Canadian Hemophilia Society
Help Stop the Bleeding

PODCAST SERIES

HEMOPHILIA GENE THERAPY – FROM DREAM TO REALITY

EPISODE 13

IF GENE THERAPY FOR HEMOPHILIA B WERE AVAILABLE TOMORROW, WOULD YOU WANT TO RECEIVE IT?

PARTICIPANTS

James Foley, Ireland; Brian O'Loughlin, Ireland; David Page, Canada; Joseph Walsh, Ireland

HOST

Brian O'Mahony, Chief Executive Officer, Irish Haemophilia Society

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Intro 00:00
This is HEMOPHILIA GENE THERAPY - FROM DREAM TO REALITY, a show coproduced by the Canadian and Irish hemophilia societies. Here's your host, Brian O'Mahony.

Brian O'Mahony 00:16
Hello and welcome to the second in our video and podcast series, Hemophilia Gene Therapy - From Dream to Reality. This is a co-production between the Irish Haemophilia Society and the Canadian Hemophilia Society. My name is Brian O'Mahony, the Chief Executive of the Irish Haemophilia Society. I'm your host for today's podcast. During the last 40 years, we have witnessed tremendous advances in care and treatment for people with hemophilia, even more so in the last 10 years, a lot of innovation. Gene therapy has been a dream for most of those 40 years, and the last two to three years, two gene therapies for hemophilia B have been approved by regulatory bodies, and one, Hemgenix, has been marketed in multiple jurisdictions around the world. But are they for everybody? So in this video / podcast, we will ask four people with severe hemophilia B to answer this question, "If gene therapy for hemophilia B were available tomorrow, where you live, would you want to receive it?" So let's meet our guests. The four people taking a part in the podcast are James Foley from Ireland, Brian O'Loughlin from Ireland, Joseph Walsh from Ireland, and David Page from Canada. You're all very welcome, James. I will start with you. So can you tell me where you live, what you do, what your age is, and perhaps what your current treatment regime for hemophilia B is?

James Foley 01:38
Yeah, perfect. Cheers. Thanks, Brian. So my own name is James Foley. I'm from Tralee, County Kerry in Ireland. I'm 34 and I'm an accountant, and I'm on prophylaxis weekly, and it's the extended half-life I'm on currently.

Brian O'Mahony 01:53
So you're already winning, James, because you're from County Kerry, which as people know is where God would have come from if he had the choice. Joseph Walsh, same question to you.

Joseph Walsh 02:04
I'm from Dublin, Clondalkin. I'm 65 years old. I'm on prophylaxis every week for factor IX.

Brian O'Mahony 02:14
What do you do for living Joe?

Joseph Walsh 02:16
I'm a journalist.

Brian O'Mahony 02:18
Journalist. I'll come to you next, David. David Page.

David Page 02:22
Hi there. Thanks for doing this. I live in a small village about an hour outside Québec City. I'm treated with EHL prophylaxis once a week. I work actually part time for the Canadian Hemophilia Society. I'm 73 years old, but my father lived to 96 and my aunts lived to well into their one hundreds. So I'm hopeful that if I do get access to hemophilia gene therapy, I could enjoy it for a long time.

Brian O'Mahony 02:47
And finally, Brian O'Loughlin.

Brian O'Loughlin 02:51
Hi there. I'm Brian O'Loughlin. I live in Sutton, which is north of Dublin. I'm a public servant the last three or four years, but prior to that, I was an industrial designer for 30 years. I'm on weekly prophylaxis with extended half-life factor IX.

Brian O'Mahony 03:06
And your age, Brian?

Brian O'Loughlin 03:08
Fifty-five.

Brian O'Mahony 03:10
Fifty-five, thank you. So again, I'll start with you. James, are you interested in receiving gene therapy? Not interested or unsure?

James Foley 03:18
Oh, no, I'm 100% interested in getting gene therapy, yeah. And why is that? Because I have the severe factor IX hemophilia. A lot of my problems are my joints. So I'm just after in December of 24 I had an ankle fusion, and seven weeks ago, I just had my elbow replaced. So to be honest, the reason why I want the gene therapy is to protect the rest of my joints. You know, my shoulders aren't great. My right elbow is the same. I'm actually due for another elbow replacement on my right so I think it's just more just the quality of life, more than anything, is what I wanted it for.

Brian O'Mahony 03:52
And how's the elbow replacement recovery going for you?

