PODCAST SERIES
HEMOPHILIA GENE THERAPY – DREAM OR REALITY?

EPISODE 10

A DEBATE ON HEMOPHILIA A GENE THERAPY

PARTICIPANTS
Matt Cundill, Cleaven Pagani, David Page, Rick Waines, Paul Wilton and Emil Wijnker

Matt Cundill 00:00
This is GENE THERAPY FOR HEMOPHILIA: DREAM OR REALITY?, a show on behalf of the Canadian Hemophilia Society. Here’s your host, David Page.

David Page 00:12
Hi, welcome to the podcast series GENE THERAPY FOR HEMOPHILIA: DREAM OR REALITY?. I’m David Page. I've been a volunteer, staff person, and now part time consultant with the Canadian Hemophilia Society for more than 40 years. Over that time, I’ve witnessed tremendous advances in care and treatment for people with hemophilia. Gene therapy has been a dream for most of those 40 years. However, the question remained. Was it just a dream, or would it become reality? In the last year, gene therapies for hemophilia A and B have been approved in the U.S. and, Europe and most recently for hemophilia B by Health Canada. But are they for everybody? In this podcast, I will ask four people with severe hemophilia A, all members of the Canadian Hemophilia Society Blood Safety and Supply Committee, to debate the question: “If gene therapy for hemophilia A were available in Canada tomorrow, would you want to receive it?” So let me introduce our debaters. For the yes side, Cleaven Pagani from Calgary, Alberta.

Cleaven Pagani
Hi, thanks for having me on the show.

David Page
And Rick Waines from Victoria, BC.

Rick Waines
I am coming to you live from the unceded territories of the Lkwungen people, known today as the Esquimalt and Songhees Nations. I'm pleased to be here.

David Page
And now for the no side. Paul Wilton from London, Ontario.

Paul Wilton 01:34
Pleasure to be here, David, and my esteemed colleagues.
And Emil Wijnker from Woodstock, Ontario.

It's my pleasure to be here as well. I look forward to a great debate.

David Page 01:44
Let me say at the outset that the sides and the teams were chosen by the toss of a coin. The debaters are being asked to argue their side as best they can. Their statements do not necessarily represent how they really feel. Our goal is to present the benefits and risks of gene therapy in an entertaining way. Please sit back and enjoy the debate. – MUSICAL INTERLUDE
To get things going, Cleaven Pagani for the yes side, you have 90 seconds to tell us why, if hemophilia A gene therapy were available tomorrow, you would want to receive it.

Cleaven Pagani 02:22
Thanks, David. A big thing for me would be the ability to travel more easily. I've always wanted to do a long backcountry biking trip or canoeing or hiking trip. And as it stands now, I'd have to pack a lot of medications and paraphernalia for injections. It'd be quite difficult to do any of that kind of stuff with all of the supplies. So a successful gene therapy treatment would allow me to actually pack a normal sized bag and do some of those things that I've wanted to do. I also work away from home sometimes and bringing medication that needs to be refrigerated can be an issue, especially during long hot road trips. And in the winter, it can be particularly troublesome when attempting to keep medication from freezing in our 40 below weather like we had here in Alberta two weeks ago. So gene therapy would eliminate that problem for me. Another one is that clinics currently give out about one to three months supply of coagulation products. Gene therapy would free me from being tied to the clinic. You know, some people might want to take a job or go to school in a foreign country. And that would be made possible or at least much easier if you didn't have to keep going back to the clinic for products. Lastly, I could potentially avoid more joint surgery. I've had an ankle surgically fused due to the pain and joint damage. The other ankle is quite damaged and painful as well. And the continuous factor VIII from gene therapy might make it possible to avoid another ankle surgery.

David Page 03:49
And now Cleaven's teammate from team yes, Rick Waines. Go, Rick.

Rick Waines 03:53
So I guess for me as I'm getting older, I have some anxieties about venous access. I also have some anxieties about ending up in a care home with staff who are needle phobic and unable to, you know, gain venous access. And despite the fact that we have subcutaneous options these days, I'm still not crazy about being taken care of by folks who may not be able to handle that treatment. I also feel like as I get older, the burden of treatment seems to be sort of exponentially higher. The older I get, I have less patience for my medications. And while that might seem like a triviality, I guess I feel like it's actually a psychological burden that I would be delighted to be freed from. And also just having the psychosocial break from having a lifelong, chronic, life threatening disease would be a great benefit to my mental health and well-being. And I think that's about my time.

