Webinar Transcript

Accessing Emerging Treatments for Childhood Dementia

8 September 2023

[Kris - Childhood Dementia Initiative]

Hello everyone, welcome to our first childhood dementia research webinar. It's just turned 80'clock.

[Kris - Childhood Dementia Initiative]

And I can see people entering the webinar. I think I'll probably just get started though, we've a lot to get through this morning.

[Kris - Childhood Dementia Initiative]

So for those who don't know me, I'm Kris Elvidge, head of research at Childhood Dementia Initiative.

[Kris - Childhood Dementia Initiative]

Thank you so much for joining us. Before we get started. I'd like to begin by acknowledging the traditional owners of the various lands on which we meet today.

[Kris - Childhood Dementia Initiative]

childhooddementia.org
hello@childhooddementia.org

I'm joining you from Melbourne and acknowledge the Wurundjeri Woi Wurrung people of the Kulin nation, and pay my respects to their Elders past, present and emerging.

[Kris - Childhood Dementia Initiative]

In this webinar we're going to hear a case study of how the special access scheme was used in Australia.

[Kris - Childhood Dementia Initiative]

To gain access to an experimental drug for one patient with Lafora disease. You will hear from the biotech company, the treating clinician and the mother of the patient.

[Kris - Childhood Dementia Initiative]

To ask questions, you can type them in the QA box at any time. And we'll have time for questions at the end.

[Kris - Childhood Dementia Initiative]

Our first speaker is Vicki. Vicki is the co-founder and vice president of Parasaill, a clinical stage biotech startup based in Boston.

[Kris - Childhood Dementia Initiative]

In this role, Vicki oversees patient community outreach, drives program development and assists with both study design and general commercial management.

[Kris - Childhood Dementia Initiative]

Vicki is going to tell us about the experimental enzyme replacement therapy, VAL 1221 and Lafora disease.

[Kris - Childhood Dementia Initiative] 07:32:27

Over to you Vicki

[Vicki Wong] 07:32:31

Thank you, Kris. Give me just a few seconds so I can start sharing my screen.

[Vicki Wong] 07:32:53

Okay, can everyone? Kris, can you confirm that you can see my screen? I just want to double check before I start.

[Kris - Childhood Dementia Initiative] 07:33:02

No, we can't see it.

[Vicki Wong] 07:33:05

Oh, hold on just a second. Let's see. Here we go.

[Kris - Childhood Dementia Initiative] 07:33:17

Yes, that's better. Yes.

[Vicki Wong]

There we go. Perfect. Thank you so much. Oops.

[Vicki Wong]

Well, thank you so much for the introduction, Kris. And as she said, I will be speaking today on utilising the special access scheme.

[Vicki Wong]

Treatment of, VAL 1221 for a single patient with Lafora. And so just a quick company overview for those of you.

[Vicki Wong]

Who don't know us, Parasail, we are a clinical stage biotech startup and we are focused on developing innovative biologics for the treatment of rare neuromuscular and metabolic diseases.

[Vicki Wong]

We own all of our intellectual property and development rights to our entire product pipeline as well. And our technology platform utilises a novel antibody enzyme fusion designed to specifically degrade intracellular aggregates.

[Vicki Wong]

For today's purpose, we will be discussing our lead product, which is, VAL 1221 and that has been specifically designed to degrade glycogen and to degrade glycogen and polyglucosan aggregates.

[Vicki Wong]

And for those of you who don't know our company history specifically, Parasail was previously Valerion Therapeutics and when the opportunity arose to restart the company a large part of that decision was the opportunity to have patient focused leadership and patient-focused goals where we could really dedicate efforts to helping patients who have historically been vastly underserved by current treatment

[Vicki Wong]

options. And part of that effort has been utilising the special access scheme and other compassionate use programs.

[Vicki Wong]

As it's known in other countries, which we'll talk about in a few minutes.

[Vicki Wong]

So, just a little bit of detail on VAL 1221, our lead product and it's mechanism of action.

[Vicki Wong]

VAL 1221 is administered systemically by intravenous infusion and it's an antibody enzyme fusion with the unique ability to deliver full-length protein cargo.

[Vicki Wong]

Where then it is able to degrade intracellular aggregates and in the case of Lafora,those aggregates are called Lafora bodies.

[Vicki Wong]

So our antibody enzyme fusion is comprised of 2 main components, the Fab antibody and also an enzyme known as acid alpha-glucosidase.

[Vicki Wong]

otherwise known as GAA. And so it's through these 2 components.

[Vicki Wong]

That we also have a dual mode of, of uptake. I will move myself down here.

[Vicki Wong]

So the first mode of uptake is, cell internalisation of the enzyme GAA via the M6P receptor upon cell internalisation then the receptor directs, shuttles the enzyme directly to the lysosome.

[Vicki Wong]

Upon entry GAA then begins its glycogen aggregate degradation activity. The antibody portion is internalised through the ENT2 transporter also known as the equilibrative nucleoside transporter.

[Vicki Wong]

and this allows for additional glycogen clearance in the cytoplasm.

[Vicki Wong]

And the cytoplasm is just gelatinous fluid that fills all cells.

[Vicki Wong]

And so what's interesting is that this ENT2 transporter is highly upregulated in post mitotic cells, especially in cardiac muscles and skeletal muscles and also in the central nervous system.

[Vicki Wong]

And interestingly enough, in diseases where there is central nervous system pathology such as stroke and epilepsy, we see that there is an elevation of this transporter in the brain and at the blood brain barrier as well.

[Vicki Wong]

And so it's these 2 components that provide this dual mode of uptake, which then gives 1221.

