ADEPT 8: Workshop on Drug Dosing in Pediatric Patients with Renal Impairment

"Setting the Scene"

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Disclosures

- The views expressed in this presentation are my own and do not constitute an official position of the FDA.

- I have no conflicts of interest to disclose.

Objectives

- Provide a high-level overview of the challenges associated with establishing dosing for drug products with potential use in pediatric populations with renal impairment (RI).

- Review the structure of this workshop.

- Introduce the topic areas we will be discussing at this workshop to attempt to address these challenges.

- Describe the goals that could be achieved by the end of this workshop.

Acronyms

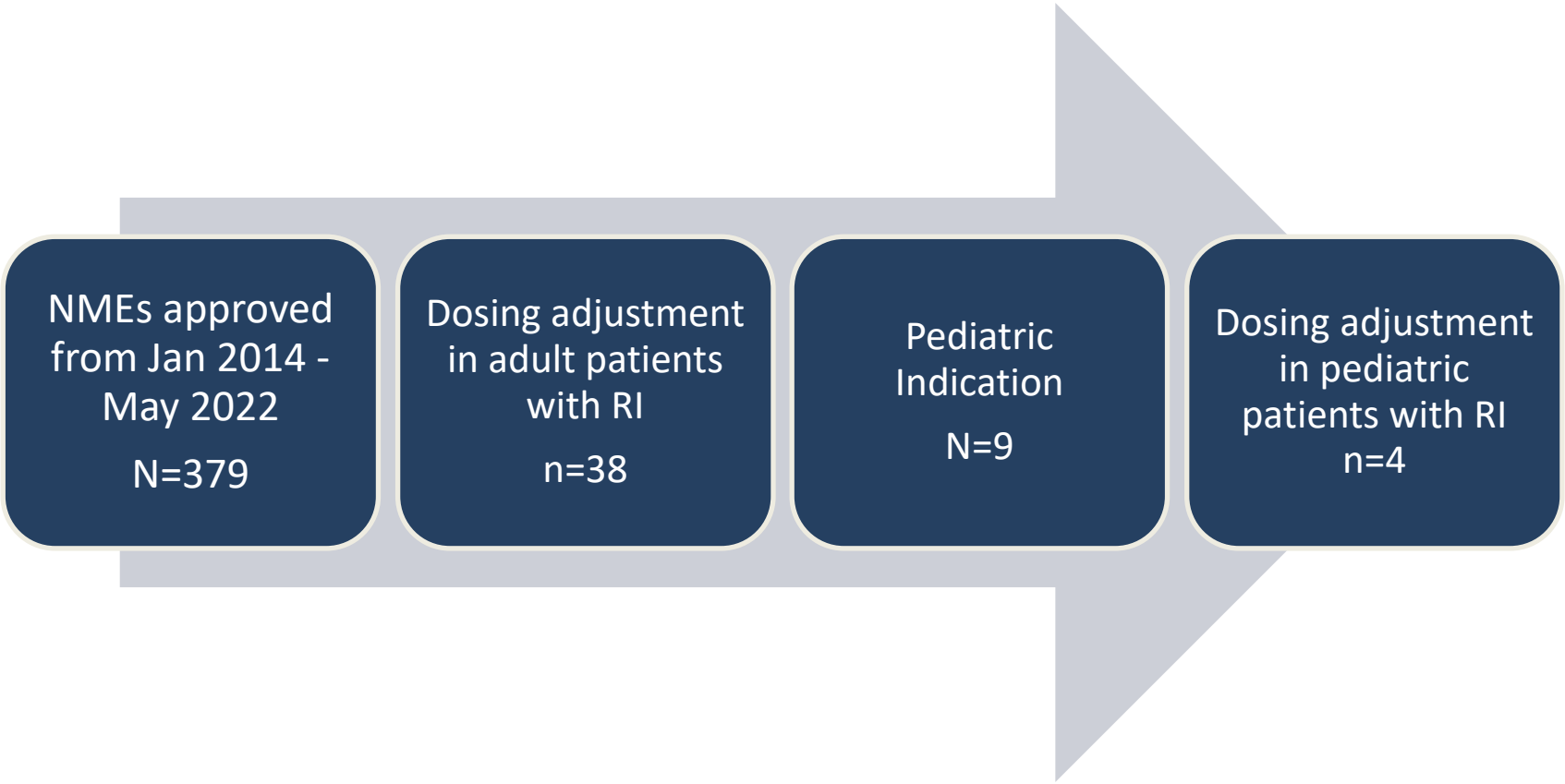
- CKD: Chronic Kidney Disease
- GFR: Glomerular Filtration Rate
- eGFR: Estimated GFR
- PK: Pharmacokinetic
- PD: Pharmacodynamic
- RI: Renal Impairment

Why are we here?

