The G word transcript

Sarcoma awareness

**Helen:** Hello and welcome to the G Word. My name is Helen Webb and I'm the Product Lead for the bioinformatics pipelines at Genomics England. On today's episode, I'm joined by Dr. Prabs Arumugam, Director of Clinical Data and Imaging and the Caldicott Guardian for Genomics England. Prabs trained in medicine at St. Bartholomew’s and the Royal London and is a histopathologist. He has also completed his PhD at the Barts Cancer Institute. Kirsty Russell also joins us and is the product manager for cancer long-read sequencing at Genomics England. Prior to joining Genomics England, Kirsty worked as a clinical scientist in the NHS and was the lead for cancer whole genome sequencing at the Southwest Genomic Laboratory hub.

The three of us will be in conversation with Lizzie Mordey, a clinical trials coordinator whose husband, Stevie, sadly passed away last year in July after receiving a diagnosis of sarcoma at the age of just 27. Sarcomas are cancers that can affect any part of the body on the inside or outside, including the muscle, bone, tendon, blood vessels, and fatty tissue.

On average, 15 people in the UK are diagnosed with sarcoma cancer every day, but awareness of its signs and symptom symptoms remain low. July is Sarcoma Awareness month, and for today's discussion, our guests will explore the use of genetic testing in sarcoma as well as the challenges and opportunities associated with integrating genomic data into clinical practice for sarcoma management.

Prabs would you be able to tell us a little bit more for people who are not aware of some medical disciplines, what a pathologist does?

**Prabs:** A pathologist is someone that looks at tissue specimens, kind of a broad term. So, we have multiple specialties, but histopathologist is what most people commonly refer to.

So when a small lesion tumour or cancer is taken out, or a large or an excision occurs, we will to have a pathway to handle that tissue. Where we fix it, take small sections, stain it and look it under a microscope ultimately. And we're trying to make a diagnosis from the tissue about the tumour origin, if it is a tumour. And we will help the oncologist in terms of guiding individual patients' treatments. We do also do things like post-mortems, so when someone unfortunately dies and for unknown causes, we can also do post-mortem to look and try and identify those cause as well. And so, yeah, that's broadly what a histopathologist does.

**Helen:** Kirsty. I think clinical scientists are a specialty that a lot of people will not have come across in the past, and one that's very important in genetic testing. Could you tell us a little bit more about what a clinical scientist does?

**Kirsty:** So a clinical scientist is sort of someone, I guess that works a little bit in the background of the healthcare setting. And so these are people who work on a scientific discipline and their sort of job is to develop and analyse tests, which can be used for patient management. And there's a lot of different disciplines that fall under this clinical scientist umbrella. So genetics is one of them. We also have things like haematology, biochemistry, immunology, and so on and so forth. But the clinical scientists work really closely with the clinicians and other colleagues in healthcare science disciplines, including pathology. And we sort of in genomics work to analyse and interpret genetic changes, which can be used for patient management. And the clinical scientists that work within genomics can specialize in rare disease, cancer, or bioinformatics. But there's quite a wide range of different types of clinical scientists.

**Helen:** There's so many different kinds of brains that come together in genetic testing, and it's amazing to see how they all operate together.

Lizzie, we are going be talking about your experience quite extensively with sarcoma, so we'll be talking about your husband, Stevie. I was wondering if you could give us a picture of who Stevie was as we talk about him so that we can hold a complete picture in our head.

**Lizzie:** Yeah, of course. My favorite subject to talk about. Yes, Stevie was an amazing man. We knew each other from the age of 14. Met at school, got together at 16. He was huge – 6 foot 5, blonde, very funny. His humor was incredibly self-deprecating, which was just hilarious. He made me laugh every day. He was a mega nerd, super into gaming. I'm currently wearing his gaming headset and I look really ridiculous. And yeah, he was just into all things nerd, loved all Lord of the Rings, that kind of thing. And yeah, he just loved friends. Had so many friends. They supported us through the whole experience, which was amazing. So we honestly couldn't have done it without them. And that was kind of a testament to who he was. He made everyone like him. That's kind of who he was.

**Helen:** So just to give our listeners a honest and fair representation, Lizzie, we think you look fabulous in your gaming headset. So would you mind walking us through Stevie's diagnosis and, what the experience was like for you on, on the journey?

**Lizzie:** Yeah, yeah, sure. So yeah, we were both 27 when it all kind of kicked off. Everything was fine, completely happy and healthy. And then in the middle of the night I woke up and Stevie was having a seizure and I ended up calling an ambulance and he went to hospital and then he kind of had a brain scan to see what was going on, and they found a brain tumour and then did a full body scan and found quite a few other tumours.

At that point they didn't know what was going on and. It kind of set off several months really, of us not knowing what type of cancer it was. They initially did a biopsy on one of his lung tumours, and that came back inconclusive. So he had a seizure on the 7th of November, and then eventually they decided, oh, we're going to operate on the brain tumour, and kind of go and biopsy that as well. So the first biopsy was inconclusive, so we might as well take the brain tumour out and we'll biopsy that as well and hopefully that will be conclusive. So he had his brain surgery on the 20th of December, right before Christmas. So then he was, had his big scar over Christmas and everything, but luckily he was home for Christmas day, which was amazing.

But unfortunately, that was also inconclusive. I don't really know the science, but my understanding is, it was really late-stage cancer, so it kind of, it's all metastasized. It all just sort of looks like nothing at that point, which is why everything was inconclusive. He had a tumour in his arm, which they tried to biopsy, also inconclusive. So mid-January they kind of said, look, it's been a really long time now. It's really aggressive. We are just going to guess it's a sarcoma and just give you some chemo based on that assumption. And then kind of in the background to this, the arm biopsy was sent for full genome sequencing and then that took a really long time to come back.

I don't really know why. I think it was longer than normal. I think it's normally quicker, but there was like loads of delays with the lab or something, I can't remember, but it did take quite a long time to come back, but eventually did come back. Then they confirmed that it was a sarcoma. So luckily that was right because he'd been having chemo for quite a few weeks by then.

But that first chemo was amazing. Like he was like a different man after that. So that was really good, and it was nice to know that that's what we were working with for kind of the next decisions of which chemo to try next and that kind of thing. So yeah, it was good to finally have a diagnosis, but it was kind of a long road getting there, but luckily something eventually without the full genome sequencing, we probably would've never known. We were originally with the cancer of unknown origin team, and then we got moved to the sarcoma team. So it was good that we knew.

**Helen:** Thank you for sharing that with us. That must have been a rollercoaster ride of an experience.

Prabs, would you be able to tell us a little bit about the interplay between pathology and genetics in the diagnosis of cases that might be like Stevie's? - obviously not his specifically.

**Prabs:** Yeah. Okay. So the difficulty is that malignant tumours or soft tumours are rare. And actually it's diagnostically incredibly difficult to kind of, or it's a challenge, let's put it like that.

And the reason is, is that, you know, it's sometimes difficult to tell from one another. I think there's, the last time I looked, there's somewhere between 80 and 100 different classifications of sarcomas. And actually, pathologists generally find it quite difficult or to struggle to actually make those.

So sarcomas usually are kind of regional or national level MDTs even to just kind of make that diagnosis because it's such a super specialised field. So you first got to work out what is the origin of cell, you know, is it soft tissue, is it bone? And then within that actually, which of those kind of differentiations actually is it? So it is quite hard. And then the added complexity of that is that quite a lot of those sarcomas and the subgroups in them have quite what you might call characteristic genes or gene fusions. So SS18 is fusion in synovial sarcoma, for instance, or alveolar rhabdomyosarcoma have FOXO1. So there's lots of very specific mutations that also go with those specific different types of tumours as well.

And again, you want to know about is it soft tissue? So retinoblastomas have RB1 mutation, so even if it's soft tissue or if it's bone origin, like, what is the mutations associated with those and what's the interplay between them is incredibly complex. So as a kind of how do you approach this, what do you do and where's the integration from that? It's really quite challenging. So at the moment, there's quite a lot of relationship between the pathology and here's the molecular testing that we're looking at. And routinely labs at the moment are kind of taking immunosuppressants or FISH, we'll look at PCR tests, but whole genome sequencing, which NHS England currently offer standard for sarcoma at the moment is incredibly useful because actually in the same case with Stevie, you can make a diagnosis that previously wasn't there or there's a lot of uncertainty around that, and that's a real value for whole genome sequencing in sarcoma.

