

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

Episode 3: Clinical Studies

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 clinical studies and why they are important to patients who have multiple myeloma or one of its precursor conditions. You'll also hear from three patients who have participated in clinical studies. They'll share their experiences and talk about the steps they took to enroll in the studies. 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.

In recent years, there's been a lot of exciting progress in myeloma care and treatment. Myeloma patients are living longer. New treatments are emerging—treatments that are not only safe and effective but that also cause fewer side effects and improve quality of life. All of this was made possible because of research done in clinical studies.

Patients with a myeloma precursor condition—that is, monoclonal gammopathy of undetermined significance or smoldering multiple myeloma—have also benefited from clinical studies, which have provided key insights into the biology of the disease and helped clinicians identify patients who are more likely to progress to multiple myeloma. This information could potentially lead to treatments that prevent progression to full-blown myeloma.

Contrary to common belief, clinical studies are NOT just for patients who are running out of options. Clinical studies are available for patients at all stages of disease, whether they have a myeloma precursor condition, are newly diagnosed with multiple myeloma, or are in a later stage of relapse. Our three guests today—Lonni McDonough, Louise Kraft, and Tricia Charamut—all made the decision to enroll in clinical trials, each of them at very different stages of their disease.

There are two main types of clinical studies that we will discuss in this podcast: interventional studies and observational studies.

Interventional studies, which is what most people think of when they hear the phrase “clinical study,” are designed to evaluate the safety and efficacy of new treatments. Patients in these studies receive early access to some of the newest drugs and therapies in development.

Observational studies, on the other hand, observe patients over a long period to determine their health outcomes based on a number of different aspects of their disease.

Louise and Tricia participated in interventional studies.

Louise was first diagnosed with multiple myeloma in 2016 after several months of feeling exhausted and having difficulties walking.

Louise Kraft: So I think my first clue was in December of 2015 my grandson was born in September. So he was only three months old but by December I wasn't able to lift him anymore. And I—and he was not a big baby.

After getting her diagnosis, Louise was treated with Kyprolis-Revlimid-dexamethasone induction therapy followed by an autologous stem cell transplant. Her Revlimid maintenance therapy worked for a while, but within 3 and a half years, her myeloma had relapsed.

Louise’s health care team offered her another stem cell transplant, but her family was apprehensive. The last transplant had been very hard on Louise. They didn’t want to see Louise go through that again. As an alternative, her doctor suggested that she try a clinical study. Louise was surprised, because she had always believed that a clinical study was a patient’s last resort.

Louise Kraft: Because we had a friend that had pancreatic cancer and his last step would have been to go—go to a clinical trial. So that was my misconception that it was a clinical trial was what you did when all other avenues were exhausted and that was your last chance for a cure or survival.

Louise’s doctor explained that the study she was recommending was looking to find out whether a four-drug therapy consisting of Darzalex, Kyprolis, Pomalyst, and dexamethasone was more effective than a standard three-drug therapy.

Louise Kraft: So I called MMRF and talked to one of the nurses there. I talked to a friend who does clinical trials for a job, and she went through all the paperwork with me, prayed for guidance. And talked to the doctor and, ultimately, she called me at home, and I asked her, “What do you think is my best chance to get better?”

Louise and her doctor agreed that the clinical study was the best option. She enrolled in the study and, after 6 months of treatment, she was determined to be MRD negative. She is still in the study as of today and expects to stay enrolled until her disease progresses.

Tricia also enrolled in an interventional study. She was in an earlier stage of her myeloma when she joined the study. Tricia was first diagnosed with smoldering myeloma in 2005 after a few months of swollen lymph nodes, worsening anemia, and fatigue.

Tricia Charamut: So, I saw my local oncologist for nine years and I had blood work every three to four months for those nine years, and it turned out the numbers changed in 2014. And so, that point it was ready for another bone marrow biopsy and they determined that it was actually active myeloma at that point, and it was time to start treatment.

Tricia was referred to the Dana Farber Cancer Institute, which was only a couple hours from her home. The doctor there recommended a clinical study that was looking to determine the best timing for a stem cell transplant in patients with early-stage myeloma: early—that is, after induction therapy—or later, after relapse *from* induction therapy.

Tricia, who had worked in health care and understood the importance of clinical studies, made the decision to enroll. She ended up in the early-transplant arm of the study, meaning that she received the standard induction treatment of Revlimid-Velcade-dexamethasone followed by an autologous stem cell transplant and Revlimid maintenance therapy. She achieved a complete response, and she has maintained that response for 8 years and counting.

