Global Action. Local Change.

KDIGO Controversies Conference on

Diagnosis and Management of Patients with Fabry Nephropathy

Breakout Group Questions

Topic Group 1: Screening & Diagnosis

A: Screening strategies

Q1: Should Fabry disease be screened systematically at any age and if so in what populations?

Q2: Should Fabry disease be screened for in the newborn period?

Q3: What is the best screening strategy for early diagnosis of Fabry disease? (e.g., newborn screening, high-risk screening of symptomatic patients, cascade screening of family members)

Q4: What is the impact of positive genetic diagnosis on asymptomatic patients and how can this be mitigated?

Q5: What techniques should be used in any of the above screenings?

Q6: What signs and symptoms should trigger screening for Fabry disease in individuals without a family history of Fabry disease? What is the importance of drug-induced phenocopies?

Q7: Are there any clinical manifestations which are pathognomonic of Fabry disease?

Q8: At what age should we screen for Fabry disease in symptomatic patients?

Q9: At what age should we screen for Fabry disease in asymptomatic family members? Should all family members be screened according to pedigree analysis or should symptom triggers be used? If so, which symptoms?

Q10: What is the role of genetic counselling and prenatal diagnosis?

B: Establishing disease status

Q11: What are the recommended assessments at different ages for monitoring kidney involvement in Fabry disease? At what intervals should assessments be repeated?

Q12: Which Fabry patients should have a kidney biopsy or a follow-up biopsy?

Q13: What are the indications for kidney biopsy in a known Fabry patient?

Topic Group 2: Enzyme Replacement Therapy (ERT)

Q1: Is current ERT effective in Fabry disease and if so for what aspects of the disease?

Q2: When to treat (and when not to treat). Do we know when to initiate ERT (e.g., age, sex, presence/absence of clinical manifestations, non-classical disease patients)?

Subquestions within **Q2**:

- Which patients should be treated? Which patients should not be treated?
- What is the role of the GLA variant, or the residual alpha-galactosidase A activity, regarding initiation of therapy?
- When should ERT be discontinued (how is treatment failure defined)?

Q3: How to monitor therapy. What criteria can be used to determine the effectiveness of ERT and how can ERT best be monitored?

Subquestions within **Q3**: (For each criterion, explain adequate timeframe)

- Should renal globotriaosylceramide burden serve as the primary outcome measure?
- Is there a role for "trials" of ERT for a limited time period in advanced disease?
- What is the role of biomarkers (plasma (lyso)Gb3 or urinary (lysoGb3))?

Q4: What is the evidence for dose response of ERT?

Subquestions within **Q4**:

- What is the role of the GLA variant, or the residual alpha-galactosidase A activity on choice of therapy?
- What is the role of neutralizing antibodies on effectiveness of ERT and choice of therapy?

Q5: Is there a role for expert centers in the diagnosis and treatment of disease burden and ERT prescription? Would this be different in low- and middle-income countries (LMICs)?

Q6: Are there clinically relevant drug interactions with ERT (e.g., amiodarone)?

Topic Group 3: Non-specific standard of care therapy

Q1: What types of Fabry-specific adjunctive treatments are most likely effective?

Q2: Can a kidney care strategy be recommended for LMICs including standard of care for preventing progression?

Q3: What are the criteria for introducing renin-angiotensin-aldosterone system (RAAS) inhibitors?

Q4: What is the endpoint for RAAS inhibitors treatment and other anti-proteinuric therapies in Fabry disease?

Q5: What are the optimal antiplatelet agents for use in Fabry disease?

Q6: Should there be primary prevention for stroke in Fabry disease?

Q7: What is the optimal treatment for neuropathic pain?

Q8: Should patient-reported outcome measures (PROMs) or even patient-reported experience measures (PREMs) be routinely collected in Fabry registries, and if so which ones?

Q9: Is there a role for a trial that investigates effectiveness of ERT versus optimal standard of care in attenuated phenotypes?