[Vicki Wong]

It's unique targeting and treatment potential. So we have cell penetration through the antibody internalisation, providing active cytoplasm delivery.

[Vicki Wong] 07:37:29

We have brain targeting which takes advantage of disease specific changes in the transporter expression and also we have glycogen clearance through the GAA enzyme activity

[Vicki Wong]

Okay. And for those of you who aren't familiar with Lafora, I just wanted to give a brief overview of the disease as well.

[Vicki Wong]

It is an ultra rare form of progressive myoclonic epilepsy.

[Vicki Wong]

It's worldwide prevalence is approximately 4 and 1 million.

[Vicki Wong]

It is genetically based so it is an autosomal recessive disease and in most cases there is a mutation in one of 2 genes, either the laforin or malin genes and these mutations result in the buildup of Lafora bodies and they are poorly branched, poorly soluble but hyper phosphorylated glycogen aggregates.

[Vicki Wong]

And so the disease is hallmarked by recurrent seizures. Onset of symptoms typically start in late childhood or early adolescence.

[Vicki Wong]

Over time these seizures become worse and more progressive. And then as their seizures become worse, other clinical features also begin to show, which include difficulty walking, muscle spasms, and of course dementia.

[Vicki Wong] 07:39:00

And so what we're here to talk about today specifically is the special access scheme. And under the Australian Therapeutic Goods Administration, which is the equivalent of the United States Food and Drug

Administration, they say that generally therapeutic goods must be included in the Australian Register of Therapeutic Goods, the ARTG, before they can be lawfully imported into, supplied

[Vicki Wong]

In or exported from Australia. However, they do have the special access scheme mechanism which allows patients and physicians to access what they call unapproved treatments for a single patient on a case-by-case basis.

[Vicki Wong]

And one of the advantages to this special access scheme is that they allow any unapproved treatment regardless of its stage of development or whether a clinical trial has commenced

[Vicki Wong]

There are several categories to the special access scheme and in this case our patient Angelina fit under a category A which allows immediate access to patients who patients who are seriously ill

[Vicki Wong]

And to the right of the slide, this is actually an updated form. We had used a previous form.

[Vicki Wong]

I think they released this, the form soon after we had submitted the previous version, but it's very similar.

[Vicki Wong]

And so what we were responsible for was providing all of the product details of VAL 1221, its trade name, dose, strength, frequency and route of administration.

[Vicki Wong]

And so what was the process, challenges and benefits to this special access scheme? I wanted to highlight first just the key players that were involved and that was of course the family, the medical team, and then us, the biotech company.

[Vicki Wong]

All of us were really new to this process, the special access scheme. And so everyone really had to be willing and committed to pursue this process.

[Vicki Wong]

And it became clear early on that everyone was very willing and very committed and working in a really great collaborative effort.

[Vicki Wong]

And that is what really expedited this process overall. And so the challenges going into the special access scheme for us, it was mostly the unknowns, the unknowns of the Australian regulatory process in general, the unknowns of the customs importation process as well.

[Vicki Wong]

And then also the ethics committee approval timeline. This was our first foray into the Australian regulatory system.

[Vicki Wong]

So we really didn't know what was to come. And then of course drug availability, and that was the manufacturing timeline on our side.

[Vicki Wong]

And the benefits of course are obvious. I think, for critically ill patients just access to treatment that they otherwise would not have been able to receive.

[Vicki Wong]

And that's whether they perhaps may be ineligible for current clinical trials, but in this case it would have been you know having to wait for the clinical trial to start and you know who knows that could take months or years to begin.

[Vicki Wong]

And then from our perspective, also this was beneficial because it provided us insight into potential future development pathways in Australia.

[Vicki Wong]

So how does the special access scheme compare to other compassionate use programs? As far as the formal process is regarded, it was a fairly straightforward, formal process, which was really helpful.

[Vicki Wong]

It was really just the category A form, submitting that information and then allowing Dr. McDougall and his team to do their end and submit the program to the Australian authorities and then also in terms of customs.

[Vicki Wong]

They were really, they readily accepted the SAS. Documentation. We have come across challenges with other country customs processes where they have not been as willing to accept documentation or wanted to impose some sort of importation tax and we didn't see that with Australia.

[Vicki Wong]

So that was definitely an advantage as well. And then interestingly compared to the United States program, which is called the expanded access program, the US has a much longer formal process just in terms of the application, not only the application itself, but also the approval turnaround time.

[Vicki Wong]

And the FDA, the food and drug administration, also required a company to have IND approval and that stands for Investigative New Drug and that is typically required to have an IND approval before a company can begin a clinical trial.

[Vicki Wong]

So that was very, very involved as well. And so we are now currently registered on clinical trials.gov

[Vicki Wong]

under the intravenous VAL1221 Lafora Expanded Access Protocol known as LEAP

[Vicki Wong]

And that is our clinical trial program, if you'd like to look that up as well.

[Vicki Wong]

Yeah. So one of the questions I was asked was, actually how, what did we learn from this process and how could we potentially extend our knowledge to global access for other emerging therapeutics for childhood.

[Vicki Wong]

Dementia in general. This is a very tough question to answer because it's so broad.

[Vicki Wong]

Specifically speaking for our product pipeline potential, there is the opportunity to create additional antibody fusions to target protein aggregates in childhood dementia.

[Vicki Wong]

So there is potential there, for future antibody fusions to be made. Otherwise it really is.

[Vicki Wong]

Disease and therapeutic specific because countries have such different regulatory processes. So you really have to jump through those hoops I guess and that will be different for every country. And then also finding potential treatments for the target disease, the disease that you're trying to find treatment for.

[Vicki Wong]

And then of course getting all the key players involved. Is the patient and family willing to try the unapproved treatment?

