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

2020–2021

THE ANNUAL REVIEW

A MESSAGE FROM PTN LEADERSHIP

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The COVID-19 pandemic has continued to challenge us in unparalleled ways and we are grateful for the commitment the Pediatric Trials Network (PTN) has exemplified in learning more about COVID as related to our youngest of patients.

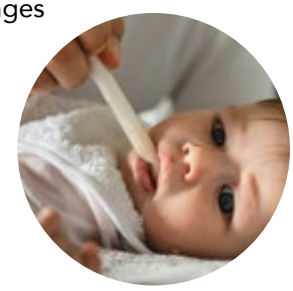
PTN's Pharmacokinetics, Pharmacodynamics, and Safety Profile of Understudied Drugs Administered to Children per Standard of Care (POP02) Study continues to make strides in supporting the treatment of younger COVID-19 patients and is currently evaluating several therapeutics to potentially treat COVID-19 pediatric patients younger than 21 years of age. In fact, POP02 has been engaged in a multi-institution, multi-study collaboration with National Institutes of Health (NIH) called The Collaboration to Assess Risk and Identify LoNG-term outcomes for Children with COVID (CARING for Children with COVID). This collaboration has worked to make de-identified data (or data that cannot be linked to a person's identity) from children with COVID publicly available, in order to accelerate research on this important topic. The POP02 team was the first study to reach the important milestone of submitting these data and having them become available, and it is a testament to their tremendous effort and dedication. Click **here** for more on this.

Additionally, this year PTN has released more than 20 publications and informed new label changes for clindamycin and diazepam.

The Annual Review is recognition of all our hard-earned accomplishments over the past year. We look forward to all that is to come and am grateful for your commitment to determining the safest and most effective use of medications and devices in children.

CLINDAMYCIN AND DIAZEPAM LABEL CHANGES

Under the Best Pharmaceuticals for Children Act (BPCA), the PTN worked to provide the FDA with information to inform label changes for clindamycin and diazepam over the last year. Both label changes provide doctors with the necessary information to prescribe the most appropriate doses of the medications to children.



CHANGING LABELS

As a result of research conducted through the Best Pharmaceuticals for Children Act (BPCA) program, led by the PTN, the following label changes have been made:

- **Acyclovir** for treatment of neonatal HSV infection/ encephalitis (label changed for dosing and safety)
- **Ampicillin** for treatment of sepsis and/or meningitis (label changed for safety)

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CHANGING LABELS (continued from page 1)

- Caffeine for non-antimicrobial medication given to intensive care unit newborns (label changed for efficacy, safety, and dosing)
- Clindamycin for treatment of infections in children (updated to include dosing guidelines for children with obesity)
- Clindamycin for treatment of infections in infants (updated to include dosing guidelines for premature and term infants)
- Diazepam for treatment of epilepsy (updated to include pharmacokinetic data for infants and children)
- Doxycycline for treatment of diseases such as Rocky Mountain Spotted Fever and methicillin resistant staph aureus in children under 8 years of age (label changes for safety and efficacy)
- Lisinopril for hypertension (label changed for treatment of pediatric renal transplant patients)
- Lithium for treatment of bipolar disorder (label changed for efficacy, safety, and dosing – BPCA legacy)
- **Lorazepam** for seizures (label changed for efficacy, safety, and dosing)
- **Mercy babyTAPE device** to assess weight without electricity in infants from birth to 90 days of age
- 2D and 3D Mercy TAPE devices to assess weight without electricity in children 2 months through 16 years of age
- Meropenem for complicated abdominal infections (label changed for safety and dosing; efficacy extrapolated)
- **Propylthiouracil** for hyperthyroidism (label changed for safety and dosing)
- **Pralidoxime** (relabeled for use in organophosphate poisoning)
- Sodium nitroprusside for hypertension (label changed for efficacy, safety, and dosing)

HIGHLIGHTING PTN STUDIES AND ACCOMPLISHMENTS

Digoxin Study Reaches Enrollment Goal

In the summer of 2021, The Pharmacokinetics and Safety Profile of Digoxin in Infants with Single Ventricle Congenital Heart Disease study reached the targeted enrollment goal for its study population of infants with Congenital Heart Disease (CHD). Thanks to the hard work and diligence of the enrolling sites and the whole PTN team, the target enrollment goal was reached efficiently.

The Digoxin Study is collecting safety and efficacy data on infants with single ventricle CHD to determine the appropriate dosing and safety measures of the study drug, digoxin. Digoxin is approved by the U.S. Food and Drug Administration (FDA) to treat heart failure in patients with congenital heart disease. However, there has not been enough safety and efficacy data to determine proper dosing of this drug in pediatric patients with single ventricle CHD.

