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

July 2017 • Issue 20

PTN Post

A Message from the Lead Principal Investigator

Danny Benjamin, MD, PhD, MPH

Welcome to the twentieth issue of the PTN Post, your quarterly source for information about the work of the Pediatric Trials Network (PTN). In this issue, we have exciting news and science to share:

- We have come out of a successful Pediatric Academic Societies (PAS) meeting where PTN co-hosted a booth, held a symposium, and presented three abstracts. Read about Julie Autmizguine's PAS abstract on Trimethoprim-Sulfamethoxazole (page 2).
- Because children need access to treatments that have undergone appropriate evaluation for safety and efficacy, CTTI has responded with recommendations that address many of the common challenges of conducting this research (page 1).
- Emboldened by the commitment and engagement of our sites, staff, patients, and their families, PTN forges ahead towards making drugs safer and more effective for use in the youngest patients. Case in point, see below for an update on the Timolol Study (page 2).

As always, thank you—your care and enthusiasm undergirds the progress of this important work.

Clinical Trials Transformation Initiative Releases New Recommendations to Improve Studies of Antibacterial Drugs for Children

The Clinical Trials Transformation Initiative (CTTI) released new recommendations to improve the quality and efficiency of research studies used to develop antibacterial drugs for children. In addition, many of the suggested strategies and practices could be applied to streamline clinical trials of other types of drugs and medical devices for children.

These recommendations resulted from a collaborative effort among research sponsors, parents, investigators, clinicians, and regulators from the US and the EMA (European Medicines Agency), who provided practical suggestions for the timing of

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Established by the FDA as a public-private partnership in 2007, CTTI comprises over 90 member organizations working to develop and drive adoption of practices that will increase the quality and efficiency of clinical trials.

For more information about the new recommendations, check out the resources via the CTTI website: blog post, recommendations, and a recorded webinar. You can also find links to CTTI, and other resources for physicians on the PTN website.

News Bite

We welcome your input about topics of interest for future issues.
Please contact us with your suggestions via the PTN website.

Clinical Trials Transformation Initiative Releases... *(cont.)*

pediatric trials, streamlining trial design, facilitating informed consent, and fostering global and community partnerships to conduct trials that can improve children's health.

The time from approval of a new antibacterial drug for use in adults to pediatric labeling can be 5 years or longer, potentially delaying appropriate use of medicines for this vulnerable group. Antibacterial resistance is on the rise in children, and the very young can be particularly susceptible to severe illness or death from these pathogens. Despite the great need for more treatment options, many trial sponsors have challenges enrolling pediatric patients in antibacterial drug trials.

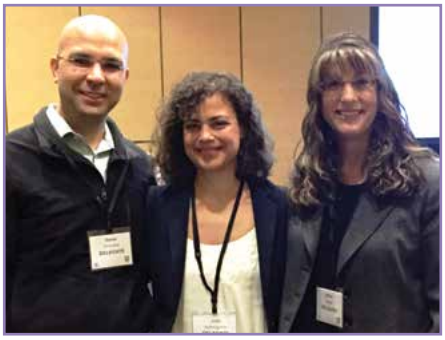
The CTTI recommendations are meant to help researchers design trials that are less burdensome for families, as well as to support improved practices for approaching parents for consent during the stressful time of a child's illness. This emphasizes the need for better engagement with parents throughout a clinical trial, including during the initial design stage. "This work matters to the lives of families like mine," said Breck Gamel, a parent participant in the CTTI effort. CTTI studied other clinician concerns as well, which helped to identify educational gaps in pediatric labeling and the need for better engagement with other healthcare providers.

Population PK of Trimethoprim-Sulfamethoxazole in Infants and Children

By Julie Autmizguine, MD

Trimethoprim-sulfamethoxazole (TMP-SMX) is used for the treatment of community-acquired methicillin resistant Staphylococcus aureus (CA-MRSA). However, TMP-SMX lacks FDA-approval for this indication and the optimal dosing for CA-MRSA treatment in infants and children is unknown. The goal of this multicenter study was to characterize the pharmacokinetics (PK) of TMP-SMX in the pediatric population. We included infants and children <21y who received enteral TMP-SMX per standard of care for any indication. Plasma PK samples were obtained while children were receiving TMP-SMX. We then developed a population PK model for both TMP and SMX, and performed dose-exposure simulations.

From 16 sites, a total of 153 children with a median age of 8 y (range: 0.1-20.2 y) contributed 240 PK samples. We found that both TMP and SMX elimination (clearance) increased with weight and age. In addition, TMP clearance was lower in children with reduced renal function, and SMX clearance increased when serum albumin was lower. Volume of distribution for both TMP and SMX was proportional to weight. Results show that a TMP/SMX weight-based dosing of 8/40 mg/kg/day divided every 12 h reached adequate plasma concentrations and would be optimal for term infants and children with CA-MRSA.



Daniel Gonzalez, PhD (left), Julie Autmizguine, MD (center), and Barrie Harper (right) at PAS Meeting

PTN's Timolol Study Now Enrolling

By Chad Livingston.

The PTN Timolol study will enroll 100 infants between the ages of 0–60 days postnatal age into a randomized double-masked treatment cohort and 10 infants into an untreated cohort. Under the leadership of Dr. Chiara Melloni (DCRI PI), and Drs. Beth Drolet, and Kristen Holland from the Medical College of Wisconsin, the PTN Timolol study is now actively enrolling at 4 sites. The primary objective of the study is to describe the efficacy of 0.25% and 0.5% topical timolol as assessed through change in the hemangioma volume—the data received will be presented to the FDA to support the use of timolol for the treatment of infantile hemagiomas.

PTN Timolol Sites Actively Enrolling:

1. Ann and Robert H. Lurie Children's Hospital of Chicago: Sarah Chamlin, MD
2. Medical College of Wisconsin: Beth Drolet, MD
3. University of Texas Health Science Center – Houston: Adelaide Herbert, MD
4. Cincinnati Children's Hospital Medical Center: Adrienne Hammill, MD

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.