Session 1: Summary

Moderators: Rachel Glaser, Robert Colbert

Summary

- There was general agreement that **PJIA and RA are similar diseases** to justify the relevance of data in RA to support the efficacy of a drug in PJIA
  - Differences in nomenclature, however similar clinical manifestations, pathogenesis (HLA associations, synovial fluid), response to treatment, and specific therapeutic targets
- While some differences noted (uveitis, presentation of early onset-JIA), greater heterogeneity within PJIA population and within RA population (seropos vs. seroneg) than between PJIA and RA
  - Response to treatment of uveitis similar between adults or children
  - Treatment of early and later JIA is the same
- **Unique safety considerations in PJIA need to be considered**
  - Growth/development
  - Suggestions for safety assessment included data from registries or RWE

Session 2: Summary

Moderators:

Marc Gastonguay

Lily Mulugeta

Summary

Several examples were presented where-

- Dose selection rationale for past pJIA programs relied on matching effective exposures in adult RA; this is consistent with clinical experience with dosing of biologics in pJIA
  - In general, PJIA programs did not have dedicated phase 2 dose ranging for efficacy.
  - Most programs, typically only one dose is assessed with the randomized withdrawal study design.
  - **PJIA exposures were generally within the therapeutic exposure range from RA pivotal trials.**

- **Response (ACR and subcomponents) was similar or better in PJIA when compared to RA**
  - Although difficult to compare given totally different study designs between RA and pJIA

Summary

- Accurate assessment of E-R relationships is difficult in the context of pediatric drug development
  - **Designs that do not randomize the exposure range/small sample size may lead to misguided inference about E-R**
- But, do we really need E-R data in pediatric patients anyway?
- Rather, **the focus should on exposure-matching given that disease similarity has been established**
  - Need for higher doses in younger/smaller patients is NOT unexpected but should be assessed
  - Anti-drug antibody is relevant and the expected impact on PK should be assessed;

- Strong scientific investigation of all trials lead to improved understanding; there are no failures
- **Move towards formal assessment of trial results in the context of prior information**
- When a lower dose is approved in adults because of a specific safety consideration that may have limited applicability in pediatric patients, the approach to the pediatric dose selection needs further consideration.
- RWD may be informative in understanding factors influencing individual patient dose titration

Session 3: Summary
Moderators: Becky Rothwell, Dan Lovell

Summary

- **For 1st in class:**
  - PK/PD studies are needed to confirm that response is similar to that in adult RA trials
  - No existing perfect biomarker: CRP was discussed, with some concerns; other biomarkers will depend on the MOA
- **For subsequent in class or drugs with well established MOA:**
  - Matching effective exposures in adults is sufficient
- **Safety may be different in children and needs to be assessed:**
  - The safety issues we are most concerned about are rare or very rare; the type of data that are needed can't be obtained in the traditional pre-market or pre-approval
  - Robust post-marketing or real world data sources, such as disease-based registries, will be useful to provide long-term safety data

Summary

- **Emphasis on need for pediatric friendly protocols (early input from pediatric investigators and patient representatives)**
  - Studies need to be designed to accommodate US patients
  - Use sparse PK sampling
  - Use of outcomes that are of interest to the physicians or families
  - Use of established networks experience with design of studies in pJIA
- **Early initiation of pediatric studies and not AFTER the marketing of medications in adults**
  - Delayed access to effective medications, despite an existing medical need of children with JIA
  - Enrolling adolescents in adult trials may provide early access but has many disadvantages including exposure to placebo, impact on ability to enroll younger patients in later trials
    - Instead may consider a parallel-group pediatric study conducted concurrently with adult phase 3 trial
- **Alternative approaches when there is uncertainty with matching exposures**
  - Use of external control from registries
  - Basket trials/master protocols

Session 4: Summary
Moderators: Lynne Yao, Lisa Rider

Summary

- **The approach for evaluating drugs for JIA should be exposure-matching and providing access.**
  - Response should also be assessed during PK studies, as supportive evidence of efficacy, but the primary objective of the study and the basis for approval will be matching adult effective exposures
- **Depending on the nuances of the MOA and residual uncertainty after the adult program (e.g. potential age related differences in target expression), additional information, such as efficacy assessment may be needed**
  - A set of bridging biomarkers, if appropriately justified, could potentially be used to increase our confidence in borrowing adult data
  - Bayesian borrowing of adult data or other pediatric data could inform the design of an adequate and well controlled study, when needed
  - The adult program should be designed to adequately assess dose response and potential biomarkers that should inform the pediatric study including appropriate dose early in clinical development
- **Long-term safety assessment is critical and is likely to be done post approval in pediatric patients**