James Foley 03:56
Yeah, yeah, fantastic. Much more movement in it, stronger, no pain, which is great. Before I had the actual replacement, I was on prophylaxis every second day, which was a lot, because I was taking 5000 units, and because I've was getting so many bleeds into the left elbow that went up to 8000 units, and there was a lot of hospital admissions as well, just for pain management.

Brian O'Mahony 04:19
So Brian, I'll come to you next. Are you interested in receiving gene therapy? Not interested or unsure.

Brian O'Loughlin 04:25
I would be interested definitely, if it were to become available.

Brian O'Mahony 04:30
Why would you be interested?

Brian O'Loughlin 04:32
I'm in reasonably good shape in terms of joints and things so far. So I've had quite a lucky run of it. But ultimately, to remove certain limits on just day-to-day living really. There's places I wouldn't go on holidays that I'd like to see. There's things that I've never done that I'd like to do. And I guess from a longevity point of view as well, to be in the best of health with family for as long as possible, and to remove certain limits that I've come to accept over the years. So yeah, I would definitely consider it most enthusiastically if it was possible.

Brian O'Mahony 05:02
So a clear rationale, but different from James where he was more about protecting his joints. Joseph, can I ask you, are you interested? Not interested or unsure?

Joseph Walsh 05:12
I'm unsure, but very open minded. I was part of an earlier test, I think sometime a good while ago …

Brian O'Mahony 05:20
That's right, when we had, a company coming in, looking at a potential clinical trial, and there were meetings and AAV antibody tests.

Joseph Walsh 05:28
I was concerned at the time. I was concerned that … I think there was a problem that maybe you could, if it didn't work, you could become immune to factor IX treatment, which was a worry. And I was just concerned about something like that happening. You know what I mean, that you could be worse off now. I'm not sure if things have changed since.

Brian O'Mahony 05:47
In fact, just to clear that one up. Joe, that's not the case, that if gene therapy doesn't work for somebody, you can always go back to your previous treatment.

Joseph Walsh 05:55
My uncle Harry became immune to treatment, but he didn't get gene therapy. So it could happen either way, I suppose. My position is that I'll be 66 in a month's time. I've had two knee replacements and two elbow operations. The fact is that the treatment is working very well for me. My problems all stem from history. I think everyone else is younger than me. I feel I can travel wherever I want to go with the treatment. It's working well for me.

Brian O'Mahony 06:24
David certainly isn't young than you. David, coming to you?

David Page 06:28
Yes, I have been interested in gene therapy. Unfortunately, I was too old for one of the clinical trials. 65 was the deadline. And for another one, you had to be AAV antibody positive, and I was negative, so I wasn't eligible for that trial either. So I have been interested, and I'm waiting to see if it becomes commercially available, or

perhaps there'll be another clinical trial that I can be eligible for. But, I maintain my right to change my mind right up to the last minute.

Brian O'Mahony 06:58
So you'd be willing to look at a licensed gene therapy or indeed participating in another clinical trial.

David Page 07:04
That's correct.

Brian O'Mahony 07:06
Can I delve with each of you a little more deeply into the reasons for your current thinking on this, in terms of relation to current health, but also in terms of the safety, the efficacy, logistical decisions, and your readiness for this or lack of it. I'd like you to think about in terms of factor IX gene therapy, or to think currently about safety, the effectiveness and the monitoring and follow-up required. Can I start with you, James?

James Foley 07:32
I suppose, basically, just with the gene therapy, I know the results are varied. You're not guaranteed certain results. And so I think just with my life at the moment, just being in another hospital, and just the way my joints are, it would be that nice to, I suppose, not worry that, when's my next bleed? When is it? When's it going to happen, you know? So the way I see it, I'm damned if I do and I'm damned if I don't, in regard to the gene therapy. Now, I know there is complications, I suppose, with the liver, and I know that it is a virus and it is an add-on to your DNA, but if I did go for it, and it didn't work out, so be it, I still have the prophylaxis to fall back on. But regarding the actual gene therapy, even if I got a rise of 30%, I'd be very happy with that.

Brian O'Mahony 08:23
If you got a factor IX expression of 30% or above, you'd be very happy with that?

James Foley 08:27
I would Yes, yes. So basically, my clotting level, it's less than 1% so actually it would be a miracle to have 20 or 30% and anything above that, then fantastic.

Brian O'Mahony 08:40
So you'd set your expectation on expression, ideally at 30% plus. How would you feel if you had gene therapy and you got 10% or 5%?

James Foley 08:50
Well, obviously, I suppose it'd just be another knock, but at the end of the day, I still have the prophylaxis there, and I can still take that and, to prevent further bleeding. But like I said, you're damned if you do, and if you're damned if you don't. So I'm very willing to take that risk, fingers crossed, that I do get those kinds of results with the gene therapy.

Brian O'Mahony 09:10
And if you were getting gene therapy tomorrow, ideally, what would your expectation be in terms of how long it would be durable for? How long the factor expression would last?

James Foley 09:19
From what I know anyway, how long it could last, could be 10 years, could be more, which is great, you know, I'm thirty-four. So it'd be great to enjoy life now instead of waiting maybe another 10 years until the new product comes out, you know, regarding gene therapy. So, yeah, like to be honest, the only thing is just a quality of life for me at the moment, and even traveling, it'd be great not to carry factor with me traveling, you know, especially for work or holidays, you know, things like that, because you have to get letters from the doctor to say you can carry X amount of medication on a flight with you.

Brian O'Mahony 09:51
David, I'm going to come to you next with the same question in terms of safety, efficacy, the follow up required what you're thinking so.

David Page 10:00
I've got, you know, several reasons for wanting gene therapy. I think right now, even though I have good prophylaxis, I do fall below 10% a lot of the week. So my ABR, my annual bleeding rate. is up around six, which is probably too high. So I'd be hoping that I could get better results with gene therapy. I think something in the neighborhood over 15% would be good. That seems to be sort of a critical point above which people don't bleed very much. I also have terrible veins, and they're getting worse all the time. Nurses hate to see me coming because they have trouble with my veins. That's not going to get better when I'm 80 or 90. So I think that would be another factor that leads me to be more interested. And certainly travel. I gets harder and harder to travel as you get older, insurance and all of those things. So I think having a solid factor IX level would be helpful and allow me to be much more mobile.

Brian O'Mahony 10:57
What about durability? David, if you would have gene therapy. How long would you hope it would last?

David Page 11:03
Well, I hope to live to about 100 so maybe 27 years would be good. And from what I've seen of the durability in not only the one that's commercialized, but in some of the earlier versions of factor IX gene therapy, this seems very durable well beyond 10 years. So I'd be hopeful that it would be, well, my lifetime, anybody, and maybe James's lifetime too, if he's even though he's only thirty-four.

Brian O'Mahony 11:24
So you want to get to the age of 100 with this so you're a pretty optimistic guy. Brian, I'm going to come to you next: safety, effectiveness and the monitoring and follow-up required.

Brian O'Loughlin 11:38
I don't have really any concerns about safety at this stage, because I think it's been around long enough that it's reasonably well understood. I think you're a fine advertisement for that now yourself. So I wouldn't be particularly worried from a safety point of view, to be honest. To be realistic on expectations. I'd take 10%. if I got it 30, it'd be nice, but I wouldn't feel shortchanged if I got 10. I think that would make a substantial improvement on things. I'd like to think that it would be a 10-to-15-year kind of thing. I'm 55 now. If I got to 70, when the body's going to slow down naturally anyway, and got those 10 or 15 active years, I think that would be very worthwhile. I would be very mindful, though, of tempering expectations. I spoke to you about this a little while ago. I was enrolled on a clinical trial, and a week or two before the study starts, I had an irregular liver function result, and I wasn't able to participate. And having got invested in the process, and despite best efforts, got my hopes up, and then it was yanked away at the last second. I found that psychologically the hardest probably thing I've had to deal with to do with my hemophilia over the years. So if there was a possibility of gene therapy coming along, I would be very much baby steps and tempering expectations and planning on the least and take anything above as a bonus. But I think that managing one's expectations and protecting your psyche really from a blow as much as your body, is an important thing I think that people should take on board or give some thought to beforehand.

Brian O'Mahony 13:13
And that's a good additional point, actually, Brian, the need for psychological support before gene therapy, during gene therapy, and even after gene therapy, for example, if somebody loses expression.

Brian O'Loughlin 13:24
Very much so. To live your life and then to have on the horizon that it could then get pulled at some stage, or even if just the level that you turn out with at the end isn't what you were expecting, and you have to sort of

rewrite your own internal route map, but just to be cognizant of those possibilities at the start of the process. So it doesn't just land on your lap, because it can be quite hard to cope with.