[Vicki Wong]

Is the physician willing to try an unapproved treatment? Is a drug company willing to participate and do they have availability of the drug product on hand and how soon will that be ready.

[Vicki Wong]

So all of these factors come into play. It's a very broad question and difficult to simply copy and paste simply because every country's regulatory processes will be different and then of course depending on the drug in question and the drug company question you know they may or may not be willing to proceed down this path.

[Vicki Wong]

And so what are our future plans? We are a very, very small startup and so we will need to seek additional venture investments and partnering and we are also seeking additional grant opportunities.

[Vicki Wong]

We've been in the throws of that for the last few months and will continue to do so.

[Vicki Wong]

It's an incredibly tough economic climate right now.

[Vicki Wong]

So hopefully something will go our way in the near future. Given our positive experience with the special access scheme.

[Vicki Wong]

I think there's also the potential to explore a new sub-company in Australia and potentially take advantage of the positive drug development infrastructure that Australia has.

[Vicki Wong]

Just briefly looking into it, the government I think has is willing to provide some or partial reimbursement of you know clinical trials in Australia and there may be some grants as well that are available.

[Vicki Wong]

So that's definitely interesting and we will be looking into that as well. And then seeking funding to expand our products

[Vicki Wong]

In a pipeline for other aggregate based diseases and childhood dementia as well.

[Vicki Wong] 07:48:00

So that's it for today. I just wanted to say thank you to everyone and to the Childhood Dementia Initiative for including us in this conversation.

[Vicki Wong]

We've, in what little spare time we have, done a little bit of research into your work and I'm so impressed by the progress that you guys have made and look forward to.

[Vicki Wong]

What your work will be in the future and then to Dr. Allen McDougall and the team at Liverpool Hospital.

[Vicki Wong]

We can't say enough about the great collaborative environment that you guys have provided for us.

[Vicki Wong] 07:48:38

So that's been really great. So thank you for that. And then last but not least, the Markou family.

[Vicki Wong]

Niki and Angelina. We just want to thank you for your patience and for your trust in this process as well.

[Vicki Wong]

So thank you very much. Back to you Kris.

[Kris - Childhood Dementia Initiative]

Thanks Vicki. So moving on now to our second speaker. We have Dr. Alan McDougall

[Kris - Childhood Dementia Initiative]

who trained at Royal Prince Alfred Hospital in Sydney and the National Hospital for Neurology, Queen Square London.

[Kris - Childhood Dementia Initiative]

He also gained a PhD from Sydney University. Dr. McDougall has been a staff specialist in neurology department at Liverpool Hospital in Sydney since 1997 and head of the neurology department there since 2007

[Kris - Childhood Dementia Initiative]

Dr. McDougall is going to tell us about the challenges of obtaining this new and unregistered treatment through the special access.

[Kris - Childhood Dementia Initiative] 07:49:40

Over to you Dr McDougall

[Dr Alan McDougall] 07:49:43

Thank you very much, Kris and thanks for the invitation to speak. I'll just make that full screen. Is that working now?

[Dr Alan McDougall] 07:49:54

You can see my screen?

[Kris - Childhood Dementia Initiative] 07:49:54

Yes, just to go to the slide show. Yep, that's it.

[Dr Alan McDougall] 07:49:59

All good, yeah, okay, thanks. And, So again, thanks for asking me to speak, Kris.

[Dr Alan McDougall] 07:50:04

And, and again, I'd like to thank Vicki and her team at Parasail and Dustin and of course the Makou family and Niki sitting right here next to me.

[Dr Alan McDougall] 07:50:15

So we'll just go through things. So, just a little bit of background about Angelina.

[Dr Alan McDougall]

So Angelina is currently aged 19. She was previously a very healthy, well young lady, an A-grade student, very physically active.

[Dr Alan McDougall]

In 2018 about the age of 14 there was the onset of seizures with initially eyelid flickering and unresponsiveness.

[Dr Alan McDougall]

She then developed myoclonic jerks and then more generalised seizures. Her EEG, brainwave test was very abnormal and I can show you that. The MRI scan looked normal.

[Dr Alan McDougall]

And given that Angelina was 14, she was initially investigated and the diagnosis was made at one of our children's hospitals.

[Dr Alan McDougall]

But at the age of 17, Angelina's care was transferred to the adult hospital under my care. So that's just a picture of

[Dr Alan McDougall]

Angelina's EEG, which shows a lot of abnormal electrical activity, which shouldn't be seen and that's indicative of seizures.

[Dr Alan McDougall]

In terms of progress, initially, Angelina was tried at the children's hospital on multiple anti-seizure medication, but unfortunately that didn't stop all of her seizures.

[Dr Alan McDougall]

Other problems came along, so intellectual and cognitive function wasn't as good. Her grades at school.

[Dr Alan McDougall]

Were getting worse. She had emotional issues. She was more emotional. Some problems with memory and then also over time there were problems developing around speech in terms of slowing.

[Dr Alan McDougall]

Of speech and slurring of speech and then movement problems with difficulties running and difficulties walking. And obviously, you know, this was a great concern to the children's hospital and to the family and multiple.

[Dr Alan McDougall]

Tests were done. And then a gene test confirmed Lafora disease, which as Vicky's already said is a problem with glycogen or glucose build up, particularly in the central nervous system and brain but in other organs as well.

[Dr Alan McDougall]

And this disease, as we've already heard, is rare. It comes on suddenly in late childhood or adolescence with seizures followed by progressive neurologic decline with impaired thinking and memory, emotional disturbance, movement problems, balance problems, speech problems.

[Dr Alan McDougall]

Sometimes or often with visual impairment as well and unfortunately this you know is a progressive disease which leads to early death.

