Changes in Plasma and Urinary Metabolites After Elamipretide in Barth Syndrome Patients: Analyses from the TAZPOWER Study

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INTRODUCTION

Elamipretide (PDI-106543) is a mitochondrial transport enhancer, or mitochondrial retromer, that localizes to the inner mitochondrial membrane. It is designed to restore the mitochondrial dysfunction that occurs in Barth syndrome (BTHS), a rare X-linked disorder that is caused by a mutation in the TAFazzin (TAZ) gene. TAZ localizes to the mitochondrial inner membrane, and it is the enzyme responsible for the remodeling of cardiolipin. Elamipretide has shown beneficial effects in patients with BTHS in previous clinical trials, including reducing symptoms and improving physical performance.

METHODS

TAZPOWER Study Design

The TAZPOWER study (NCT03098797) was a 28-week, randomized, double-blind, placebo-controlled, multicenter trial to evaluate the safety and efficacy of elamipretide in patients with BTHS.

RESULTS

Exploratory targeted metabolomic analyses were performed to assess changes in plasma and urinary metabolites for patients with BTHS receiving elamipretide and placebo in TAZPOWER.

Acylcarnitines

- There was a trend for decreased acylcarnitine levels in both plasma and urine (normalized to creatinine) following elamipretide treatment, but this decrease did not reach statistical significance (p<0.05).

3-Methylglutaconate

- There was a strong trend for decreased 3-methylglutaconate concentration in both plasma and urine, but this did not reach statistical significance compared with placebo (p>0.05).

Taurine

- Compared with placebo, circulating taurine increased significantly in the elamipretide arm after 12 weeks of treatment (p<0.01).

CONCLUSIONS

- Metabolic analyses performed in patients with BTHS receiving elamipretide and placebo in TAZPOWER suggest that elamipretide treatment may have beneficial effects on mitochondrial function and metabolism in BTHS.

REFERENCE