Brian O'Mahony 13:42
And I know that the new WFH guidelines on gene therapy talk quite a lot about psychological support at every stage of the process. Joe, can I come to you? What are your thoughts?

Joseph Walsh 13:54
To be honest, I don't really know much about it, because I haven't I investigated. Like I say, the long-life treatment I'm on at the moment seems to be working fairly well for me. I've had other health issues, I've had a cancer scare and prostate issues, and I just haven't had problems with hemophilia in the last 10 years, and I haven't had serious bleeds. I mean, the point about veins, veins is getting more and more a problem. If it was available, I'd certainly like to have it. I wouldn't jump to the top of the queue, though, because I think that there's clearly people here who would need it more than I would, but I'd certainly, I'd certainly look at it. If it was available, it seems to be the future. It seems to be the present. And, you know, my safety fears, I'd obviously have to read up on that, but I'd be happy to take it, I think, after reading them up on it. I don't feel an urgent need for it.

David Page 14:44
Brian, can I jump in there. That’s an interesting point that Joe makes about perhaps other people needing it more. To me, this could mostly benefit younger people. They could have it for a longer time and maintain their joints in better shape and be more active, as opposed to an older person like me, whose joints are pretty well finished already. Now I'd like to maintain them as they are. And the other issue is there may not be doses for everybody, and they may be a limited number of people who can get it in the early years, and so maybe younger people would benefit more.

Joseph Walsh 15:13
No, I'm not saying that. I think everyone here deserves it. I'm not trying to make that point at all. I'm just saying it's only when Brian rang me and said, you want to take part in this. I said, yeah, the weekly treatment is working for me. I haven't had a bleed in a good few years. That's the only point I’m making. I think everyone deserves it.

Brian O'Mahony 15:29
But you made another important point, Joe, and I think that is that you haven't given it a huge amount of thought yet. But if it became an option for you, you would do that. You'd look at all the information.

Joseph Walsh 15:40
Yes, absolutely.

Brian O'Mahony 15:42
I think the key here is that this is a therapy which you can only get once. You can't be re-dosed. You can't predict for any individual how long it will last, what factor level he will get, and whether there are any safety considerations. So it is, to an extent, somewhat going into the unknown, although there's quite a bit of use now globally, and I think our view, certainly as an organization, would be that we want people to make a fully informed personal decision. So for each of you, I think it would be a question of going through all of the parameters, all of the knowns and unknowns, look at your expectations and trying to manage those before you make a decision. I mean, unlike any other therapy, you get this once, you can't get it again, and you can't predict what outcome you'll get. Now, you can look at the results of the clinical trials. You can look at the real world evidence which is coming forward, which shows, you know, a significant proportion of people getting very good outcomes, but you can't predict what outcome any individual will get, and unlike factor, you can't change the dose, you can't change the treatment, you can't change the frequency. So I'm interested in your thoughts, all of you, about the fact that you can't predict any of those. you would be going into a situation where you'd have to

set your expectations and then manage them, knowing that you may not achieve all of your expectations. You may achieve them all. You may achieve none of them. How do you all deal with that uncertainty? James?

James Foley 17:06
I suppose with my level being less than 1%, getting hopefully 30%, obviously, that would be the dream. But, you know, I suppose that would be my expectation going in and I suppose maybe if I got five or 10, obviously, it'd be a bit of a knock, because I'd have to continue to take prophylaxis, but at the end of the day, like, it makes no difference to me. You know, the reason for me doing this is for, literally, like I keep saying, this is for the quality of life. It's for nothing else. I just want to stay out of hospital. I've missed a lot of work, you know, because of my bleeds, and I'm kind of struggling financially because I've been off so much this year, and mentally, it's kind of hard to cope with. I think I've spent nearly … what … two to three months this year in hospital alone, and like that's excluding appointments and follow-ups. So I just kind of just want to enjoy life. I remember my first bleed started when I was 11. It's been bleed after bleed since. It'd just be lovely just to get a break from that. And just after I had the replacement and the ankle fusion. It'd be great that like nothing else triggers, like my knees and my shoulders It'd be nice to just kind of move on from it, put everything behind me and start the new chapter. And that's how, like I said, if I got the 30% raise, I wouldn't have to kind of worry about both accessing and taking needles, worrying about carrying it places. To me, that's such a relief.

Brian O'Mahony 18:29
Brian, what about you? And as you mentioned earlier, you had a psychological blow in the past when you were approved for it, then it was pulled. So in terms of the uncertainty of the outcome, how would you deal with that?