**Helen:** Prabs you mentioned the MDT or the multidisciplinary team that's involved in this diagnosis. So Kirsty, I think that's a great time for you to come in and talk about from a clinical scientist perspective - what goes on behind the scenes during whole genome sequencing? As Lizzie said, it often can take a little bit longer than expected due to the complexity of it. Could you walk us through some of what is involved in whole genome sequencing for cancers like sarcoma?

**Kirsty:** Yeah, so typically at the moment for whole genome sequencing, we will have to get, receive a tumour sample. This normally comes from pathology as Prabs was saying, and we need a slightly different type of sample to be able to perform whole genome sequencing than what we do from standard of care. So that requires like an extra biopsy or a different type of sample to be taken.

So typically when we do a standard of care test, and the typical pathology route is you get something called formalin-fixed paraffin embedded tissue, which is basically when it was treated so that the histopathology can look at the slide and sort of look at the different cells and things like that.

But for optimal whole genome sequence and we need a fresh bit of tissue, so that's like as close to as it comes out of the body as possible. So this sort of sampling rate is a little bit different from whole genome sequencing and sometimes that can cause delays and things like that, in the genetic testing, because it's a different sampling route that has to be taken.

But when we receive a sample in the genetics lab, so we'll typically sort of go through the referral, and work out whether the testing that has been requested is appropriate for the patient and the methodology that we would use. So, in sarcoma testing, as Prabs mentioned, a lot of the standard of care testing, so that's the stuff that's done with whole genome sequencing. These would be things like FISH testing and things like that, and they can get done directly on the paraffin-embedded tissue that we would receive for whole genome sequencing that's different. So the route in which we take and how we process this samples are quite different due to the different types of methodology and the different types of sample that we use.

So the clinical scientists will be involved in working out what type of test is appropriate and sending it down that route. For whole genome sequencing in particular we then have to, we, so we effectively have to extract the DNA from the sample. So that's sort of, you degrade the tissue and then pull out the little bits of DNA that we can then test, and then we'll send it away to get sequenced through whole genome sequencing. And then those results are returned through Genomics England, processed through the pipelines, the analytical part here, and then the results are then returned to the clinical scientists who do the interpretation of the results that they receive. The interpretation can be quite extensive when you're looking at whole genome.

So if you imagine like in typical sarcoma care, you're looking for single changes, and that's quite easy to analyse. But when you're looking at whole genome, you can get many, many, many of those changes. And then the clinical scientist has to look at all those changes and work out what is important for the patient, and they will analyse this and then return it as part of a clinical report, and this will go back to the referer, who's normally from pathology, and that's sort of the general process for how it flows through the analytical steps of clinical scientists.

**Helen:** Lizzie, do you want to walk us a little further through Stevie's journey and also sort of, I guess, your journey going onwards from there?

**Lizzie:** Absolutely. I guess first off, just to say it's really useful to hear you speak about all of that. I've come from sort of a more kind of science background. I did a science degree. I've worked with healthcare professionals a lot of my career, and I totally get everything that's going on and all the pressures and everything. But even then as the patient or the loved one going through it, it's so hard not to get frustrated with all of those delays.

I just think it's really valuable to hear and understand just what goes into that, just to kind of help you realise why it's happening and why it's taking X-number of weeks and that kind of thing. And I just think that's really valuable. It was partly because the journey had been so hard and everything's so uncertain and your kind of not expecting it, and I don't think any of our healthcare team are expecting it. You know, everyone just says, oh, we'll just take a biopsy and we'll find out where the tumour started and that will solve all of our problems and we'll know everything. And then every time you get told, we don't know, we can't figure it out. It is kind of another setback or frustrating. And it's frustrating as well when you're kind of dealing with such an aggressive cancer and it feels like every week or every day you wait, you know, every day you wait and you can't start chemo because they don’t know which chemo to give you feels huge.

So it was hard, but luckily for me, Steve was amazing and he was just an absolute trooper the whole time. Never complained. He was still completely himself, had all of his humour and everything. So he made the experience for me better, which is crazy because he was the patient. But yeah. It was, it was kind of okay, but it was just like, you just got to deal with it, haven't you? It's only okay because it has to be okay, but yeah.

**Helen:** I guess as you've highlighted there, from the patient side, often a lot of the processes happening behind the scenes are sort of not very transparent and that there are so many people involved and from so many different disciplines to try and work through, what is going on with the patients and how to proceed.

