KDIGO Controversies Conference
Common Elements in Uncommon Kidney Diseases

CONFERENCE OVERVIEW & OBJECTIVES

Olivier Devuyst & Lisa Guay-Woodford

Amsterdam, June 16-19, 2016
The Global Burden of Rare Diseases

- Rare diseases: $\sim$6,000 – 8,000 disorders
- Affect $\sim$30 M patients in EU and in the USA, > 300 M worldwide
- 80% of rare diseases have a genetic origin
- Typical challenges: variable phenotypes, fragmented data, lack of standards, poor knowledge for disease mechanisms and natural history
Rare Kidney Diseases

- Rare kidney diseases: > 150 disorders
- Overall prevalence: ~60-80 cases per 100,000
- At least 10% adults and virtually all children on RRT
- Fifth most common cause of ESRD (Diab > HT > GN > PyeloN)

- Patients with inherited kidney disorders rarely die (progresses in RRT)
- However: poor health, poor quality of life, multisystemic complications

→ *children with severe congenital nephropathies can be dialysed from neonatal age onwards, but face many decades of life with ESRD and have a high likelihood of changes in physical, cognitive, and psychosocial development.*
Inherited Kidney Disorders: Segmental Distribution

**Glomerular diseases**
- Congenital steroid-resistant nephrotic syndrome
- Denys-Drash syndrome, Fraser's syndrome
- Wilms' tumour, aniridia, genitourinary abnormalities, and mental retardation (WAGR) syndrome
- Pierson's syndrome
- Nephropathy syndrome
- Schimke immuno-osseous dystrophy
- Mitochondrial disorders with steroid-resistant nephrotic syndrome
- Fabry's disease
- Alport's syndrome
- Benign familial haematuria (thin basement membrane)
- Fuch's syndrome (Alport's syndrome with macrothrombocytopenia)
- Alport's syndrome with leiomyomatosis
- Familial amyloidosis

**Proximal tubule**
- Renal glucosuria
- Dicarboxylic aminoaciduria
- Lysinuric protein intolerance
- Proximal renal tubular acidosis
- Hypophosphataemic rickets
- Nephropathic cystinosis
- Primary renal Fanconi's syndrome
- Fanconi-Bickel syndrome (hepatoencephalopathy)
- Lowe's syndrome
- Dent's disease, types 1 and 2
- Hereditary renal hypouricaemia
- Cystinuria, types 1-3

**Thick ascending limb and distal convoluted tubule**
- Bartter's syndrome, types 1-4
- Familial hypocalciuric hypercalcaemia
- Neonatal severe hyperparathyroidism
- Autosomal dominant hypocalcaemia
- Gitelman's syndrome
- Pseudohypoaldosteronism type 2 (Gordon's syndrome)
- Ellis-van Creveld syndrome (EAST syndrome)
- Hypomagnesaemia, types 1-6
- Familial juvenile hyperuricaemic nephropathy

**Collecting duct**
- Liddle's syndrome
- Distal renal tubular acidosis
- Pseudohypoaldosteronism type 1
- Nephrogenic diabetes insipidus, types 1 and 2
- Nephrogenic syndrome of inappropriate antidiuresis

Kidney Function and Homeostasis

Emotional Burden of an Inherited Disease

- Family secrecy
- Inadequate information
- Ambivalence towards diagnosis
- Uncertainty, anxiety
- Denial
- Anger, depression
- Reproductive decisions
- Parental blame

V. Torres, KDIGO-ADPKD
Rare Inherited Kidney Disorders: Opportunities
Application of -omics technologies in rare kidney diseases

Biopsy

Urine

Transcriptome
Epigenome
Genome
miRNAome
Proteome
Metabolome
Clinical Information

Multiscalar Pathway and Network Analysis

Molecular disease ontologies
Diagnostic tests
Prognostic biomarkers
Therapeutic targets
Fragmentation of patient-related information represents a major obstacle for rare disease research.

