

**Best Pharmaceuticals for Children Act (BPCA)  
Renal Disease Working Group Conference Call and Webcast  
October 19, 2011  
11:00 a.m.–11:50 a.m. ET**

**Participants**

Lauren Agoratus, M.H.A.  
Kimberley Benner, Pharm.D.  
Joseph Flynn, M.D.  
Abraham Karkowsky, M.D.  
Frederick Kaskel, M.D., Ph.D.  
Guoying Liu, Ph.D.  
Uptal Patel, M.D.  
Michael Reed, Pharm.D., F.C.C.P., F.C.P.  
Douglas Silverstein, M.D.  
Amy Taylor, M.D., M.H.S., F.A.A.P.  
Perdita Taylor-Zapata, M.D.  
Phil Walson, M.D.

**Discussion**

Dr. Taylor-Zapata explained that the mission of the BPCA pediatric therapeutic area outreach is to identify and address the scientific gaps in knowledge in pediatric therapeutics in drugs, biologics, and devices. The Pulmonary, Hematology, and Renal Disease working groups have been charged to summarize current knowledge, standards of care, and existing data; identify barriers and gaps in knowledge; and suggest ways to address barriers and gaps.

The working groups are engaged in ongoing discussions and are in the final stages of developing key gaps and final recommendations. The final recommendations will be presented and discussed at the 2011 BPCA Annual Meeting on December 8–9, 2011.

At the end of September, Dr. Taylor-Zapata sent the working groups a document with instructions and a template for final recommendations. The groups were asked to develop a paragraph on scientific gaps, a needs assessment list, a brief reference list, and a blueprint for closing the gaps. The document includes a template that the groups may use. Recommendations should be prepared by the first week in November.

Dr. Kaskel said that the working group should divide into subgroups to prepare recommendations. The group has previously discussed the following areas:

- Anemia. Dr. Kaskel, Dr. Susan Furth, and Dr. Brad Warady will form a subgroup to work on this area.
- Acute kidney injury (AKI). Dr. Stuart Goldstein will lead the AKI subgroup, which will look at continuous renal replacement therapy (CRRT). Dr. Kaskel suggested that Dr. Flynn may also wish to contribute to this area.

- Osteodystrophy. On the last call, the group discussed new data on osteodystrophy and fibroblast growth factor 23 (FGF-23) in adults, but it may be too early to look at that agent. He recently heard from Dr. Anthony Portale about a monoclonal antibody in Phase II adult studies of FGF-23. The group also discussed the lack of guidelines for vitamin D dosing.
- Chronic kidney disease (CKD). The group discussed statins and treatment of dyslipidemia in CKD and biomarkers. A subgroup could discuss biomarkers across all of the gap areas.

Dr. Flynn asked about anemia, and Dr. Kaskel explained that it is a priority area for this year. Anemia is a controversial topic for the Centers for Medicare and Medicaid Services and the U.S. Food and Drug Administration (FDA). Data are needed to support the contention that anemia is different in children than in adults. He asked whether Dr. Flynn wanted to be part of this subgroup and noted that CRRT is in use throughout the country but has not been well studied. Dr. Flynn said that the lack of a device indicated for children is a fundamental issue.

Dr. Kaskel said that the group should take advantage of existing networks to gather information. Examples include the Prospective Pediatric CRRT Registry Group and the Chronic Kidney Disease in Children (CKiD) study. Dr. Flynn suggested the North American Pediatric Renal Trials and Collaborative Studies and the Midwest Pediatric Nephrology Consortium. He said he would be participating in a conference call with the American Society of Pediatric Nephrology to discuss these groups.

Dr. Kaskel said that the CKiD network recently produced observational data on the incidence and prevalence of osteodystrophy, acidosis, dyslipidemia, hypertension, and anemia, along with data on treatment. The group can develop surveys from that data set and query site investigators for more information.

Ms. Agoratus asked about the gastrointestinal effects of immunosuppressant medications. Dr. Kaskel agreed that this is an important issue and could be a separate gap area. He said that Ms. Agoratus was leading efforts in this area.

Dr. Silverstein noted that CKD and AKI were listed together in the group's discussion points table, but the category should be changed to only AKI. He asked about the feasibility of studies. Osteodystrophy is a major issue, but FGF-23 should be studied in adults first. Vitamin D would be difficult to study in different types of dialysis. Studies of anemia and AKI would be feasible, directed, and focused. The FDA is interested in evaluating devices for pediatric use and erythropoiesis-stimulating agent (ESA) dosing. There is interest in comparing the effects of ESAs in children and adults.

