NICHD - PEDIATRIC TRIALS NETWORK

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Pediatric Trials Network
Leading the Way

Eunice Kennedy Shriver National Institute of Child Health and Human Development

A project of the Best Pharmaceuticals for Children Act

What is the Pediatric Trials Network?

"Create an infrastructure for investigators to conduct trials that improve pediatric labeling and child health."

- Sponsored by the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)
- Success - improve dosing, safety information, labeling, and ultimately child health
- PI – Danny Benjamin, MD PhD MPH – Duke Clinical Research Institute (DCRI)

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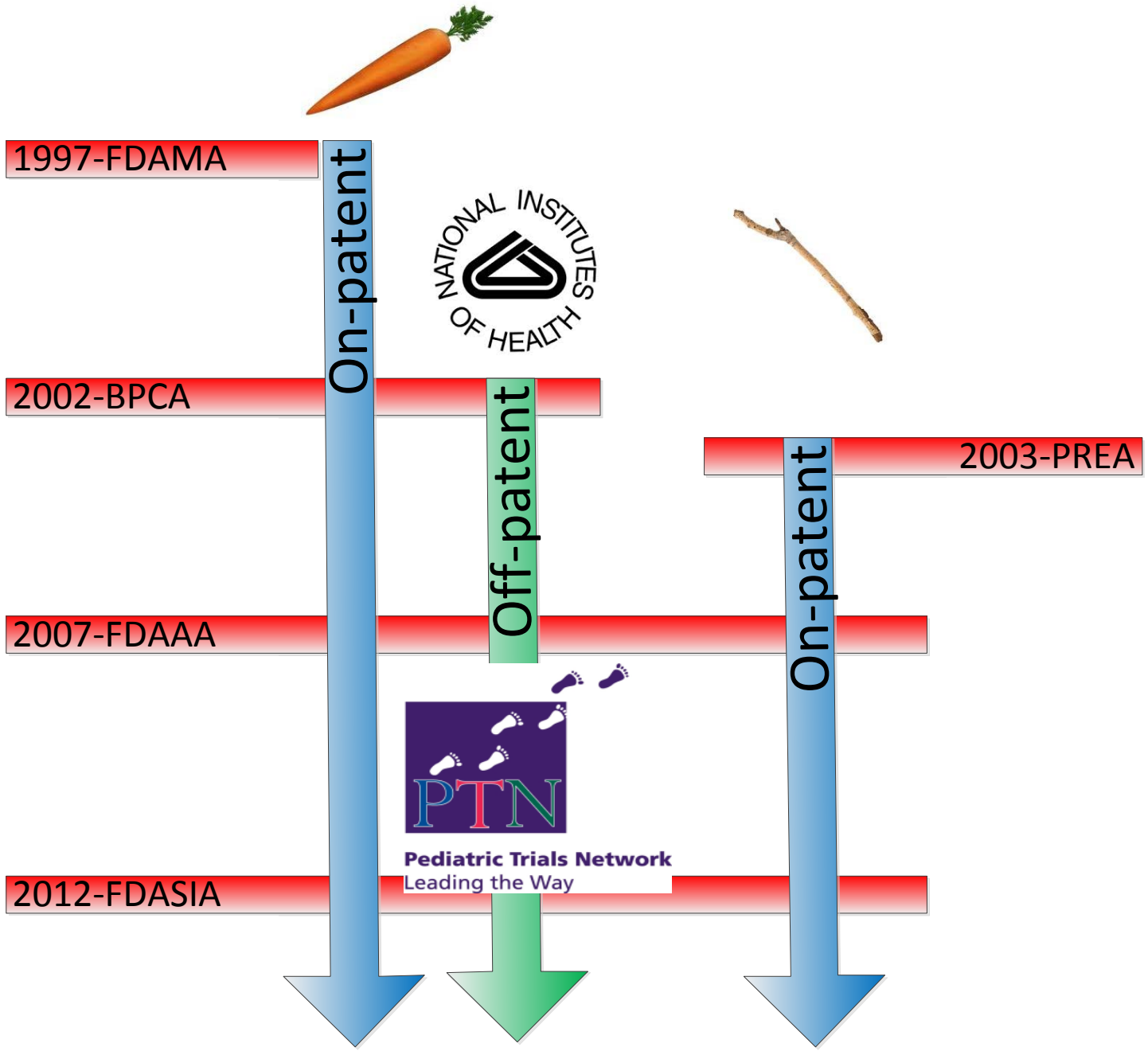
1997-FDAMA
On-patent
NATIONAL INSTITUTES OF HEALTH
2002-BPCA
Off-patent
2003-PREA
On-patent
2007-FDAAA
PTN
Pediatric Trials Network
Leading the Way
2012-FDASIA

