**What Happens When a Cancer Trial Leads to Unexpected Results?**

**SickKids VS Leukemia**

**Hannah:** When Beatriz’s son, Santiago, was just three-years-old, a doctor delivered the news no parent ever wants to get.

**Beatriz:** And he told me, he looked me right in the eyes and he said, as a father, you need to go tomorrow to this appointment. As a doctor, I will tell you, go home and get some rest. But that he didn't have a good feeling about this.

**Hannah:** Santiago had a type of blood cancer known as acute lymphoblastic leukemia, or ALL for short. Beatriz knew the road ahead wouldn’t be easy. But she also knew Santiago’s chances were pretty good. The survival rate for ALL was high – likely between 85 and 90 per cent. But Santiago would need aggressive treatment. And the side effects could be severe and long-lasting. Plus, relapse was still a risk.

**Dr. Gupta:** And, you know, I often tell families and colleagues as well that, you know, 85, 90, 95 percent, all these numbers sound really great unless it's your own child that we're talking about, right? And then even a 10 percent chance of relapse or a 15 percent chance of relapse is absolutely terrifying

**Hannah:** That’s Dr. Sumit Gupta, a paediatric oncologist and clinical investigator at SickKids. For decades, oncologists have been treating kids with ALL the same way. And for decades, that 85 to 90 per cent survival rate hasn’t really budged. But is there a different type of therapy that could tip the scales? By treating smarter could we, one day, potentially eliminate the risk of relapse?

These questions kept Sumit up at night. That’s when he and his colleagues got an idea – one that brought them closer to answers than they ever thought possible.

You’re listening to SickKids VS. I’m Hannah Bank, and this is SickKids VS Leukemia.

**ACT 1**

**Hannah:** Paediatric cancer is rare. But in Sumit’s world, Santiago’s diagnosis is the most common one he sees. I asked him to tell me more about ALL.

**Dr. Gupta**: So, ALL. We always talk about it as being one of the miracles of modern medicine. So this was a disease that, if you went back to the 50s and 60s, was essentially a nearly universally fatal disease. Children did not survive this. And when you talk to people who have some memories of that time or trained under people who had memories of that time, you talked about making kids comfortable, and that was it. So the majority of children with ALL, when they get diagnosed, are treated with anywhere from a two and a half to a three-year period of chemotherapy. And that usually involves 10 or 12 months of intensive chemotherapy and then a couple of years of very low intensity chemotherapy after that. Relapse is when therapy fails for whatever reason and the leukemia actually comes back. And at that point, we know that there's something about that child's leukemia that is stronger than most childhood leukemia. And so then we have to use relapse treatments that are far more aggressive.

**Hannah:** If you listened to the SickKids VS Cancer’s Shadow episode in Season Five, you’ll remember we talked about “late effects” of chemotherapy. Because chemo, although lifesaving, is highly toxic.

**Dr. Gupta**: When I first sit down with the parents of a child with cancer and I talk about chemotherapy, I usually tell them like most of our chemotherapy is pretty dumb, right? It can't tell the good, healthy, regular cells in the body apart from the bad, you know, unhealthy cancer cells. When you give chemotherapy, it hits both healthy and cancer cells, and then thankfully healthy cells recover, whereas we hope that the cancer cells don't. Now we're really good at dosing it, we're really good at getting kids through the complications that they might see, but in the end it's still poison, right?

**Hannah:** For decades, chemo has been the standard of care for kids with leukemia. Kids like Santiago.

**Beatriz:** He turned four in the hospital, and all those nurses on the eighth floor rallied together to make a birthday party for him in his bedroom. I still have the huge card in my room. They hand drew these things and like I needed that. Like, I was planning his first real birthday party and we had to cancel everything. So that was really nice to see and I knew that they cared. Nobody's going to sit and draw a Spiderman or Lightning McQueen from scratch on their break if they don't care.

