Discussion: Innovations in Rare Disease Clinical Programs

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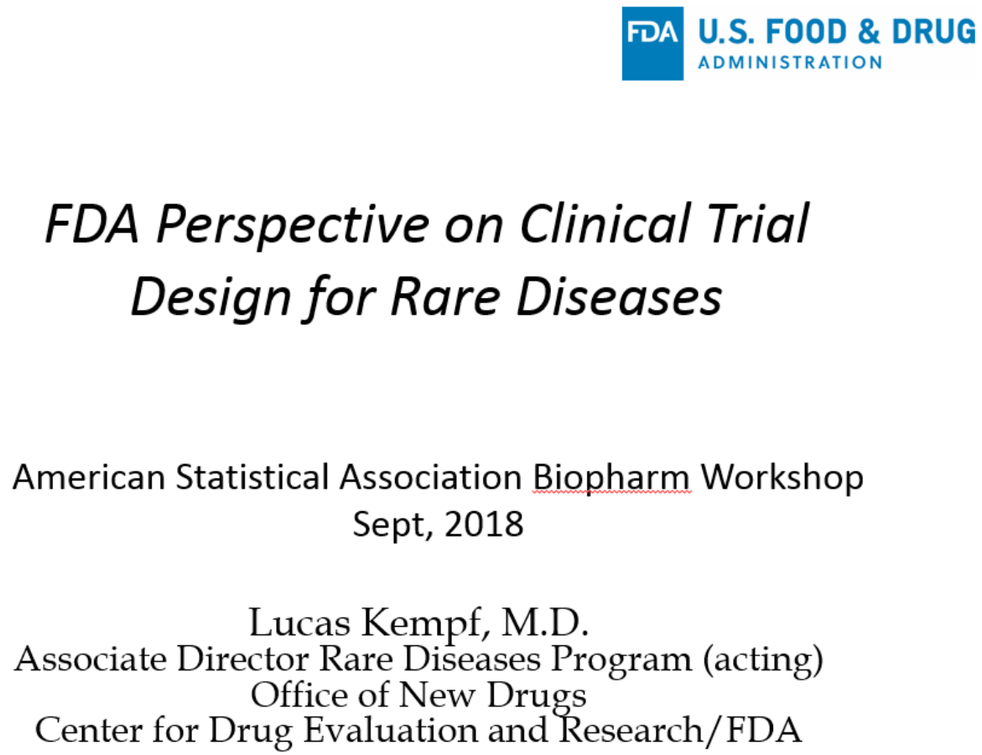
Lilly

FDA Perspective on Clinical Trial Design for Rare Diseases



- Rare diseases are not so rare (10%)
- Hallmarks of rare diseases
- Rare Disease Program Responsibilities
- Use missing data to its fullest
- Reduce variability with efficient trial execution
- Randomize to promote enrollment
  - Avoid placebo
  - More subjects allocated to experimental arm (2:1 or greater)
  - Allow rescue treatments
- Room for Innovation
  - Adaptive Designs & Interim Analyses
  - Platforms

Combining Clinical Progression Modeling with Innovative Trial Design in Rare Disease Trials

Case Studies in Designing Clinical Trials in Rare Disease

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- Common approaches to reduce heterogeneity are not feasible
  - Large sample sizes to overcome heterogeneity
  - Subgroup identification
- Solutions should involve more efficient use of available information data
  - Incorporation of multiple sources of information
    - Natural History Studies
    - Augmented Designs
  - Design innovations
    - Adaptations
    - More powerful methods
- Simulation is a key tool to understand operating characteristics when applying innovative designs and leveraging multiple sources of information

Making the Most of What You Know

- Bayesian Borrowing
  - Offers a structure for incorporating existing information in to the analysis
- Master Protocols
  - Borrow within a platform, reduce heterogeneity
- Natural History Studies
  - Begin with the end in mind
- Patient Advocacy Groups
  - Physicians, relatives are the experts