- Needs:
  - Pediatric patients with RI deserve access to safe and effective therapies with well-characterized dosing.
  - Current approved labeling for drug products reveals a paucity of established dosing for pediatric patients with RI.

Khurana M, Egger GF, Yao L, Thompson A, Pallidis C, Goldstein SL, Laskin BL, Tuchman S, Malley MA, Uhlig K. Overcoming Barriers to Drug Development in Children with CKD. Clin J Am Soc Nephrol. 2023 Apr 13. Epub ahead of print. PMID: 37055225

Pediatric Renal Impairment Dosing in Labeling



NME: New Molecular Entity
RI: Renal Impairment

What are the Challenges?

- Defining renal impairment for the purposes of drug disposition
- Evolving estimation methods for renal function
- Accurate and consistent estimation of GFR across the pediatric age range
- Accounting for growth and renal maturation
- Limited data for pediatric patients with RI from clinical trials
- Limitations of establishing pediatric dosing from adult patients with RI

ADEPT 8 Workshop: Structure

- Attendees: stakeholders from academia, government, non-profit organizations, industry, patients, and parents/caregivers

- 3 Focused Topic Sessions
  - Short focused presentations
  - Moderated Q&A Panel Discussions

ADEPT 8 Workshop: Focused Topics

What constitutes renal impairment in pediatric patients for the purposes of PK characterization and drug dosing?

- Strengths and limitations of existing estimating methods for specific populations
- What clinicians and other stakeholders need to know about special populations
- How to assess renal function within the scope of clinical trials

ADEPT 8 Workshop: Focused Topics

Translating adult renal impairment data in pediatric patients with renal impairment

- Translating adult renal impairment PK data to pediatric populations
- Reliance on BSA Indexed vs. individualized GFR values in adult renal impairment dosing – Implications for pediatric renal impairment dosing
- Extrapolation of exposure-response for safety and efficacy from adult data

ADEPT 8 Workshop: Focused Topics

Future Directions: Dosing in pediatric patients with renal impairment

- Case example illustrative of challenges and potential approaches
- Role of modeling and simulation to derive pediatric dosing
- What are the opportunities for generating clinical data to assess the impact of RI on PK in pediatric populations

What We Hope to Achieve

- Develop a shared understanding of the key challenges and knowledge gaps limiting the establishment of accurate dosing for drug products in pediatric populations with RI.

- Generate potential strategies to overcome these challenges.

- Articulate future directions for a shared commitment from stakeholders to advance dosing for pediatric patients with RI.

Relevant Scientific and Guidance Documents

- **Pharmacokinetics in Patients with Impaired Renal Function — Study Design, Data Analysis, and Impact on Dosing and Labeling. FDA Guidance for Industry**
https://www.fda.gov/regulatory-information/search-fda-guidance-documents/pharmacokinetics-patients-impaired-renal-function-study-design-data-analysis-and-impact-dosing-and-impact-dosing

- **Matzke, GR et al. "Drug dosing consideration in patients with acute and chronic kidney disease-a clinical update from Kidney Disease: Improving Global Outcomes (KDIGO)" Kidney Int. 2011; 80(11): 1122-1137.**
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- **Filler, G, Yasin A, and Medeiros M. "Methods of assessing renal function." Pediatric Nephrol. 2014; 29(2): 183-192.**
https://link.springer.com/article/10.1007/s00467-013-2426-7

- **Al-Khouja, A, et al. "Dosing recommendations for pediatric patients with renal impairment." J Clin Pharmacol. 2020; 60(12): 1551-1560.**

- **Schijvens, AM, de Wildt SN, and Schreuder MF. "Pharmacokinetics in children with chronic kidney disease." Pediatr Nephrol. 2020; 35(7): 1153-1172.**

Thank You