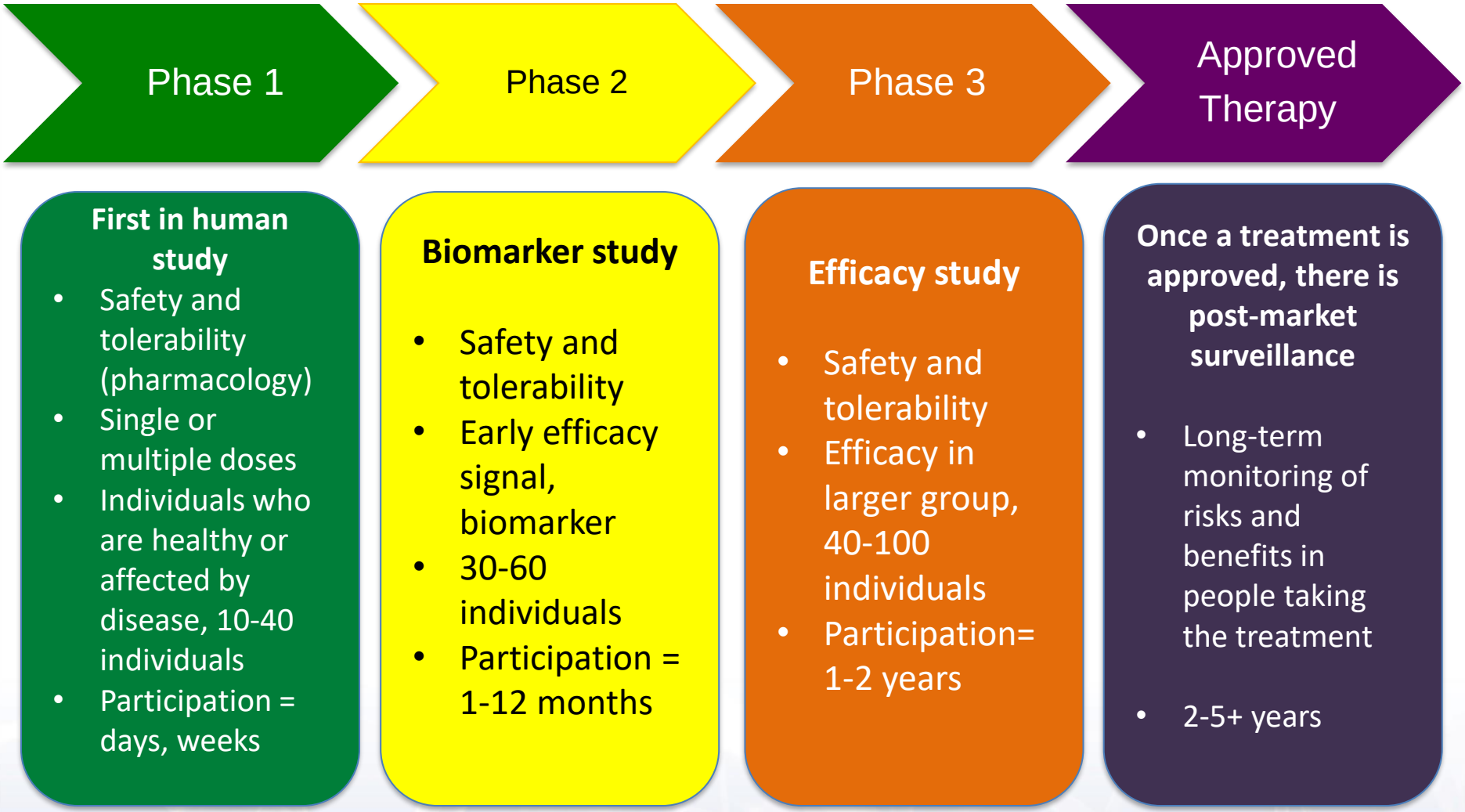
Traditional Timeline for Phases of Clinical Trials



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Study Protocols

- Protocols describe how clinical trials are to be conducted; study protocols are reviewed by regulatory agencies, like the FDA and EMA, for approval to initiate a phase of a trial.
- The study protocol describes -
  - Purpose of study
  - Eligibility and target number of participants to be enrolled
  - Duration of study and number of visits
  - How the study will be carried out
    - Safety monitoring
    - Information to be gathered about participants
    - Endpoints – biomarkers, efficacy measures
  - Determinants for terminating the study
  - Analysis and security management of data

Clinical Trials – Becoming Informed

- How do you know if a trial is happening?
  - ClinicalTrials.gov – search for Friedreich ataxia
  - FARA clinical trial list – www.curefa.org/network
  - FARA patient registry – www.fapatientregistry.org
- Are you a candidate for the clinical trial?
  - Inclusion and exclusion criteria
    - Criteria are established to determine measurable benefits and risks of treatment; these criteria aim to enroll a homogenous group of participants, meaning the participants have similar characteristics like symptoms, stage of disease, age range, gender, ethnicity
    - There might be additional criteria not listed in study announcements
  - Screening is performed to determine if person qualifies to be a study participant.

