

A Message from the Lead Principal Investigator



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In the last issue of the *PTN Post*, we noted that the completion of the meropenem study, and the resulting label change allowing treatment of abdominal infections in infants under 3 months of age, laid the ground work for the Pediatric Trials Network. The label change is an important milestone and underscores the continuing significance of the work we do. With that in mind, I'd like to review the progress we have made to date in other therapeutic areas.

In addition to meropenem, two other advances were made through work under the Best Pharmaceuticals for Children Act. The use of sodium nitropruside was approved in 2014 for blood pressure management in children, with label

The submission of the clinical study report, sometimes referred to as CSR, is an important event for each molecule studied by the PTN. When we submit the CSR under our current relationship with NIH and FDA, it's a signal that we believe that sufficient data have been collected to secure a labeling change. In effect, we are asking the FDA if they agree that a labeling change is warranted, and if not, what the next steps are for the PTN.

As of June 1st of this year, CSRs for BPCA legacy (prior to PTN) and PTN-led studies submitted to the FDA include the following:

- **Lorazepam** for seizure control to determine efficacy, safety, and dosing (BPCA legacy study and PTN)
- **Isotretinoin** for treatment of neuroblastoma to determine efficacy, safety, and dosing (BPCA legacy)
- **Hydroxyurea** for treatment of sickle cell disease to determine PK and bioavailability of a liquid formulation (this is a PTN partnership submission with NHLBI)
- **Ampicillin** for treatment of complicated infections in pre-term neonates to determine safety and dosing (PTN)
- **Fluconazole** for prevention of candidiasis in neonates and infants to determine efficacy, safety, and dosing, prevention of candida infections for infants and children on ECMO, and treatment of invasive candida for infants <12 months of age (PTN)
- **Lisinopril** for treatment of hypertension in pediatric renal transplant patients to determine PK and safety (PTN)
- **Clindamycin** for treatment of complicated infections to determine PK and safety for obese children (PTN)

- **Acyclovir** for treatment of neonatal HSV infection/encephalitis to determine dosing and safety (PTN)
- **Lithium** for treatment of bipolar disorder to determine efficacy, safety, and dosing (BPCA legacy)
- **Metronidazole** for treatment of abdominal infections to determine dosing and provide additional safety data (PTN)

With an eye toward the future, we anticipate submitting data for the following trials in 2016.

- **Diazepam** for seizure control to determine improved dosing (BPCA legacy and PTN)
- **Lorazepam** for sedation to determine efficacy, safety, and dosing (PTN legacy and PTN)
- **Clindamycin** for treatment of soft tissue infection to determine efficacy, safety, and dosing (PTN in partnership with NIAID)
- **Sulfamethoxazole and trimethoprim** for treatment of soft tissue infection to determine efficacy, safety, and dosing (PTN in partnership with NIAID)
- **Caffeine citrate** for treatment of apnea of prematurity to determine efficacy, safety, and dosing (PTN in partnership with NHLBI)
- **Methadone** for treatment of pain and opiate withdrawal to determine safety and dosing (PTN)
- **Rifampin** for treatment of complicated infections in neonates to determine safety and dosing (PTN)
- **Clindamycin** for treatment of complicated infections in neonates to determine safety and dosing (PTN)

The 2015 BPCA Annual meeting will be held on December 9, 2015 on the NIH Campus in Bethesda Maryland. Web conferencing will be available for those unable to attend in person.

Check the [PTN website](#) for upcoming details.



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changes for efficacy, safety, and dosing. More recently, the TAPE study resulted in FDA marketing clearance for a new device, the first of its class, to more accurately assess weight to determine pediatric dosing.

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A Message from the Lead Principal Investigator *(continued)*

Thanks to the hard work and dedication of PTN investigators and sites, the list of accomplishments is long, but there is much more work to be done to determine the safest and most effective use of medications and devices in the pediatric population. This issue of the *PTN Post* celebrates the progress we've made and the work that lies ahead. You will also read about opportunities to learn more through upcoming meetings and contributions to the literature. As always, we welcome your input about topics of interest for future issues. Please contact us with your suggestions via the [PTN website](#).

Since October of 2014, PTN faculty members have published ten manuscripts in professional journals. Refer to the list below for more information about these PTN-led studies.

