# Elamipretide treatment in an infant with Sengers syndrome

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## Introduction

Sengers syndrome (SS) is a rare cause of early onset cardiac failure, congenital cataracts and hypotonia caused by homozygous disease-causing variants in the AGK gene. Average published survival of children presenting in infancy is 4.2 months[1]. SS and Barth syndrome have overlapping phenotypes and both are thought to lead to depletion of mitochondrial cardiolipin[2]. Elamipretide is a tetrapeptide which is known to target the inner mitochondrial membrane and thought to bind to cardiolipin and reduce its damage[3], thus theoretically useful in both syndromes. We recently diagnosed a boy that was homozygous for a founder mutation (p.Ile348AsnfsTer38) carried by approximately 1% of Icelanders. He presented at 3 weeks of age with severe hypertrophic cardiomyopathy, bilateral cataracts and significant hypotonia.

## Methods

In collaboration with Stealth BioTherapeutics the boy received elamipretide for ~ 6 months (starting at 3 months of age) through a compassionate care protocol, in addition to established beta-blocker treatment. Here we summarize data from weekly clinical global impression evaluations[4] and bi-weekly echocardiograms during the 6 months of treatment. This compassionate care protocol was approved by the appropriate local authorities.

## Results

Pharmacokinetic studies indicated that drug exposure was similar to other elamipretide trials. Our patient showed subjective improvement from the prior week evaluation in 13 of 21 visits (~62%) and only was felt to worsen on one occasion. His global score went from markedly ill to borderline ill during the treatment period (Figure 1). Specifically, our patient's cardiac condition improved in the first few weeks of treatment and remained stable. Left ventricular end-diastolic internal dimension increased by 53% (Z-score from -2.7 to +0.7). Ventricular septal thickness decreased from Z-score 4.7 to 3.5 and left ventricular posterior wall thickness decreased from Z-score 5.8 to 4.7 (Figure 2 A and B). There were no obvious side effects that were attributable to elamipretide. The patient demonstrated intermittent lactic acidosis and neutropenia which were thought to be related to his condition.

## Conclusions

The treatment of a single individual with SS suggests that elamipretide is well tolerated in patients with SS and may have helped stabilize the patients cardiac function. Further studies are required to define the role of elamipretide in SS.

## Update

The patient underwent PEG placement after approximately 6 months of treatment and had severe outcome, with cardiac decompensation followed by multi-organ failure and death. This may indicate that patients with neonatal presentation of Senger syndrome are extremely sensitive to external stressors such as anaesthesia and surgery.

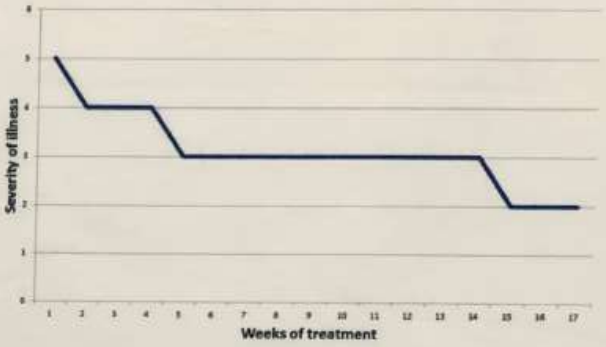


**Figure 1. Severity score during the first 4 months of treatment**

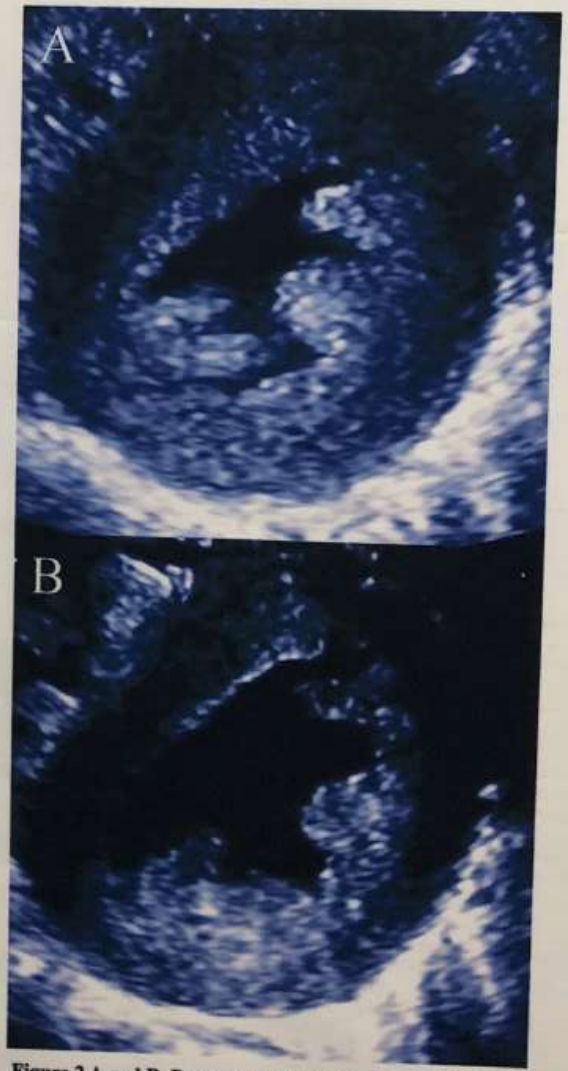


**Figure 2 A and B. Parasternal short axis view of the left ventricle in end-diastole at week 1 (A) and week 20 (B) of treatment.**

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