

Rachael McCormack, Founder of Societi Foundation talks to Professor Despina Eleftheriou about the latest research into Kawasaki Disease treatment.



Professor Despina Eleftheriou, Professor of paediatric rheumatology, infection, immunity and inflammation at UCL Great Ormond Street, Institute of Child Health is the lead clinician in the largest and single greatest clinical trial in Europe for Kawasaki Disease treatment – the

biggest scale trial in a generation. Despina talks to us about the trial and the potential for transformational outcomes for children with Kawasaki Disease.

Rachael: Welcome Despina. You are the lead clinician in the largest clinical trial for Kawasaki Disease treatments in a generation – the KD-CAAP trial. It's got a great name! So, can you tell us what KD-CAAP is and just how significant the trial is?

Despina: Thank you very much Rachael, and thank you for inviting me to do this interview. KD-CAAP is an acronym we're using that stands for Kawasaki Disease Coronary Artery Aneurysm Prevention trial and it's a trial that Professor Paul Brogan and I are leading. We will aim to recruit 262 children with Kawasaki Disease and run the trial across Europe in a number of different countries including in the U.K.

What we're doing with KD-CAAP is trying to establish whether it's safe and it's effective to use corticosteroids, otherwise known as steroids, in addition to standard care, which is IVIG and aspirin, to try and prevent coronary complications in children with Kawasaki Disease. If we show that this is an effective and safe treatment approach, we can then use steroids and change clinical practice to use them for all children with Kawasaki Disease across Europe. If this works, we can prevent coronary complications and we can change the outcomes for the hearts of hundreds of children across Europe.

Rachael: You mention coronary artery aneurysms – that's the most serious complication of Kawasaki Disease isn't it. So, why steroids? What led you to believe that they could help in the treatment of this most serious consequence?

Despina: Steroids makes sense because they've been used to treat other inflammatory conditions for years, so we know they're effective and safe. We also know that children in Japan, where Kawasaki Disease is of increased frequency, have benefitted from steroid use upfront. I think it's really time we see if this very simple approach – it's a medicine you take by mouth and it's a very cheap medicine – works for our children in the U.K. and in Europe.

Rachael: It's really interesting to know that we're drawing on the expertise and proven treatment approaches elsewhere and it seems that they are relevant to our European children. But it's not always the case, is it? So, this trial is very important. What do you think it could mean for children affected by Kawasaki Disease in the future if the trial approves what you believe it might?

Despina: Yes, Rachael, I really want to emphasise why this trial is important and why we developed the trial as well. A number of different studies arising from a number of different countries across Europe have really highlighted that the rate of coronary complications in children with Kawasaki Disease, are much higher than we had previously appreciated. This is no longer acceptable; we need to change this, and we really need to develop better treatment. If we prove that steroids – as I say they are very cheap and a very simple intervention. We can give steroids by mouth, children can take them at home if need be and it's a cost effective intervention – we can change the rate of coronary complications and can prevent these children's hearts from being affected. We now know that essentially these heart complications – the coronary artery aneurysms – are the one single defining factor of long-term outcomes for children with Kawasaki Disease. If we can address that and reduce the coronary complications, we can give these children's hearts a better future.



Rachael: *Kawasaki Disease is of course the leading cause of acquired heart disease in children isn't it? So, finding a treatment that can prevent the very serious heart damage that happens for too many children, seems to be absolutely critical and a phenomenal driver for your work. Within the clinical trial, there's obviously a lot going on – you've talked about a number of hospitals involved across Europe. It's obviously a big scale clinical trial. How long is it going to take and when will we know if what doctors are looking at, at the moment in terms of using steroids, is an effective treatment for children with Kawasaki Disease?*

Despina: I want to emphasise that clinical trials involve a number of different people, and they take a lot of organisation and there's a lot of work that goes into trying to get centres up and running recruiting patients. We're very thankful to the conect4children network which is a pan-European network supporting clinical trials in paediatrics that has taken this on. I'm also very grateful to Sara Walker, Cara, Helen and Yolanda from the MRC Clinical Trials Unit for really looking into the everyday conduct of the trial. A number of co-investigators and very importantly Rachael, I want to thank you for getting all the right people round a table to actually design and prepare this clinical trial years ago. So there's a lot that happens before a clinical trial starts recruiting. We need 262 children. We got our first patient in January 2021, and we need three or four years of recruitment. We're hoping to be recruiting until 2024 and we will see the analysis of the results at that stage. We'll be able to share this with the community, scientists, colleagues and very importantly with patients and families as well.



Rachael: *Fantastic! It's a long-term programme of work and I remember very clearly, the conversations that we had – the very first conversations about the prospect of this trial in May 2016 at your offices Despina, together with valued colleagues. We wrestled with – if we were going to put our collective muscle behind pursuing some research – what should it be?! And KD-CAAP was very much the result. You've led, since that time, a very broad team of clinician's and statisticians and data specialists and trial specialists – brilliant people, all of them – that has allowed this to come to fruition. And you're right to mention our European funder, who, without them, this wouldn't have been possible – this would have been an ambition and something that we knew was the right thing to do but it wouldn't have been able to come to reality, so huge thanks from me too to conect4children for bringing this to reality.*

Thank you, Despina so much. Your time today is hugely important. Your time supporting Societi is valued every single day. We appreciate your insights and your expert knowledge. I'm sure that families must feel reassured that huge advances are being made into changing outcomes for children with Kawasaki Disease and your support is key to that in continuing to have your expert input into our work is so very appreciated. Societi as you mention is a partner in the KD-CAAP trial team. We've got responsibility for patient and public involvement throughout the trial and both yourself and Professor Paul Brogan – members of our Scientific Advisory Board – have been key to making sure that the trial moved out of paperwork and became a reality – which is so exciting for all of us. I had mixed feelings when the first patient was recruited at the beginning of the year but every patient matters in this trial and if we're going to change outcomes for children, this trial is absolutely key.

Thank you, Despina, I really appreciate your time this morning

Despina: Thank you, Rachael, thank you for inviting me and thanks to everyone who has made KD-CAAP a reality. Let's get some more patients some more centres up and running across Europe and let's see this trial to the end – Thank you!