I guess I just want to loop back a little bit before we carry on with Stevie's journey. Something that you mentioned was that, prior to the whole genome sequencing, Stevie's tumours were being treated as cancers of unknown primary. So that is one of the areas where, genetic testing is, is particularly valuable. And I wonder, Kirsty, if you could, I know that you've had experiences as a clinical scientist with cancers of unknown primary, and genetic testing. Could you walk us through why genetic testing, particularly whole genome sequencing is so important for cancer of unknown primaries?

**Kirsty:** Yeah. So in cases of cancer of unknown primary, like fundamentally, there's no specific test that you can order because you don't know what the cancer type is. So when you're testing a cancer unknown primary, you're not looking for a specific treatment option or anything like that. You're kind of looking for a way of classifying the type of tumour that it is. As you mentioned, like that's probably your experience of it, is like you went through it with Stevie and it was a cancer of unknown primary, but you've used the genetics to understand that it was a sarcoma.

And that's kind of where whole genome sequence and comes and into its own in those kind of cases. So the typical sort of testing pathway normally looks for specific variants, which are specific to those cancer types, and for cancer of unknown primary as I said, we don't have that. So, in order to sort of classify that type of tumour, you have to look much wider than you would in sort of normal testing, and whole genomes can inform that.

So when you're looking to [classify tumour types, there are specific types of changes which are associated with different tumour types. So in sarcoma in particular, as Prabs mentioned, you can get these gene fusions and they can sort of indicate what type of cancer you're looking at. Where it becomes really interesting is when you look at the whole genome as a whole. And like you look for patterns, so not specific genetic changes, but patterns of genetic changes. So you might see those types of variants that you would look for specifically for something, but as a whole you can sort of work out from the patterns, what type of tumour it is. And that is something actually we're looking at a little bit more, particularly for sarcomas and cancer of unknown primaries, is using those patterns that you can see in the genetic data to then sort of loop back and try and suggest a sort of classification for that tumour type. And that's one of the sort of areas where whole genomes can really give value. And hopefully that's something you experienced with Stevie

**Helen:** Prabs you mentioned. That's pathology interplays with genetics a lot. And Kirsty has also mentioned that it's the pathologist who is ordering the genetic testing often - I wonder in this scenario where you don't have genetic information before you have the genetic information. What kind of things when you're looking down a microscope at a slide of cells in a case something like sarcoma where it's very difficult to know what you're looking at. What, what are you going on as you're sitting at the microscope? Are there certain changes? Can you walk us through that journey, which sounds like it's quite difficult?

**Prabs:** Normally, like in Stevie's case, you take, a patient will present with some kind of a lesion or a lump using sarcoma. Or there's some kind of symptoms then, so you want to take a biopsy, and like Kirsty said the normal route is you take that piece of tissue, put it into formula, and it gets fixed, and we embed it in something called paraffin. So we call it formalin-fixed paraffin embedded, it’s basically kind of like a hard block and then we'll cut very thin sections through it. So that's what we put on a glass slide. And to be honest, that hasn't really changed for about 20 or 30 years. That's quite a traditional method. It works and is very useful. And the important bit there is we add a stain which correlate to hematoxylin and eosin. The important bit is that we want to look at the kind of the cells in that.

So, you know, normal cells will have a relative homogeneity, so look very round they have smooth edges, those are kind of simple things we're looking for. But in cancer, they tend to go a little bit, morphologically, they look a little bit odd. So the nuclear in the middle of the cells look a really little bit wonky or they're kind of like discordant.

They're kind of distance between the cells looks a bit odd. So there's each cancer in each tumour will have certain appearances down the microscope. We start looking for, and it's those what you call morphological changes that we're trying to identify. And so suddenly you'll go, oh look, that doesn't look right. This is probably tumourous. And there might be a series of, look, it's these features that correlate with this tumour, but you might also want to do something called immunohistochemistry. So you can add a bit of a protein stain to some of these uncut sections, and you want to see if they're staining positive.

So specific markers, you might want to look at cell border markers, you might want to look at vascular type markers. And the pathologists, usually the experts there, they'll say, look, actually this is properly relevant to this. I want to run this very small panel to look for it. So we'll get a better sense from it. And historically that was it. That's all we used to really do. And you get a sense of where you're going go from there. And in the last few years we started at more tests. So FISH is a type of cytogenetic study was trying to add in, which is very successful, especially in haematological disease as well.

