Pregnancy Outcome After Exposure to Migalastat: A Case Study

Haninger-Vacariu N,1 El-Hadi S,1 Pauler U,2 Foretnik M,1 Kain R,3 Schmidt A,1 Skuban N,4 Barth JA,4 Sunder-Plassmann G1

1Division of Nephrology and Dialysis, Department of Medicine III, Medical University of Vienna, Vienna, Austria; 2Department of Medicine I, University Hospital St. Pölten, Lower Austria, Austria; 3Clinical Institute of Pathology, Medical University of Vienna, Vienna, Austria; 4Amicus Therapeutics, Inc., Cranbury, NJ, USA

INTRODUCTION

- Fabry disease is a rare X-linked lysosomal storage disorder caused by deficiency of α-galactosidase A (α-Gal A), encoded by the GLA gene.
- The resulting accumulation of globotriaosylceramide (GL-3) produces a wide variety of debilitating signs and symptoms, including cardiomyopathy, renal failure, cerebrovascular events, and gastrointestinal manifestations.
- The first clinical symptoms of Fabry disease typically occur during childhood, and, if left untreated, the burden of disease increases over time.
- Until recently, enzyme replacement therapy (ERT), consisting of infusions of agalsidase alfa or agalsidase beta, was the standard treatment approach for patients with Fabry disease.
- Migalastat is a small-molecule pharmacological chaperone designed to bind selectively to α-Gal A and facilitate its proper trafficking to lysosomes, where dissociation of migalastat then restores endogenous enzyme activity.
- In the phase 3 FACTS (NCT00925301) and ATTRACT (NCT01218659) trials, migalastat was shown to provide clinical benefits for patients with Fabry disease and amenable mutations and was generally well-tolerated.
- Migalastat is now approved for long-term treatment of Fabry disease in patients ≥18 years old in the European Union, Switzerland, Israel, Australia, and Republic of Korea and in adults and pediatric patients in Canada.
- In rabbits, developmental toxicity was observed at maternally toxic doses.
- As a result, migalastat is not recommended during pregnancy.

OBJECTIVE AND METHODS

- To describe the medical history and outcome of a Caucasian woman with Fabry disease who became pregnant, despite hormonal contraceptives, while being treated with migalastat during the phase 3 ATTRACT trial.
- The 18-month, randomized, active-controlled study aimed to assess the effects of migalastat on renal function in patients with Fabry disease previously treated with ERT.
- Patients of reproductive potential agreed to use medically accepted methods of contraception throughout the duration of the study and for up to 30 days after the last migalastat infusion.
- Pregnancy outcome after exposure to migalastat is shown in Figure 2.
- The patient's medical history prior to migalastat treatment is shown in Figure 2.
- Details of migalastat treatment and of the third pregnancy are shown in Figure 4.

CASE REPORT

Patient History

- The patient was a Caucasian woman with Fabry disease aged 35 years at the time of migalastat initiation and 37 years at the time of pregnancy.
- Her family history is shown in Figure 1.
- Her father had Fabry disease (generation II), and all 3 surviving siblings (all females) also have Fabry disease (generation III).

Treatment With Migalastat

- Details of migalastat treatment and of the third pregnancy are shown in Figure 4.

CONCLUSIONS

- Except for low birth weight, pregnancy outcome in this case was normal despite exposure to migalastat for 18 weeks during the pregnancy.
- Migalastat therapy during pregnancy is not advised.

REFERENCES


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CONFLICTS OF INTEREST

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DISCLOSURE

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