Our third guest, Lonni, was first diagnosed with smoldering multiple myeloma in April of 2021, when a routine bone scan revealed that she had early osteoporosis. After more testing, she was referred to a hematologist-oncologist, who determined that she had high-risk disease and suggested treatment.

Lonni lives in rural Idaho and didn't have ready access to a myeloma specialist, so she began calling around to find one. She ultimately connected with a doctor at the University of Miami, who suggested that she participate in an observational clinical study looking at methods to predict disease progression.

Lonni McDonough: he was just, like, "Hey, I wanted to let you know that this is something that I'm working on." And it's really difficult to understand who's gonna progress and who's not gonna progress, that's the issue with smoldering, so you're constantly kind of, you feel like you're waiting for the other shoe to drop, right? Like, "When is it gonna happen?" and there's no

real good markers. And so he said, "I'm working on this pregnancy test," right, for—that's what he called it, for smoldering.

Lonni had known since shortly after she was diagnosed that she wanted to participate in a clinical study and was excited for the opportunity.

Lonni McDonough: because you don't feel like you have a lot of control. You feel like the disease is in control, right? And I really wanted to kind of take my power back, in a way, and feel like I was doing something to contribute, and then also feeling like I was in control.

Lonni's smoldering myeloma has not progressed. If and when it does, she will have the opportunity to participate in a follow-up study examining the use of a bispecific antibody treatment early in the course of myeloma therapy.

Before enrolling in a clinical study, patients and caregivers should have all the details of the treatment of observational plan explained. It's important to ask questions to make sure you understand everything that will happen in the study and take time to carefully consider your options.

Louise Kraft: I would say just make a list of your questions, ask what kind of side effects will I have. Do you have any statistics yet on the effectiveness of it? What do you think as my doctor, do you think this is a good choice for me? How long will I be on it? Just any question you have just write a list of those questions and discuss those with your doctor. And I have to say, she was wonderful, very patient with me. She even like I said called me at home and spent about a half hour on the phone with me. Because it's a big decision and she understood that. So I, yeah, I would just say make a list of all your questions and make sure that they're answered to your satisfaction.

A myeloma specialist can help identify studies that are available and help evaluate whether you are eligible to participate. Doctors, research nurses, and advanced practice providers involved in the study can also help evaluate eligibility and provide more details about any available trials, including where and how they will be carried out.

Participants in any clinical study receive care according to a carefully designed plan, known as a study protocol. This protocol is developed by medical experts and scientific investigators to help researchers learn as much as they can while protecting the health of participants. As Tricia learned, these protocols can be modified if needed to help keep patients safe.

Tricia Charamut: originally when I started the trial I had a fainting issue at work and they determined that the medications were all just too strong

and they lowered them all. So, I was surprised. I was like, oh, okay, 'cause I thought at that point I was gonna have to go off the trial because I thought maybe I couldn't handle the medication. But they can alter things when necessary, because in most trials, I don't think people realize that the individual patient is more important than the outcome.

Clinical study protocols for patients with cancer don't allow for patients to be given a placebo, which is an inactive compound used in place of the drug being tested.

Tricia Charamut: Some people think they're a Guinea pig or whatever. I felt that my life and my history and my health was more important than any trial or anything else.

Clinical studies typically take place at academic care centers, hospitals, or clinics that are staffed with myeloma experts. For some patients, such as Louise and Tricia, those centers may be close by or within a few hours' drive.

For Lonni, access to specialists and centers hosting myeloma studies was a challenge given her location. However, because she is in an observational study, there is more flexibility and her visits to the more-distant study site are limited to once a year.

Lonni McDonough: I know that it's difficult for a lot of people to make the time and do the travel, and it can be a hindrance for some people. But just know that, you know, especially in an observation trial, where you're only having to go once a year, I think that is a plus, to be honest. And basically, you utilize tools like this, you know, Zoom. So, in-between, if I have questions or he has to get ahold of me, we basically do telemedicine, which is great.

When considering participation in a clinical study, it can be helpful to connect with other patients who may be able to help you understand their own experiences in a clinical study. You can also contact the MMRF Patient Navigation Center to ask about your options and which studies may be available in your area. Additional sources include the MMRF's Clinical Trial Finder and the National Institutes of Health website, www.clinicaltrials.gov. Links are available in the box below this video.

Louise Kraft: look at all options. Ask your questions, listen to the answers, put everything in your notebook so you have it there so you don't forget.

If after careful consideration you decide to enroll in a study, you will be asked to provide consent before receiving any tests or treatments. Many other safeguards

are also in place to ensure that studies are performed safely and ethically. Before any patients are enrolled in a study, ethics committees and institutional review boards review study protocols to ensure that they are safe and that patients will be well protected. These include protocols for data protection and privacy.