But whole genome sequencing is where there's kind of a lot of interest because actually you can start delineating quite clearly, cytogenetic studies really beautifully in these kind of panels that like Kirsty's working through. And that's the important bit is that actually that's where the direction that you want to head towards.

So the real value here is for instance, chondrosarcoma, which is the bone tumour. They historically tend not to respond very well or if at all to chemotherapy and radiotherapy. So actually, if you can make that distinction really early on that this is tumour that is just not going, is going to be ultimately resistant to that kind of therapy. Whereas you can define, I don't know, things like rhabdomyosarcoma, respond actually to chemo, radio and the resection. So that's that kind of individualised diagnostics and then leading to the therapy that we're trying to delineate a lot clearer and we're getting a lot more centrum as well.

**Helen:** Excellent. I'm just going to elaborate a little bit more on the FISH testing just to say that, what we are looking for there is we are looking at fluorescence of two different genes and we are checking that genes that have broken apart during processes in cancer, have been put together in a way that is unexpected. Am I describing that in a scientifically correct way? Prabs and Kirsty?

**Prabs**: Yeah. You sound like a pathologist Helen.

**Helen:** Yeah. A recovering, geneticist from old days. Lizzie, would you like to walk us a little bit further through Stevie's journey? So we've gotten to the point where he's had his first chemo and it, it had a very positive effect and it felt like things were getting better.

**Lizzie:** Yeah, yeah, definitely. Just to caveat that we did know that it was going be terminal at that point, but obviously any extra months is good. To be fair, by the time he'd started chemo, it'd been nearly two months since his seizure, and that's a long time considering how advanced his disease was, and he was very, very poorly.

And then, as I said, the chemo, I'm going to say it was like a miracle cure, but obviously it wasn't a cure, but it was, it was amazing and he luckily had very few side effects, so he did really well on the chemo as well. We actually got married after his diagnosis. So we managed to get married, which was also amazing. He was really kind of well on, on our wedding days, so that was really good. And yeah, it, it was great from there. Unfortunately, after that, the kind of next type of chemo they tried just was not effective, so he really only had those six sessions of chemo, and then he had four sessions of the next chemo, but he was just rapidly going downhill that whole time, really.

**Lizzie:** And I think that's kind of the next point to make really, is that it's not just about knowing that it's a sarcoma, but as Prabs mentioned, some sarcomas don't respond well to chemo and others do, and all of that kind of nuance. I mean, I remember the frustration from a patient point of view when you're told, oh, we're going try this chemo, but we don't really know, like sarcoma's so rare, we don't really know what works, what doesn't work. We're just going try this one and see what happens. And then the kind of delay is kind of a month or couple of months before you realise, oh, actually that this whole time it hasn't been doing anything. So all of that information is only a good thing in my eyes. If you can kind of start learning more about. What will work in terms of tailoring treatment as well as just finding out that something's a

**Helen:** In terms of hopes for the future of what will happen for sarcoma patients. Can you, you give us a sense from your perspective as a pathologist with extensive genetics background as well as imaging, and new AI algorithms that are becoming available. What sort of things are we hoping for in the future from your perspective?

**Prabs:** So that is a very good question, Helen. Look, I think the important bit is how we try and get to a position where stories like Stevie's are not the usual precedent, but are rare. So how do we advocate the notion of making quicker and better and more accurate diagnosis?

That that's where we all want to get to, because I think our treatments are pretty good. I think the way we operate is fantastic and our oncological surgeons have great kind of techniques to remove tumours, chemotherapy and advancements is progressing really well, but it's just how we make these diagnosis and technology that we are looking at. You know, beyond whole genome sequencing and the new advances is where there's real interest. So, we run a program here in Genomics England, where we're trying to link the whole genomes also to the pathology. So actually, is there really early kind of morphological changes from those genetic variants that we can actually see down the microscope, you might call it, but it's actually digital pathology image.

How does that link to potentially predicting treatment outcomes? So actually, can you even say that, you know, this person with these type of changes on the image is actually probably going to respond to this therapy and actually, their survival might be quite poor, but they might do also quite well if you can give them this alternate therapy.