Fifty study participants have been recruited for this study, where the drug digoxin was given as part of standard of care to treat heart failure. Study participants are infants <6 months of age who have single ventricle CHD and who have received an initial surgery to correct it, and whose healthcare team is planning on providing digoxin treatment. Each year about 40,000 infants born in the U.S. are diagnosed with CHD, with single ventricle CHD being the most serious and complex form of the disease. MORE

Funding Received to Study Device Used to Treat Overactive Bladder

PTN received funding from the Best Pharmaceuticals for Children Act (BPCA) to study a device to treat Overactive Bladder (OAB) in pediatric patients. The project is planned as a collaboration with industry partner Laborie Medical Technologies Corp, who will provide devices for the study.

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HIGHLIGHTING PTN STUDIES AND ACCOMPLISHMENTS (continued from page 2)

Overactive bladder affects up to 47% of children and can be influenced by conditions such as recurrent urinary tract infection (UTI), psychiatric & developmental disorders, and obesity. This condition can negatively impact the quality of life of children and exacerbate or lead to other chronic health conditions. The most common medication therapies are oxybutynin (Ditropan) and solifenacin (Vesicare), and are approved by the Food and Drug Administration (FDA) in children and adults. However, there is concern that there can be long-term side effects of oxybutynin, which includes memory problems and possible development of dementia in late adulthood.

The device is a posterior tibial nerve stimulation (PTNS), called the Urgent PC System, and will be used to treat OAB. This device is approved to treat OAB in adults, however there is not enough safety and efficacy data yet to approve it as a treatment for children with the condition. To prescribe PTNS devices, such as the Urgent PC system, into future OAB therapies for children, the PTN will test the safety and efficacy of the device in children ages 5 to 21 years old. Safety events or side effects such as electrode site reaction, electrode site infection, and residual will be tested and data will be validated via the Vancouver Dysfunctional Elimination Syndrome (VDES) questionnaire.

Testing the Urgent PC system as a PTNS device therapy in children with OAB will further demonstrate the PTN's ability to study medical devices. Data from the study will be submitted to the FDA for consideration of adding pediatric data to the device label. MORE

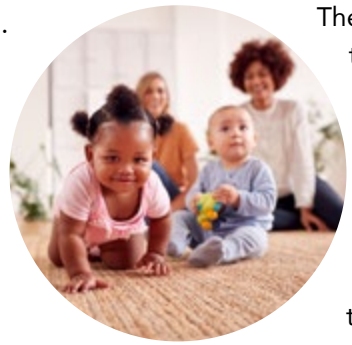
LAPS Trial Meets Study and Sub-Study Milestones

The PTN Long-term Antipsychotic Pediatric Safety (LAPS) Trial, which aims to assess the long-term health of risperidone and aripiprazole in children, has enrolled more than 500 children in the main study. Risperidone and aripiprazole have been shown to be effective for the treatment of conditions such as schizophrenia and bipolar disorder in adults and children. However, it is common for these drugs to be prescribed without FDA approval for conditions such as attention-deficit disorder, obsessive-compulsive disorder, and major depression. Regardless of indication, little is known about the long-term health risks and quality-of-life benefits for their use in children.

In addition to the main study, the team has established a sub-study registry that will continue to collect height and weights, from home, via the Pattern Health mobile app. This will allow for continued longitudinal assessment of pathologic weight change associated with these antipsychotics. In addition to the use of the app, parents of participants will also complete quality of life questionnaires, every six months, for their children participating in the sub-study. The team has enrolled more than 250 children in the sub-study portion of LAPS. MORE

ANA Study Updates Protocol to Include New Medications

The PTN's Anesthesia and Analgesics in Children (ANA) study has updated its study protocol to include new medications to be studied in pediatric populations. These new medications being studied, known as drugs of interest (DOI), include morphine, oxycodone, and ketamine. Although often prescribed by providers for anesthetic and analgesic (or pain relief) reasons, the safety, efficacy, and dosing information of these medications have not been established in pediatric populations.



The PTN is thrilled to add these medications to the ANA study, which has enrolled participants aged 2 to 17 who currently receive anesthetic or analgesic drugs as part of their routine care. Once this study is completed and data are analyzed, the PTN will submit results to the Food and Drug Administration (FDA) to change the label of the medications studied and establish information and dosing guidelines for children. MORE

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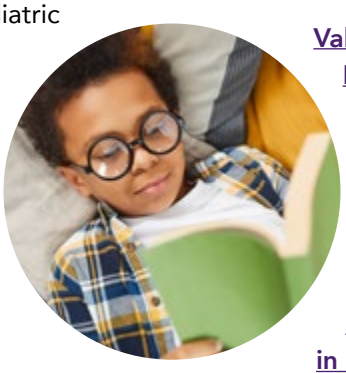

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