Fabry Disease Progression with and without Enzyme Replacement Therapy

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Objectives: Fabry disease is a rare inherited lysosomal storage disease, where kidney complications are a common and serious manifestation. Enzyme replacement therapies (ERT) with agalsidase-α and -β were investigated for a therapeutic effect on renal function in Swiss adolescent and adult Fabry patients. A model to describe the time course of estimated glomerular filtration rate (eGFR) was developed.

Methods: Data from 52 patients (25 female, 27 male) with ERT with a total of 373 observations and data from 20 patients (all female) without ERT with 73 observations were available. Age ranged from 17 to 67 years. eGFR was computed with the chronic kidney disease epidemiology collaboration (CKD-EPI) formula [1]. Non-linear mixed effect modeling was applied and covariates such as age at baseline, gender as well as drug and dose effects were investigated.

Results: A linear relationship between age and eGFR described best the available data. Female Fabry patients without ERT appeared to have a slight decrease of eGFR, whereas eGFR appeared to stabilize or slightly increase with ERT. Male Fabry patients showed decreasing eGFR during ERT, which was comparable or greater than eGFR decrease in males prior to ERT and greater than eGFR decrease in females without ERT. There was no apparent effect of prescribed ERT doses on the eGFR slope. Age at baseline was included as a covariate of the eGFR intercept of the linear model.

Conclusions: Available data and performed modeling suggest a positive effect on kidney function (i.e. eGFR change over time) at licensed ERT doses in female but not in male adolescent and adult Fabry patients. Future investigations are warranted to investigate whether higher ERT doses are associated with improved kidney function in male Fabry patients.

References: