

Myeloma Matters: A Podcast Series from the Multiple Myeloma Research Foundation

Episode 2: Targeted Immunotherapy

Transcript

Narrator: Welcome to the *Myeloma Matters* podcast, hosted by the Multiple Myeloma Research Foundation and focusing on patients' experiences with and perspectives on multiple myeloma topics that matter to anyone affected by this blood cancer.

In this episode, you'll learn about targeted immunotherapy, a unique type of myeloma treatment that actively targets myeloma cells. We'll hear from three patients who have been on a targeted immunotherapy to get a sense of the patient experience. And we'll discuss how these patients wound up receiving targeted immunotherapy.

Please note that every myeloma patient is unique: the information in this podcast is not intended to replace the services or advice of trained health care professionals. Please consult with your health care team or contact the MMRF Patient Navigation Center at 1-888-841-6673 if you have specific questions about your health.

The path to a diagnosis of multiple myeloma looks different for everyone. For patients like John Wayland, myeloma is first detected during a routine physical. John was diagnosed with multiple myeloma in 2016 after his primary care physician decided to follow up on some abnormal bloodwork results.

John Wayland: Called me on President's Day, 2016 in the afternoon. I remember I was grilling. My sister and brother-in-law were in town. And he said, "I'm going to need to make a referral to a hematology oncologist." And so, I said, "Well, that certainly is not good news."

For others, myeloma isn't detected until it has significantly affected other organs. This was the case for Erik Ellefsen and Brenda Clark, the other guests we'll hear from in this episode.

Erik was a 33-year-old high school principal in southwest Chicago when he started developing vision problems. When he visited his eye doctor, he learned that he had a hemorrhage in his retina. The doctor knew it was an issue with either his blood or his brain and referred him for an MRI and bloodwork.

Erik Ellefsen: But then when I went for the blood test, it was like those old, it's like the oil commercials where they showed the old viscous oil versus the new oil. Like the blood was barely coming out of my veins.

Likewise, Brenda was diagnosed with multiple myeloma after seeking care for another health concern. In January 2010, Brenda knew something wasn't quite right. She was recovering from knee replacement surgery and contacted her cardiologist to tell him she wasn't feeling well. After running some tests, Brenda's cardiologist told her to go to the emergency room right away.

Brenda Clark: So I went and they gave me a vial and they said, "We need you to go ahead and provide a sample for us." And I said, "What?" And the doctor at the emergency room said you're in renal failure.

After running more tests to determine the cause of her renal failure, Brenda's doctor called in a hematologist who diagnosed her with multiple myeloma.

Brenda Clark: And he said I tell you what, I said, he said once we get you in treatment, then all this other may fall into place.

Multiple myeloma treatment typically begins with several cycles of induction therapy, which typically consists of three—sometimes even four—types of medications. These cycles of therapy are usually followed, in patients who are eligible, by an autologous stem cell transplant and maintenance therapy with Revlimid.

For many people, this initial treatment strategy works well: most patients respond to a point where the level of M protein in the blood drops. This was the case for John, who had over 2 years of a response after getting a stem cell transplant and standard maintenance therapy.

John Wayland: So my induction therapy was Revlimid, Velcade, Dexamethasone. And I think we did either six or seven cycles. I had a very fast and strong response to the drugs. And that led up to an autologous stem cell transplant at UM in – it started in September of 2016. I had a very good result from that. I got down to no discernible M spike, et cetera.

And given the kind of higher risk profile that I had, I continued immediately after the stem cell transplant on maintenance therapy with Revlimid, Velcade and Dexamethasone.

But not everyone responds to this treatment. Some people with aggressive forms of myeloma may require several different medications or even a second stem cell transplant to get their disease under control.

That was the case for both Brenda and Erik. For them, standard treatment approaches weren't enough, and they had to quickly move on to new kinds of therapy or, in Erik's case, a second stem cell transplant. Erik received several rounds of therapy and two stem cell transplants within 9 months of being diagnosed. In that time, he estimates that he spent 60% of his time in the hospital for treatment.

Erik Ellefsen: I spent a significant amount of time in the hospital. Because they had me in and they did pheresis and they started on the, you know, at that point in time Velcade/dex. And then they'd send me home and it would get worse. And I'd come back, and then they'd do pheresis again and Velcade/dex, and then they realized well, sending me home, it gets worse. And then they sent me to a different hospital.

Yeah, so that was the crazy, like, they were just trying to keep me alive. Find a treatment. They didn't know what to do with me, because I had manifested in such an unusual way for them.

Brenda achieved a very good partial response after her transplant, but she also developed severe side effects from her treatments, including neuropathy and blood clots.

Even among patients who initially respond well to induction therapy and transplant, many experience a relapse or recurrence of their disease that requires additional treatment. Multiple myeloma is characterized by periods of relapse and remission, and most patients need to try several treatment approaches to control their disease. John, Erik, and Brenda all reached points in their myeloma journey where they required a new approach to treatment. For John, that point came more than 2 years after his stem cell transplant, when his maintenance therapy stopped working. For Erik and Brenda, that point came much sooner.

Fortunately, there are now many options available for treating myeloma that has relapsed or that does not respond to treatment—what is referred to as “refractory myeloma.” These options include several approaches and agents that are showing promising results in clinical trials. One of the most exciting new approaches to myeloma treatment is targeted immunotherapy, which has emerged as a strong option for many patients who require new treatments for their myeloma—including John, Erik, and Brenda.

