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Variability of GFR Decline in Alport Syndrome: Insights from a Provincial Database

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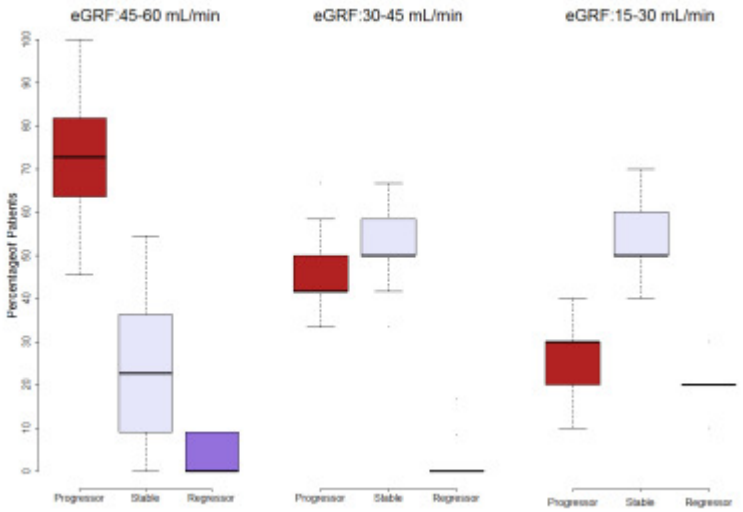
BACKGROUND: Alport syndrome (AS) is one of the inherited causes of CKD due to mutations in the collagen genes making up the glomerular basement membrane collagen. Design of clinical trials for intervention in AS proves challenging without a clear understanding of renal progression over time as observational data is lacking due to small sample size. We present here the utilization of population based data in a simulation to mimic clinical trial recruitment and endpoints to provide insights in trials design for AS.

METHODS: AS patients were identified within a provincial CKD clinical database (PROMIS) in British Columbia, Canada for this observational simulation study. Patients were excluded if they have fewer than 4 eGFR-MDRD measurements or 2 as a study entry point to generate 100 random samples. Primary outcome was annual rate of eGFR change over 2 years categorized into: > -5 mL/min per year (progressor), -5 and 2 mL/min per year (stable), >2 mL/min year (regressor).

RESULTS: 37 pts met inclusion criteria; median follow-up was 48.2 months, and median age of 36. The sample sizes for each random sample at the 3 enrolment eGFR levels were: 11, 12 and 10 respectively. Of those that 'enrolled' at eGFR 45-60 mL/min, 72.7% (IQR:63.6%,81.8%) progressed, and 22.7% (IQR:9.1%, 36.4%) remained in stable state.



For those recruited at eGFR 30-45 mL/min, 41.7% (IQR:41.7%,50%) had disease progression and 50% (IQR:50%, 58.3%) remained in stable state. Of

those enrolled at eGFR 15-30 mL/min, 50% (IQR:50%,60%) were in stable state, 30.0% (IQR:20%, 30%) had disease progression, and 20% (IQR:20%,20%) had an improvement in eGFR.

CONCLUSIONS: Heterogeneity and non-linearity of AS renal progression ought to be taken into account when designing trials of interventions aimed at improving renal outcomes.