PEDIATRIC TRIALS NETWORK

Making drugs safer & more effective for use in the youngest patients

2023

THE ANNUAL REVIEW

A MESSAGE FROM PTN LEADERSHIP

2023 was another busy and exciting year for the **Pediatric Trials Network (PTN)**. This year, the Network upheld its commitment to improving pediatric care by changing labels, performing research, connecting with partners, and sharing science. The PTN would like to thank its participants, members, and partners for their continued support in making a difference for children and families worldwide!

This year, the PTN contributed data to two U.S. Food and Drug Administration (FDA) medication label changes. FDA label changes help health care providers prescribe the safest, most effective dosages of medicines to children. These label changes make 19, in total, that the PTN has informed to date.

Three PTN studies reached milestones in 2023. Pharmacokinetics, Pharmacodynamics, and Safety of a Single Dose Intravenous Methadone in Healthy Adult Volunteers (MTH02) enrolled its first participants; CUDDLE added seven medications to the list of those being studied; and the Safety of Sildenafil in Premature Infants study opened its third and final cohort. Including these, the PTN supported six ongoing studies in 2023, and one new study is expected to begin enrolling in 2024.

Throughout 2023, the PTN connected with its partners at the Pediatric Academic Societies Annual Meeting and the International Children's Advisory Network (iCAN) Summit. Events at these meetings included a debate between PTN investigators and informational sessions on the work of PTN and iCAN.

Since last year's report, the PTN has released four new publications and three new results-at-a-glance summaries. Additionally, the PTN started sharing its methods for analyzing various biological samples with the scientific community. Please read on for more details on all of the PTN's accomplishments and thank you again for your continued commitment!

Danny Benjamin, MD, PhD, MPH
Pediatric Trials Network,
Principal Investigator

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Pediatric Trials Network,
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THIS YEAR THE PTN...CHANGED LABELS

Levetiracetam label change

In 2023, A pharmacokinetic (PK) study by the PTN contributed to a label change for levetiracetam, an anti-epileptic drug. The FDA updated the dosage information for levetiracetam based on the PTN studies **Pharmacokinetics of Anti-epileptic Drugs in Obese Children (AED01)** and **Pharmacokinetics of Understudied Drugs Administered to Children per Standard of Care (POP01)**. This was the 19th FDA label change informed by PTN research. **MORE**.

Rifampin label change

The PTN also contributed PK data to change the FDA label for rifampin, an antibiotic. The FDA updated the dosage information for rifampin based on the PTN study **Pharmacokinetics (PK) of Antistaphylococcal Antibiotics in Infants**. This was the 18th FDA label change informed by PTN research. **MORE**.

PTN label changes to date

Under the **Best Pharmaceuticals for Children Act** (BPCA), the PTN provides the FDA with research and data to inform updates to medication labels so that health care providers can prescribe the most effective doses of medications to children. As a result of research performed through the BPCA program, led by the PTN, the following label changes have been made:

- Acyclovir
- Ampicillin
- Caffeine
- Clindamycin (x2)
- Diazepam
- Doxycycline
- Levetiracetam
- Lisinopril
- Lithium
- Lorazepam
- Mercy babyTAPE
- 2D and 3D Mercy TAPE
- Meropenem
- Propylthiouracil
- Pralidoxime
- Rifampin
- Sodium nitroprusside

...PERFORMED RESEARCH

Methadone study for adults

In mid-2023, the PTN enrolled the first participants in its study **Pharmacokinetics, Pharmacodynamics, and Safety of a Single Dose Intravenous Methadone in Healthy Adult Volunteers (MTH02)**. The study completed enrollment in early 2024.

MTH02 is evaluating how healthy adults process methadone administered intravenously to determine the optimal dose and to understand variations in drug disposition. Methadone is already approved by the FDA for pain management in adults. Results from MTH02 will help update information on dosing methadone for adults, and they will lay the foundation for studies to label methadone for treating acute pain for children. **MORE**.

CUDDLE study update

The PTN study **Pharmacokinetics and Safety of Commonly Used Drugs in Lactating Women and Breastfed Infants (CUDDLE)** added seven additional medicines to determine safety for both mothers and their breastfed infants. These additions are a substantial milestone in determining the safety of medications passed through breastmilk. **MORE**.

Sildenafil study update

In the summer of 2023, the PTN opened the third cohort in the second phase of the **Safety of Sildenafil in Premature Infants** study. This is a major study milestone as it will help determine the safety of a higher dose of sildenafil in premature infants. The study aims to assess the safety of sildenafil in premature infants at risk of bronchopulmonary dysplasia (BPD) and determine preliminary effectiveness and pharmacokinetics. **MORE**.

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...PERFORMED RESEARCH (continued from page 2)

Ongoing PTN studies

The PTN has six currently enrolling studies. **Learn more** about ongoing and completed PTN studies.

- A Prospective, Blinded, Cross-Over Trial of the Exposure-Response Relationship of Terbutaline Sulfate in Adults with Asthma (TBS02)
- Anesthetics and Analgesics in Children (ANA)
- Commonly used drugs during lactation and infant exposure (CUDDLE)
- Pharmacokinetics, Pharmacodynamics, and Safety Profile of Understudied Drugs Administered to Children per Standard of Care (POP02)
- Safety of Sildenafil in Premature Infants (Sildenafil II)
- Pharmacokinetics and Safety of Commonly Used Drugs in Lactating Women and Breastfed Infants (BMS02)

PTN studies recruiting soon

- Guanfacine for Hyperactivity in Children with Down Syndrome (HYP01)

Clinical study reports

The PTN has seven clinical study reports (CSRs) that are with the FDA for review.