**Hannah:** Now at SickKids, Santiago started on his treatment plan right away. At the same time, a clinical trial was taking shape—one that involved a promising immunotherapy drug called blinatumomab.

**Dr. Gupta:** It's an antibody that targets a protein called CD19 on the surface of the leukemia cell itself. And then the other side of that antibody recruits your own immune system, your own what are called T-cells, to come attack that leukemia cell. So it's kind of like a homing mechanism, right? It like attaches to the leukemia cell and waves to your own immune system T-cells to say, hey, come attack this. This isn't supposed to be here, right?

**Hannah:** In 2015, a blinatumomab study showed promising results in kids and adults whose leukemia had relapsed multiple times. And researchers could see the side effects of the drug were pretty manageable. Knowing this, Sumit and his colleagues started designing a *new* clinical trial – *this* one with kids who had newly diagnosed ALL. Half their participants would simply get their regular chemo. The other half would get the same chemo plus two months of blinatumomab.

**Dr. Gupta:** And I got to tell you, when we started to pitch this idea across different groups and different physicians, oncologists, and things like that, people were a little nervous, totally understandably, right? Here's a new agent, and you're going to give it to like you want to give it to a group of patients, a group of children, that already have a 90 percent outcome. Does that make sense, right? Like new agents, usually we save for the kids with cancers that have outcomes that are terrible. But the counterargument we had is, look, we have no confidence that we are going to be able to improve outcomes for standard risk ALL past the 90 percent using traditional chemotherapy. So we have two choices. Either is to say, we're done. It's good enough. Or we say we're willing to take a little bit more of a risk… So we opened in July of 2019, and we had calculated that to see the difference that we thought we were going to see, or that we hoped we would see with blinatumomab, that we needed about 5,500 kids to go on the trial.

**Hannah:** Five thousand, five hundred kids. That’s more than five thousand, five hundred parents who would have to be willing to take that risk too. Parents like Beatriz.

**Beatriz:** I want to say we still weren't even discharged from the very first admission when we had found out. Two doctors came to me. My partner was with me at the time. We were both there. And they explained the trial to us. They never pushed anything on me. They just explained it. They were very adamant on letting me know that regardless, he was going to get the same care. It was just that if we had agreed to this, they have this plan to follow. I could pull out at any point I felt uncomfortable, or if I felt his body didn't mesh well…. This whole cancer journey is something I've never experienced before. The medications I had already seen gave horrendous side effects, so I might as well take the other door and see. I know that there's children that signed up for this trial that had no other choice because of how high risk they were. That could have been their only chance. And if I had the opportunity to help that science for all the kids that didn't make it and continue pushing through when it did not seem like a dangerous choice whatsoever considering the unknown we were already in… It really was just a no brainer.

**Hannah:** Beatriz had made her decision. But would she ever really know if it was the right one?

**ACT 2**

**Beatriz:** I won't lie to you. The first three days were rough.

**Hannah:** Santiago’s now enrolled in the clinical trial. And he’s placed in the group that’s getting blinatumomab. He had fevers. He had chills. But thankfully, after a few sleepless nights, those side effects seemed to pass. Santiago was simply adapting to the new therapy. And he wasn’t the only one.

Blinatumomab has a short half-life, meaning it doesn’t last in the body for very long. In order for the treatment to work, patients need to get a continuous infusion of the drug for a full 28 days. At every hospital involved in this trial there were hundreds of nurses learning how to administer this therapy for the first time. It needed to be safe. It needed to be practical. And it needed to be portable.

You’re about to hear from Sue, a nurse here at SickKids. For patients like Santiago, and their families, she made the unknown so much more manageable.