[Dr Alan McDougall]

The treatment up until now really has been to treat seizures. And with anti-seizure medications and symptomatic treatment around behaviour and movement.

[Dr Alan McDougall]

There's been no specific treatment available for the disease unfortunately. Just a little bit more background about Lafora Disease. So way back in 1911, doctor Rodriguez Lafora.

[Dr Alan McDougall]

Described in patients with this sort of illness, inclusion bodies, which he found in many tissues when the tissues were examined, including the brain.

[Dr Alan McDougall]

The disease was actually better described in 1965 by doctors Schwarz and Yanoff. In 1986 a good test was worked out which was an axillary skin biopsy.

[Dr Alan McDougall]

So that’s an armpit skin biopsy, particularly looking at sweat glands where you can see accumulation of these Lafora bodies and I'll show you a picture of that in a second. In the 1990s, with advances in genetics, the genetic abnormality was identified and the cause identified.

[Dr Alan McDougall]

And as Vicki's already told us, the Lafora bodies are abnormal glycogen or sugar accumulation.

[Dr Alan McDougall]

Due to a defect in the enzymes which break them down, a genetic defect. And normally the sugar or glycogen serves as a store of energy in many tissues including the brain but when this glycogen accumulates too much it actually damages the cells and causes cell death.

[Dr Alan McDougall]

And hence the disease symptoms that we have heard about. This is a microscopic picture of a sweat gland from the axillary skin biopsy and you can see with the arrows these little I guess they're purpley coloured.

[Dr Alan McDougall] 07:54:52

Bodies or dots they shouldn't be there, they're the actual Lafora bodies. So they're the accumulation of the glycogen and before we had the gene test available that was how the diagnosis was made by doing a skin or auxiliary biopsy and looking under the microscope to see these, Lafora bodies.

[Dr Alan McDougall]

Okay, so back to Angelina. In 2020 she was transferred to Liverpool Hospital, the adult hospital and as we've heard already she had severe epilepsy with generalised seizures. Absence seizures and myoclonic seizures.

[Dr Alan McDougall]

Progressive decline in her thinking and memory function and decline in other neurologic functions like movement and mobility, and speech and general physical function.

[Dr Alan McDougall]

Vicki has already given us a lot of information about the VAL1221 medication.

[Dr Alan McDougall]

So this was developed by her company and the preceding company. And as we heard, it's an antibody enzyme fusion drug.

[Dr Alan McDougall]

It's given via intravenous infusion. So in Angelina's case, she's getting an infusion.

[Dr Alan McDougall]

Every 2 weeks. Initially, of course, the company would have performed animal studies to show safety, tolerability and effect in animals.

[Dr Alan McDougall]

We were very lucky in this situation in that the company had already done a trial in humans.

[Dr Alan McDougall]

For a different disease. So there's another disease associated with sugar or glycogen buildup called Pompe disease, which is different from the disease we're talking about today.

[Dr Alan McDougall]

And this is a muscle disease. And this medication had been tried in people with Pompe disease.

[Dr Alan McDougall]

So we knew that it was safe to administer to humans and I think this was very vital in terms of getting a medication approved and used because I think it would have been very difficult if we'd had no human safety data.

[Dr Alan McDougall]

I think it would have been really probably impossible from our point of view to do that. This medication.

[Dr Alan McDougall]

Or, this drug therapy had been identified by Angelina's mom, Niki, probably before I met Niki and Angelina and she'd written to the our federal health minister, Mr. Greg Hunt, MP to seek approval to use.

[Dr Alan McDougall]

And I'll just show you the reply. He forwarded that onto the therapeutic goods administration which Vicki's mentioned about and I think it's good just to go through the reply that came from the TGA.

[Dr Alan McDougall]

So, you know, the first thing they said was the Australian government is committed to ensuring that Australians can access the most safe and effective medical treatments.

[Dr Alan McDougall]

As we've heard, medications being used in Australia must be included on the register of therapeutic goods which is administered by the therapeutic goods administration.

[Dr Alan McDougall]

Now that's really for drugs that are widely available and have been, you know, very well studied.

[Dr Alan McDougall]

So this medication which is experimental is certainly not under that category and would require, to get on that category, would require further investigation in clinical trials.

[Dr Alan McDougall]

However, there are times when approved and available products may not meet the needs of all patients and situations. So it was certainly the case in Angelina's situation because there were no treatments that were shown to have any benefit in this condition affecting the history of the condition.

[Dr Alan McDougall]

So there are provisions in the Australian regulation such as the special access scheme or SAS. To allow doctors and patients access,in inverted commas, unapproved treatments from overseas.

[Dr Alan McDougall]

And the SAS refers to arrangements that allow health practitioners to access an unapproved therapeutic.

[Dr Alan McDougall]

Medication or good for a single patient on a case by case basis. So it wouldn't be available in this situation to do a large trial of multiple patients but for a single patient we could potentially access a medication or therapeutic agent.

[Dr Alan McDougall]

There's and I won't bore you with the next one, but there's different pathways.

[Dr Alan McDougall]

Category A, category B. I think there's also a category C depending upon how much research had been done into the drug and the severity of the patient's condition.

[Dr Alan McDougall]

So we'll focus on the category A, which is, how we achieve this medication. And this can be used by medical practitioners to allow.

[Dr Alan McDougall]

Immediate access for patients defined as seriously ill, with a condition from which death is reasonably likely to occur within a matter of months or from which premature death is reasonably likely to occur in the absence of early treatment.

[Dr Alan McDougall]

So I think that was what allowed us to get access to this medication on the SAS. The next step is that the importation could be arranged by a doctor, a pharmacist, a hospital, patient or appropriate wholesaler or importer.

