Long-term multisystemic efficacy with migalastat in ERT-naive and ERT-experienced patients with amenable GLA variants

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Fabry disease (FD) is an X-linked, multisystemic disorder caused by GLA variants resulting in α-galactosidase A deficiency. Migalastat has demonstrated multisystemic efficacy in phase 3 clinical trials and is approved for treating FD in patients with amenable GLA variants. Here, we report long-term efficacy of migalastat in phase 3 FACETS (NCT00925301, ERT-naive), ATTRACT (NCT01218659, ERT-experienced), and open-label extension studies (N=97; mean age: 46.4 years; males, 38%). Incidence of Fabry-associated clinical events (FACEs; predefined renal, cardiac, and cerebrovascular events) was assessed in all patients. A Cox proportional hazard analysis was performed to identify predictors of FACEs. eGFR slope was assessed with simple linear regression in patients on migalastat for ≥2 years (n=78).

Over a median follow-up of 5.1 years, 17 (17.5%) patients experienced 22 on-treatment FACEs, leading to an incidence of 48.6 and 47.9 events per 1000 patient-years for ERT-naive and ERT-experienced patients, respectively. FACE incidence in ERT-naive males with classic FD (based on α-galactosidase A activity and multiorgan involvement) was 61.5. Over 18 months in ERT-experienced patients, migalastat was associated with lower FACE incidence versus continued ERT but analysis was limited by small patient number and shorter exposure with ERT. eGFR remained stable in ERT-naive and ERT-experienced patients (mean [SD] annualized eGFR change: −1.6 [3.1] and −1.6 [3.6] mL/min/1.73 m², respectively). Baseline eGFR is a predictor of FACEs in migalastat-treated patients, highlighting the importance of preserving renal function. FACE incidence and eGFR slope with migalastat compared favorably with historical reports of ERT, supporting long-term multisystemic efficacy with migalastat.