- Metronidazole, with data from ABS01
- Oxycodone, with data from BMS01
- Oxcarbazepine, with data from AED01 and POP01
- Furosemide, with data from FUR01 and POP01
- Ondansetron, with data from BMS01
- Topiramate, with data from AED01 and POP01
- Fluconazole, with data from Safety of Fluconazole Prophylaxis in Infants

...CONNECTED WITH PARTNERS

Investigator spotlights

Throughout 2023, the PTN highlighted three investigators to share their experiences with the Network and pediatric clinical research. Read the responses of Dr. Chi Hornik, Dr. Matthew Laughon, and Dr. Susan Rahman.

Chi Hornik

Matthew Laughon

Susan Rahman

PTN investigators and a patient advocate debate

In late April 2023, the PTN sponsored a session at the Pediatric Academic Societies Annual Meeting in Washington, D.C. The event involved quick debates between PTN investigators on topics related to pediatric clinical research. A patient advocate from the International Children's Advisory Network (iCAN) and student with experience participating in pediatric clinical research shared her thoughts on each topic. The event was attended by more than 100 people. Participation from the audience, as well as the perspectives offered by the patient advocate, made for engaging debates. MORE.

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…CONNECTED WITH PARTNERS (continued from page 3)

PTN at the annual iCAN summit

During the summer, members of the PTN presented at the 2023 International Children's Advisory Network (iCAN) Summit in La Jolla, California. Global Trials Associate Director, Phyllis Kennel, and Research Communications and Engagement Specialist, Meagan Daly, presented to a group of young people and industry representatives. The presentation familiarized the group with the important work of DCRI Pediatrics and PTN. The presentation also provided updates on the ways in which iCAN participation has helped inform the work of PTN. MORE.

PTN and iCAN anthology

The PTN partnered with the International Children's Advisory Network (iCAN) to produce an anthology that highlights iCAN members' perspectives on the pediatric clinical research process. A formal publication will soon be produced as a way of engaging families in the clinical research process. View the digital version.

The *PTN Post*

Throughout 2023, the PTN released four issues of its newsletter, the PTN Post. If you missed an issue, find it linked below, or subscribe to the *PTN Post*.

- Issue 42 (December 2023)
- Issue 41 (September 2023)
- Issue 40 (June 2023)
- Issue 39 (March 2023)

…SHARED SCIENCE

PTN methods for analyzing drug concentration

Many PTN studies measure the concentration of medicines in children's bodies. The PTN collaborates with several laboratories to develop and validate methods for analyzing biological samples. The PTN is now sharing these methods with the research community. The PTN Methods page contains a list of drugs studied by the PTN along with the type of sample (plasma, dried blood spot, urine, cerebrospinal fluid, and breastmilk) used to evaluate drug concentration. There are over 200 methods available for 90 drugs. MORE.

Results At-a-Glance

The PTN shares what it's learning with research participants and the public through results-at-a-glance summaries. These summaries describe the key information, including results, of PTN studies and publications in a format that is quick and easy to read. The PTN is continuing to develop results-at-a-glance summaries for publications to ensure the knowledge generated from the PTN is shared, especially with study participants who make it possible. In 2023, the PTN created three summaries on PPE, metronidazole, and clindamycin. Read these and all of the PTN's results-at-a-glance summaries.

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...SHARED SCIENCE (continued from page 4)

Published Research (2022 – 2023)

Assessing clinical site readiness for electronic health record (EHR)-to-electronic data capture (EDC) automated data collection. Eisenstein EL, Zozus MN, Garza MY, Lanham HJ, Adagarla B, Walden A, Zimmerman KO, Kumar KR. *Contemporary Clinical Trials*, May 2023.

Safety of sildenafil in premature infants at risk of bronchopulmonary dysplasia: Rationale and methods of a phase II randomized trial. Lang JE, Hornik CD, Martz K, Jacangelo J, Anand R, Greenberg R, Hornik C, Zimmerman K, Smith PB, Benjamin DK, Laughon M. *Contemporary Clinical Trials Communications*, December 2022.

Use of Real-World Data and Physiologically-Based Pharmacokinetic Modeling to Characterize Enoxaparin Disposition in Children With Obesity. Gerhart JG, Carreño FO, Loop MS, Lee CR, Edginton AN, Sinha J, Kumar KR, Kirkpatrick CM, Hornik CP, Gonzalez D; Best Pharmaceuticals for Children Act - Pediatric Trials Network Steering Committee. *Clinical Pharmacology & Therapeutics*, August 2022.

Exposure-safety relationship for acyclovir in the treatment of neonatal herpes simplex virus disease. Ericson J, Benjamin DK Jr., Boakye-Agyeman F, Balevic SJ, Cotten MC, Adler-Shohet F, Laughon M, Poindexter B, Harper B, Payne EH, Kaneshige K, Smith PB; Best Pharmaceuticals for Children Act - Pediatric Trials Network. *Early Human Development*, July 2022.

View a full list of publications from the PTN.