David Page 05:00
Very convincing arguments from the yes side. Now the no side, arguing that they would not be interested in hemophilia A gene therapy, even if it were available tomorrow. From team no, Paul Wilton.

Paul Wilton 05:12
Twenty-five years ago, I was so excited about gene therapy. Hemophilia could be one of the first genetic diseases to have a cure, and in a very dark sort of competitive way us bleeders could claim to have bragging rights, our diseases cured before yours. If this aspirational therapy could be a reality, I could live a normal life, no more bleeds, no more restrictions, no more needles, no more pain. But our dreams of days past were just that,
dreams. The gene therapies available today are not full cures. You get one shot at gene therapy and once you're in, you’re in; it cannot be retracted or repeated. The outcome of gene therapy for an individual patient cannot be predicted. For all those guys out there with commitment issues, this may not be the therapy for you. And for all you bleeders who lived through frequent hospital visits and traumatic poking and prodding, recipients of gene therapy can expect many hospital visits and blood draws in the first months after administration. Did you know that most gene therapy patients require corticosteroids for many months? And do you know what the side effects of corticosteroids are? I do not need weight gain in the belly, face or back of the neck. And get this! Did you know your doctor may recommend reducing your alcohol consumption after gene therapy? Read my lips: deal breaker.

David Page 06:34
And to complement Paul Wilton’s arguments on the no side, team no’s Emil Wijnker.

Emil Wijnker 06:39
I don't think I would be jumping on the bandwagon to receive gene therapy if it were available today for a number of reasons. Number one would be the lack of efficacy demonstrated for hemophilia A gene therapy so far. Some of the results coming out of studies have been really promising for some of our factor IX gene therapies. But factor VIII hasn't shown the same degree of efficacy. I'm a very cautious patient when it comes to my hemophilia treatment. I for one am still on a regular half-life factor VIII product. So I'm very slow to adapt. And I take a lot of information into consideration when I make the choice to switch my therapy. And there doesn't seem to be enough information out there yet for me to feel confident making this switch or jumping on with a hemophilia A gene therapy treatment. As Paul mentioned, the corticosteroids required for some of the AAV vector-based gene therapies really pose a huge red flag for me. I don't want to take those on with the side effects that are presented with corticosteroids. And the fact that once you've received such a gene therapy treatment, you're likely to be precluded from receiving them in the future. If there's no guarantee that the current therapy would be efficacious, I'm not sure I want to commit to that one treatment and roll the dice that it might work for me, it might not, for how long? I don't know. I really just am one of those people who really wants more information to be able to make a sound decision. And I don't feel like there's enough information out there to convince me that gene therapy for hemophilia A is right for me, now.

David Page 08:16
Some very clear concerns from the no side. Now on to the second stage of this debate, the rebuttals.
MUSICAL INTERLUDE – The no side goes first. Paul Wilton and Emil Wijnker, please give us your reactions to the arguments from the yes side.

Emil Wijnker 08:38
I really appreciate Cleaven's argument for travel. I get that one hundred percent. I love to travel myself and taking all of the factor VIII replacement therapy paraphernalia with you as you travel is a huge pain in the butt. I'm not so sure though, if gene therapy would really get rid of all of that, especially at the beginning of treatment, considering all of the follow up that's required at the outset of gene therapy. Right now, I don't think it would pose an immediate solution to some of those concerns. But I certainly hear that argument one hundred percent.

Paul Wilton 09:08
While I have tremendous respect for my colleagues and how they feel about this and in their own personal right, I would say Cleaven's risk tolerance is quite a bit higher than mine. I would look at the risk benefit differently than him with the risks of gene therapy. It would seem to outweigh the convenience of some of the things he mentioned around supplies and freezing and keeping things cold.
And now Cleaven Pagani and Rick Waines from the yes side, and I'd like to hear more about the arguments around efficacy because you know, these therapies do bring people up to, you know, a mild hemophilia level, and that would be quite attractive in terms of lowering bleed rates. So please, please go with your rebuttals.

Rick Waines 09:55
I've been on emicizumab for a while and I have had the benefit of having ... presenting now as someone with mild hemophilia. It’s been a great change for me. There’s still a great many barriers to I guess ... what we’re talking about is, you know, dreams, I think. And if you have dreams of spending a year overseas—and who hasn't had those—they've never been accessible for folks with hemophilia A, and I guess as I get older, and I think about some of those unfulfilled dreams, I think seriously that gene therapy could provide an avenue for some of those long held desires to ... to find a place and or at least to, yeah, to experience something that other folks get to do.

