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Clinical Outcomes in Patients Switching from Agalsidase beta to Migalastat: a Fabry Registry Analysis

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Objectives : Fabry Registry data (07APR2023; NCT00196742) were used to compare outcomes among 83 patients (44 male) treated first with agalsidase beta (≥1 year; median duration 3.7 years), who then switched to migalastat as their second primary Fabry therapy (≥6 months; median duration 2.6 years).
Methods : Outcomes (estimated glomerular filtration rate [eGFR], plasma globotriaosylceramide [GL-3], plasma globotriaosylsphingosine [lyso-GL-3], interventricular septal wall thickness [IVST], left posterior wall thickness [LPWT], left ventricular mass index [LVMi]) were compared using within-person mean difference between the last pre- and last post-switch assessments and using linear mixed models across all assessments in the pre- and post-switch periods to estimate annual change.
Results : In the last post- vs. last pre-switch assessment, mean difference [95% CI] analysis revealed significantly decreased eGFR (-3.19 mL/min/1.73 m^2 [-6.27, -0.11]) and increased plasma GL-3 (1.25 µg/mL [0.61, 1.88]) and lyso-GL-3 (10.91 ng/mL [1.07, 20.75]), with no significant differences in echocardiogram measures after switching to migalastat. In linear mixed models, eGFR decreased significantly over time in both periods (pre-switch: -0.85 mL/min/1.73 m^2/year; post-switch: -1.96 mL/min/1.73 m^2/year; both $p<0.0001$); rate of decline was significantly steeper post-switch (p-difference=0.01). Plasma GL-3 was stable pre-switch (-0.04 µg/mL/year, p=0.14) and increased significantly over time post-switch (0.44 µg/mL/year, p=0.0003; p-difference=0.0003). These trends were consistent across phenotypes. LPWT was stable pre-switch (0.08 mm/year, p=0.26) and significantly decreased post-switch (-0.57 mm/year, p=0.0008; p-difference=0.0013); this was seen primarily among later-onset patients. IVST and LVMi trajectories varied significantly by phenotype (p-interaction <0.05). Among classic patients, IVST and LVMi slopes were stable/decreasing pre-switch, and significantly increasing post-switch; among later-onset patients, slopes were stable/further decreasing post-switch.
Conclusions : Overall, eGFR and GL-3 trajectories worsened post-switch across phenotypes, while cardiac measures stabilized/improved post-switch among later-onset patients. These real-world findings indicate variability in long-term outcomes after switching from agalsidase beta to migalastat, underscoring the importance of careful monitoring. Funding: Sanofi.