Targeted immunotherapy gets its name from the fact that it actually *targets* cancer cells based on the presence of certain markers found on the surface of myeloma cells. These therapies boost the body’s ability to focus on and kill myeloma cells specifically. This is a major step up from older approaches, which used therapies that killed both good and bad cells.

The markers that are used as targets for immunotherapy are proteins with names like CD38 or SLAMF7. These proteins are found on the surface of both myeloma cells and healthy cells—though myeloma cells tend to have higher amounts of them, which is why they are useful as targets for anti-myeloma therapy. Different drugs are able to target different markers; for example, Darzalex and Sarclisa were designed to target CD38, whereas Empliciti was designed to target SLAMF7.

Many new immunotherapies that are approved for use in multiple myeloma patients or are currently in development target another myeloma surface marker known as B-cell maturation antigen, or BCMA. BCMA is an especially attractive target for immunotherapies because it is found in abundance on almost all myeloma cells. A wide variety of novel immunotherapies target BCMA, including antibody-drug conjugates like Blenrep, chimeric antigen receptor, or CAR T-cell therapies like Abecma and Carvykti, and several new bispecific antibodies that are currently in clinical trials.

The newest of these targeted immunotherapies, such as CAR T-cell therapies, have been able to induce responses in most patients with multiple myeloma – including those that have relapsed from several other prior therapies.

John, Erik, and Brenda were all offered some form of these new immunotherapies in a clinical trial setting. For John, this occurred after he'd experienced several episodes of relapse despite getting two rounds of stem cell transplant and three different combinations of maintenance therapy. Given the urgency of his situation, he was enrolled in the MagnetisMM trial, which was investigating a bispecific antibody that targets BCMA plus another drug that helps enhance the expression of BCMA on myeloma cells.

John Wayland: I was hopeful that the approved and available pharmaceutical out there would keep things under control and, you know, together with the stem cell transplant. And we kind of rapidly—over a five-year period—worked our way through everything that was kind of approved and available.

There really wasn't enough time to continue waiting for cilta-cel nor was there enough time to go through apheresis due to the modification of the cells, et cetera. And number two, what Doctor Hoffman seen is one fo the study investigators, I think, indicating that the bispecific antibody therapies are showing as promising results. So those two decision points put together led us towards the BiTE trial.

John started treatment in the clinical trial early in the spring of 2022, and he's extremely optimistic; he achieved remission after only four months. As of August 2022, John was gearing up for bone marrow biopsies and imaging studies that would determine how deep that remission is. Early in the trial, he was challenged with more intense fatigue and nausea than he'd had with other therapies, and he had to manage a case of low-grade cytokine release syndrome. John and his oncologist agreed to a reduction in one of the two study medications, which provided significant relief of his symptoms. John is confident that his participation in the MagnetisMM trial will help not only himself, but others with multiple myeloma.

Erik expressed similar sentiments about the broader value of clinical trial participation. Erik's myeloma was well managed after his second transplant, but it never went away. After 11 years of maintenance therapy, the treatment started to take a toll on his well-being, so he spoke with his doctor about next steps. His doctor recommended a clinical trial of a CAR T-cell therapy.

Both Erik and Brenda were enrolled in CAR T-cell therapy clinical trials to help manage their disease, which never went into remission for either of them. Erik was, in fact, actually enrolled in two clinical trials, as the first therapy didn't work as well as his oncologist had hoped. Nevertheless, for both Erik and Brenda, CAR T-cell therapy was the answer they'd been looking for.

Brenda Clark: Let me say this, after I had the first CAR T-cell and you have to go back every so often to get checked and everything. So it was about two weeks later, yeah, two weeks later after I had had the CAR T cells, so Doctor Flynn said your multiple myeloma is gone.

And when he told me that, the relief that I felt, the joy that I felt, I still remember that.

Erik's myeloma also responded quickly to his second CAR T-cell therapy. Both Brenda and Erik have been fortunate to be in remission for a while without needing additional treatment for their myeloma. Erik has been off treatment for more than a year and Brenda for four years. Unfortunately, Brenda's myeloma has since relapsed since her treatment in 2016, and Erik's myeloma appears to be coming back, as well. Despite this, both Brenda and Erik consider their treatments a success.

Erik Ellefsen: I think the one thing I've learned about CAR T, people talk about it so positively that then we ask that kind of, what's the overall response rate? And then when you hear the overall response rate, it's actually kind of disappointing. Because it's like, you know, they said 10 months. And I'm like, what? I'm doing all this for 10 months? But then I realize like now, a year after my second one, it's like oh yeah, I'd do this for 10 months.

After more than a decade of nearly continuous treatment, Erik cherished the break.

Erik Ellefsen: I think it is that sense of just living life without the ties to treatment. My schedule, my life schedule for 12 years, for really 12 years, was so tied to the ups and downs of what the drugs would make me feel and how they'd make me feel, and even I traveled a lot for work for a period of time, and it's like, well, I can't travel here because this, this. So your life is built all around myeloma, and then it's really this interesting

phenomenon that I've experienced this last year of self-reflection, of feeling more like myself.