[Dr Alan McDougall]

They also mentioned that the importers should check whether there's any additional restrictions on the importation of the product.

[Dr Alan McDougall]

And the other Australian legislation such as by the Security Act and the Gene Technology Act. That wasn't an issue for us and didn't apply, thank goodness.

[Dr Alan McDougall]

They also mentioned in the letter from the TGA that the special access scheme is reliant on the pharmaceutical company being able to supply the product to Australia.

[Dr Alan McDougall]

And that's likely to depend on its stage of development and other considerations. And the TGA administers this scheme to facilitate access to the so-called unapproved medications.

[Dr Alan McDougall]

But it is not involved with the actual supply or the cost of the goods. So, there is obviously a cost implication for bringing these medications into the country.

[Dr Alan McDougall]

Both the cost of the medication as well as the cost of shipping, and then obviously administration, etc.

[Dr Alan McDougall]

And then just in terms of the rest of the letter, that our pharmacy be in contact with the company Enable Therapeutics, it was called Enable Therapeutics at that time. The pharmacy would need to confirm if Enable Therapeutics were able to supply the medication and whether this can

[Dr Alan McDougall]

be done under a compassionate access or other program and you know depending upon the cost and obviously a decision to grant access to such programs would be made by

[Dr Alan McDougall] 08:01:42

The company. So there's, you know, there's a lot of discussion and information needs to be aware.

[Dr Alan McDougall]

We have a lot of help from our hospital pharmacy with the SAS application. But in fact the SAS application was probably the easiest part of this whole process.

[Dr Alan McDougall]

You know, the drug had been used in humans. It was safe. Been shown to be safe.

[Dr Alan McDougall]

You know, the company were willing to work with us. We were willing to work with the family, with Niki and Angelina and the company to try and see if this would benefit Angelina.

[Dr Alan McDougall]

So the SAS actually was the least of our problems in terms of doing this.

[Dr Alan McDougall]

There was obviously multiple correspondence back and forth about shipping. How it should be shipped, shipping costs, storage, how it should be stored.

[Dr Alan McDougall]

How it should be prepared by pharmacy and administration. And you know it is difficult, not difficult, but there is a burden on the family.

[Dr Alan McDougall]

The drug is administered every 2 weeks via intravenous infusion. So Angelina, Niki and the nurses have to come in.

[Dr Alan McDougall]

To the hospital to our infusion centre every 2 weeks and stay for 4 or 5 h. So it is a significant time burden.

[Dr Alan McDougall]

There's also, you know, the burden on the hospital in terms of having that infusion centre available and our nursing staff and supplies etc but obviously we're happy to support that as best we can.

[Dr Alan McDougall]

Hospital pharmacy was fantastic in terms of working with us with the SAS application and with importation storage and preparation and administration of the medication.

[Dr Alan McDougall]

But the other important thing was we needed approval of course to use this medication because this had never been used in this condition.

[Dr Alan McDougall]

Medication wasn't available in Australia. So there was a lot of discussion with your colleagues at the hospital with the doctors in charge of the infusion centre and with our hospital clinical ethics committee to make sure that you know we were doing the right thing and that it was above board to be doing this and we very lucky that everyone was very supportive around this, recognising that, you know, this Lafora body disease is

[Dr Alan McDougall]

terrible and you know this would be potentially of benefit to Angelina. So after all of that, Angelina received her first dose of medication in June.

[Dr Alan McDougall]

Of 2022 last year. Currently she has had 30 infusions, maybe 31, I'd have to count them up. Every 2 weeks.

[Dr Alan McDougall]

In the ambulatory care unit. Infusions last 4 or 5 h. They were well tolerated.

[Dr Alan McDougall]

We've seen no problems at all with the infusion. We've been monitoring routine blood tests and blood pressure and all other parameters and there have been no issues seen with that.

[Dr Alan McDougall]

In fact, it's been a very easy medication to administer apart from the time burden, with no problems from our side.

[Dr Alan McDougall]

Now how's Angelina gone on this? Well, you know, for one patient, it's very hard to.

[Dr Alan McDougall]

To prove a benefit or to prove that it doesn't work but you know we feel that her functional capacity such as feeding herself, speed of walking.

[Dr Alan McDougall]

The speed of doing tasks like dressing yourself, etc, seem improved. Her gait is better, she can run.

[Dr Alan McDougall]

Whereas previously, you know, she could only walk. So we've certainly seen improvement there. We think that her cognitive function improved.

[Dr Alan McDougall]

She was more alert and she seemed to be remembering more things. So, you know, I think from those sides we would be very.

[Dr Alan McDougall]

Positive, that we think that there has been benefit but of course we can't prove that based on one patient.

[Dr Alan McDougall]

Unfortunately, however, seizures do remain an ongoing problem and really are still a significant issue and Angelina's on a lot of anti-seizure medication which you know itself can cause problems.

[Dr Alan McDougall]

So we're seeing benefit in some things, but perhaps not in the seizures, would be, I guess, my clinical view of this.

[Dr Alan McDougall]

So what have been the challenges? Well, The first step obviously is to identify which medication might be a benefit in, you know, a particular condition.

[Dr Alan McDougall]

And all of that hard work was done by Angelina's mum, Niki, who's going to speak next.

[Dr Alan McDougall]

So once that was identified that there was a potential medication which might be beneficial in clearing the glycogen or sugar buildup.

[Dr Alan McDougall]

We, we then need to work out how to do this. The other challenge of course is the cost of the medication.

[Dr Alan McDougall]

So you know there's a cost of shipping, a cost of customs, there's also the cost of the medication itself depending upon, you know, what arrangements are made with various companies.