And that's where we all want to head towards. So we call it the multimodal program. We think it's quite an interesting way, but I think there's lot of interest in garnering like different sources of data together to make those diagnoses better. And I think we've always historically kind of looked at it, here's a radiology scan. We think it's probably related to this. Here's pathology, we think it's this, here's genome, we think it's that. And actually it's now fusing that all together in a way that is useful. How do you make that ultimately return that to our patients? That's the important bit here. How do we try and avoid these kind of stories in the future?

How do we make sure that we're making those decisions earlier? And you know, there's really interesting studies out there. Actually the idea of tumours shred, like kind of shed off little cells, so floating cells, so tumours in the bloodstreams, can you pick them up even before they've actually started forming a mass?

Really interesting questions that people are asking us, and I think we as Genomics England can only help drive that research that kind of inquisitively to big organisations like the NHS is advocating the kind of notion of research. So we've brought in a company called Grail who're doing a very similar test. So look at tumour markers in blood.

And it's happening in the NHS. And I think that this is going to become a hotbed for research and that will ultimately drive how we develop, and ultimately it's return to our patients. And I think that's going to be unique.

**Helen:** With very rare cancers. Like all of the very different types of sarcomas, the subtypes, tumour agnostic clinical trials may become important in finding treatments in the future. Kirsty can you start us off on why that is and what it might be like?

**Kirsty:** Last couple of years, we've started to see more sort of therapeutic approvals for drugs, targeted therapies based on genomics, but not linked to a specific cancer type. And historically, a lot of the clinical trial studies have been done on particular cancer types looking for particular genetic change.

And the drug approvals are based on this. More recently, these clinical trials have started to become a bit more tumour agnostic, which is great for tumours like sarcoma where they're rare and probably not prevalent enough to have like a clinical trial and hard to recruit to. And that's probably why at the moment there's like very limited sort of targeted therapies available for things like sarcoma.

And these tumour agnostic biomarkers will be great in driving that forward. And like I said, in the last couple of years, we've had a few of those starting to appear. So the most prominent one is probably NTRK inhibitors. So these are targeted therapies which target specific fusion that involves the NTRK genes.

And this is approved for all cancer types regardless of sort of where it's from. So a sarcoma patient who has an NTRK fusion would. Be able to access this therapy. And actually NTRK fusions are more prevalent in rare cancers like sarcoma. So, if you have a sarcoma, you're actually more likely to have an NTRK fusion than say a lung cancer.

And we're always only able to start doing that now because of these clinical trials that are moving into a more sort of tumour agnostic space. And hopefully with things like whole genome sequencing where we're starting to look wider than these sort of targeted things, we can start to include more patients into those kind of clinical trials through identifying these kind of genetic changes as well.

So, yeah, it is looking very promising that things are sort of moving more in that direction, and I think that'll open up a lot more therapeutic options for patients with rare cancers like sarcoma.

**Helen:** Lizzie. So I guess I should ask you, in your professional life as a clinical trials coordinator, do you work with cancer?

**Lizzie:** Yeah, I don't work in cancer for my kind of professional life. I do work in other trials. I mean, I guess I would just say about trials. I am a big believer in taking part and I always think it's so important for patients and their families to take part. It's just amazing all the work that's done across all disease areas.

But I guess if I'm here as the sort of patient representative, I should just say as well, it's completely personal decision. And it's just doing what, what's right for you and your situation. I mean, if me and Stevie had been offered a trial, we would've done it straight away regardless. But I can see a situation where, you know, you've got so many appointments anyway, and you know, we are lucky, we live really close to Adam Brooks Hospital, but when you're going four times a week to have various appointments for various things - a study appointment might not be what you want to do. So I do feel the need to kind of put that in there. But personally, I think it's great things to do and I would encourage people who are considering it to take part because that's the only kind of way we can find new treatments and help people in the future. And I think that's all super important.

**Helen:** Lizzie, unfortunately, Stevie passed away last year, almost a year ago. I know that you have a very active interest in health research and in public and patient engagement with health research. Can you tell us what your journey going forward has been like since he passed away?

