Presenting Author Name
Cheryl Rockman-Greenberg

Presenting Author Category
Faculty

Research Category
Clinical

Abstract Title
In utero enzyme replacement therapy for life-threatening hypophosphatasia: promises and challenges

Background
Hypophosphatasia (HPP) is a rare metabolic disorder caused by pathogenic/likely pathogenic variants in the ALPL gene leading to impaired bone and teeth mineralization and non-skeletal manifestations. Seven clinical forms have traditionally been recognized, classified by age of onset and severity. The most severe forms are life-threatening, clinically appearing at birth (perinatal) or in the first few months of life (infantile), with historically very high morbidity and mortality. The introduction of enzyme replacement therapy (ERT) with human bone-targeted alkaline phosphatase (asfotase alfa) has dramatically improved the outcome for patients, especially survival rates for patients with perinatal and infantile HPP (JCEM 2016;101:334-42). However, significant morbidity and deceased quality of life remain in many of these patients with life-threatening HPP treated with ERT postnatally and, in some cases, mortality persists. In utero initiation of ERT (IUERT) may offer significant benefits for babies with life-threatening forms of HPP over initiation of treatment postnatally, comparable to the benefits documented for IUERT for infantile-onset Pompe disease. IUERT can take advantage of the unique window antenatally to enhance fetal bone development and mineralization and change the natural course of life-threatening HPP.

Objective
To add life-threatening HPP to the list of disorders that meet criteria for IUERT.

Methods
The IUERT protocol is being finalized by the In Utero consortium led by Dr. Tippi Mackenzie (UCSF) and will be submitted to the FDA. Attitudes to IUERT and feedback of individuals with lived experience with HPP will be collected through a RedCAP survey that will be distributed by 2 North American patient advocacy organizations- Soft Bones Canada and Soft Bones.

Results
Attitudes to IUERT and feedback of individuals with lived experience with HPP will be collected through a RedCAP survey that will be distributed by 2 North American patient advocacy organizations- Soft Bones Canada and Soft Bones.

Conclusion
We anticipate IUERT for HPP will be endorsed by the HPP community of patients and families, will be approved by the FDA and will offer significant advantages over postnatal initiation of ERT for life-threatening HPP.

Authors

Name	Role	Profession
Pranesh Chakraborty	Co Author	Associate Professor
Marie-Eve Robinson	Co Author	Assistant Professor
Karen Fung-Kee Fung	Co Author	Full Professor
Aziz Mhanni	Co Author	Associate Professor
Emma Canepa	Co Author	Graduate
Billie Lianoglou	Co Author	Graduate
Anna Zhao	Co Author	Graduate
Tippi Mackenzie	Co Author	Full Professor
Cheryl Rockman-Greenberg	Presenting Author	Full Professor