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Leading the Way

SCAMP Hits a New Enrollment High in January

January was a record month for enrollment into the PTN's Safety Study of Clindamycin, Ampicillin, Metronidazole, and Piperacillin-tazobactam in Infants with Complicated Intra-abdominal Infections (SCAMP). Eleven patients were recruited into the study, bringing total enrollment to 36.

Study PI Micky Cohen-Wolkowiez credits the commitment of the sites for this achievement. "The site investigators and study coordinators work hard to identify and consent patients into this important trial," he observes. "Without their efforts, we'd never get any closer to understanding how best to use these drugs in the NICU."

The antibiotics being studied in SCAMP are frequently used to treat complicated intra-abdominal infections, which are common and often fatal in premature infants. These infections often occur as a result of necrotizing enterocolitis (NEC), the pathogenesis of which involves intestinal mucosal injury, usually associated with intestinal ischemia and bacterial overgrowth. NEC has a high mortality rate, and, in extremely-low-birth-weight infants (≤1000 grams), mortality for surgical NEC is nearly 50%. Survivors often suffer from complications, including stricture formation, and life-long morbidities such as short bowel syndrome. Infants who have had NEC are also at increased risk of poor neurodevelopmental outcomes.

Combinations of clindamycin, ampicillin, metronidazole, and piperacillin-tazobactam, meropenem, and gentamicin are recommended treatments for this condition; however, the safety and efficacy of these antibiotics in infants with complicated intra-abdominal infections have not been established.

The PTN is seeking to fill this information gap with SCAMP. Approximately 374 infants will be enrolled at approximately 60 sites. For more information about the study, visit clinicaltrials.gov.

A Message from the Lead Principal Investigator

Danny Benjamin, MD, PhD, MPH

Welcome to the twelfth issue of the PTN Post, your quarterly source for information about the work of the Pediatric Trials Network (PTN).

The new year is off to a tremendous start, as the many labors of the PTN continue to bear fruit. Trials like SCAMP have accelerated enrollment; other studies, like furosemide (featured on page 2) are busily recruiting sites. Findings of several studies are in the process of being disseminated at academic meetings (like PAS) and in the published literature. Label changes to drugs frequently used in infants and children are not far behind. It's an exciting time to be involved in the PTN.

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

PTN to Present Findings at PAS 2015

The PTN will have a big presence at this year's annual meeting of the Pediatric Academic Societies. Several researchers will be presenting results from PTN studies at the conference, to be held April 25–28, 2015, in San Diego. Presenters will include:

- Jeremiah Momper of UC–San Diego, making a platform presentation titled "Population Pharmacokinetics of Fluconazole in Extremely Low Birth Weight Infants"
- Michael Smith of the University of Louisville, presenting a poster titled "Pharmacokinetics of Multiple-Dose Intravenous Clindamycin in Obese Children"
- Jessica Ericson of Duke University, presenting a poster titled "Effectiveness of G-CSF in hospitalized infants with neutropenia"
- Jessica Ericson of Duke University, making a platform presentation titled "Safety of Acyclovir in Infants with HSV in the Era of High-dose Therapy"
- Lawrence Ku of Duke University, presenting a poster titled "Safety of Enalapril in Young Infants"

More details about the upcoming meeting may be found at the PAS website.

The PTN Wants YOU: Sites Needed to Study Furosemide in the NICU

More than 60,000 infants are born ≤29 weeks gestational age each year in the United States, and nearly 40% of those develop bronchopulmonary dysplasia (BPD). Because the consequences of BPD can be catastrophic, neonatologists frequently use diuretics such as furosemide to reduce pulmonary edema, improve pulmonary mechanics, minimize exposure to mechanical ventilation, and, ultimately, to prevent BPD. The understanding of the safety profile of furosemide in premature infants, however, is limited.

The PTN is conducting a phase 2, randomized, multicenter, placebo-controlled, dose-escalating, double-masked safety study evaluating the safety and preliminary effectiveness of furosemide in premature infants at risk of BPD. Approximately 120 infants will be enrolled at 25 sites. Total duration of study participation is 35 days—28 days of treatment and 7 days of safety monitoring, and data on hospitalization will be collected until hospital discharge.

We are actively seeking sites to participate in this study. If you are interested, please contact Maurine Morris (project leader) at maurine.morris@duke.edu.

PTN Clindamycin Obesity Study Moving Full Steam Ahead

The Safety and Pharmacokinetics of Multiple-dose Intravenous and Oral Clindamycin in Obese Children study has achieved numerous milestones in the past months. The database was recently locked, the pharmacokinetic (PK) analysis is ongoing, and the clinical study report is currently under review with the Food and Drug Administration. Additionally, principal investigator Michael J. Smith, MD, of the University of Louisville will be presenting preliminary findings from the study at the upcoming annual meeting of the Pediatric Academic Societies (see preceding page).

Antimicrobial agents such as clindamycin are often employed as first-line therapies for the treatment of methicillin-resistant *Staphylococcus aureus* (MRSA): use of clindamycin among children hospitalized with this disease increased from 21% in 1999 to 63% in 2008. Over the same time span, rates of childhood obesity have also increased, and we know from studies in adults that the PK of drugs used in the obese can be markedly different from that of their lean peers. As such, specific dosing recommendations for this population are often required.

To date, no PK data exist to guide clindamycin dosing in obese pediatric patients. This study will fill this gap. For more information, visit clinicaltrials.gov.

Stay Tuned: Results Forthcoming from the Lisinopril Trial

The manuscript deriving from the Safety and Pharmacokinetics of Lisinopril in Pediatric Kidney Transplant Recipients study is in the final stages of peer review. The authors are hopeful for its publication in the spring or summer of 2015. Stay tuned for information about their findings in the future issues of the PTN Post.

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**.

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