But Erik and his doctors think that these novel treatments have broader potential. As Erik's oncologist told him, these novel therapies are paving the way for a brighter future in multiple myeloma treatment.

Erik Ellefsen: He told me in March. Erik, I truly do think for the first time that we might be able to cure this. You know? And so to have that hope where I think early on, so many patients' lives, and there's a hopelessness that comes with myeloma that can be, and I've felt it at times. And it's just like, can be debilitating and overwhelming. And so to have that hope that there's something next and to have this option and that for now, the next best hope are these kind of treatments that you're talking to patient about.

Treatment advances have also offered hope to Brenda, who reminds herself that even if there isn't a cure, myeloma treatment is advancing every day.

Brenda Clark: And the key to all of this is staying alive long enough so that you can get to that next drug or that next treatment that they have coming out. Because it's just around the corner and you just trying to get there to make sure that you can get that next treatment or get that next drug.

These improvements in treatment and the ever-advancing understanding of myeloma biology take a lot of work, and clinical trials are a key piece in putting together the puzzle. Although their experiences differed, John, Brenda, and Erik all received life-saving treatment thanks to the opportunity to participate in immunotherapy clinical trials.

Erik Ellefsen: I mean, that's where I encourage some of my other friends too, when they go into these places of like, should I do a trial or not. It's like yeah, do it. Because you're helping yourself. But then you're helping so many other patients behind you, whether it works or not.

Narrator: Let's hear more from John, Erik, and Brenda, who are joined by Mary DeRome from the MMRF, who'll share more about their experiences with targeted immunotherapy treatments, and their insights on what factors to consider when deciding whether a clinical trial is right for you.

Mary DeRome (MMRF): John, Erik, and Brenda, thank you so much for being with us today on our *Myeloma Matters* podcast dealing with the topic of targeted immunotherapies and multiple myeloma. This is arguably the most important and most talked about topic in multiple myeloma today.

You guys are all myeloma warriors with experience in having these immunotherapies, and we are really interested to hear about your experiences

with them—how well they worked and any words of wisdom you might have for other patients who are considering these therapies.

Let's talk about how getting a targeted immunotherapy might be different than getting some of the other more traditional drugs that you've been on.

Erik, let's start with you.

Erik Ellefsen: The biggest difference for me was just the extent of what the immunotherapy required—the hospitalization. It was the time in the hospital that was different, whether it is the oral medication or the infusion process.

Mary DeRome (MMRF): Brenda, did you find it similar with your CAR T experience?

Brenda Clark: Absolutely. Also, with the [autologous] stem cell stem [transplant] I remember that just prepping for stem cell was different, and it was more intensive for me.

I had a lot more problems with the stem cell than I did with the CAR T.

Mary DeRome (MMRF): John, how about your experience with bispecifics?

John Wayland: For the bispecifics, it was much different than the two stem cell transplants I had previously. There was a required hospitalization for initial dosing, mainly to determine what side effects you might experience, particularly for anybody who's might have a heavy cytokine release syndrome issue. But outside of that, it is weekly treatment in the hospital, and I have a daily oral. It's very similar to what I found for maintenance medications. The difference, really, was in terms of the magnitude of side effects that I experienced, which were significantly higher than I had had in the past.

Mary DeRome (MMRF): We're going to talk about CAR-T therapy right now with Brenda and Erik.

You both mentioned that preparing for the CAR-T therapy was challenging. How does preparing for that particular therapy compare to preparing for, let's say, an autologous stem cell transplant?

Brenda, you mentioned that, for you, the CAR-T preparation was not as bad as the stem cell transplant. Can you talk about what made these procedures more or less challenging for you?

Brenda Clark: With the stem cell transplant, you had to actually give yourself a shot so that you could increase your count. That was challenging. With CAR T, I didn't have to do that. I had an outpatient, as opposed to an inpatient, stem cell

transplant. That was more challenging. Also, I lost my hair with the stem cell transplant, which for me was devastating. With CAR T, I didn't have that.

I did have to spend 14 days in the hospital for CAR T, but I didn't find that challenging. I had my laptop and my movies, so that was not as challenging. Also, I didn't have the side effects that I had with the stem cell transplant.

Mary DeRome (MMRF): Erik, how about you? How did your CAR T compare to your stem cell transplant?

Erik Ellefsen: The stem cell transplant is much more difficult overall: the preparation, the chemotherapy, the side effects. I actually did a double transplant, so I went back-to-back with mine. The weight of that, back-to-back, was really difficult for me when I look back at it. The biggest challenge for me was more mental and emotional, in the sense that it was a trial. I didn't know a lot of details. Part of my being on it was that the doctors are also trying to figure out some of those things.

In comparison: when I was diagnosed and then went through the stem cell process, that was all rushed because of the situation that I was in. Whereas, with the CAR-T therapy, I had the time to mentally and emotionally prepare. Which actually, in some ways, was a detriment. Because I found that the anxiety and my anxiousness for something I didn't know a whole lot about started to kick in.

So these were very different experiences. Challenges in certain ways. But CAR T was much more, overall, preferable to the stem cell transplant.

Mary DeRome (MMRF): A lot of patients probably share that view.

When you were getting ready for your CAR T, were you worried about whether or not it was going to work for you?

Erik Ellefsen: Oh, 100 percent. I think the worry is like—they said it's similar to the stem cell transplant.