[Dr Alan McDougall]

Challenges in terms of shipping the medication to make sure it was not damaged or degraded in its shipping in terms of temperature, storing it in our pharmacy, also in terms of preparation.

[Dr Alan McDougall]

There needs to be a little bit of preparation in our pharmacy in terms of getting the medication ready each fortnight for Angelina.

[Dr Alan McDougall] 08:06:58

And then of course there's challenges around administering it. So we needed approval from the hospital that we can do this, from the ethics committee and from various other groups such as our infusion centre doctors.

[Dr Alan McDougall]

There is of course a large burden on the patient Angelina, she has to come in for 4 or 5 h every fortnight.

[Dr Alan McDougall]

Burden on family, Niki and the rest of the family in terms of bringing her in every fortnight.

[Dr Alan McDougall]

There's obviously a need for hospital resources to do this so we're only managing one patient you know, I think it would be very difficult if there were more than one patient on this.

[Dr Alan McDougall]

Therapy but you know it's certainly for one person we can accommodate that and really I think from our side the special access scheme was not a barrier in getting this medication.

[Dr Alan McDougall]

However, it would have been a barrier if there hadn't been human trials. I think our ethics committee would not have approved that if there weren't human trials, I think our ethics committee would not have approved that if there weren't human trials.

[Dr Alan McDougall]

The other challenge for a single patient of course is assessing the outcome. And the effect of treatment. And that's very difficult on one patient, but I know I know Parasail are looking at doing more trials and Vicki's already spoken about that on larger number of patients which I think would be beneficial.

[Dr Alan McDougall] 08:08:12

And that was the end of my talk there. Okay.

[Kris - Childhood Dementia Initiative] 08:08:20

Thank you. Dr. McDougall. That's great.

[Kris - Childhood Dementia Initiative] 08:08:24

So, lastly, we're going to speak with Niki Markou. Thank you so much for joining us Niki.

[Kris - Childhood Dementia Initiative] 08:08:34

I know it's a tricky day for you. Niki is super mom to Angelina.

[Kris - Childhood Dementia Initiative] 08:08:39

She also serves as the director of family support for the US based patient organisation, Chelsea's Hope Lafora Children Research Fund.

[Kris - Childhood Dementia Initiative] 08:08:51

She's also been an incredible family advocate for CDI, inputting to many of our programs and also raising awareness through videos, one of her videos now has over 4 million views.

[Kris - Childhood Dementia Initiative] 08:09:05

Which has done incredible things for improving awareness of childhood dementia. And she's also been featured in a recent documentary called Fighting the Rare about Lafora disease, which is an awesome documentary.

[Kris - Childhood Dementia Initiative] 08:09:19

I recommend you watching it. So, Niki. How did you find out about the medication and get the balll rolling?

[Niki]

Hi, Kris.

[Niki]

We were doing research and with Chelsea's hope, there was a webinar where Vicki and Dustin from, now Parasail (they were Enable), they did a webinar to tell us about that.

[Niki]

Also with the researcher Matthew Gentry, and they explained to us the benefits.

[Niki]

So I reached out to Vicki, found some more information and then passed that on to Dr.

[Niki]

McDougall. And also I spoke to yourself, Kris, and said, what can I do?

[Niki]

How can I get approval in Australia? And you advised me to email the Health Minister.

[Niki]

So I did that and got a positive response, which was great. I couldn't believe it.

[Niki]

I, you know, so I passed all that information on to Dr. McDougall and everyone worked together.

[Niki]

We all worked as a team. And it all worked out. If that's the best way to put it?

[Kris - Childhood Dementia Initiative]

Yeah. It's been an amazing effort and a lot of persistence from everybody involved.

[Kris - Childhood Dementia Initiative]

And obviously this isn't possible for everybody because a lot of stars need to align for this to happen.

[Kris - Childhood Dementia Initiative]

Including probably, the biggest problem is often the company having drug available that they are willing to supply.

[Niki]

Yes.

[Kris - Childhood Dementia Initiative]

So, what would you say have been the hardest parts for you?

[Niki]

Maybe putting it together. Having many phone calls or emails or trying to find a way. But then yeah, when we got the green light I think it was, the challenge was getting the drug to Australia, that was the challenge.

[Niki]

And it was very stressful the whole time it was in the air. I was like, oh my god, please stay okay.

[Niki]

It was very, it was quite funny. But, it did get here, but that was, the time, the time was very challenging, the waiting game.

[Niki]

Because with Lafora disease, you know, every day counts. They progress quite quickly. So like, hurry up, hurry up.

[Niki]

Because of course, you know, the quicker you get it to them, the more likely that the disease will slow down or you know not make as much damage.

[Niki]

So yeah it was the, it was the waiting.

[Kris - Childhood Dementia Initiative]

And you have been very open about the fact that Angelina has been able to access this medication. Have you had

[Kris - Childhood Dementia Initiative]

A lot of families contact you and wanting to know how it's going.

[Niki]

Yes, I've had a lot of families contact me all the time. They still contact me all the time and you know they want, you know, evidence. But you know it was very hard.

[Niki]

We never had evidence other than to show that it was safe. So we, you know, someone had to be first on the dance floor and we were, and I just hope other other countries can do that too for patients just like Angelina.

[Niki]

Someone has to do it first. And sometimes there isn't enough evidence you know but if it's safe why not give it a go. Because I think it's worth giving it a go.

[Niki]

You've got nothing to lose. I mean, this is, you know, a terminal disease.

[Niki]

You know, they're progressing. Why not try and see if you can change their timeline and give them a better quality of life.

[Niki]

I believe Angeline has had a better quality of life. She's still walking and talking. She could have been wheelchair bound or bed bound by now.

