Dual X-ray Absorptiometry in Children with Hypophosphatasia
Treated with Asfotase Alfa: a Pooled Post Hoc Analysis

Jill H. Simmons, MD;1 Eric T. Rush, MD;2 Anna Petryk, MD;2 Shanggen Zhou, PhD;3 Gabriel A. Martos-Moreno, MD, PhD3

1Department of Pediatrics, Vanderbilt University Medical Center, Vanderbilt University, Nashville, TN, USA; 2Children’s Mercy Hospital, University of Missouri–Kansas City School of Medicine, Kansas City, MO, USA; 3Alexion Pharmaceuticals, Inc., Boston, MA, USA; 4Covance, Inc., Princeton, NJ, USA; 5Hospital Infantil Universitario Niño Jesús. IIS La Princesa, Universidad Autónoma de Madrid, CIBERObn, ISCIII, Madrid, Spain

INTRODUCTION

- Hypophosphatasia (HPP) is the rare, inherited, metabolic bone disease with systemic consequences caused by deficient tissue-nonspecific alkaline phosphatase (TNALP) activity.
- Children with HPP commonly present with impaired skeletal mineralization, rickets, bone pain, fractures, premature loss of primary teeth, short stature, craniosynostosis, stiffness, muscle weakness, and reduced physical function, including compromised ambulation.1
- Asfotase alfa (Strensiq®, Alexion Pharmaceuticals, Inc., Boston, MA, USA) is a human recombinant TNALP enzyme replacement therapy approved for treatment of patients of any age with pediatric-onset HPP.1
- Children with HPP treated with asfotase alfa have shown improvements in skeletal radiographic findings, growth, strength, motor function, pain, and disability.2
- In clinical studies of astasfa asf, changes in skeletal abnormalities and mineralization defects were assessed using several modalities, including skeletal radiographs, bone biopsies, and dual x-ray absorptiometry (DXA).

STUDIES INCLUDED

Subcutaneous Asfotase Alfa

OUTCOME MEASURES

- Change from Baseline in height-adjusted BMD (BMDht) and bone mineral content (BMCht) Z-scores and absolute values for BMD and BMC assessments of the lumbar spine and whole body (including the head) measured by DXA.
- Correlation between changes in DXA measures (BMD and BMC Z-scores and absolute values) and other skeletal/bone histomorphometry assessments.
- Radiographic Global Impression of Change (RGI-C) scale score.12
- Rickets Severity Score (RSS).13
- Osteoid thickness, osteoid volume, and mineralization lag time

LIMITATIONS

- The analysis population had a wide age range and a limited number of female patients.
- There was no cross-calibration of DXA scanners between participating centers; comparisons were made with each patient’s Baseline data to mitigate this limitation.
- DXA whole body scans included the head, which may have overestimated BMD in younger patients.
- The relative contribution of astasfa alfa vs. natural accumulation of BMD due to growth in the observed improvements in DXA measures is unclear.

CONCLUSIONS

- Based on the data from this pooled post hoc analysis, DXA BMD Z-scores, which are most commonly used in clinical practice, are not a useful measure of bone deficits in children with HPP either at Baseline or in response to treatment.
- Other complementary measures, including functional outcomes, should be considered.

ACKNOWLEDGMENTS

This study was sponsored by Alexion Pharmaceuticals, Inc., Boston, MA, USA. Editorial and writing support was provided by Bina J. Patel, PhArmD, CMPPh, of Peloton Advantage, LLC ( Parsippany, NJ, USA), an OPEN Health company, and funded by Alexion Pharmaceuticals, Inc.

DISCLOSURES

JHS was a clinical study investigator and received honoraria/travel support from Alexion Pharmaceuticals, Inc. ETR received consulting fees from Alexion. AP is an employee of and may own stock/options in Alexion Pharmaceuticals, Inc. SZ is an employee of Covance, Inc., and provided statistical services for the analyses under contract to Alexion. GM-M was a clinical study investigator and received institutional research funding and/or grant support from Alexion.

REFERENCES