My worry was like, "Oh, I have to go through this again." That was worry number one. Worry number two was, "I don't really know a whole lot about it." I knew people who'd gone through this stem cell transplant process, so I could ask them questions to prepare myself, whereas I didn't necessarily have that opportunity for CAR T.

The clarity for the doctors was much less. Then there's that big question, "I'm going to go through all of this and it may not work?"

The combination of those factors really created some anxiety.

Mary DeRome (MMRF): Let's talk about after you were in the hospital for your CAR T. Coming home, what was the role of your caregiver? What did they have to know? Knowing what you know now, is there anything that you wish your caregiver could have done differently?

Brenda?

Brenda Clark: My husband was my caregiver.

He was watching for any changes in my behavior or cognitive functioning. He was also looking out for fevers, chills, things like that. Anything out of the ordinary, neurological issues, anything like that that was not normal for me. He also was my chef, my cook, and my housekeeper. He did a lot of things. When I was first going through that, it was before DoorDash and before grocery delivery. He had to do all of that himself.

Looking back, one thing I wish he could have done was asked for more help. Because he felt like he needed to do it all himself, and he didn't want to ask anyone. Plus, he was worried about infection, and he didn't want me to be exposed to anyone. So he wanted to just be there and do it all. I wanted him to know he didn't have to do it all, but he wanted to.

Mary DeRome (MMRF): Sounds like he did a great job.

Brenda Clark: He did an excellent job.

Mary DeRome (MMRF): Erik, what was your situation like with your caregiver?

Erik Ellefsen: To Brenda's point about having a caregiver who feels like they have to do it all, we've learned over time to create a caregiving team. That caregiving team is my wife, my sister-in-law, my mother-in-law, and my father-in-law. It is this group of people that has different roles, responsibilities, opportunities. It doesn't rely solely on one person even though my wife is definitely the chief of the caregivers. She's working full-time, taking care of her job and her work but then also taking care of me.

My sister-in-law was willing to come in for a month from Europe to live with us, work from our home, and do the things that she needs to do while she drives me places and does a lot of errands...that is the shared nature of it.

When I look back at the perspective of, "What might be an encouragement," it is about sharing roles and responsibilities. I got both of my CAR Ts during COVID, so there was also heightened anxiety of contact with other people. I love people and I love being around people, so just having consistent conversations of, "What does it mean to stay safe? You know, to allow yourself to heal, allow your immune system to come back?" But also, for your overall well-being, the

connections and contact that we need as patients who spend significant time alone.

Mary DeRome (MMRF): As if going through this therapy isn't bad enough, you had COVID on top of all of that, which just made everything more complicated.

Erik Ellefsen: The two weeks in the hospital was really... take your entertainment stuff and catch up. But it was actually surprisingly a place of peace and quiet before moving back into the space of home and the busyness of life.

Brenda Clark: I looked at it as a two-week vacation. I enjoyed being in there. I was able to read. I was relaxing. I enjoyed it, just being there and just being by myself and not having to worry about anything.

Mary DeRome (MMRF): For your caregiver, it's like the calm before the storm.

Brenda Clark: Absolutely. But he was able to come to the hospital. We played cards, and we just did all kinds of little things that we really would not have had a chance to do at home. It was really calming there.

Mary DeRome (MMRF): John, tell us about your experience when you were starting your bispecific treatment and how that went for you and your caregiver.

John Wayland: I was delayed starting because I had COVID in February. I actually went on a drug holiday starting in December 2021 and was originally scheduled to start in the trial in January. It was delayed because of a COVID infection, and I continued because they hospitalize you in the same floor that patients going through stem cell transplants are going through, even though you're just there for observation.

Of course, everybody is very careful about potential infections. I was delayed until mid-March in terms of starting the clinical trial treatment. Given that I had never really had significant issues with any of the pharmaceuticals and I'd taken pretty much all of them over the past five years, I really did not have any foresight or thought that I would have side effects from this trial treatment—that it would create issues for me where I would need more caregiver support and wouldn't be able to return to work. I didn't have a Plan B around any of this.

One thing I will say is that you should always expect the best but prepare for the worst. I did not prepare for the worst, which left us a little bit behind the eight ball. From the caregiver perspective, my husband—Ulysses—was really responsible for 100 percent of everything. It was everything around the house, transportation to and from your appointments, everything.

In my prior stem cell transplants, as well as the clinical trial treatment, I really did not establish a larger universe of caregivers to support the primary caregiver. That is something that people should take to heart and prepare for.

Mary DeRome (MMRF): Almost like the caregiver also needs a caregiver.

John Wayland: Absolutely.

The other issue I had to adapt to—and this is important for patients and probably everybody who goes through this—is that when you're the patient and you require a caregiver, you have to adapt your mentality to it. You're going to be frustrated. You're going to want to do things on your own. I know I had to really adapt my overall responses and everything else to understand where I am, the importance that Ulysses is bringing to the table. Everybody just has to learn to function in a different role for a period of time.

Mary DeRome (MMRF): It really is a life-changing experience.

Did the target of the immunotherapy that you had—at least, Brenda, for your first one and Erik, actually, it's for both of the ones you had. The target was BCMA. Did that mean anything to you when you were considering these treatments? Does it mean anything when you're thinking about future treatments?

Erik, did that mean anything to you?

