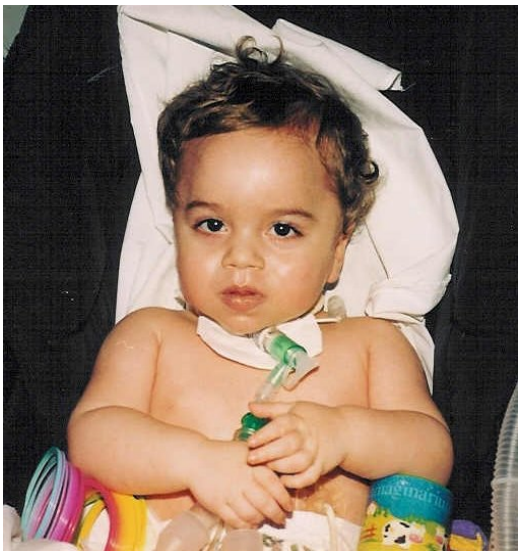
Lucas Story

Written by: Javier, Lucas father, Spain

Lucas was born on 3rd February 2002. Apparently everything was fine with him and he seemed to have normal strength, but soon he started to experience the first problems.

When he was one month old he showed difficulties during feeding. He was unable to feed properly and he failed to gain weight. His muscles were bulky and, from the moment he was born, he also had cyanosis around his mouth.

Although the lack of weight gain was very stressing for us, and there were very good reasons to think Lucas was seriously ill, his paediatrician failed to notice that something was very wrong with him until he was 4 months old.



Lucas, age 3, enjoying Summer time

After some medical tests, an echocardiography revealed that he suffered a cardiac condition called hypertrophic cardiomyopathy. Lucas was hospitalised, immediately, to determine what exact disease was causing his cardiac problems, although from the first moment a metabolic disease was suspected.

Because of his symptoms and the few things that we had read in the internet, from the beginning of his hospitalisation period we were pretty sure that he was suffering from Pompe disease. Unfortunately we were right. Even like that, and due to a general lack of efficiency in the diagnosis process, doctors were unable to provide us with a confirmed diagnosis of Pompe disease until he was 7 months old. By that time his deterioration had really began.

The day before entering the hospital, Lucas was able to breath by himself, to move his arms and to kick his legs. He had little strength but his movements were acceptable. Three months later he had lost all mobility in his legs, and, because of 2 consecutive pneumonia he contracted at the hospital, he lost his ability to reach acceptable oxygen saturation levels, and doctors decided to provide him with a permanent supplement of oxygen, which at the end proved to be a wrong decision.

After his Pompe disease diagnosis was confirmed, doctors were very pessimistic about his evolution, and told us that there was nothing to be done. In any case, from the very first moment, the Spanish Association for GSDs provided us with a great deal of information about the disease, and we were fully aware of the ERT trials that Genzyme was performing.

We applied for compassionate use of the drug, as Lucas access to ERT was the only chance to save his life. However, due to the very limited production, compassionate use at that time was limited to very exceptional cases, and we had to knock at many doors until it was finally granted to Lucas, just by the time he was 9 months old.

By that time his cardiac situation had worsened although it was not still life threatening. His respiratory status had deteriorated very rapidly also, and he became dependent on a CPAP after another pneumonia, which again proved to be a wrong decision.

He started ERT at a dose of 20 mg/kg bi-weekly with very good tolerance. However, we did not notice any immediate improvement from the muscular, cardiac or respiratory point of view.

Just one month after he started with ERT he had a cardio respiratory failure during his bath. Although he was literally dead during seven minutes, doctors were able to resuscitate him with no neurological damage. Obviously, using a CPAP was not the right option for him and the respiratory failure took place because of poor ventilation and high CO2 levels.

He had to be trached and ventilated and he entered the paediatric ICU were he spent the following months. After he was trached, we noticed a significant gain in strength that took place since he was 10 months old until he was 23 months old. He regained strength in his arms and had a much better head control.

Initially, we attributed this gain in strength to ERT, although now we think that perhaps it was mostly due to the fact that he had the help of a ventilator. The reason is that, although he was gaining strength, his cardiac situation was worsening. This was in complete contradiction with the results published in the scientific literature, which described good muscular evolution only for a set of patients, but a generalized cardiac improvement for all patients, at least in those cases in which appropriate dosages were used.

It seemed clear that 20 mg/kg bi-weekly was not working sufficiently for Lucas. Even like that, ERT was playing a role, as his cardiac deterioration was not going so rapidly as before. The scientific literature stated that different doses had been used with different versions of the enzyme; including 20 mg/kg bi-weekly, 40 mg/kg bi-weekly, and 40 mg/kg weekly. So Lucas doctor decided to apply for a dosage increase to 40 mg/kg bi-weekly when he was 12 months old. However, the increase was refused arguing that production was still very limited.

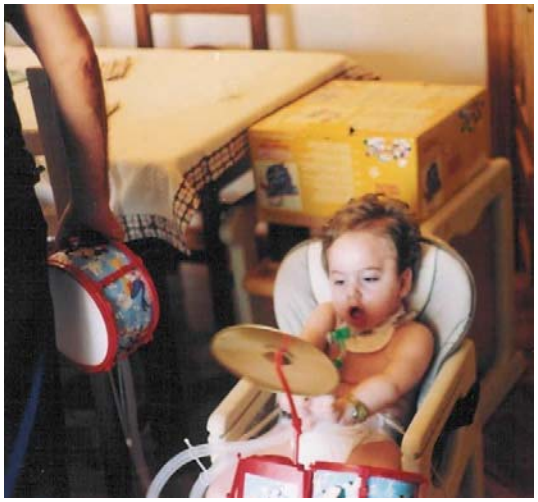
As a result of that, his cardiac ejection fraction continued to go down and almost reached the verge of compatibility with life when he was 20 months old. By that time, he got another pneumonia that only worsened the situation, as it led to a very dangerous episode of supraventricular tachicardia. His poor cardiac status revealed that he was going to die if nothing was done, and finally Genzyme agreed to increase the dose to 40 mg/kg bi-weekly, just one year after he started with ERT.

