Industry Perspectives

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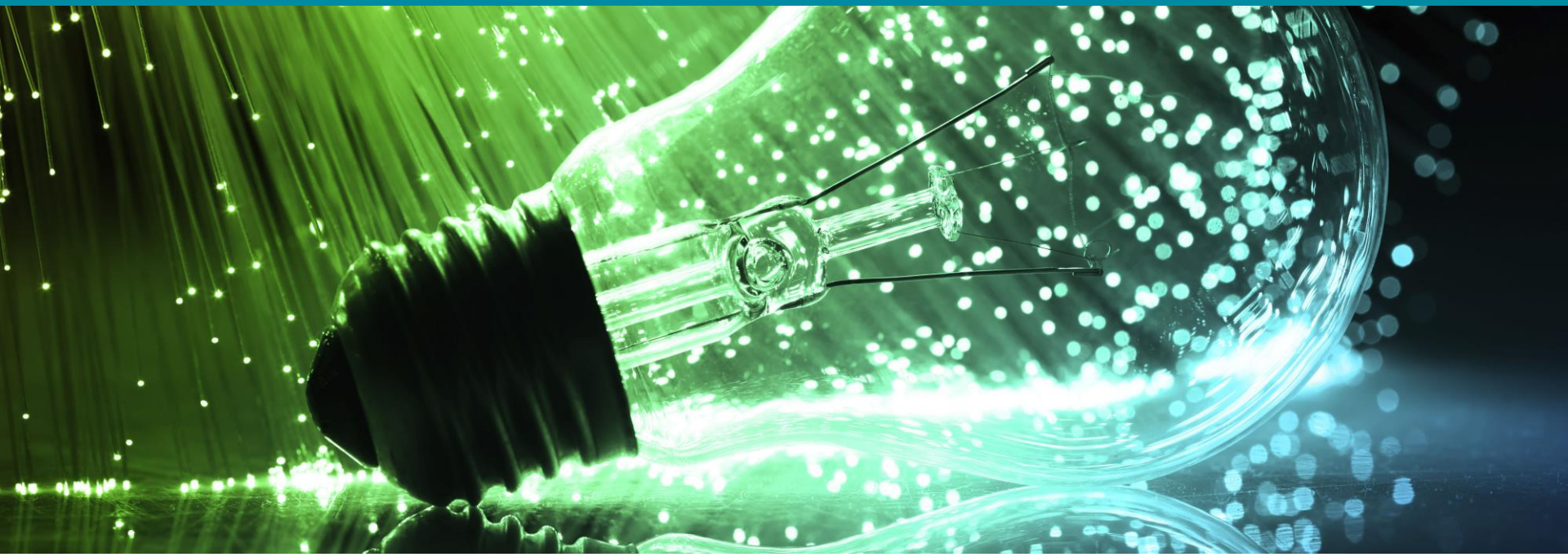

Disclaimer

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.

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