Erik Ellefsen: When I first started, it's like, "No. I don't even understand what this means." I made them draw diagrams. I made them explain it. Now, I asked the hard question, like, "Okay, why am I now just becoming aware of this?"

There is that place for the doctors where they are still a few steps ahead of us. It didn't mean much for me on the front end. For me now, it just made me more educated and aware for the next step.

Mary DeRome (MMRF): Brenda, so you've had two CAR-Ts, right? Only the first one was BCMA-targeting. But you actually had that BCMA one twice. Now you're going to have the next CAR-T, which has a different target. What does that mean for you?

Brenda Clark: Well, for the BCMA it meant something for me because I had done the research. I knew that that's what I wanted to receive. When they told me, "This is what it was going to target," I was like, "great." I was looking forward to that. Now, because I've had the BCMA, I know that that didn't work because of the second CAR-T cell that I had.

Now I'm asking, "Okay, what's another marker?" But my next thing is, "How do you know I really have that marker?" I'm hearing, "Well, everyone has it with multiple myeloma. Everyone has this marker."

But how do you know I have this marker?

Mary DeRome (MMRF): That makes sense to ask that question.

John, your treatment—unlike the treatment that Brenda and Erik had, which is CAR-T and what people say is a one-and-done—used bispecifics, which is different. You do have to go back to get treatments. Is it weekly or biweekly you have to get treatments?

John Wayland: For the trial that I'm on, which is two drugs—the bispecific therapy drug that I'm on is called elranatamab—is a weekly subcutaneous injection that I go to the hospital every Wednesday to receive.

It is coupled with a second oral medication called nirogacestat, which is a daily pill that I take at home. Originally, I was taking a full dose, two pills in the morning, two in the evening, 12 hours apart. That really was the drug that was causing the majority of my side effects. We were able to, thankfully—with permission from the trial—reduce my dosage by half. Now I take it once a day and it has made a significant improvement in my side effects.

Mary DeRome (MMRF): I know that the nirogacestat has something to do with the target BCMA, which is what the elranatamab is targeting. Do you know what that drug does, the oral drug? Like how it helps your therapy work?

John Wayland: In layman's terms, what I understand of the drugs and the way that they interact is that the bispecific antibody therapy that I'm on is a BCMA-targeting bispecific, similar to the CAR-Ts that we've been talking about. One of the challenges, for all of this immunotherapy—whether it's CAR-T or bispecific—is durability. Nirogacestat is targeted at inhibiting the malignant cell's ability to shed the BCMA proteins, such that it continues to be a viable target for the bispecific antibody therapy overall.

Mary DeRome (MMRF): From what you said, it sounds like nirogacestat was the one that was causing you a lot of difficulties as far as side effects. Can you elaborate on that?

John Wayland: At the full dose of nirogacestat, I had a low to mid-level cytokine release syndrome issue.

I had breathing difficulty. I had a constant cough, all of which was related to this, which nothing solved. I also had a lot of gastrointestinal issues. I actually lost 35, almost 40 pounds between mid-March and mid-May. That was after being 20

pounds down from December of last year to March. I really got to a fairly unhealthy weight overall.

I was also requiring a lot of support in terms of blood transfusions, given significant levels of anemia and very low platelets. I also required plasma infusions, et cetera. Overall, the side effects were significant in terms of the first couple of cycles of my treatment.

Mary DeRome (MMRF): It sounds like the dose reduction has worked, so that's great.

John Wayland: Wonderfully.

Mary DeRome (MMRF): Are you gaining some weight back?

John Wayland: I am. I'm actually up about 10 pounds, so I'm happy about that. I have appetite. I can eat. I am starting to gain some weight back. That's all very good news.

Mary DeRome (MMRF): Good for you.

Brenda and Erik, you've mentioned that being off treatment for an extended period of time after you began your CAR-T has really changed how you handle things in life.

Brenda, let's start with you. What has changed with your so-called one-and-done therapy?

Brenda Clark: Well, I'm not tied to a treatment. I have freedom of movement. Or I had. I'm back on treatment now, but I had freedom of movement. If I wanted to go on a trip, I could just plan on going on a trip. You don't really think about things like that. Most people think, "Oh, Well, I'll just plan a trip and I'll go."

If you're in treatment, you can't just plan a trip and go because you have to plan around when you have to go back to get your blood drawn or when you have to go to a doctor's appointment. Your time is not your own. Also, being off treatment gave my body time to heal. I have little, small, roly-poly veins. So it gave my veins a chance not to have to be stuck or not to have blood drawn. Just to be off the medication was good, and it made my body feel like it was recovering from whatever it was going through. So just to be off the medication for a while was good for me.

Mary DeRome (MMRF): After being on treatment for so long, being off treatment must be really almost life-changing.

Erik, was it like that for you?

Erik Ellefsen: I 100 percent agree with Brenda. There are times where I forgot I was a myeloma patient. I lived in normal rhythms of life. I felt much more like myself. I looked much more like myself. One friend saw me, and he was surprised because he's like, "Erik, you look like I remember you." So, there are these places where you get to live life more freely. You get to forget about the myeloma at times and forget about it controlling your life and the rhythms of your life.

I will also say of all the side effects and everything, I was so glad and realized that like, "I don't have to take dexamethasone for a while." Not only physically but mentally, emotionally, energy-wise—this was the first treatment where I felt like I regained some normal life.

