KDIGO Controversies Conference on the Management of Patients with Diabetes & CKD

-- Breakout Group Questions --

1. Safety of Treatments in Diabetes & Kidney Disease

What is known (and what needs to be known) about the safety of:

- Diverse pharmacologic treatments in the diabetic patient, particularly in relation to GFR. Is the diabetic CKD patient in any way different compared to other CKD patients at equivalent renal function?

- Glucose-lowering agents used in diabetes and kidney disease, including:
  - Metformin
  - Sulfonylureas
  - Thiazolidinediones
  - Insulin

- Novel and recently approved treatments:
  - DPP-4 inhibitors
  - GLP-1 agonists
  - SGLT2 inhibitors

- Treatments under development, including:
  - Endothelin receptor antagonists
  - Pirfenidone
  - Others

- Cardiovascular and other therapies in diabetes and kidney disease, including:
    - Blood pressure-lowering agents
    - Lipid-lowering therapies
    - Antiplatelet agents and antithrombotics
    - Treatments for anemia
    - Novel and in development approaches: Vitamin D, antioxidants, other agents

- How should the safety of agents being developed in this population be studied in the future?
    - How do we select patients who are most likely to have a positive benefit-risk profile
    - What are the most important outcomes to be considered?
    - What should be required to achieve regulatory approval, and/or guideline recommendations?

2. **Efficacy of Glycemic Control**

- Does glucose lowering *per se* prevent ESKD in people with diabetes and kidney disease? At what stage of kidney disease might this be best known or studied?
- Do specific classes of agents have particular nephroprotective or harmful effects?
- What is the impact of more intensive glycemic control on cardiovascular events in this population? Is there a similar or different effect on mortality?
- What is the importance of hypoglycemia in this population?
- What is the effect of lifestyle measures on diabetic nephropathy?
- How does one assess glycemic control in diabetic subjects with chronic kidney disease?

3. **Therapies for Protecting Kidney Function**

- What treatments are proven to be effective at improving kidney function?
- What is the relevance of short-term changes in kidney function induced by treatment?
- Should surrogate endpoints (e.g., albuminuria) be used in clinical trials and proposed to regulatory agencies?
- How should GFR be measured in clinical trials?
- Use of new biomarkers in monitoring potential nephroprotective effects
- Can renal structure be used as primary endpoint in clinical trials?
- What are ideal patients to test the nephroprotective effects of a new agent? (i.e., prevention of development vs. prevention of progression)
- Which are the most promising agents or approaches that should be prioritized for future study?
- How should promising agents be identified and selected for outcome studies?

4. **Therapeutic Effects on Cardiovascular Risk & Other Outcomes**

- What is the impact of lifestyle intervention on CV outcomes in patients with DKD?
- Why are effects of metabolic control on micro- & macro-vascular outcomes different?
- Is there any new information that might change the conclusions of recent guidelines on blood pressure lowering and lipid modification in diabetes and CKD?
- Are there still options for using dual blockade in DKD?
- Is lower the BP target the better in DKD?
- How are residual risk and unmet medical need defined for the increased CVD risk in DKD patients?

- What is known about the risk-benefit ratio of antithrombotic agents and anticoagulants in CKD?
- Are there new agents in development (e.g., CETP inhibitors, PCSK9 inhibitors, mineralocorticoid receptor antagonists) that might be particularly promising for people with diabetes and CKD?
- Do any new agents in development have important caveats that require specific study in people with diabetes and CKD?
- Are there any CKD-specific therapies that are effective at reducing cardiovascular risk in diabetes and CKD (e.g., iron therapy)?