Perspective of an Adult Investigator on Inclusion of Adolescents in Adult Phase 3 Trials

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Overview

Inclusion of adolescents 12 and up into adult phase 3 trials for IBD

- Feasibility
  - Potential challenges
    - Ideas to overcome them

Feasibility

- Recruitment
- Impact of study procedures on subjects
  - What do we do in adult studies that may not be acceptable to adolescents and their families?
    - Placebo control, and duration thereof
    - Need for objective (invasive) assessment of disease outcomes
- Operational aspects
  - Who will medically manage during the study?
    - Adult GIs neither comfortable nor competent to manage adolescents
    - If it will be the pedi GI and staff, how many centers have IBD co-localized?
    - If not co-localized, study management more complex, even if under one IRB approval

The Adult GI Perspective

- For the site PI, an additional source of subjects, but not ones that most of us actually see
- Most adult GIs neither comfortable nor competent to manage adolescents
- Challenges in study organization
  - One IRB submission, but a more complex one
  - If it will be the pedi GI and staff, how many centers have IBD co-localized?
  - If not co-localized, study management more complex, even if under one IRB approval

Limitations to enrolling in same protocol as adults

- Special concerns with regard to growth and nutrition
  - Adult GI does not have the training or competencies to evaluate these aspects
- Invasive procedures (colonoscopy)
  - Deemed a necessary part of outcomes measures/endpoints
  - Likely at baseline, end of induction and end of maintenance
- Lack of centers with dual expertise in adult and pedi IBD
- Lack of operational unity even within centers that do have both
- Desire of pedi Gis to be recognized for their contributions
- Concern over placebo control
  - For randomization of responders, perhaps 12 weeks for induction
  - For treat-through design, could be 1 year

Potential Solutions

- Enroll adolescents in same trial as adults
  - Sites with strong pedi and adult investigators could perform as a single site
  - Would need to identify whether there is a single PI or co-Pis (adult and pedi)
  - Also could have distinct pedi and adult sites
- Compel same study procedures for adolescents as for adults
- Adopt overall study designs that are less onerous for adolescents for adults as well
  - Do we truly need colonoscopy at end of induction, or might regulatory requirements be satisfied by PRO+inflammatory biomarker at end of induction and colonoscopy at end of maintenance
  - Shorten maintenance, especially in treat-through design
  - Head-to-head studies
    - Avoids placebo for all
    - Need for double—dummy design adds complexity in execution, questions about unblinding at end of study, risk for the sponsor

Potential Solutions

- Completely separate, but simultaneous, trial
  - alternate design that parallels adult RCT
  - additional protocol specified safeguards for the pediatric patients, in terms of assessing response and earlier access to exit to open label "rescue"

Potential Solutions

- "Piggy-backing" children in same study
  - operationally unified in terms of recruitment
  - possibility for some differences in procedures
  - may be analyzed separately, if study endpoints are different

Phase of study considerations

- Difficult to envision enrolling adolescents in Phase 2 dose-ranging studies
  - Possibly at the higher end of age range after most aspects of growth complete
  - Probably not according to calendar age, but rather maturation

Conclusions

- There are real challenges to enrolling adolescents in adult Phase 3 trials
- Some of these may be addressed by adapting/omitting some study procedures
- Consideration should be given to easing procedures for patients of all ages