

Lucas story

Lucas was born on 3rd February 2002. Apparently everything was normal 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 his feeding sessions. He was unable to finish his meals 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. Then an echocardiography was performed and an hypertrophic cardiomyopathy was diagnosed. Lucas was hospitalised immediately to determine what exact disease he had, although from the first moment a metabolic disease was suspected.

Because of his symptoms and the few things that we read in the web, 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 had lost his ability to reach acceptable oxygen saturation levels and doctors decided to supplement him with oxygen continuously.

After his diagnosis was confirmed doctors were very pessimistic about his evolution and told us that there was nothing to be done. In any case, since we suspected that he had this terrible disease from several months before his diagnosis was confirmed, we were able to collect a great deal of information about it, and we were fully aware of the trials that Genzyme was performing with ERT.

We applied for compassionate use, so that Lucas could have access to ERT as it 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.

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 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 a poor ventilation.

He had to be trached and ventilated and he entered the ICU where 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 I am almost convinced that it was due to the fact that he had the help of a ventilator. The reason for that 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 at least in those cases in which appropriate dosages were used.

It was obvious that 20 mg/kg bi-weekly was not enough for him. 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 of the 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 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 tachycardia. 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 increased 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 effects of the new dose did not show up either with respect to muscular strength. 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 almost 3 years old he was not able to do most of the things he did when he was younger as he had experienced a very severe loss 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 way. Lucas had left the hospital for the first time when he was 16 months old, but we had to hospitalise him very frequently due to respiratory crisis, fever, etc. After the dosage increase to 40 mg/kg bi-weekly the visits to the hospital were not so frequent.

Even like that we were convinced that that 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 continuous losses of mobility, and we felt 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

to provide that increase, as such doses were not used in the trials. However, our claims were supported by the articles by the team of Dr. Van der Ploeg and Dr. Reuser, where they claimed 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.

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 results were dramatic as his heart size was reduced very rapidly to normal size and his heart finally reached normal functionality. In relation to mobility he has not regained any, but the deterioration we were observing has stopped completely. He is conserving the little mobility he had in his arms. It is a pity that the dose increase was not granted before, because perhaps he could have better mobility now, but the fact is that we are very glad that he is not losing anymore the little mobility he still conserve.

We can conclude that we are very happy that Lucas is receiving ERT because thanks to it he is alive with us. 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 a few months over 3 years of age. The tolerance of the drug has always been perfect both at low and high doses, and he has never had 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 disable child, dependent on us in every aspect, he is much more stable now and less prone to complications as infections, fevers, intolerance to feeding, sleeping difficulties etc. He just feels much better.

Our experience tell us that there are two key issues for an optimal utilization of the drug: early intervention and the use of appropriate dosages, which clearly differ for each patient. Lucas has proved that he needed high doses and that he can tolerate them. I am convinced that if he had been treated with higher doses at a younger age he would be in a much better shape now, surely much closer to normality. At least, what his evolution and his tolerance of the drug has proven is that if a more intensive pattern of drug administration had been used from the beginning he would not certainly be in a worst position now. There is not too much scope for errors with this disease.

In relation to the future, I want to keep optimistic, even if I have my feet on the ground and I know that the situation is very hard and the disease has done most of the damage on the muscular system. Any improvements in ERT (both in quantity and quality) and the emergence of new therapies such as gene therapy will certainly be welcome although I doubt that they would be able to regenerate the muscles of Lucas. Perhaps the only hope for a real cure for a child who has been treated late with ERT relies on muscle regeneration through stem cell therapy, which still seems to be far away.

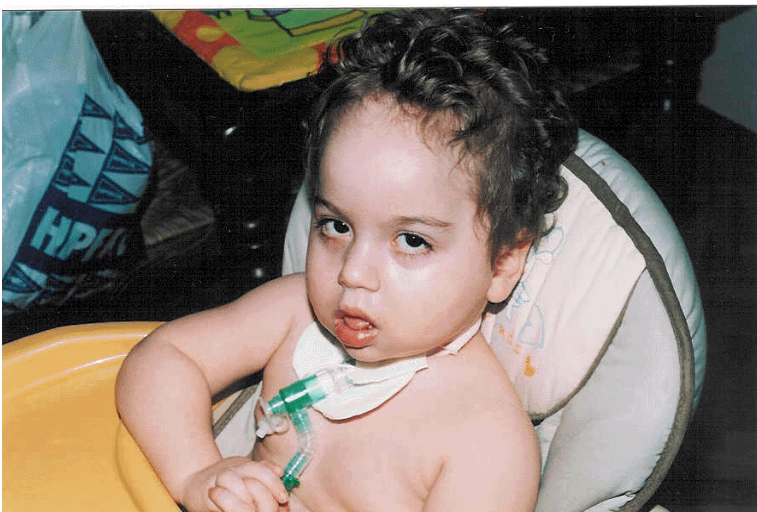
Javier, Lucas father



Lucas playing music



Lucas enjoying the Summer



Lucas at the age of 3