**Sue**: So to make this immunotherapy portable for children for 28 days, we really need to give them equipment that supports them to be in the outpatient setting with minimal complications so it works well. And so one of the ways to give them the infusion bag, so this big heavy bag of medicine, all the I.V. tubing and this small portable infusion pump, was to put it all together in a bag that carried the equipment for them. And so the bag we were using was an adult infusion carrying bag. It had a single strap. So sort of like a sling bag design. And it was pretty flimsy. At that time I thought, well, that's that doesn't look like it fits a child very well. It doesn't look like it's comfortable to wear all the time. And we want them to play and go to the bathroom by themselves. We don't want six and seven year olds to have someone go to the bathroom with them. We want them to go to school, possibly. Like there were all these things we wanted for these children. So I thought, well, if there isn't one, why don't we just make one? So I decided it should be the patients and families to tell us what is the best bag, because they're the people who are going to be at home and using this equipment. We learned a lot. We learned that they wanted it to look like a backpack. They didn't want it to look like a medical bag. That the stigma associated with the current bag identified the child as being sick. They wanted it to be more sturdy. They wanted it to have a handle. Imagine that. A handle that you could pick it up and carry.

**Hannah:** After a prototype was made and more feedback was received, the Blina Backpack was created. Another great feature of the Blina Backpack? Patients could choose their own design. For Santiago, that meant his had to have sharks.

**Beatriz:** It was great. We could have been stuck in the hospital for a whole month. And this let him go out. He even went to dad's soccer game with this. Once the medication adapted to him, regardless of what they were giving him on the side with part of the treatment, he didn't get sick too much at all. And really, he was super active. We had to slow him down. His energy levels were back. And he tolerated this medication amazingly.

**Hannah:** By the end of the month, Santiago was feeling a lot better. And, as it turns out, so were many other kids around the world….

**Dr. Gupta:** You go into this trial not expecting to have results until not just the trial ends, but all well-designed clinical trials have what are called interim points of analysis. And this is where, at pre-planned times, people confidentially take a look at the preliminary results to make sure that something really, really, really good isn't happening or really, really, really bad isn't happening. Because if something really, really good is happening, then it's not ethical to do the trial anymore, if you've already proven that one arm is better than the other. And if something bad is happening, like an unanticipated side effect, or the experimental arm is clearly worse and you know that really early, then it's not ethical to keep continuing the trial as well.

**Hannah:** It was June of 2024. And Sumit's team was about to receive their first round of results from the clinical trial.

**Dr. Gupta:** I can tell you exactly because I don't think I'll ever forget it. My family and I and my partner and I were actually on vacation. We had this like, lovely, lovely time in northern Italy, and we were actually flying back. And I got a text from the head of the COG ALL committee, this amazing guy named Dave Teachey, who's out of CHOP, Children's Hospital of Philadelphia in the US. And all the text says is, do you have a minute? I really need to talk to you. It's like, well, no, Dave, I'm like over the Atlantic Ocean. And he goes, okay, are you on the email? I'm like, yeah, I am. He's like, I'm sending you something. And essentially, he and John, the statistician, sent me the results. The numbers and all of that sort of stuff. So I'm literally sitting there on the plane, opening up these things and looking at it. And it's slowly sort of dawning on me what these numbers are and what they mean and, you know, you probably can tell, like, I'm not at a loss for words very often, but you know, my partner actually looked at me from across the aisle and actually asked me like, are you okay? You're really pale. And I think it took me a good five, seven minutes to like, even be able to respond as I sort of processed these. And then, you know, I said a couple of holy whatevers, right, such and… we just changed global treatment for this disease, right? Like it was immediately obvious. This is the new standard of care for nearly every kid with this disease across the world.

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**ACT 3**

**Hannah:** Those numbers that left Sumit speechless on the plane? Here are a few of them. In the trial, one group of patients had a 90 per cent survival rate with chemo alone. But when they added blinatumomab? That number jumped to 97.5 per cent. And for patients at even higher risk of relapse — their survival rate with chemo alone was 85 per cent. Add blinatumomab, and it climbed to 94 per cent. That’s not just a small bump. That’s a gamechanger.