- **EPIRARE**: European Platform for Rare Disease Registries (www.epirare.eu)
- **PARENT**: Patient Registries Initiative (www.patientregistries.eu)
- **RD-CONNECT**: An integrated platform connecting databases, registries, biobanks and clinical bioinformatics for rare disease research (www.rd-connect.eu)
- **IRDiRC**: International Rare Diseases Research Consortium (www.irdic.org)
- **EURenOmics**: European Consortium for High-Throughput Research in Rare Kidney Diseases (www.eurenomics.eu)
- **ORPHANET**: The portal for rare diseases and orphan drugs (www.orpha.net)
- **EURORDIS**: The European Organization for Rare Diseases (www.eurordis.org)
- **Center for Mendelian Genomics** (www.mendelian.org)
Inherited Kidney Disorders: Health Policies

- To ensure that approaches developed at highly specialized tertiary care centers can be adopted in facilities that cover the majority of population.

- To promote the implementation of clinically relevant genetic testing and to ensure delivery and impact of genetic information to physicians, patients and society in general.
Patient Organizations and Research on Rare Diseases

Julie R. Ingelfinger, M.D., and Jeffrey M. Drazen, M.D.

Comment on: Efficacy and safety of sirolimus in lymphangioleiomyomatosis.
Common Elements in Uncommon Kidney Diseases: Challenges and Topics

- Technological advances in diagnosis
- Consequences of improved genetic diagnosis
- Management of renal function, optimal pediatric transition care
- Challenges in trial design and conduct
- Development of novel biomarkers or surrogates
- Translation of new knowledge into clinical programs
- QOL issues
- Policy initiatives – various parts of the world

→ Implementation of the resources in low-income countries?
KDIGO Controversies Conference
Common Elements in Uncommon Kidney Diseases

• Address **common clinical and patient issues** across the field of rare kidney diseases.

• Identify **controversial topics** and outstanding knowledge gaps

• Propose a **research agenda** to resolve these issues

• Determine whether there is sufficient evidence base for providing guidance in clinical management

• Systematically integrate **patient perspectives**
Controversies Conferences examine what is known, what can be done with what is known and what needs to be known on topics of clinical relevance in nephrology.

- Current practice recommendations
- Clinical questions and outstanding issues
- Research agenda

- **Gitelman Syndrome** (Brussels, February 2016)
- **Complement-Mediated Kidney Diseases** (Barcelona, November 2015)
- **Fabry Nephropathy** (Dublin, October 2015)
- **Nephropathic Cystinosis** (Lisbon, December 2014)
- **Autosomal Dominant Tubulointerstitial Kidney Disease** (ADTKD) (Boston, September 2014)
- **Autosomal Dominant Polycystic Kidney Disease** (ADPKD) (Edinburgh, January 2014)
Global panel – Multidisciplinary expertise

- Adult nephrology
- Pediatric nephrology
- Genetics
- Epidemiology
- Pathology
- Imaging
- Research & Development
- Patients & caregivers
- Design of clinical trials
- Regulatory authorities
- Patient organizations
KDIGO
Plenary Sessions 1
Friday June 17, 9:00 to 18:30 hrs

• Plenary lectures covering major themes

• Balanced review of the literature

• Highlighting controversial issues

• Introduction to the prioritized breakout questions
Scope of Work

KDIGO Controversies Conference on
Common Elements in Uncommon Kidney Diseases

June 16-19, 2016
Amsterdam, The Netherlands
# KDIGO Controversies Conference on Common Elements in Uncommon Kidney Diseases

## Breakout Group Roster

### Conference Co-Chairs

Olivier Devuyst - Switzerland
Lisa Guay-Woodford - USA

### Breakout Group Members

#### Diagnostic Challenges (Amsterdam Room)

<table>
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<th>Diagnostic Challenges</th>
<th>Management of Renal Function Decline (Haarlem - Eindhoven Room)</th>
<th>Challenges in Clinical Study Design in Rare Kidney Diseases (Rotterdam Room)</th>
<th>Translation from Research to Clinical Care (Den Haag Room)</th>
<th>Practical &amp; Integrated Patient Support (Koepelzaal Room)</th>
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#### Breakout Group Co-Chairs

