

# SEBELIPASE ALFA AS ENZYME REPLACEMENT THERAPY IN THREE PAEDIATRIC PATIENTS

Jiménez Núñez C, Álvarez Criado J, Pérez Robles T, Gabaldón Garnica P, Jiménez Vicente C, Moreno Palomino M, Lucena Martínez P, Herrero Ambrosio A.

Hospital Pharmacy Service, Hospital Universitario La Paz, Madrid, Spain

ATC code: A16 - Other alimentary tract and metabolism products

## Objective

Evaluation of enzyme-replacement therapy with sebelipase alfa in three paediatric patients with lysosomal acid lipase deficiency (LALD)

## Methods

- Observational, retrospective study involving three patients treated with sebelipase-alfa (administered intravenously at a dose of 1 mg/kg/2 weeks). Preparation of the medication was carried out by the Hospital Pharmacy Service.
- From clinical history we obtained: age, diagnosis, analytical values of total cholesterol, low density lipoprotein (LDL), high density lipoprotein (HDL), triglycerides (TG), alanine aminotransferase (ALT) and aspartate aminotransferase (AST), liver size and fibrosis before and during treatment with sebelipase alfa, and adverse events.
- The efficacy was evaluated by normalizing the analytical values of the lipidic and liver profiles in 3 patients who participated in the clinical trial until April 2018.

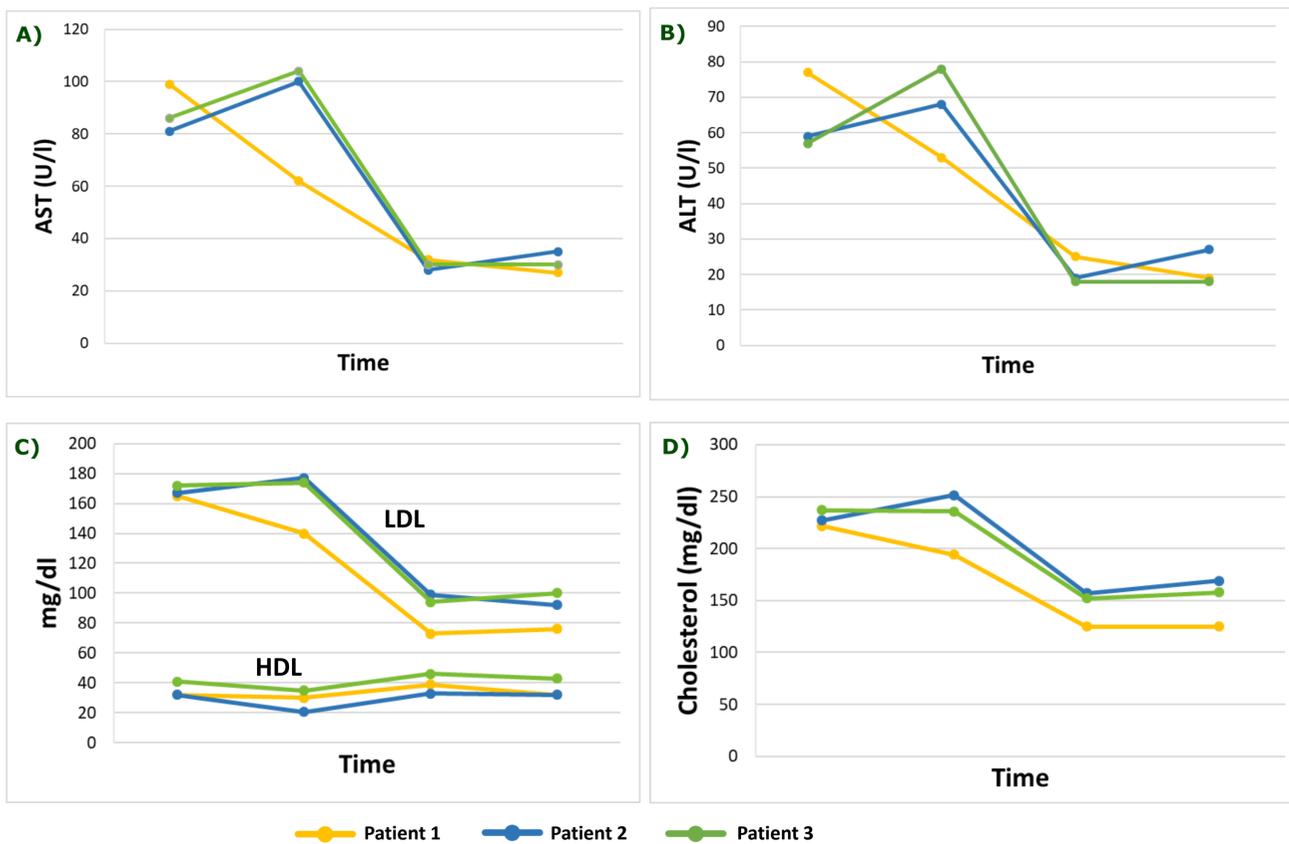
## Results

Three male brothers with 12, 15 and 17 years old diagnosed with LALD before 5 years, heterozygous for mutation in the LIPA gene c.894G>A, c.256C>T.

On April 2018, patients had been in treatment with sebelipase alfa 225, 183 and 229 weeks (112, 91 and 114 doses), and all of them got the normalization of the analytical values of lipid and hepatic profile (except one patient in triglycerides and two patients in HDL). Hepatomegaly reversed in all patients.

Relative to safety, two patients suffered diarrhea, and infusion-associated reactions weren't reported.

	Basal (mean)	Final (mean)	Change from baseline (%)
AST (U/I)	88,67	30,67	<b>-64,88</b>
ALT (U/I)	66,33	21,33	<b>-65,99</b>
Total cholesterol (mg/dl)	227,23	150,67	<b>-34,19</b>
LDLc (mg/dl)	163,67	89,33	<b>-46,90</b>
HDLc (mg/dl)	28,50	35,67	<b>+1,55</b>
Triglycerides (mg/dl)	174	130	<b>-2,10</b>



Figures: Variation of AST (A), ALT (B), LDL and HDL cholesterol (C) and total cholesterol (D)

## Discussion

- The results in these three paediatric patients correspond to those obtained in the pivotal trial, where improvement of the analytical values of the hepatic (AST and ALT) and lipid (CT, LDL, HDL) profile was observed.
- Reductions in AST and ALT levels suggest that sebelipase alfa may have potential value in reducing the risk of fibrosis and progression to cirrhosis among patients with lysosomal acid lipase deficiency.
- Improvements in serum lipid values may help to decrease cardiovascular risks associated in these patients.
- The treatment has been well tolerated, with no apparent severe adverse events, including infusion-associated reactions

## Conclusions

LALD is a rare disease, and sebelipase-alfa is the first drug authorized for its treatment. The response to treatment with sebelipase-alfa has been favorable from the beginning, with an improvement in the studied variables and a good safety profile in the reported cases

