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SIGNIFICANCE OF GENOTYPIC ALPHA GALACTOSIDASE A MUTATIONS IN FABRY DISEASE TREATMENT

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Fabry disease (FD) is a rare inherited X-linked lysosomal storage disorder caused by a deficiency in alfa-galactosidase A (α-GAL). It is resulting in the accumulation of glycosphingolipids that leads to multiple organ dysfunction and ultimately signs and symptoms of the disease. The aim of this study was to examine the significance of genotypic α-GAL mutations in the treatment of FD. The disease can be divided into a severe, classical phenotype, and a milder nonclassical phenotype. Numerous α-GAL mutations are described in gene mutation databases. Missense, nonsense, consensus splice site, cryptic splicing, and frameshift mutations are reported. Enzyme replacement therapy (ERT) can lead to a significant clinical improvement. Depending on the α-GAL mutation, there are various recommendations for initiation of ERT in adult male and female patients with classic Fabry mutations, later-onset Fabry mutations or α-GAL variants of unknown significance. ERT with recombinant human agalsidase alfa and agalsidase beta is currently available therapy. Although there are no uniform guidelines, development of signs or symptoms related to FD should be an indication to start ERT. Treatment with ERT should be combined with adjuvant treatments for specific disease manifestations. Migalastat is a new oral pharmacological molecule developed as an alternative treatment to intravenous ERT for patients with FD and amenable mutations. Migalastat and ERT have similar effects on renal function in patients with FD. Long-term treatment of adult Fabry patients should involve timely ERT, regular assessment of disease progression in all patients, use of appropriate adjunctive therapies and multidisciplinary team approach.

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