Dr. Kaskel asked about the feasibility of studying dyslipidemia in CKD. Dr. Silverstein said that there is not much information about dyslipidemia in end-stage renal disease, especially with hemodialysis. Studying the treatment of hyperlipidemia may be easy; the only question is what outcome indicator to use. Hyperlipidemia is important, and it was part of the CKiD study.

Dr. Kaskel asked about biomarkers for dyslipidemia treatment. Dr. Walson said that a group in Heidelberg, Germany, is looking at intima-media thickness (IMT) in CKD. He said that he has

been working on biomarkers of immune function, and this issue should be added to the group's gap areas. He would be willing to help with a group in this area. Dr. Kaskel noted that there was a recent article in the *New England Journal of Medicine* on genome-wide association between GLCCI1 and response to glucocorticoid therapy in asthma. This type of work is not being done in pediatric renal diseases. The working group should include transplant immunologists. Dr. Walson said that the endocrine group may address vitamin D. Dr. Kaskel said that baseline data on vitamin D could be collected without a large trial.

Dr. Walson said that the working group should propose all of the gaps it identified, and the larger group should make decisions about feasibility. The group should submit consensus recommendations—organized by priority and feasibility—and individuals in the group should submit additional recommendations for discussion.

The group discussed whether the purpose of studies was to add to science or to labeling. Dr. Kaskel noted that there is a lack of information about disease processes. For example, the lowering of adult hemoglobin targets has affected children, but there are no data in children. More studies are needed before pediatric recommendations are put in place. These studies would add to the science and affect the labeling. The goal of CRRT studies is to examine the use of devices in pediatrics and understand the science of drug clearance. It was suggested that studies could contribute information about optimal dosing, which is part of the BPCA mandate. Under BPCA, even negative studies are added to the label. Dr. Taylor-Zapata said that labeling is a key factor for BPCA, but additional steps may be needed to improve the science and ultimately improve the label.

Dr. Patel said that a pediatric rheumatologist at Duke University is completing a 5-year trial of statins in lupus patients. The goal was to evaluate anti-inflammatory effects and cardiovascular risk. The researchers used surrogates of cardiovascular risk such as IMT. A study combining IMT with endothelial function would be important because the goal is for pediatric renal disease patients to survive well into adulthood. Dr. Kaskel noted that five CKiD sites are studying IMT. Drs. Flynn, Patel, and Reed will work on this area. Dr. Walson noted that there are papers showing that vitamin D is protective against statin-induced myopathy. Dr. Kaskel said he would like to add Dr. Jeffrey Saland, a pediatric nephrologist working on lipids with the CKiD study, to the working group.

Dr. Kaskel said he talked with Drs. Goldstein and Warady about the AKI and CRRT, and Dr. Warady said that Amgen is interested in supporting research on ESAs in pediatrics. An international meeting on AKI and CRRT will be held in Cincinnati in February 2012. Dr. Kaskel will talk with Dr. Goldstein after the conference call about recommendations for AKI and CRRT.

Dr. Taylor-Zapata thanked the group for its suggestions. She noted that the group should not write grant submissions; it should develop recommendations for studies that may be funded. Those recommendations will be further prioritized at the BPCA Annual Meeting. Funding of studies is not guaranteed. The Pediatric Trials Network is doing most BPCA studies, but it can partner with other organizations and networks. She will send the recommendation instructions and template to the group.

Dr. Walson said he would submit a recommendation about measures of immunosuppression. Dr. Taylor-Zapata said she would send the group a list of members who volunteered in each area.

Dr. Kaskel noted that a meeting on pediatric clinical trials would be held on Friday, October 21 at the National Institutes of Health Natcher Conference Center. Dr. Kaskel will send the group a link to the meeting webcast.

**Action Items:**

- The group will prepare its recommendations by the first week in November.
- The CKD and AKI category in the discussion points will be changed to only AKI.
- Dr. Kaskel will talk with Dr. Goldstein about recommendations about AKI and CRRT.
- Dr. Taylor-Zapata will send the group the recommendation instructions and template and a list of members who volunteered in each area.
- Dr. Kaskel will send the group a link to a meeting webcast on pediatric clinical trials.