Mary DeRome (MMRF): Erik, what would you say to a patient who is considering an immunotherapy? If you're taking a CAR-T, it can be really great. You can go back to living a normal life. But it's not like it's not without risk, and it's not without side effects. What would you say to a person who was talking to you about it and wanted your advice about that?

Erik Ellefsen: What myeloma patients do is constantly and consistently ask lots of questions, do research. It's exhausting, but I do think there is a place for it. It's like, "Okay. I've exhausted or—I have pretty much exhausted, you know, the other opportunities." Because even in this, one of the great worries is we don't want to run out of the next treatment or the next treatment that might be in line. This is not a solution. It's not a cure. It's just a continuation of the treatment process. So ask, "have I exhausted the steps along the way to get me to this?" But the CAR-T side of things... I would do it again over regular treatment most anytime, if the possibility was there.

Mary DeRome (MMRF): Brenda, would you say the same?

Brenda Clark: Absolutely. I agree with Erik. I'm looking forward to more CAR-T cell therapy treatment options. That to me is where I'm going with it. If I had a choice between regular treatment and CAR-T, I'm going with CAR-T.

Mary DeRome (MMRF): John, you know, you're in a different boat with the bispecific. We're looking forward to our first approval in the bispecifics arena in the not-too-distant future. What would you say to a patient who might be considering going on a bispecific?

John Wayland: I would absolutely recommend it. I needed something that was available immediately with where I was. That was one of the reasons that we went bispecific instead of CAR-T. The side effects notwithstanding, you're going to have those pretty much from any treatment and just being up front with your doctor and your medical team going through that looking for a solution. The

overall therapy has been great. I have reacted wonderfully to it.

In fact, I'm in definitional remission right now. I just had a new bone marrow biopsy yesterday, and imaging studies will take place next week to see how deep that is. I'm very, very excited about that. I was as excited as Brenda and Erik, and I'm sure lots of patients out there, when I found out past the initial two doses I no longer had to take dexamethasone. What a blessing that was.

I was ecstatic. In mid-November, after I complete seven cycles of treatment, I'll move to biweekly. So that leash to the hospital will be a little bit longer, allow for a little bit more normalcy.

I really do believe that immunotherapy is where the cure will be found.

Mary DeRome (MMRF): There is a lot of hope in this field, particularly in immunotherapy. There are more drugs being approved all the time. John, what can you tell us about your experience of being on a clinical trial?

John Wayland: The clinical trial experience has been great. It's a bit more involved in terms of interactions with the hospital. One of the nice things is that you see your doctor much more often.

Generally, it's a once-a-week schedule with him and his team. Going into it, similar to what Erik related, you do have to adjust and accept where you are in the treatment continuum. We all as patients understand the importance of the clinical trials and the development of these new drugs.

We don't have another choice. You shouldn't have an issue because you've got to go forward with it. But I did find educating myself as much as possible with publicly available materials and conversations with the medical team was very important, but I was comfortable from day one going into it.

Mary DeRome (MMRF): Brenda, what was your experience like on the clinical trial?

Brenda Clark: I highly recommend clinical trials. With the CAR-T, that was not my first time with being exposed to clinical trials.

I will say that my preference is phase 2 and phase 3. I'd been on some phase 1 clinical trials; I'm not a big fan of phase 1 clinical trials.

Mary DeRome (MMRF): How come?

Brenda Clark: Well, because that's the first time that that drug is actually being introduced. I had some side effects from some of those drugs that I'm glad probably didn't make it to the market. They just had numbers to them and no

names. Some of those were not too good. But, overall, my experience with clinical trials has been really good. I would not have had access to the CAR-T without a clinical trial. I'm a big advocate for clinical trials. Especially when it relates to CAR-T.

Mary DeRome (MMRF): Erik, with the CAR-T's that you've taken, have you taken them on clinical trials or have they been approved?

Erik Ellefsen: Both of mine were phase 3 clinical trials. I came at the end of all of the work that patients like Brenda did in phase 1. I had the benefit of the doctors having better information, better knowledge. They were in the place of the final revisions or refining and getting that final data.

For the one trial I was on, the CAR-T was approved a few months later. Being in that stage is probably very different than what Brenda and John experienced at the front end, being on the front end of these processes. For me it was very normative in a lot of ways. There was more information.

The doctors were more comfortable and confident in what they were doing. Even the nurses and the medical team were more confident in their processes. The one thing I had to learn to temper was their excitement and positivity at that time. Because these were going to be—my first one in particular—approved, so there was real excitement.

But then to really temper that excitement and energy and to look at it for me practically and realistically and ask, "Okay, what does this mean overall for all myeloma patients? Where do I fit into that bigger picture?" That was one thing that I learned. But clinical trials overall... I am alive because other people have done them.

If my treatment journey takes me to a clinical trial, I will sign up—because people did that for me, to get to this stage.

Mary DeRome (MMRF): Going through phase 1 or phase 2 trials, but especially phase 1—when it's really the first time that these drugs are in people—what they're really trying to do is figure out what the best dose is to give people. Essentially, it's like finding the highest dose you can give people without having too toxic side effects.

But that information is so important, allowing drugs to move either farther along the clinical trial continuum or discontinue them if they turn out that they're too toxic. It's something that's important for all patients to do, and it's a great thing when you can really donate yourself to be able to get that information.