**Sue:** It’s surreal really… to think about how many children will not have to suffer a relapse of leukemia and go through, you know, very toxic relapsed chemotherapies. I think it's just, it's unbelievable.

**Beatriz:** And they came to me one day super, super excited, and they said that it was officially going to be like standard care if it fit for the children. And they were so happy and they said to Santi, they were so proud of him for being part of it and that, like, we made the right choice. Now it was confirmed for me that we made the right choice for sure.

**Dr. Gupta:** And so then we landed eventually… I did cry a little bit on the plane, which was quite embarrassing, but like… so then we land, we're in the cab, driving home. Now I'm on the phone with Dave and we're both like, holy crud, like what, what is, and like, you know, who can we tell what? And then over the next week, you're slowly able to tell more and more people. Because at that point, you have to stop the study, right? Like, not only do you have to stop the study, but then anyone who was in the appropriate timeframe but didn't get blinatumomab should now freaking get blinatumomab.

**Hannah:** Santiago started school in early 2025 – exactly one day after receiving his final chemo treatment. A few months later, he celebrated his fifth birthday. This time with mini golf and a big party at home.

**Beatriz:** I try to let him lead as normal of a life as possible. And he's very open about everything. One thing I always told him is every kid you meet, please teach them about your port. Because the last thing I want is for boo boos to happen for no reason. So he's very open with that when the situation comes and he's not scared to tell them to kind of stay away from his body or whatnot. So that's also a blessing too. But he's integrated beautifully. Like, beautifully.

**Hannah:** For kids with ALL, this trial completely changed the trajectory of their care, and their chances of relapse-free survival. But I wanted to know… could we now say we’d cured this type of cancer?

**Dr. Gupta:** It gets us a whole lot closer. But is that the end of the story? No, absolutely not. There’s a few things we have to figure out still, right? One is a few kids still relapse. And why? All of those prognostic factors that made us know that a kid was more or less likely to relapse, those are all in the context of kids getting chemotherapy. Maybe those factors are still the important ones when you add blinatumomab, or maybe not. Maybe there are totally other factors. And then the question is, well, why do those small number of kids relapse? Is there something different about that kid's leukemia? Is there something different about that kid's immune system? All of that sort of stuff is, we need to sort out as well. And then the big, super exciting thing is, maybe we don't need all that chemo anymore. If all of a sudden our outcomes are that good, maybe we can peel back some of the chemotherapy without sacrificing relapse rates, right? Now that's an even more difficult study design to put together, which is exactly what we're trying to do now.

**Hannah:** Now that scientists know more, they can do more. But to keep advancing, there needs to be more research. More clinical trials. More participants in these clinical trials. And even more support.

**Sue:** None of this is possible without philanthropy. There are only so much health care dollars and clinical trial research dollars to support doing clinical trials work. And so, we're very fortunate to be able to access philanthropic dollars to support the work of clinical trials themselves, never mind the, you know, the added opportunities to think about how can we improve the care of children on clinical trials and how can we improve the overall experiences for children diagnosed with cancer and their families.

**Beatriz:** For the mothers, I want to tell them to trust their gut. Do not let the outside noise in. It is absolutely not worth it. I'm sorry he had to go through this for sure, and I'm sure every parent is going to be heartbroken to see their child suffering. But we're all human, and part of learning and growing is suffering. And I do believe that. We're able to change science and motivate so much with that. And the children are what's going to get us through this.

**Hannah:** From SickKids Foundation, I'm Hannah Bank. Thanks for listening. To support breakthrough research and care at SickKids, please visit SickKidsFoundation.com/podcast. And if you liked this episode, subscribe and rate us wherever you listen to podcasts. SickKids VS is produced by me, Neil Parmar, Jasmine Budak, Liz Surani, Charlotte D’Arcy and Rebecca Ostroff. This episode was written by Rebecca Ostroff. Sound design and editing by Quill. Check out our show notes for related links and resources. Until next time.