How PTN works

1. NIH develops a priority list of off-patent therapeutics
   - http://bpca.nichd.nih.gov/prioritization/status/documents/priority_list_10-26-2012.pdf
2. Investigators submit study concept sheet to PTN
3. PTN Administrative Core reviews science and feasibility
4. If approved, PTN forms protocol development team
   - protocol chair, thought leaders, pharmacologists, operations experts
5. NIH provides small amount of funding for protocol development
6. PTN sends protocol and budget to NIH
7. PTN selects sites from rapid start network based on site study interest & availability, previous history of enrollment
8. PTN executes trial

PTN Network Steering Committee

Name	Role	Center
Daniel Benjamin, MD, PhD	Network PI	Duke University, Durham, NC
Gregory Kearns, Pharm D, PhD	Chair, Clin. Pharmacology Core	Children's Mercy Hospital, Kansas City, MO
Edmund Capparelli, Pharm D	Chair, Pharmacometrics Core	UC San Diego, San Diego, CA
Andrew Muelenaer, MD	Chair, Devices Core	Virginia Tech Carilion School of Medicine, Roanoke, VA
John van den Anker, MD, PhD	Co-Chair, Mentorship Core	GWU School of Medicine & Health Science, Washington, DC
Kelly Wade, MD, PhD	Co-Chair, Safety & Ethics Core	Children's Hospital of Philadelphia, Philadelphia, PA
Michael O'Shea, MD	Co-Chair Devices Core	Wake Forest University Medical Center, Winston-Salem, NC
P. Brian Smith, MD	Network Co-Investigator	Duke University, Durham, NC
Michael Cohen-Wolkowiez, MD, PhD	Network Co-Investigator	Duke University, Durham, NC
Matthew Laughon, MD	Committee Member	UNC Memorial Hospital, Chapel Hill, NC
Ian Paul, MD	Committee Member	Penn State College of Medicine, Hershey, PA
Michael Smith, MD	Committee Member	Univ. of Louisville, Louisville KY
Anne Zajicek, MD, PharmD	Branch Chief	NICHD, Bethesda, MD
David Siegel, MD	NICHD COTR	NICHD, Bethesda, MD
Perdita Taylor-Zapata, MD	NICHD COTR	NICHD, Bethesda, MD

Pediatric Trials Network – Progress Since 2010

Contract Scope of Work

- Projects
  - 16 clinical trials
  - Phase I-II studies
- Enrollment
  - ~100 children enrolled per project
  - 1600 total enrolled
- Therapeutic areas
  - Primary contract included hypertension; but had flexibility with respect to number and type of areas
- Flexibility with respect to data submitted to FDA but reasonable goal of ~4 product submissions (by 2015)

Accomplished

- Projects
  - 30 total projects; 18 clinical trials
  - Phase I-IV studies
- Enrollment
  - Over 100 sites enrolling
  - > 5000 children enrolled
- Across therapeutic areas
  - Hypertension, Neonatology, ID, Obesity, Neurology, Psychiatry, Critical Care, GI, Pulmonary, Hematology, Oncology
- Data for 9 products submitted to FDA and >20 products with planned submission by 2017

PTN - Lessons Learned

- Have frequent discussions with FDA/NIH
- Keep protocol simple
- Make inclusion criteria “inclusive”
- Minimize exclusion criteria
- Minimize blood draws
- Use labs/procedures done per standard of care
- Work with experienced sites

Innovation

- Data access
- Federated IRB
- Master contracts
- Partnerships with funding, etc.
- Obesity dosing
- Neonatal studies
- Education

- Master protocols
  - POPs
  - Multi-arm PK/PD studies
  - Multi-arm safety studies
  - Antipsychotics
  - Anesthesia