Brian O'Loughlin 18:42
Well, for me, I'd be setting my expectations at the lowest likely result and then can treat anything else above that as a bonus, pretty much. So if there's a reasonable expectation of a range from, say, 10 to 40, I would just try and convince myself 10 is what you're going to get, and then if it turns out to be more, so much the better. So I think that's the way I would manage it personally. I would convince myself that the lower end of the range is what's likely to happen and then be happily surprised if something better comes along. I couldn't really handle the disappointment otherwise.

Brian O'Mahony 19:16
You take quite a sensible approach of setting a relatively low expectation and then hoping to achieve more than that.

Brian O'Loughlin 19:25
Purely just as a psychological safety net, as a cushion, because the previous time I didn't realize there were so many things that could go wrong. But as it turned out then, I had a slightly positive result for the AAV, so that would have been a complication as well, but that didn't go up until after. And actually, I'm in the hospital tomorrow to have a liver scan, so that only came to rise from that clinical trial. So still trying to get my liver fixed. So you don't know what other things are going to come along. So the only way I could really go along with this process would be to expect the least and be happily surprised at anything better that comes along. I'm very fortunate. I don't really have target joints. I don't get a lot of bleeds. I'm less than 1% but the prophylaxis is working really quite well. So I can get through as things are. Better would be nicer, and lots better will be really nicer, but I'd be managing expectations down to the low end. It's the only way I could really progress.

Brian O'Mahony 20:21
Joe, what about yourself? How do you deal with all the uncertainty of not being able to predict the outcomes?

Joseph Walsh 20:28
I'd want to read up and see what the risks are to my liver for anything like that, and then I'd weigh it up. Maybe I am being a bit naive and thinking I haven't had any bad bleeds recently. That doesn't mean I couldn't get them,

but just listening to what James is saying there, I can see the difference. The damage done to my ankles and my knees is done. Having gene therapy isn't going to change that end of it, it would prevent other serious bleeds. So that's actually a huge thing that I hadn't considered when I think of it, and then the risk, you just have to … I mean, it sounds, from what's been said here … I'd have to read up on it, but you take risks with everything. Any time you have an operation, it's a risk. Medication is a risk. So if I was happy enough that the risks were at a minimal risk level or whatever, I'd certainly go along with it. I wouldn't be too worried.

Brian O'Mahony 21:20
David, what about yourself?

David Page 21:24
With the commercial product, it looks like about 90% of the people are getting a really good response, well in the therapeutic window. So 90%, I'd take a chance with that. I think the risks are pretty low of a bad outcome. If it was a clinical trial, that's a bit of a different thing, especially an early clinical trial. You don't know what the results are. There are different doses at the beginning. You may not get a good expression. You've got no data, really, on safety. So, you know, I'd be interested in a clinical trial, but the unknowns are a lot more daunting there, but with a commercial product, I would certainly be ready to accept the risks and see what happens.

Brian O'Mahony 22:02
And obviously with gene therapy, if any of you are considering gene therapy, it's important you talk to your consultant hematologist, and your primary lead for this in terms of getting a better understanding of what it involves. But also, I think the hemophilia societies will be doing a lot of work in terms of education. And let me ask all of you one quick question about that. In terms of education on this, would you prefer individual consultations with the patient organization or small group meetings, where you could discuss this in small groups together? Any thoughts on that?

David Page 22:36
I like small group meetings. I mean, this discussion has been really interesting. It's great to hear other people's viewpoints.

Joseph Walsh 22:43
I agree. I agree. I think a group discussion would be perfect.

Brian O'Loughlin 22:47
I'll go along with that, now I think small groups will be a good way forward.

James Foley 22:51
I think individually or by groups, whatever you feel more comfortable with. I did it individually, which was fine. And it's nice to get other people's opinion here on the group. So I think it's nice always to be honest.

Brian O'Mahony 23:03
And actually, I don't see any reason why we can't do both. We can have individual consultations using, perhaps also the World Federation of Hemophilia shared decision-making tool, but also small group meetings. We've always found that in a small group, somebody else asked a question and makes a point that you hadn't thought of. That's interesting. I hadn't thought of that, so it's a good way to absorb information. So look, I think we will close it there. Thank you all very much for taking part. I think it was a very stimulating discussion, and hopefully we will talk to you all soon on this again.

Signoff 23:42
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