Lizzie: The start of the journey from him passing away was, Obviously hard and I basically did nothing. Well, I kind of stopped working. My work were amazing, so that was sort of super helpful. Went on a few holidays. My family kind of took me under their wing. My dad took me away, whisked me away, on a few holidays, that kind of thing, which was, which was really nice. And then, yeah, I started back at work. So as I mentioned before, I work in clinical trials and. It was really amazing going back to work. I kind of find a lot of value in my work. I think it's really important. So that was really nice to kind of get back on the horse and start that up again. And then, a few months ago, really, I sort of finally came to the decision that I'm maybe ready to do a bit more in terms of things around sarcoma and feeling like I want to give back and what can I do next, and that kind of thing.

I obviously speak to patients and the public a lot for my work. Really a big believer in public involvement and research and always considering what your patients or your participants want when you're designing a study and all of that, all of that stuff, and I've always been really interested in it. I've never been the kind of the kind of person that anyone wants to speak to, because I've never had a condition and I'm kind of, you know, kind of not, not who I would've done PPI before, but no one cared what I had to say, but I finally felt like, oh, I actually do have something to say now. And you know, Stevie's journey was hard, but if we can make someone else's journey better, that's only a good thing.

And speaking to patients and hearing from that patient voice is so important in that. So that's why I kind of contacted Sarcoma UK and said, is there anything I can do? And that's kind of how this journey started. This sort of new journey of, of being a bit more involved in their research and sarcoma research, and I think it's only kind of up to go from here. I'm so interested in doing as much as I can to sort of support work like this really.

**Helen:** Yeah. And it is so important for all of us working behind the scenes to be able to speak to patients. And it's something that's very important to us here at Genomics England. And the more opportunity we get to do it, the better we can hopefully make the lives of patients in the future. So it's invaluable to us and we're very grateful that you do it. Lizzie, I'd like to ask you, so in terms of the future for sarcoma patients, what do you hope for?

**Lizzie:** Personally, I would, I would hope for quicker diagnosis. And I know that's super hard to do and I think as we've discussed before on this call, it's such a rare thing and it kind of often doesn't fit the standard clinical pathway and that that's one of the reasons why it's so frustrating. So anything that we can do on that front, I think would be hugely valuable to anyone experiencing a journey like what me and Stevie went through. And yeah, advances like genome sequencing are really amazing in supporting that. Yeah, as I mentioned as well, any information about types of treatment, you know, the diagnosis is important, but then the other aspect of getting a diagnosis and a specific diagnosis is understanding what's most likely to help.

And as Prabs mentioned, you know, sometimes it's not the outcome in terms of long life might not be what everyone wants to hear, but what changes you can make to the quality of life in the time you have with your loved one is so valuable. Like, as I said before, getting to marry Stevie was one of the best days of my life, and we wouldn't have been able to do that if we hadn't have known what he had, what was likely tell what, what chemo to give him. So, Anything we can do to help that and improve that is really the way to go.

**Helen:** one of the things that we know about whole genome sequencing that patients sometimes find valuable is knowing about whether their cancer is hereditary or not. Did you and Stevie have that experience?

**Lizzie:** Yes, actually we did. Yes. So, part of the results that came back to us when we found out that it was a sarcoma that Stevie had was they made it quite clear to us that it was. Not hereditary. And it was nice in sort of two ways. The first is that it was quite important to Stevie that some people might find that worse, but for him it was quite nice that it was just a random fluke, bad luck, almost like nothing he'd done out of his control.

He sort of found peace with that. And the other really important factor was, the fact that it wasn't hereditary. So, we didn't have any children, but he has lots of young nieces and nephews that he was very, very close to. And it was really important to him that there was no kind of genetic component that could affect his siblings or her children. So that was really important to him as well. Gave him a lot of relief, I think.

**Helen:** So I feel so privileged to have been able to have been part of this conversation. It's been amazing to have patient perspective with the background of what's happening, uh, with pathology and genetics. Lizzie, thank you for entrusting us and our listeners with your story, and it's been a great pleasure to talk to you.

**Lizzie:** Thank you very much. Thank you for having me. This was, I'm super excited about being here. So it is been, it's been great and it's been really nice to hear the kind of behind the scenes, as you say, the sort of background, what goes on. And as we mentioned before, that's sometimes lost a little bit when you are the patient or the loved one going through the journey. So I think it's really amazing to hear. All the good work that everyone's doing.

**Helen:** I had like to thank all of our guests today for joining me in a discussion about genetic testing in sarcoma and how we can help to drive research in this area to ensure quicker and more accurate diagnosis for patients with sarcoma.

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