Let's talk about your relationships with your care teams.

Is it like a collaborative thing where you discuss different treatment options, then decide which one might be the best for you based on your goals and what's happening in your life? If you did have that collaborative experience with your care team, what can you recommend to other patients to be able to establish that relationship?

John, let's start with you.

John Wayland: I do feel that my relationship with my hematologist-oncologist and care team here in Miami is extremely collaborative and has been very good. We have very detailed, open discussions around all topics and have throughout this treatment. I actually decided when I had my initial stem cell transplant here at University of Miami in 2016—and, when that failed, in 2018—to pursue a second transplant but at the University of Arkansas for Medical Sciences at their myeloma institute.

That is the first time in my life that I've needed to speak to a physician about seeking a second opinion. I was a bit nervous about doing it, and I remember my doctor calling me—I sent him an e-mail first to tell him. I was going to slide out an e-mail and discuss it at an appointment later. He called me that same day and said, "I just want you to know I fully support your going for a second opinion. You should never feel badly about that. Arkansas is a great institution."

I transitioned back to Miami after my second transplant failed. My primary doctor's always been here in Miami.

When we were looking at the other options, we had a lot of conversations around CAR-T and bispecific antibody therapies. The doctor's view on those and their similarities, differences, et cetera helped me arrive at a decision. But really, it was driven by time and my needs more so than anything else.

Mary DeRome (MMRF): Once you start the CAR T process, it can be at least a month before the product is ready. That can be difficult for patients, depending on where they are in their disease. They may need something very quickly—something more off-the-shelf—which is more of a bispecific thing at this point. But it's great that your doctor supported you in seeking a second opinion. You were able to come back to that same care team after going somewhere else.

John Wayland: I was. I did all of the induction therapy and the transplant in Arkansas. I then had a couple rounds of extended chemotherapy after I was back. We did that in Miami; I transitioned back. They worked together. It was a fantastic experience.

Mary DeRome (MMRF): It's just amazing that everybody was so cooperative.

Brenda, what was your experience with your care team?

Brenda Clark: I have an excellent care team. I couldn't ask for a better care team. It's important that you have a multiple myeloma specialist working with you. That's what I have. I have a team of specialists working with me, and they collaborate among themselves to talk about patients and to see what's the best care for that patient. Then they come back and they talk to the patient about the care. They don't talk over you. They talk with you. They help you to understand exactly what's going on with your care and what you need.

As far as clinical trials are concerned, they're always looking for clinical trials that you may fit into. My team was heavy into research, which I'm grateful for because I like research. That's what they do. A lot of people come to them for treatment.

Mary DeRome (MMRF): The more myeloma patients your doctor sees, the better off you are.

Brenda Clark: Absolutely. They're more comfortable with it. They would not have a problem with getting a second opinion. I wouldn't need to, because they are the specialists there. Why would I need to go somewhere else to find out what they already know?

Mary DeRome (MMRF): If you have a doctor and you say to your doctor you want to have a second opinion and your doctor says, "I don't advise that," you know that you need another doctor.

Erik, what was your experience with your care team?

Erik Ellefsen: I've been blessed. When you talk about collaboration and care, it's really at the heart of the entire team that I've gotten to work with. In particular, my doctor for the last 11 years (Dr. Jeffrey Wolf at UCSF) exhibits that personally and professionally. Just how he lives that out is really fun to watch. I didn't choose him for that reason. He was recommended to me by the MMRF when I moved back to California.

We clicked right away. He's always been open to conversation, and he always gives me the options or even recommendations. But what led me even on this CAR T journey was that I was on a treatment that just became too onerous for me, and it was helping and it was working and it was managing the myeloma but my overall life capacity and wellness and...it was just not going well.

So he said, "Well, let's try something different because we want you to live the best life possible." That's always been my great appreciation. And his team has been incredible. One of the doctors in particular, Dr. Nina Shah, she became a great friend. Because I did Moving Mountains for Myeloma with her, you know, a trip to Iceland and got to know her and became a friend before she became my

doctor for one of the trials.

To build the relationships and to build the friendships and to build the connectivity—the biggest thing is that, with this time around with my current doctors, they see me as a person first and then a patient second.

That's really one of the biggest things I felt a lot of times early in my treatment and early in my disease.

I felt like I was a problem to be solved, a patient to be treated and not a person. I really feel like the reverse is true of my current team and current doctors. I'm a person first, a patient to be treated second, and the myeloma to be solved, third.

Mary DeRome (MMRF): Let's talk about some of the patients you have met along the way during your treatments and whether you've taken advantage of multiple myeloma support groups.

John, what can you tell us about that?

John Wayland: I have not been involved in a support group per se. I have kept up with several patients that I met during my stem cell transplants to understand how they're doing overall, but I have not yet involved myself in the support groups around multiple myeloma or blood cancers. I haven't felt a need overall from that support perspective. I just have been busy with everything else.

Mary DeRome (MMRF): Brenda, have you made any friends during your journey and do you utilize the support group?

Brenda Clark: I have not utilized the support group. I have throughout my journey actually been a mentor and talked with other people who have multiple myeloma or who have been just diagnosed with multiple myeloma. But as anything formal, no.

Mary DeRome (MMRF): Erik, how about you?