[Niki]

And I think physically she is stronger. She's still very strong and I believe it is because of the infusion.

[Niki]

So to me she's had a better quality of life.

[Kris - Childhood Dementia Initiative]

And what would your advice to families be?

[Niki] 08:13:25

To give it a go. You know, make those calls. Talk to the doctors.

[Niki]

Contact your governments and see what you can do, how you can get it in your country or, you know, to see if there are, you know, to see if there is a drug out there.

[Niki]

So do your research, contact companies. Or, you know, Kris, you were a lot of help for me.

[Niki]

I emailed you a lot of times, called you a lot of times to see if you think this is a good idea, do you think this could work or if I didn't understand it, a process, I called you.

[Niki]

So that was, you know, that was very helpful. So educating yourself, finding out what it means, and understanding it to see if it is a pathway.

[Niki]

For your child.

[Kris - Childhood Dementia Initiative] 08:14:11

Yeah, I think your international networking capability has been an amazing benefit. And that's a credit to you.

[Kris - Childhood Dementia Initiative]

And is there anything else you wanna add before we move on to questions?

[Niki]

Stay hopeful, be positive, try, it doesn't hurt and take away what you can from this webinar.

[Niki]

If there's any questions that we haven't answered that we can, we can do that afterwards.

[Niki]

But I'm very thankful that it worked out really well for Ange getting the access to this treatment.

[Niki]

Thank you to Dr. McDougall and Vicki, many phone calls with Vicki to try and find a way.

[Niki]

Because as you said, it was the first time. So we had to work together. So working together as a team was the most important thing, you know, finding a way.

[Niki]

Because I believe there's always a solution to every problem. And you just have to try.

[Niki]

And if you can. If it works, it works. And thankfully it worked for us.

[Kris - Childhood Dementia Initiative]

Okay, thank you Niki and thanks so much for your insight and thanks for joining us. So now if you wouldn't mind turning your camera on and start going through some questions

[Kris - Childhood Dementia Initiative]

And so the first question that's come up in the question and answer box is from Lisa.

[Kris - Childhood Dementia Initiative]

And she asks, is data being collected as it would be in a formal clinical trial with standardised test, validated outcome measures etc.

[Dr Alan McDougall]

I could answer that. So yes, we are. We're looking at seizure diary.

[Dr Alan McDougall]

We're looking at functional assessments such as measures of walking speed and other functional things. As well as, cognitive assessment.

[Dr Alan McDougall]

So yes, we are doing that, but you know, with one patient, it's very difficult to.

[Dr Alan McDougall]

To know how that would compare to not being treated. So that's why, you know, we need larger trials as Vicki and her company are organising.

[Kris - Childhood Dementia Initiative]

There's a question from Simone but I think that might be better for maybe Vicki to address after the talk, because

[Kris - Childhood Dementia Initiative]

I think it is a very individual question, rather than general. So, a question from Glenn Bennett.

[Kris - Childhood Dementia Initiative]

How long did it take from finding the drug, doing the paperwork to the first delivery of the drug?

[Niki]

9 months. I think I started talking to Vicki in about October. And I started, yeah, making the negotiations and then.

[Dr Alan McDougall]

June was the first one.

[Niki]

For the first drug, was that when it was? Or finding the drug.

[Dr Alan McDougall]

The first infusion was June 22. Yeah. So 9 months.

[Niki]

So it was it was long in, I mean it feels short, but when you're waiting it feels very long.

[Niki]

And you know, with a Lafora disease patient, it does feel. Yeah. And I think that was a short timeline compared to a lot of other processes.

[Niki]

I know a lot of international families had a lot longer timeline. Like even the US, I think they only just got approval.

[Niki]

This year. So I feel quite fortunate that it was only 9 months, even though it felt very long, but it can take a lot longer.

[Kris - Childhood Dementia Initiative] 08:17:56

So yeah, a question from Danny. If the Pompe phase 1, 2 trial and safety data was not available.

[Kris - Childhood Dementia Initiative] 08:18:06

Would it have been possible to take some additional steps and then go through the

[Kris - Childhood Dementia Initiative] 08:18:14

Special access scheme?

[Dr Alan McDougall] 08:18:17

Can I answer that? Look, I think that would have been very difficult and practically impossible in that situation.

[Dr Alan McDougall] 08:18:26

I don't think that the special access scheme would necessarily have been a problem but our hospital and our ethics committee would not have approved.

[Dr Alan McDougall] 08:18:34

Use of the medication that hadn't been shown to be safe in humans. So I think it would we couldn't have done that unless there was already human safety data.

[Dr Alan McDougall] 08:18:45

We're not in a position to do what's called a phase one or phase 2 trial looking at safety and tolerability of a medication.

[Dr Alan McDougall] 08:18:54

A new medication, that wouldn't have been possible. We would have needed that data first before we could have administered it.

[Kris - Childhood Dementia Initiative] 08:19:03

And Rose Mooney asks, what's the first step if you're interested in finding medication that your child might be able to access.

[Niki] 08:19:16

Contact whoever it is that you found that information, email them, contact them, call them, get advice of someone.

[Dr Alan McDougall] 08:19:24

Who understands the data. Or, you know, someone in the medical field. Like me, I spoke to you Kris and I spoke to Dr. McDougall

[Dr Alan McDougall] 08:19:34

How do you find a drug? How do you even know it exists?

[Niki]

Oh, well, because we had the webinar.

[Dr Alan McDougall] 08:19:39

So our Lafora disease researchers and experts told us about it and because it was in the pipeline beforehand. And then of course Vicki said that the company went down and they took over the assets.

[Dr Alan McDougall] 08:19:54

And that and we knew about that. So that was, public knowledge that we had known about.

