Phase 1b trial with Genzyme Corporation in patients with Niemann-Pick B – A Patient's Perspective

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At our recent Family Conference, James Dyson, NP-B, shared his experiences on participating on the Phase 1b clinical trial in Niemann-Pick Type B patients to evaluate the safety and tolerability of an investigational enzyme replacement therapy recombinant human acid sphingomyelinase (rhASM). This is what he had to say:

My name is James and I have Niemann-Pick type B. I was diagnosed when I was 3 years old and have since wandered, thankfully, through life with very few serious concerns to my health. Very briefly, thanks to the fight of my parents, I attended normal school. When I was 12 years old, concerns for my huge spleen reached a head and I was offered a partial splenectomy, which was pioneering surgery at the time and more than likely the main reason I have such good health now. Since leaving school, I have trained with the fire service, owned my own business, driven double decker buses and coaches for First Group and now I am currently employed with South Western Ambulance Service as a Paramedic. I am also a qualified welder and training to be a blacksmith. I live in Tavistock, Devon, with my wonderful wife Bev and my step son and daughter, Danny & Alex.

I am currently the only person participating on the Phase 1b Enzyme Replacement trial in Manchester. I made enquiries into the trials around April 2013 and after a short while had telephone conversations with Simon Jones and Brenda Pimlott. We discussed the trial and what was involved and at this stage, every emphasis was on whether or not I would even be suitable. Honestly at first, I did have concerns about the safety of this drug and I was also dubious about the amount of time the trial would take out of my life. I discussed with Simon visiting the Welcome Trust to start the screening process to see if I was suitable and was overwhelmed when I arrived by how friendly the staff at the facility were.

Very shortly after screening started and after a long discussion with Simon, quizzing him about my concerns, I became more apprehensive that I wouldn't be accepted than I had previously been about safety issues.

I have spent my whole life burying my head in the sand, trying to live my life to the full and rarely thinking about the future as I knew my health would only ever be getting worse. This year, a routine check-up raised concerns about my liver and unfortunately being a paramedic not only means I understand these issues, but I have also seen people who have suffered these problems. Discussing a treatment with Simon that was not only expected to work but would actually reverse years of damage was amazing and emotional because for the first time in my life I could potentially look forward to a full and normal life.

As the screening approached completion, it didn't look good. My liver was causing concerns and my bilirubin levels we're too high. Simon and I discussed that I had recently been unwell with a usual chest infection and that I had just finished six horrendous night shifts and the test was done again, this time I scraped through. In the end it all came down to my liver biopsy results and as it turned out, we we're told I was suitable about fourteen hours before the infusion was due to start.

The infusion started late morning with a tiny 0.1mg/kg dose. I can remember looking at this tiny amount of Fluid in a syringe driver and thinking, I hope everyone who developed this in the states had got this right. As the infusion was given, everyone was stood round and regularly asked me how I felt. Although initially, I had told Simon I would be very matter of fact about how I felt, I couldn't help but find myself questioning even the slightest itch. The dose took no time at all to be given, and the subsequent 72 hours we're very un-eventful, to the relief of everyone. My time was taken up with the regular observations, scans and ECG's that were required.

The infusions are given through a cannula in one arm and bloods are taken through a second in the other. You are constantly connected to a wireless ECG machine which monitors you day and night for your entire stay, so there is no leaving the facility. I am not bothered by needles and so although it is uncomfortable for 10 or 20 seconds, while the needle is inserted, it's not painful every time blood is required & none of the other tests are painful or uncomfortable.

The week post infusion was as if nothing had happened and I looked forward to the 0.3mg/kg dose. This dose was very similar, however the week after the infusion I started to notice some mild spleen discomfort, the occasional 'stitch' like sensation on and off through the week. After the 3rd dose at 0.3mg/kg, I was convinced my spleen was shrinking. At first I thought it was in my head but, my abdomen started to feel different like things were loose and in a slightly different area. To everyone's surprise my clinical examination on my 4th visit showed my spleen had shrunk. Only by a small amount but it was definitely shorter. I was thrilled. This visit was for 0.6mg/kg dose and I was really excited about how everything was going and how much change, this dose would have. On the Wednesday night around 30 hours after the infusion, I started to feel lethargic, my shoulders and hips began to ache and my temperature spiked. Immediately everyone was on top of it and Tolga, the facility medic was called. There is always a doctor on duty, mainly Tolga, day and night throughout the whole time I'm in the building. I had been warned that this would probably happen by Simon at the start, but I think everyone was surprised at how quickly the drug was working. The feeling I get is similar to flu, but it is different by how quickly it hits you. One minute your sat feeling fine and the next minute you ache, feel lethargic and your joints feel tired. Similarly it wears off just as quick, and within half an hour you feel fine again.

The 0.6mg/kg reaction lasted overnight. The 1mg/kg reaction lasted until the following afternoon. The week following the 0.6mg dose left me feeling tired, whether that was the drug or not I don't know. After the 1mg dose I was absolutely fine, I had no lethargy or spleen discomfort. Unfortunately though my in hospital bloods showed some markers elevated and

given how unwell I had felt, the decision was made to go back for a week to 0.6. On this infusion I had no reaction in hospital or at home. The week prior to the family conference we rechallenged the 1mg dose again and this time I had no reaction, similarly to the 0.6. As this is printed hopefully I will be on a 2 or even 3mg dose, the maximum amount for this trial. If all goes well with the 3mg dose, then I will no longer need to stay in hospital after the infusion and will be discharged the same day.

In summary, the drug appears to be working very well and it looks to be the rapid removal of years of storage that makes you feel rubbish for several hours, a small price for all the benefits.

I can hand on heart say this so far is proving to be an amazing chapter in my life, the start hopefully of a second life. I am regularly told each visit how my tests are improving, I can physically feel my organs shrinking, my blood clots like normal now, I hardly ever bruise, where previously I had no idea how I had caused them. I no longer wake 3 times a night with spleen pain, there are so many small changes that I have noticed even at this early stage, and I would without any shadow of a doubt sign up again tomorrow.