Global Action. Local Change.

KDIGO Controversies Conference on

Challenges in the Conduct of Clinical Trials in Nephrology

- Breakout Group Discussion Questions -

Breakout Group A: Renal Outcomes including CKD Progression
Group Leaders: Joe Coresh, Peter Rossing

Breakout group A will discuss the challenges raised in the plenary session on "Defining optimal outcomes in trials assessing renal disease progression." Discussion topics will include:

1. Is there now consensus on the optimum outcome for CKD progression trials and how it should be assessed?
2. Is there consensus on how to measure change in GFR efficiently during trial follow-up (e.g., slopes)?
3. Under what circumstances is directly measured glomerular filtration rate necessary?
4. Under what circumstances could albuminuria be accepted as a marker of CKD progression?
5. Is there consensus on the most appropriate surrogate outcomes for specific renal conditions:
    a. Glomerulonephritides
    b. Polycystic kidney disease
    c. Transplantation
    d. Acute kidney injury prevention and treatment

Breakout Group B: Non-Renal Outcomes in Nephrology Trials
Group Leaders: Michael Walsh, Vlado Perkovic

Breakout group B will discuss the challenges raised in the plenary session on "Defining appropriate non-renal outcomes in renal trials" with particular attention to cardiovascular outcomes. Discussion topics will include:

1. What is the appropriate process for choosing endpoints (e.g., what components of what composites? Should we use cardio-renal composite outcomes?), and how should effects on mortality be assessed (cardiovascular versus non-cardiovascular)?
2. What is the role of surrogate outcomes?
3. How can we ensure that outcomes important to patients are measured and do these include patient reported outcome measures?
4. Is there consensus on the key outcomes for:
    a. Anemia trials?
    b. Vascular access trials?
    c. Safety (i.e., toxicity and adverse events including bleeding and infection)?
    d. Mineral-bone disease trials?
5. Can we record information in trials to assist in assessment of health economic impact of a particular treatment?

Breakout Group C: Optimizing Trial Design
Group Leaders: Martin Landray, Marc Pfeffer

Breakout group C will discuss the challenges raised in the plenary session on 'Optimizing trial design'. Discussion topics will include:

1. What is the optimum choice of trial population?
    a. Key inclusion criteria (e.g., relevant disease, possibility of benefit from intervention; narrow vs broad population; special groups or regions)
    b. Key exclusion criteria (i.e., based on safety or other issues)
2. What are the key issues when selecting active & comparator treatments (e.g., dose selection, placebo, blinding, factorial designs)?
3. Why are "run-in" periods important in renal trials and what is their optimal duration?
4. What are the principles behind selection of trial endpoints (i.e., what to include in primary, key secondary and safety endpoints; and the use of composite outcomes)?
5. How should sample size calculations be done to minimize risk of false negative trials, including:
    a. Estimating a realistic event rate
    b. Estimating a realistic treatment effect
    c. Determining follow-up duration
    d. Estimating the impact of non-adherence, incomplete follow-up or missing data?
6. What types of statistical analyses are the most robust, including:
    a. Intention-to-treat principles
    b. Appropriate and inappropriate subgroup analyses and their interpretation?

Breakout Group D: Optimizing Trial Conduct
Group Leaders: Adeera Levin, Christoph Wanner

Breakout Group D will discuss the challenges raised in the plenary session on 'Optimizing trial conduct'. Discussion topics will include:

1. What is the optimum method to identify potential participants? Can disease registries and other electronic healthcare records be used for identifying and inviting patients to participate in randomized trials, and recording patient outcomes?
2. What are the opportunities to improve both data quality and streamline its collection (including laboratory analyses)?
3. How can the model of trials be changed so large numbers are recruited per study center?
4. How can the common problem of loss of treatment adherence (i.e., drop-out and drop-in) and loss to follow-up be tackled?
5. How might trial monitoring procedures be made more efficient (e.g., statistical monitoring)?
6. How can safety reporting/pharmacovigilance be streamlined?
7. How should adjudication be more focused and streamlined?