Erik Ellefsen: For me, the support group, the relationships, have been hugely beneficial and encouraging. I don't think I would be alive today other than the fact that, early in my diagnosis, I had a couple of what I call mentors in myeloma that came alongside me who had gone through all of what I was going to go through. They had gone through it before.

Then, when I was early diagnosis, the fellow myeloma warriors that I was going through it with as we were discovering the process together.

And our support group here in San Francisco might be pretty special because we've got a legendary advocate and myeloma patient, Jack Aiello, who cares for

us, who leads us, who organizes us, who brings us together and does such an incredible job of keeping us informed but then allowing us to develop the relationships and build into each other's lives has been so important for me.

If you're around long enough and you stick at this long enough, naturally you become a mentor in myeloma yourself, where other people and newly diagnosed patients are asking questions. For me in that entire process, the place that has been most unique is that I've had to be careful of where I fit, as I'm not the typical myeloma patient in many ways. My story doesn't match with very much of the typical myeloma story. It's saying, "How can my experience be of benefit to you? How can my story be of benefit to you? What are the things that I've learned that can be helpful to you?" But then, what are the ways I need to get my story out of the way and help people understand where they're at in their own journey?

Mary DeRome (MMRF): That type of experience helps other patients understand what a variable disease this can be and how different it can be in every person. Even so, there are pieces that people have gone through. Most people have gone through a stem cell transplant. You can talk about that with other patients. As some of these other therapies become more common, you'll be able to tell your stories to the next group of immunotherapy patients that are coming up and let them know how you did.

Let's wrap up by talking about what in your experience has been helpful in your journey that you can tell other patients about and maybe advise them about? John, let's start with you.

John Wayland: I thought about this a bit. It's been eye-opening as to just how much the patient and the patient's caregiver and the people around them need to be the advocate during the totality of the process.

From my point-of-view, you're going to achieve the best result if you educate yourself, if you have an open, frank relationship with your doctor and your care team. I echo Brenda's thoughts and Erik's as well. Myeloma specialist, a group, people who see those day-in and day-out, acquaint yourself with the Multiple Myeloma Research Foundation. The materials that are put out by the MMRF are fantastic from an educational perspective.

Understand where you are in the treatment continuum and what else is out there. Exercise, take time for self-care and care for the caregiver or caregivers, as well. Be very cognizant and focused on all of that.

Mary DeRome (MMRF): It's great advice.

Erik, let's go to you. What about your experience has been most helpful that you can really advise other patients about?

Erik Ellefsen: Having come after my second CAR T, and now I'm in that process of preparing for treatment and what's coming next, there are two things that I've learned and had the opportunity to reflect on, in particular in this last year of being off treatment. First, there's hope. The hopelessness that can often be tied to myeloma and myeloma treatment is something that can be overwhelming. The hopelessness that can often kick in through treatment or at different points as you transition between treatments—I do think what I had the opportunity to do this last year of being off treatment was really reflect on my journey, educate myself as to what's coming next, but then to sit in a place of hopefulness for more life, extended life. Better life. Not just for me but for my friends. Like Brenda and John and my other friends who are going through this with me, and then also for our caregivers.

That was the second thing that I realized. I've had great opportunities to do really great things since I was diagnosed 14 years ago and really to experience life in a unique way. But I don't think I fully sat in the place of enjoying the life that I was given. This last year really put me in a place where it was like, "You know what? I need to enjoy the peace of life." I began to enjoy the health of life again. Just to enjoy the reflection moments of saying, "Who am I and who have I become?" Even some of those places of enjoying the conversations of what I lost through this journey, but yet what I've been given because of this process and because of this diagnosis and because of this journey. For me, it is that place where purposefully placing myself in a place of hope and enjoyment, because often I can be too focused on what's next. Even now as I prepare for treatment, I focus on what's next rather than enjoying today and the moments of today.

Mary DeRome (MMRF): Brenda, what advice can you give to other patients?

Brenda Clark: I agree with everything that John and Erik said. But also, you have to stay positive. You can't have a defeatist attitude about this. This has been a 12-year journey for me. One thing that I had to realize is that relapse is going to be a part of that journey.

It's nothing to be afraid of, nothing to be upset about. It's just a part of it. You've heard me talk about a train ride. I still think of this as a train ride. This journey, once the train ride stops, you get off and you get on another ride. That's how treatment is. Once this treatment stops, you get off and you start another treatment.

But you keep moving forward. You just keep moving forward. Because you're living with multiple myeloma. It's not a death sentence anymore. We're going to live with multiple myeloma, so we have to learn how to live with it. We just got to keep moving forward.

Mary DeRome (MMRF): Amazing words of advice and wisdom from all of you. Thank you so much.

Narrator: Thank you for listening to this episode of the *Myeloma Matters* podcast on targeted immunotherapies in multiple myeloma, hosted by the Multiple Myeloma Research Foundation. The MMRF would like to thank John Wayland, Erik Ellefsen, and Brenda Clark for sharing their stories and unique perspectives on targeted immunotherapy in myeloma treatment. The MMRF also thanks Adaptive, Amgen, Bristol Myers Squibb, GSK, and Janssen for their generous support of this podcast. If you have additional questions about anything you have heard today, please call the MMRF Patient Navigation Center at 1-888-841-6673 for more information.