Discussion: Innovations in Rare Disease Clinical Programs

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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

- 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