Disclaimer

The views and opinions expressed in this presentation are those of the individual presenter and do not necessarily reflect the views of the Clinical Trials Transformation Initiative.
Overview

Twelve industry representatives participated in CTTI-led, in-depth interviews

Representatives were currently or recently involved in their company’s pediatric antibacterial drug development program

Representatives included:

- Former Chief Medical Officers
- Vice President in clinical development, antibiotic portfolio
- Chief Medical Vice President, former physician lead, and physician in infectious disease units
- Therapeutic head for anti-infectives in clinical research
- Former Medical Director/Director/Lead of pediatric clinical research, drug development
- Head of biometrics unit
- Payer associate
Overview

- Representatives were from both large and small companies
- They were asked a variety of questions related to pediatric antibacterial clinical trials
Extrapolation

- The majority of representatives supported extrapolation

- Therapeutically-dependent
  - Comfortable indications included pneumonia, UTI, osteomyelitis, sepsis, HIV, skin infections, and intra-abdominal infections
  - General principle: “If it’s a disease that is an infection that occurs in pediatrics, and it occurs in adults, that’s the same infection, I would think that...I can’t think of a drug whose efficacy could not be extrapolated.”
Extrapolation (continued)

Age-dependent

- adolescents and older children was appropriate
- precautionary stance toward extrapolating for neonates
- concerns focused on older infants, those under about two years of age
- “I think neonates in general are a very complicated population…[they are] the most vulnerable population…”

Beneficial

- can avoid unnecessary studies in children or can be used to design better studies
- “…And the concept of being able to extrapolate data so that your studies were more manageable and feasible in a reasonable period of time was pretty critical, I think.”
Extrapolation – On-going Challenges

- Unclear rules about when it is appropriate to pursue pediatric labeling under these indications

- Pediatric studies come last – “on the tail end of the adult study”

- Understanding risk tolerance, particularly in younger children, and the level of data needed for FDA approval

- Conflicting regulator and payer requirements
  - “if it’s not a full phase 3 trial, sometimes you get a push back from a payer standpoint about whether that product should or shouldn’t be used in children”

- Smaller adult studies makes extrapolation harder
Reasons for Slow Progression of Pediatric Antibacterial Clinical Trials

Factors related to recruitment and enrollment were the main challenges identified:

- Parents tend to be extraordinarily risk-adverse
- Less general trust of physicians
- Ease of obtaining standard-of-care for children versus the complexity of participating in a clinical trial
- Differences in enrollment between U.S. and international sites
  - Recruitment and enrollment was far easier at international sites, primarily due to differences in parental acceptability of such trials
Suggestions for Simplifying Antibacterial Clinical Trials

- Extrapolate efficacy from adult patients
- Reduce the burden of trial participation for parents and children
  - Minimize the number of blood samples and invasive procedures
- Ease investigator burden
  - Alter eligibility criteria to make trials easier to recruit
    - Rethink requirements for the number of days of prior effective antibiotics
    - Allow evaluator blinding
    - Reconsider power calculations for non-inferiority studies
Suggestions for Simplifying Antibacterial Clinical Trials (continued)

- Rethink study design in some cases to accomplish more within a single protocol
  - Allow for multiple indications to be combined in a single trial

- Select sites with a proven track record of successful recruiting or establish a pediatric trials network
Experience with Pediatric Antibacterial Clinical Trials Sites

- Important to select sites that have experience, particularly those conducting pediatric PK studies (limited number of such sites available)

- Some sites under-perform, leading to increased trial expense timelines, and potential for lower quality data

- A challenge to using more experienced sites is increased competition among trials for the same patient population

- Networks suggested as a potential solution for the issue of site selection
The Utility of Providing Pediatric PK Data Through Peer-Reviewed Publications

Peer-reviewed publications would not serve as a good stand-alone source of information for clinicians on the pharmacokinetics of a new antibacterial drug for children

- Prescribing pediatricians in general practice would not have sufficient familiarity with the literature
- Familiarity with the published literature varies by specialty

There are well-established sources for prescribing information available for general practitioners

- “Most clinicians are going to get that information from something like Lexicomp or some other online resource through up-to-date..

Drug label provides prescribing information
Potential Reasons for a Submission Delay of Pediatric Trial Results to the FDA

Respondents had a difficult time identifying circumstances that would prompt a submission delay of study results.

Hypotheses included:

- Results do not support the use of the drug in a pediatric population
- Unable to recommend a dose to put on the label
- Time spent preparing the submission package, to avoid numerous follow-up questions
- No unexpected safety findings
- Limited interest in submission
- Perception that piece-meal data could not be submitted to the FDA (rather, must wait until studies of all age ranges are completed)
Thank you.