- Klein (US)
- Bockenhauer (NL)
- Day (FR)
- Simon (UK)
- Aymé (NL)
- Schaefer (DE)
- Ingelfinger (US)
- Roberts (US)
- Julia (US)
- Torres (US)
- Vicente (US)

#### Breakout Group Members

- Antignac Corinne (FR)
- Bleyer Anthony (US)
- Chassan* Afilal (US)
- Angelle Aris (UK)
- Baroni* David (US)
- Baek Kyongiae (US)
- Bledsoe Klemens (DE)
- Cornet Marilisa (NL)
- Bull Katherine (UK)
- Bos Marjolein (NL)
- Bergmann Carsten (DE)
- Chauveau Dominique (FR)
- Hamilton Bruno (BE)
- Goodship Tim (UK)
- Cosyns Etienne (BE)
- Goodyer Paul (CA)
- Ding Jie (CN)
- Langman Craig (US)
- Gross Oliver (DE)
- Gear Susie (UK)
- Harris Peter (US)
- Hogan Marie (US)
- Mantz Segundo (UK)
- Hone Shigeo (JP)
- Harr Nicole (US)
- Hoffmann Julia (DE)
- Hovor Ewout (NL)
- Rayner Brian (CA)
- Kashian Cliff (US)
- Harris Jess (UK)
- Korirad Martin (DE)
- Long* Albert (UK)
- Remuzzi Giuseppe (IT)
- Kleta Robert (UK)
- Kerecuk Larissa (UK)
- Fie Per (CA)
- Pinson Yves (BE)
- Serviss Laura (FR)
- Levchenko Elena (BE)
- McKerracher Gayle (UK)
- Smimh Sara (US)
- Salmi René (FR)
- Smith Richard (US)
- Orthez Alberto (ES)
- Nieuwenhoven Annet (NL)
- Torn Roser (ES)
- Stangel Bénédicte (FR)
- van't Hoff William (UK)
- Soliman Neveen (EG)
- Odaando Dwight (US)
- Vargasc-Pousso Rose (FR)
- Wanner Christoph (DE)
- Yap Hui-Kim (SG)
- Renault Daniel (FR)
- Storm Marjolein (NL)
- Vroom Elizabeth (NL)
Breakout Session 1
Saturday, June 18, from 8:30 to 12:30 hrs

- Manage time to address prioritized questions
- Discussion leaders: moderate & take notes
- Objective: Reach conclusions regarding
  - Areas of consensus
  - Areas of controversy
  - Gaps in knowledge
  - Need for interactions - expertise
- Prepare report to for Plenary Session
Plenary Session 2
Saturday, June 18, 13:30 to 16:00 hrs

- Preliminary report from Breakout Groups (20 min each)
- Questions/comments to Breakout Groups (10 min each)
Breakout Session 2
Saturday, June 18 from 16:15 to 18:30 hrs

• Manage time to address prioritized questions

• Objective:
  - Discuss feedback from Plenary Session
  - Finalize areas of consensus, controversy and gaps in knowledge
  - Propose research agenda - controversies & knowledge gaps
  - Determine whether there is sufficient evidence base for providing guidance in clinical management

• Prepare report for last Plenary Session
Final Plenary Session
Sunday, June 19 from 08:00 to 12:30 hrs

• Final reports from Breakout Groups (30 min each)

• Discussion (20 min each)

• Final Conference Summation: Wrap up and next steps
Post-Conference Report and Publication

- Medical writer (Jennifer King) to establish a draft, sent to co-chairs of each Breakout Group and conference co-chairs
- Report from co-chairs of each Breakout Group due to the conference co-chairs
- Compiled and revised manuscript by conference co-chairs due to conference participants
- Feedback from conference participants to conference co-chairs
- Manuscript submitted to *Kidney International* by the end of 2016
- Authorship – bloc & names for all participants
Enjoy the meeting - Thank you!