The new dosage had a good effect on cardiac functionality which improved significantly, although still remained below normal levels several months after the dosage increase. There was no effect however on cardiac size, which continued to be around 4 times the normal size for his age. The new dose had no positive effects with respect to muscular strength. In fact, the initial gains in strength that took place after he was trached were slowly fading away. As a result when he was around 3 years old he had lost all of his head control and most mobility in his arms.

Thus, when he was 3 years old he was not able to perform most of the things he did when he was younger, as he had experienced a very severe lost of mobility. On the other side he was feeling better. His heart was functioning better and, as a result, his health was much more stable in every aspect. Lucas left the hospital for the first time when he was 16 months old, but still we had to re-hospitalise him very frequently due to respiratory infections, fever, etc. After the dosage increase to 40 mg/kg bi-weekly the visits to the hospital became less frequent.

Even like that, we felt that the 40 mg/kg bi-weekly dose was still not enough for Lucas. The main reason was the lack of normalization in his heart, which still had a huge size. Besides, we were concerned with the permanent mobility losses, and we considered that something had to be done about that, before he could not move a single muscle.

His doctors applied for a further dosage increase, to 40 mg/kg weekly, by the time Lucas was 2 years and a half. Initially, in Genzyme they were reluctant again to provide that second increase, as such doses were not used in the trials. However, our claims were supported by the scientific publications produced by the team of Dr. Van der Ploeg and Dr. Reuser, where it was suggested that there were no proven differences in efficiency between the transgenic and the CHO enzymes and that the dose of 40 mg/kg weekly that they had used might be the most appropriate, at least for some patients.

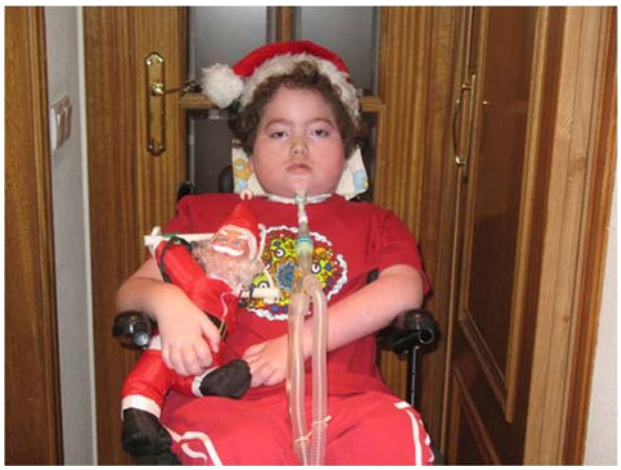


Lucas enjoying his music play

Finally, Genzyme agreed to provide a dose of 40 mg/kg weekly to Lucas by the time he was 3 years old and had lost almost all mobility. The improvement was dramatic from the cardiac point of view, as his heart size was reduced very rapidly to normal size and his heart finally reached normal functionality. However, in relation to mobility the dose increase had no effect at all.

We can conclude that we are very happy that Lucas is receiving ERT, because the treatment has saved his life. We have accepted the fact that he is not, and will never be, a normal kid. He is a happy boy however, with lots of interests, with an amazing sense of humour, and who is able to read since he was 3 years old. The tolerance to the drug has always been perfect both at low and high doses, and he has never experienced any side-effects. Apart from osteoporosis, he does not seem to show any other potential problems that could be associated to Pompe disease, such as neurological problems or hearing problems. Besides, even if he is a very disabled child, dependent on us in every aspect, he is now much more stable and less prone to complications, such as infections, fevers, digestive problems, sleeping difficulties etc. He just feels much better.

Our experience suggests that there are two key issues for an optimal use of Myozyme: early intervention and appropriate dosages, which could differ for each patient. Lucas has proved that he was in need of high doses for his cardiac recuperation, and he has been able to tolerate them without major problems. If he had been treated with higher doses at a younger age, perhaps he could also be now in a better position from the muscular and respiratory points of view.



Lucas, at the age of 8 years

In relation to the future, we want to keep optimistic, even if we have our feet on the ground, and we know that the situation is very hard as the disease has damaged his muscles very badly. An improved second generation ERT, as well as the development of other approaches, such as gene therapy, will certainly be welcomed, although we doubt that they would be able to regenerate the muscles of Lucas. Perhaps the only hope for a real cure for a child like Lucas, who has had a late access to ERT, relies on muscle regeneration through stem cell therapy, which still seems to be far away.

Lucas is now 9 years old. He has almost no movement at all, just limited to his eyes and tongue. Anyhow, he manages to use computers with a camera that catches his eye movements and with the help of an ultrasensitive switch. However he has an overall stable condition and has no major problems from the cardiac or neurological point of view. He is a happy boy and is usually in a good mood. Communication is a major problem, and the education authorities in Madrid are doing very little about that, even if there are methods of alternative communication that would allow for a substantial improvement in the exchange of information between Lucas and the rest of the world.