Panel discussion questions

Session 1: Disease Similarity in pJIA and RA

Panel discussion questions

- Are pJIA and RA sufficiently similar to justify the relevance of data in RA to support the efficacy or safety of a drug in PJIA?
  - Clinical manifestations
  - Known pathogenesis
  - Response to treatment
  - Specific therapeutic targets
- If not, what differences may preclude relevance of data in RA to support pJIA?
- What additional data/information would be needed to address these uncertainties/differences?

Session 2: Dose Selection and Response Similarity in pJIA and RA

Panel discussion questions

- Given the existing similarities between RA and pJIA and the experience across RA and pJIA programs, to what degree can efficacy data in RA be extrapolated to pJIA?
  - What are the implications, if any, of the two studies that failed to meet their primary objective (infliximab and golimumab) on extrapolation of efficacy in RA to pJIA?
  - Are there specific considerations for:
    - small molecules versus therapeutic proteins?
    - well-studied pharmacological classes versus a new mechanism of action?
  - Should there be any additional considerations for younger aged pJIA patients (2 years to 5 years of age)?

Panel discussion questions

- Pediatric dose selection for pJIA programs to date has relied on the assumption that comparable serum concentrations in pediatric patients to those observed in adult patients would produce similar clinical response.
  - Under what circumstances are dose-ranging studies necessary (i.e. targeting dose/exposures efficacious in adult patients or being evaluated in adult phase 3 trial(s) is not sufficient)?
  - What alternative approaches can be used to de-risk pediatric dose selection and improve feasibility of PK studies in this population?

Session 3: Confirmation of Efficacy and Assessment of Safety

Panel discussion questions

- In light of the case examples and presentations in this session, what do you consider the most significant strengths, barriers, and challenges to pediatric efficacy and safety trials in pJIA?
- Given this previous experience in pJIA trials and the alternatives presented here, what specific recommendations do you have for future trial designs in pJIA drug development?
- Are there different considerations for trial designs for:
  - The first-in-class product being investigated in JIA?
  - The third or later product in an established effective class of agents?
- In discussing a borrowing approach in pJIA, the differences that exist in the pediatric and adult trial designs and endpoints is a remaining challenge. Please share any comments or thoughts on this issue.

Panel discussion questions

- What are the key considerations if children are included in an adult study to gain regulatory approval for the pediatric indication? How would age-specific issues across pediatric age groups be studied (e.g. uveitis, growth, sexual maturation) under this approach?
- What are the key trial design considerations for pediatric safety assessments?
- Given the international enrollment of pJIA studies for licensing purposes, what additional issues in study timing (i.e., initiation, interim analyses) and trial design is needed?

Session 4: Moving Forward

Panel discussion questions

- What is the biggest Pro for each potential path?
- What is the biggest Con for each potential path?
- What uncertainty remains, if any, for acceptance of a specific path?
- What data should be generated in future programs to address this uncertainty?