PTN Update

- Metronidazole: 3 sites, 24 premature infants at risk for NEC. Protocol chair: Michael Cohen-Wolkowiez. Enrollment and analysis complete, CSR submitted to FDA, published PIDJ.
- Acyclovir: 3 sites, 32 infants with suspected HSV. Protocol chair: Brian Smith. Enrollment and analysis complete, CSR submitted to FDA, published PIDJ.
- TAPE weight estimate device: 3 sites, 625 children. Protocol chair: Sue Rahman, Children's Mercy Hospital, Kansas City, MO. Enrollment and analysis complete. CSR submitted to FDA, FDA cleared the 510(k) application, published Ann of Emer Med.
- Hydroxyurea: 8 sites, 40 children. Protocol chair: Kathleen Neville, Children's Mercy Hospital, Kansas City, MO. Enrollment and analysis complete. CSR submitted to FDA, published J Clin Pharm
- Opportunistic (POPS): 36 sites, 2000 children. Protocol chair: Michael Cohen-Wolkowiez/Chiara Melloni. Enrolling (>2000 enrolled to date).
- Lisinopril PK: 8 sites, 26 children with kidney transplants and HTN. Protocol chair: Howard Trachtman, NYU Langone Medical Center. Enrollment and analysis complete. CSR submitted to FDA -LABEL CHANGE, published CPT

PTN Update

- Midazolam meta-analysis: Update label to include treatment of seizures in children 2 years and older using available data. Protocol chair: Tracy Glauser. Manuscript in progress.
- Ampicillin meta-analysis: 1 site, 64 infants, PK analysis in combination with 2 retrospective studies. Protocol chair: Michael Cohen-Wolkowiez. Data collection and analysis complete, CSR submitted to FDA, published AAC.
- Obesity informatics: Database of published PK studies relevant to pediatric obesity. Protocol chair: Kevin Watt. Complete, published JAMA Peds.
- Staph microtrials: 12 sites, 63 infants, 3 anti-staph drugs. Protocol chair: Matt Laughon, UNC. Complete, published AAC
- Sildenafil: 9 sites, 41 infants with pulmonary hypertension or lung disease. Protocol chair: Matt Laughon, UNC. Enrolling.
- Clindamycin obesity: 6 sites, 23 children. Protocol chair: Michael Smith and Janice Sullivan, University of Louisville, KY. Federated IRB. Complete. CSR submitted to FDA.

PTN Update

- Methadone PICU: 5 sites, 26 subjects. Protocol chair: Kevin Watt. Complete.
- Diuretics in NICU: retrospective review: 2 sites, 679 infants. Protocol Chair: Matt Laughon, UNC. Complete. CSR submitted to FDA.
- Piperacillin-tazobactam, clindamycin, metronidazole, ampicillin safety in infants with complicated intraabdominal infections (SCAMP): 50 sites, 374 subjects, Protocol Chair: Michael Cohen-Wolkowiez. Enrolling.
- Pantoprazole obesity: 4 sites, 41 children. Protocol chair: Greg Kearns, Children's Mercy Hospital, Kansas City, MO. Complete.
- Pediatrix meta-analysis of safety of 11 drugs: Retrospective data analysis; database includes >300 sites and >800,000 infants. Protocol chair: Brian Smith. Analysis complete. Published Peds, EHD (3), PIDJ, JPGN, J Perin, A J Perin
- Fluconazole safety meta-analysis: 33 sites, 361 infants enrolled in an earlier RCT. Protocol chair: Brian Smith. CSR submitted to FDA, published CID
- Baby Tape: 8 sites, 2000 subjects. Protocol chair: Sue Rahman, Children's Mercy Hospital, Kansas City, MO. Complete

PTN Update

- Caffeine therapy for apnea of prematurity: retrospective safety, PK, and efficacy. Protocol chair: Kelly Wade, CHOP, data collection for 400 infants
- Furosemide for the prevention of bronchopulmonary dysplasia: 20 site, 120 subjects. Protocol Chair: Matt Laughon, UNC. Enrolling.
- Clindamycin/trimethoprim-sulfamethoxazole: submission of PK data from POPS
- Timolol for infantile hemangioma: 10 sites, 100 subjects. Protocol chair: Beth Drolet, Children's Hospital of Wisconsin. Protocol development.
- Sildenafil for prevention of bronchopulmonary dysplasia: 20 sites, 120 subjects. Protocol Chair: Matt Laughon, UNC. Protocol development.
- Antiepileptic obese children: 6 sites, 72 subjects. Protocol Chair: Kanecia Zimmerman, Duke. Protocol development.
- Data Repository: 10 sites, 72 subjects. Protocol Chair: Christoph Hornik, Duke. Protocol development.
- Anesthesia drugs-PK and safety: 15 sites, 50 subjects. Protocol Chair: Kevin Watt, Duke. Protocol development.
- Antipsychotic drugs – long term safety: 60 sites, 850 subjects. Protocol Chair: Linmarie Sikich, Duke. Protocol development.