FDA-University of Maryland CERSI

Analgesic Clinical Trial Designs, Extrapolation, and Endpoints in Patients from Birth to Less Than Two Years of Age

Wednesday October 13, 2021       10:00am – 1:30pm EST       All Virtual
Thursday October 14, 2021        10:00am – 3:00pm EST       All Virtual

The goal of the workshop is to address challenges related to evaluation of analgesic products in pediatric patients including population to study, endpoints, and extrapolation of adult efficacy data. The workshop will also provide a forum for discussion on the use of extrapolation as well as alternative trial designs and statistical methods. The focus of the workshop will be on well-established mechanism of actions (NSAIDs, acetaminophen, local anesthetics, opioids).

Day 1

10:00 – 10:15
Welcome/Introductory remarks: Setting the scene (DPMH)
Lily Mulugeta, PharmD (Division of Pediatrics and Maternal Health, FDA)

10:15 – 10:35
Introductory remarks
Peter Stein, MD (Office of New Drugs, FDA)
Rigo Rocca, MD (Division of Anesthesiology, Addiction Medicine, and Pain Medicine, FDA)

10:35 – 10:50
General landscape of extrapolation of efficacy in pediatric drug development and Ethical considerations in Pediatric Drug Trials
Beth Durmowicz, MD (Office of Pediatric Therapeutics, FDA)

Session 1: Extrapolation of Efficacy (goals: To define an age limit for using PK-based extrapolation (i.e. exposure-matching))

Moderators: Lily Mulugeta (FDA) and Lisa Wiltrout (FDA)

10:50 – 11:10
Development of nociception and pain—Suellen Walker, PhD (UCL GOS Institute of Child Health)

11:10 – 11:30
Pain epidemiology in neonates and infant patients—Ricardo Carbajal, MD (Hospital Armand Trousseau)

Types of pain encountered in each age cohort as compared to older pediatric patients, number of patients available for clinical trials, etc.

11:30 – 11:45
Developmental pharmacology of analgesics—Chris Mcpherson, PharmD (Washington University School of Medicine, St Louis)
What do we know about maturation of targets? Are there maturation related changes to drug disposition or targets that may suggest need for lower or higher drug exposures in this age group to achieve response similar to older pediatric patients?

11:45 – 12:05
Extrapolation of adult efficacy data to pediatric patients
John van den Anker, MD (Children’s Hospital, Washington DC)
Given the available data, is there a biological reason to believe that drugs with well-established MOA (on drugs with well-established MOAs (opioids, NSAIDs, acetaminophen, and local anesthetics) would be less effective (at similar concentrations) in pediatric patients less than 2
years of age compared to older children? If so, in which age group and what are the uncertainties? Assessment of PK and safety would be required in all age groups.

12:05—1:20  Panel Discussion (Moderators: Lily Mulugeta and Charles Berde)
Q&A: All speakers
Panelists: John Alexander (FDA), Yun Xun (FDA), Lisa Wiltrout (FDA), Tamorah Lewis; Suellen Walker, Gary Walco, Ellen Fields, Kanecia Zimmerman, John Van Den Anker

1:20—1:30  Closing Remarks – Charles Berde
Day 2

Session 2: Trial design considerations in acute pain (goals: Trial design and endpoint considerations in age cohorts where exposure-matching cannot be used as the basis for extrapolation of efficacy)

Moderators: Lily Mulugeta (FDA) and Charles Berde

10:00 – 10:05  Welcome/Introductory remarks: Setting the scene (DPMH)
Lisa Wiltrout (Division of Anesthesiology, Addiction Medicine, and Pain Medicine, FDA)

10:05-10:55  Trial Design Considerations for Acute Pain in neonates and infants:

   Academic Perspective
   Carolina Donado-Rincon and Joe Kossowsky (Boston Children’s)

   Industry Perspective
   Edress Darsey (Pfizer Pediatric Center of Excellence)

   Regulatory Perspective
   Lisa Wiltrout, MD (FDA Division of Analgesics and Anesthetics, FDA)

10:55-11:10  Outcome measures in acute pain clinical trials in neonatal & infant populations
Monique van Dijk

11:10-11:25  PTN COA development and PTN/NICHD trials for off patent drugs
Kanecia Zimmerman, MD (Duke University/Pediatric Trials Network)

11:25—11:40  Brain-derived approaches to assess neonatal & infant pain
Rebeccah Slater, PhD (University of Oxford)

11:40-12:00  Innovative trial designs including Bayesian approaches
Brian Anderson

12:00-12:40  Lunch break

12:40-1:00  Considerations for PK/PD studies
Amy Cheung, PhD (Certara)

1:00 – 2:50  Q&A and Moderated Panel Discussion (moderators: Lily Mulugeta and Charles Berde)
Q&A: All speakers
Panelists: Rigo Roca (FDA), Gerri Baer (FDA), Lynne Yao (FDA), Jinglin Zhong (FDA), James Yates (GSK), Ellen Fields, Edress Darsey (Pfizer), Dina Metwally (UMD), Gary Walco, Kanecia Zimmerman, Tamorah Lewis

2:50– 3:00  Closing Remarks/Future Direction
Lynne Yao, MD—FDA