1. Watt KM, Gonzalez D, Benjamin DK Jr, Brouwer KL, Wade KC, Capparelli E, Barrett J, Cohen-Wolkowicz M. [Fluconazole population pharmacokinetics and dosing for prevention and treatment of invasive candidiasis in children supported with extracorporeal membrane oxygenation](#). *Antimicrobial Agents and Chemotherapy* • July 2015, volume 59, issue 7, pages 3935–43.
2. Testoni D, Hornik CP, Neely ML, Yang Q, McMahon AW, Clark RH, Smith PB; Best Pharmaceuticals for Children Act—Pediatric Trials Network Administrative Core Committee. [Safety of octreotide in hospitalized infants](#). *Early Human Development* • July 2015, volume 91, issue 7, pages 387–92.
3. Harskamp-van Ginkel MW, Hill KD, Becker K, Testoni D, Cohen-Wolkowicz M, Gonzalez D, Barrett JS, Benjamin DK Jr., Siegel DA, Banks P, Watt KM; for the Best Pharmaceuticals for Children Act—Pediatric Trials Network Administrative Core Committee. [Drug dosing and pharmacokinetics in children with obesity: a systematic review](#). *JAMA Pediatrics* • July 2015, volume 169, issue 7, pages 678–85.
4. Gonzalez D, Melloni C, Poindexter BB, Yogev R, Atz AM, Sullivan JE, Mendley SR, Delmore P, Delinsky A, Zimmerman K, Lewandowski A, Harper B, Lewis KC, Benjamin DK Jr, Cohen-Wolkowicz M; Best Pharmaceuticals for Children Act—Pediatric Trials Network Administrative Core Committee. [Simultaneous determination of trimethoprim and sulfamethoxazole in dried plasma and urine spots](#). *Bioanalysis* • May 2015, volume 7, issue 9, pages 1137–49.
5. Arnold CJ, Ericson J, Kohman J, Corey KL, Oh M, Onabanjo J, Hornik CP, Clark RH, Benjamin DK Jr, Smith PB, Chu VH; on behalf of the Best Pharmaceuticals for Children Act—Pediatric Trials Network Administrative Core Committee. [Rifampin use and safety in hospitalized infants](#). *American Journal of Perinatology* • May 2015, volume 32, issue 6, pages 565–70.
6. Ericson JE, Arnold C, Cheeseman J, Cho J, Kaneko S, Wilson E, Clark RH, Benjamin DK Jr, Chu V, Smith PB, Hornik CP; Best Pharmaceuticals for Children Act—Pediatric Trials Network Administrative Core Committee. [Use and safety of erythromycin and metoclopramide in hospitalized infants](#). *Journal of Pediatric Gastroenterology and Nutrition* • March 2015 [Epub ahead of print]
7. Autmizguine J, Hornik CP, Benjamin DK Jr, Laughon MM, Clark RH, Cotten CM, Cohen-Wolkowicz M, Benjamin DK, Smith PB; Best Pharmaceuticals for Children Act—Pediatric Trials Network Administrative Core Committee. [Anaerobic antimicrobial therapy after necrotizing enterocolitis in VLBW infants](#). *Pediatrics* • January 2015, volume 135, issue 1, pages e117–25.
8. Samiee-Zafarghandy S, Raman SR, van den Anker JN, McHutchison K, Hornik CP, Clark RH, Brian Smith P; Best Pharmaceuticals for Children Act—Pediatric Trials Network Administrative Core Committee. [Safety of milrinone use in neonatal intensive care units](#). *Early Human Development* • January 2015, volume 91, issue 1, pages 31–35.
9. Hsieh EM, Hornik CP, Clark RH, Laughon MM, Benjamin DK Jr, Smith PB; Best Pharmaceuticals for Children Act—Pediatric Trials Network. [Medication use in the neonatal intensive care unit](#). *American Journal of Perinatology* • October 2014, volume 31, issue 9, pages 811–821.
10. Gonzalez D, Melloni C, Yogev R, Poindexter BB, Mendley SR, Delmore P, Sullivan JE, Autmizguine J, Lewandowski A, Harper B, Watt KM, Lewis KC, Capparelli EV, Benjamin DK Jr, Cohen-Wolkowicz M. [Use of opportunistic clinical data and a population pharmacokinetic model to support dosing of clindamycin for premature infants to adolescents](#). *Clinical Pharmacology and Therapeutics* • October 2014, volume 96, issue 4, pages 429–437.

For a full listing of PTN publications, [click here](#).

The Pediatric Trials Network (PTN) is made possible by the Best Pharmaceuticals for Children Act (BPCA). The BPCA, first enacted in 2002, provides mechanisms for studying on- and off-patent drugs in children. Visit us on the web at www.pediatrictrials.org.

The Pediatric Trials Network is supported by The Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, and U.S. Department of Health and Human Services.



An international symposium titled Recent Advances in Pediatric Drug Prescribing will be held in Toronto on September 9, 2015. Sponsored by the EnRICH program, topics focus on drug safety and issues related to prescribing of medications for children.

To learn more and register, [click here](#).

The Pediatric Trials Network made an appearance in the pages of the *Wall Street Journal* on June 8. [Check out the story online](#).