Cleaven Pagani 10:51
I could jump in as well. I agree with my colleagues that the use of corticosteroids sounds like a potentially terrible situation. There are lots of side effects that are known. I guess my rebuttal to that is it's only a temporary situation, you know, you might be able to suffer through a small timeframe of having to use corticosteroids. But once that initial immune reaction is settled, then life could hopefully resume normally. Regarding the one shot is all you get argument that was raised. I agree that there's no chance to use gene therapy again due to the limitations of the AAV vector delivery. But I guess I'd like to have some optimism that researchers will find another more effective delivery system that won't rely on AAVs and so if I could get another couple of years of protection using the current gene therapy now, maybe a more efficacious gene therapy will be made available in five, ten, fifteen years down the road. – MUSICAL INTERLUDE

David Page 12:02
So the conclusions. I will ask each of you to present in 60 seconds or less, the most important arguments in your mind in favour or not in favour of gene therapy for hemophilia A. So again, in random order, we start with Emil.

Emil Wijnker 12:18
The most important argument for me that would convince me to receive gene therapy for hemophilia A and which is probably why I'm hesitant at the moment would be the lack of, I suppose, a guarantee. And I think that sounds that might sound a little harsh, because I don't think in medical treatment, we can ever have a guarantee that a treatment would work. But I think the lack of hard evidence to support a likely or a highly likely positive outcome for hemophilia A and a highly likely long term positive outcome is one that is holding me back at this point.

David Page 12:53
And next Cleaven Pagani.

Cleaven Pagani 12:54
I guess I just want to say, we know that there's a bunch of risks to gene therapy, we know that the test groups aren't statistically very large. But if I had the opportunity to take it now, I might consider it to help collect data for future generations. I'm a father, I have daughters or grandchildren potentially someday that could be affected by hemophilia. And I'd want to help be one of those data points to make gene therapy better and a more attractive option for them potentially in the future.

David Page 13:24
Interesting. And now Paul Wilton.
Paul Wilton 13:26
My dream of yesterday hasn’t kept up with the reality of today. I’m now on a factor replacement therapy where I no longer need frequent infusions or to keep a constant eye on my factor levels. I can quickly and painlessly infuse every two weeks. The average factor level three years after gene therapy for hemophilia A is in the range of my current therapy. Some people get great results with gene therapy, but some people get no results. Gene therapies results don’t last. They say never buy a car in its first model year. Wait. Let them work out the kinks before you make your purchase. I’m happy to let the eager beavers go first and leave my options open for potentially more predictable and less risky future generations of gene therapy. I can understand why for older generations, even the greatest generation, they would be great, they would be eager to act now. But us younger folks can make a calculated gamble to wait for something better in the future. The equation has changed. The benefits of gene therapy are too low for me and the risks too high.

David Page 14:24
And finally Rick Waines.

Rick Waines 14:26
Yeah, I guess for me, I'm reminded on the Blood Safety and Supply Committee when we hear about a treatment that to my ears seems like bonkers, I think of rebalancing agents. When I first heard about them, I think a number of us were like, “This is a wacky way to treat a bleeding disorder, getting your system all out of ... affecting the balance of your clotting cascade in order to stop bleeding.” But then I'm at these conferences and somebody stands up and talks about rebalancing agents as being the only thin that works for them. And I guess what I feel like with gene therapy for factor VIII is that we all have different risk reward rubrics. We all have different ways to calculate what is going to help us lead our best life. I would want to have the ability to make those informed decisions on my own based on the information that I can get from organizations like CHS, or even a podcast like this. And so I would want to have those options available for folks who feel like that's going to be the right move for them.

David Page 15:40
Thank you to our four guests for an entertaining and stimulating debate. We hope that it has succeeded in laying out the benefits and risks of gene therapy for hemophilia A. To learn more about gene therapy, we invite you to visit the CHS Gene Therapy Education Program at www.hemophilia.ca. And watch out for a future debate on gene therapy for hemophilia B. Above all, it is important to talk to your primary medical provider or hematologist to better understand if gene therapy is the best option for you.

Matt Cundill 16:13
For more information, we invite you to check out more episodes in this series, HEMOPHILIA GENE THERAPY: DREAM OR REALITY?. This podcast series was made possible by an unrestricted educational grant from Pfizer, Canada to the Canadian Hemophilia Society.