[Kris - Childhood Dementia Initiative] 08:20:02

And who feels in the SAS for?

[Dr Alan McDougall] 08:20:06

Our pharmacists were very helpful in doing that. But, the actual form is not that complicated.

[Dr Alan McDougall] 08:20:14

I mean, I, the doctor could have filled that in, but we had great help from our head pharmacist at the hospital.

[Kris - Childhood Dementia Initiative] 08:20:20

Yeah. Yeah, from what I hear, the SAS form isn't that difficult.

[Kris - Childhood Dementia Initiative] 08:20:26

It's all the other logistics around it that take more effort

[Dr Alan McDougall] 08:20:28

Yeah. Yeah.

[Dr Alan McDougall] 08:20:36

But I should say that apparently patients and family can also fill in an SAS form apparently looking at the legislation.

[Dr Alan McDougall] 08:20:44

This is my first experience with using SAS. I'm not an expert, but just reading the legislation, I think.

[Dr Alan McDougall] 08:20:51

There's a wide range of people who could do that, Kris, yeah.

[Kris - Childhood Dementia Initiative] 08:20:55

Yeah.

[Kris - Childhood Dementia Initiative] 08:21:01

To Vicki and Allen, how much time did it pass till you saw any improvement in Angelina

[Dr Alan McDougall] 08:21:11

It's a very good question. I think there was like slow continual improvement, you know, after maybe after a few months after maybe 6 to 8 weeks we might have started to see some benefit in my view but again with a patient of one number of one trial, it's very difficult to say that but that would just be my personal view.

[Dr Alan McDougall] 08:21:33

Niki, what do you think?

[Niki]

Yeah, I think so. That sounds about right. We saw in about 6 to 8 weeks that, you know, every time she had the infusion, she was a bit more, she was quicker or she showed an ability that she hadn't done for a while.

[Niki] 08:21:44

Which was great to see.

[Kris - Childhood Dementia Initiative] 08:21:55

Just trying to, there's so many questions coming in the chat now. I'm trying to think.

[Kris - Childhood Dementia Initiative] 08:22:01

I think we've got time for about one more. There's a few questions coming in, about specific.

[Kris - Childhood Dementia Initiative] 08:22:08

Countries being able to access the drug. So I think I might pass those onto Vicki after the meeting and you can answer those ones.

[Kris - Childhood Dementia Initiative] 08:22:17

Individually and we can circulate those answers.

[Kris - Childhood Dementia Initiative] 08:22:26

Okay.

[Kris - Childhood Dementia Initiative] 08:22:32

I guess, there's been quite a few questions about who pays for what. So.

[Kris - Childhood Dementia Initiative] 08:22:39

I guess it's very, it's different, it'd be different in each, case, but I don't know if anyone wants to.

[Kris - Childhood Dementia Initiative] 08:22:47

Answer that in a general sense.

[Niki] 08:22:50

Well, I suppose I can answer that. It depends on your country. Sometimes governments can have grants that you can.

[Niki] 08:22:58

To help fund it, or you can just do crowdfunding yourself. So I did some crowd funding to help.

[Niki] 08:23:06

With the cost.

[Dr Alan McDougall] 08:23:08

But yes, it's sort of more on, depending on every scenario is different. But in my case it was dependent on the cost that I could provide to help.

[Kris - Childhood Dementia Initiative] 08:23:19

And also the hospital covers the costs of the treatment.

[Dr Alan McDougall] 08:23:23

Yes. Yes, so in Australia the hospital care is covered by, by the government so there's no cost to Angelina or Niki in terms of the hospital side.

[Dr Alan McDougall] 08:23:34

It was the supply of the medication, was the cost. Yes.

[Kris - Childhood Dementia Initiative] 08:23:38

Okay. I'm sorry to those people whose questions we haven't got to, but, we will address them.

[Kris - Childhood Dementia Initiative] 08:23:46

Thank you so much for all of your great questions. Thank you all for joining us today.

[Kris - Childhood Dementia Initiative] 08:23:58

Feel free to email me. My email address is on the slide there.

[Kris - Childhood Dementia Initiative] 08:24:06

If you have any further questions or comments. You can also scan the QR code there, for several opportunities to get involved in childhood dementia research.

[Kris - Childhood Dementia Initiative] 08:24:18

The next webinar is planned for the 31 October, which will be about the use of organoid models.

[Kris - Childhood Dementia Initiative] 08:24:24

for childhood dementia. We'll send out the details soon. You'll receive a link to a survey by email.

[Dr Alan McDougall] 08:24:27

Hmm.

[Kris - Childhood Dementia Initiative] 08:24:32

We would be grateful if you could give us some feedback on this webinar. And finally, a shameless bug for a couple of events we have coming up.

[Kris - Childhood Dementia Initiative] 08:24:42

Twentieth September is childhood dementia day and we're asking people to paint their faces, make it colourful and share it on social media.

[Kris - Childhood Dementia Initiative] 08:24:52

You can see more information about that on our website. And also we have a track coming out in November.

[Kris - Childhood Dementia Initiative] 08:25:02

For anyone who would like to get involved in that. Thank you all for your time. Thanks so much to our speakers today.

[Kris - Childhood Dementia Initiative] 08:25:09

So great to have you.

[Kris - Childhood Dementia Initiative] 08:25:17

Thank you all and we'll see you next time.

[Dr Alan McDougall] 08:25:20

Thank you.

[Kris - Childhood Dementia Initiative] 08:25:22

Thank you.

[Vicki Wong] 08:25:22

Thanks for having me. Bye.

[Dr Alan McDougall] 08:25:24

Thank you.

childhooddementia.org
hello@childhooddementia.org