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Clinical Trials – Being Informed

- How do you decide about participation in a trial?
  - Informed consent is the process of learning the key facts about a clinical trial before deciding whether to participate.
  - Informed consent is a continual process throughout the study to provide new information to participants.
  - Informed consent includes:
    - Description of expected or known benefits and risks to participation in the study
    - Details of procedures, tests and/or assessments required for participation
    - Details of length of study and required commitments, such as dietary restrictions, number of visits to a clinic, stopping of current medications or supplements, keeping a diary, limiting environmental exposures
    - Specifications on who oversees care during the study and how to access care if an adverse event occurs while in the study
    - Compensation for participation; reimbursement for expenses (e.g., travel, hotel)
    - Description of results provided to individual participants

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Clinical Trials – Being Informed

- Can a participant leave a clinical trial after it has begun?
  Yes, a participant can leave a clinical trial, at any time; however, it is better to not enroll in the study if you have reservations, serious concerns or personal circumstances that could interfere with completing the full length of the study.
  - There can be significant consequences to the study outcome and quality of data if participants withdraw, especially if the number of participants is small.
  - Participants can be asked to withdraw from the study if behavior and lack of commitment are putting the study outcome at risk.
  - Participation can be terminated if a participant experiences an adverse event requiring medical attention or hospitalization.

- Study investigators must balance their priority for participants' safety with their oversight for data quality.

What if you don’t qualify for a clinical trial?

- Can you still get the drug?
  - Expanded access - FDA regulations enable manufacturers of investigational new drugs to provide for "expanded access" use of the drug.
  - Expanded access can be considered if …
    - clinical investigators are actively studying the experimental treatment in well-controlled studies, or all studies have been completed.
    - there is strong evidence that the drug may be an effective treatment in patients.
    - the drug doesn’t expose patients to unreasonable risks given the severity of the disease to be treated.

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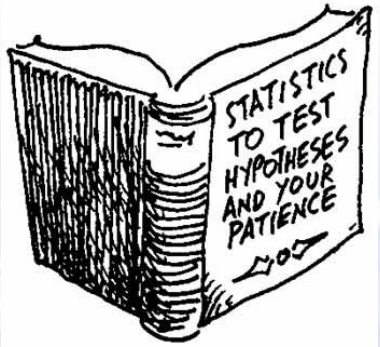
Clinical Trials – Interpreting the data/results

- A statistical analysis plan is determined prior to the start of a clinical trial.
  - Decisions are made up front on how data will be collected and documented with details on specific analysis of all the measures.
  - The statistical analysis plan includes stating what would indicate meaningful outcome(s).
- However, not all studies will reach statistical significance.
  - Remember clinical trials are EXPERIMENTS
  - Investigators need to learn from the data

(learnings include re-designing the trial or deciding to terminate further study)



Clinical Trials – Being a Participant*

* Participants are often referred to as "research subjects"

- **Be prepared by becoming knowledgeable**
  - Participation in the FA Global Patient Registry allows FARA to notify people of current research (www.fapatientregistry.org); attend informational webinars, when offered.
  - Take advantage of the informed consent process – make the best decision for you!

- **Follow the rules** – it is required for clinical trial investigators and participants to follow the approved study protocol. Participants must:
  - Comply with study visits, diets, diaries, etc.
  - Communicate effectively with the study investigators and coordinators, especially about any possible side effects
    - Report any time you visit a hospital, ER, outpatient clinic
    - *You* should not be determining what is a side effect. It is the responsibility of the study investigator to document any concern or occurrence for discussion with the data safety monitoring board.
  - Refrain from your own experiments – (changing dose, adding a supplement) - these undocumented changes will invalidate any outcomes the study was designed to evaluate.

- **Confidentiality** – sharing your impressions of study experiences with others in the study or outside the study can compromise the integrity of the data

- Clinical trials offer participants the opportunity to ...
  - play an active role in their own health care.
  - gain access to potential treatments before they are widely available.
  - obtain expert medical care at leading health care facilities during the trial.
  - help the FA community by contributing to medical research.

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FARA has created multiple resources to contribute to the research and development (R&D) continuum. These resources are available to academic researchers and industry sponsors to facilitate improved knowledge of the biology of FA and to facilitate the clinical trial process.

Many of these resources are listed on the next slide.

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FARA Resources Across the R&D Continuum

- Grant funding
- Access to academic experts & clinical network
- Assays
- Mouse models
- Cell lines and biorepository (patients' DNA and blood samples)
- Natural history database
- Gene expression data

- Clinical network sites for trials
- Patient registry / recruitment
- Patient engagement & access, retention
- Trial design advice
- Funding support / patient costs
- Serve on DSMBs
- Endpoint, biomarker advice & development

- FDA advocacy in post phase 2/3 meetings
- Serve on FDA advisory committees
- Provide testimony at FDA hearings
- Patient engagement / education

Discovery → Pre-Clinical → Phase 1 → Phase 2/3 → FDA review & approval → Approved Therapy

- Assays
- Animal and cell models
- FDA advocacy at pre-IND
- Prevalence data, disease burden
- Disease characterization
- Access to academic and clinical experts
- Validated outcome measures for clinical planning

- Clinical network sites for trials
- Clinician / Site recommendations
- FDA advocacy at post phase 1 meetings
- Patient registry / recruitment
- Patient engagement and access, recruitment
- Endpoints & Biomarkers

- Patient access & communications
- Website/newsletter/blog, social media articles
- Seminars & conferences - co-present results
- Payer engagement
- Assist w/ post-market surveillance initiatives

Adapted from the Parkinson's Disease Foundation 2013 and the Clinical Trials Transformation Initiative

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Thank you for viewing this information. If you have questions on the content, please send an email to info@curefa.org

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For additional education on clinical trial participation for Friedreich's ataxia, please visit curefa.org/trial

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