1. Clinical suspicion of Anderson-Fabry Disease

2. Measurement of α-galactosidase A activity in leukocytes (DBS and/or whole blood)
   - Very low *
   - Mildly reduced *
   - Normal

3. GLA sequencing analysis
   - Disease-causing mutation
   - Unknown variant
   - Polymorphism
   - No mutation identified

   - AFD confirmed
   - AFD excluded

   Laboratory investigations
   - Molecular and functional studies
     - In silico and mRNA analysis
     - Computational modeling
     - Protein analysis
   - Biochemical studies
     - Plasma measurement of metabolites (Gb3/LysoGb3)
   - Histological studies
     - Tissue biopsies
   - Co-segregation studies in male family members

   - AFD confirmed
   - AFD excluded

   High clinical suspicion
   Further laboratory analysis

* Results obtained by DBS need confirmation by standard laboratory diagnostic procedures
1. Clinical suspicion of Anderson-Fabry Disease

2. GLA sequencing analysis
   - Disease-causing mutation
   - Unknown variant
   - Polymorphism
   - No mutation
     - AFD confirmed
     - AFD excluded
     - MLPA
       - No mutation

Laboratory investigations
- Molecular and functional studies
  - In silico and mRNA analysis
  - Computational modeling
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  - Plasma measurement of metabolites (Gb3/LysoGb3)
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