Conference Overview and Objectives

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Disclosure of Interests

Olivier Devuyst
• Steering Committee, TEMPO Trials, Otsuka Pharmaceuticals

Vicente Torres
• Research funding from Otsuka Pharmaceuticals
12.5 million ADPKD patients world-wide were born with:

- 50% risk for ESRD by age 55 years of age (\textit{PKD1 trunc. mut.})
- 80% risk for hypertension
- 60% risk for painful kidney complications
- 20% risk for symptomatic PLD (if female)
- 3% risk for ICA rupture

Varially increased risk for cardiovascular and cerebrovascular disease, gastrointestinal disorders, hernias, neurologic and other disorders
Emotional Burden of an Inherited Disease

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

• Loss of productivity and contribution to society

European Union
• Cost of renal replacement therapy: €2 billion

United States (cost per patient)
• Mean annualized medical and pharmacy charges (GFR ≥90): $26,521
• Mean annualized medical and pharmacy charges (GFR 60-89): $21,360
• Mean annualized medical and pharmacy charges (GFR ≥90): $31,247
• Mean annualized medical and pharmacy charges (GFR ≥90): $41,806
• Mean annualized charges for dialysis services: $131,890
• Mean charges per transplant hospitalization: $119,931
Current Management of ADPKD

• Early detection and treatment of hypertension
• Treatment of other cardiovascular risk factors
• Treatment of renal complications
• Management of extrarenal associations
• Treatment of CKD
• Renal replacement therapy (ADPKD specific issues)

Challenges

• No consensus for specific recommendations
• Marked phenotypic variability requires individualized therapies
• Level of evidence for specific recommendations at best C or D
• No widely accepted practice guidelines
• Challenges shared with inherited disorders in general
Barriers to Clinical Trials

- Late decline of GFR: Necessitates very long periods of follow-up as a clinical trial endpoint (unappealing to pharmaceutical companies)
- TKV predicts renal functional decline in ADPKD, but it has not been accepted as a valid end-point by regulatory agencies
- Lack of funding for clinical trials of repurposed drugs without patent protection
- Limited resources of NIH and other government agencies to fund large clinical trials
Opportunities for intervention at multiple stages

- Early diagnosis feasible in most cases
- Cause of the disease is known
- Pathophysiology partially understood
- Large window for intervention

Late progression by mechanisms similar to other chronic nephropathies: Nephron loss, hyperfiltration, proteinuria, oxidative stress, and interstitial inflammation and fibrosis

PGD

Nephroprevention

PKD specific therapies

CKD therapies
Goals

• Assess the current state of knowledge related to the evaluation, management and treatment of ADPKD

• Identify controversial topics and outstanding knowledge gaps

• Propose a research agenda to resolve these issues

• Determine whether there is sufficient evidence base for the development of a practice guideline

• Help pave the way to harmonize and standardize the care of ADPKD patients
“A goal without a plan is just a wish”

(Attributed to Antoine Saint-Exupéry)
KDIGO Controversies Conference on ADPKD

→ Participants divided into 6 Breakout Groups:

- Diagnosis (Drs. Pei & Torra)
- Mgmt. of renal manifestations (Drs. Chapman & Horie)
- Mgmt. of hypertension & renal function decline (Drs. Schrier & Gansevoort)
- Mgmt. of ESRD in ADPKD (Drs. Eckardt & Perrone)
- Mgmt. of extra-renal complications (Drs. Pirson & Watnick)
- Practical integrated patient support (Tess Harris & Dwight Odland)

Specific questions

Essential literature
Plenary Session 1: Friday January 17, 8:15 to 14:20 hrs

- Two plenary lectures for each Breakout Group (15+5min)
  - Balanced review of the literature
  - Highlighting controversial issues
  - Introduction to the prioritized breakout questions
**Breakout Session 1:** Friday, January 17, 14:20 to 18:30 hrs

- Manage time to address **all prioritized questions**
- One group Co-Chair moderates and the other takes notes
- Objective: Reach **conclusions** regarding
  - **Areas of consensus**
  - **Areas of controversy**
  - **Gaps in knowledge**
- Prepare **report to for Plenary Session 2** (PPT presentation)

- If time allows, some optional questions can be addressed
Plenary Session 2: Saturday, January 18, 8:00 to 11:30 hrs

- Preliminary report from 6 Breakout Groups (20 min each)
- Questions/comments to Breakout Groups (10 min each)
- Feedback to be addressed during next breakout session
Breakout Session 2: Saturday, January 18 11:30 to 15:00 hrs

- Manage time to address all prioritized questions
- **Objective:**
  - Discuss feedback from Plenary Session
  - Finalize areas of consensus, controversy and gaps in knowledge
  - Propose research agenda (controversies and knowledge gaps)
  - Determine whether there is sufficient evidence base for the development of practice guidelines
- Prepare report for Plenary Session 3
- If time allows, some optional questions can be addressed
• Final reports from Breakout Groups (30 min each)
• Discussion (30 min each)

• Need for Guidelines: Discussion (30 min)
• Research Agenda & Priorities: Discussion (30 min)

• Final Conference Summation: Wrap up and next steps
Can we provide acceptable guidance in rare/ inherited disorders?

- ADPKD is not *stricto sensu* a rare disease – but close
- In rare diseases, the basis of evidence for clinical practice guidelines is generally weak: need for pragmatic attitude
- Transparency: literature search, interpretation of evidence, considerations taken when formulating recommendations
- Position document by European Medicines Agency (EMA):
  - *Rules for the production of guidelines on common diseases are also applicable to rare diseases*
  - *All forms of evidence, even anecdotal case-reports, may provide relevant information and should then be taken into consideration*

EMA Guideline on clinical trials in small populations, 2007
Bolignano D et al. Nephrol Dial Transplant 2013
Post-Conference Report and Publication

- **Report from co-chairs** of each Breakout Group due to the conference co-chairs by February 15, 2014

- **Compiled and revised manuscript** by conference co-chairs due to conference participants by March 15, 2014

- **Feedback** from conference participants to conference co-chairs due by April 1, 2014

- **MS. submitted to Kidney International** by April 15, 2014