Lonni McDonough: so, of course my husband was more concerned about that. He's in IT, right, so, yeah. And I'm, like, "I could care less who sees my data," right? But, yes, no, all of the concerns are taken care of with the paperwork, I mean, it's very legal, very well put together, they clearly say in there that your data is only going to be used for myeloma research, it's only gonna be shared for scientific purposes, you know, for this particular trial. So, I had no issues after reading through the legal documents, and my husband didn't, either, so there were no concerns whatsoever.

Patients who agree to participate in a clinical study are free—and encouraged—to raise concerns and questions as they receive treatment and may withdraw from the study at any time.

All of our guests today felt valued and cared for in the studies they were involved in. If you communicate your needs and concerns to your care team, accommodations can always be made.

Tricia Charamut: There was a lot of give and take. They were very accommodating. I had my daughter's wedding at one point, so it's like, reschedule it for another week or whatever, or snowstorm. But going there was important because they liked all their lab. Sometimes different labs read things a little differently here or there, so they want basically all their tests done at their facility, which made perfect sense to me.

Tricia spent several years in her clinical study, and she always felt like she was a priority.

Tricia Charamut: I just felt like I was gonna be well taken care of and any questions or any issues that arose, they were gonna take care of it, and they did. There was nothing that happened to me over the last eight years that they didn't know about and they didn't handle.

Clinical studies are essential to increasing our understanding of multiple myeloma and to the development of new treatments, providing an ever-growing range of options for patients at all stages of the disease. By participating in a clinical study, you are not only helping yourself, you are giving hope to other patients and to those who will be diagnosed with multiple myeloma or its precursor conditions in the future.

Tricia Charamut: What I've said to other people in the past is, without clinical trials, you wouldn't have the medicine you have today. So, somebody was in your shoes before this, and they took the chance and the risk on the trial, and that's how we have so many new medications and so many new treatments and combinations of medications and it is because patients were willing to risk whatever and go for it.

Let's hear more now from Lonni, Louise, and Tricia, as they join the MMRF's Mary DeRome in a roundtable discussion on their perspectives on what it's like to enroll and participate in a clinical study.

Mary DeRome (MMRF): Lonni, Louise, and Tricia, thank you so much for being with me today on our *Myeloma Matters* podcast.

All of you have been involved in clinical studies and/or are still involved in clinical studies. So, we're going to talk to you today about clinical studies, how you joined, why you joined, and what the outcomes were. Tricia, I'm going to start with you. How did you learn about the availability of a clinical study for your specific condition?

Tricia Charamut: When I was diagnosed with smoldering myeloma back in 2005, there was no treatment at all. I had smoldering for 9 years. Over those 9 years, I was looking at clinicaltrials.gov to see what, if anything, new would be coming along, and if there was anything good that eventually I might need. When I ended up with active myeloma, I went up to Dana-Farber Cancer Institute, and Dr. Richardson suggested a trial that he was in charge of. It was a no-brainer because it was basically the treatment I would've gotten —RVd (Revlimid, Velcade, and dexamethasone) with a stem cell transplant. The other arm got no stem cell transplant. I was hoping that I would not have to have the stem cell transplant; unfortunately, that didn't happen. I did have the stem cell transplant, and I was just taken off the trial after 8 years. It's still going on and going strong for them to find the actual numbers of which is best for people.

Mary DeRome (MMRF): So, this was the DETERMINATION trial, which was such big news this past June at the ASCO meeting in talking about multiple myeloma. Your friend Paul Richardson indeed gave the presentation about the trial. It was talked about everywhere for quite some time. Actually, it was such a big presentation that he got a plenary session. So, he was in a room with thousands of people talking about your study. It's really amazing to meet a patient who was involved in that study, which is pretty much a seminal study at this point in multiple myeloma. Lonni, let's go to you. How did you learn about the availability of a clinical study for your condition?

Lonni McDonough: Sure. At diagnosis, I was fortunate enough to get a second opinion via telehealth with Dr. Ola Landgren, who really is a leader in precursor

disease. During that first phone call, he told me that he was working on a trial called TRANSFORM, but it wasn't yet open for enrollment and would be probably about a year out. So, I just kept in touch with him and saw him speaking at other events. As soon as enrollment became open, I contacted him. He told me all of the details about the trial, and like Tricia said, it really was a no-brainer for me. It's been a really wonderful experience, and I'm sure we'll get into some more of the details later. But it is observation only, and it works perfectly for me because the trial is only in Miami. I live in Idaho, but I only have to go to Miami once a year. So, it's much more convenient.

Mary DeRome (MMRF): And Louise, how about you?

Louise Kraft: Can I first ask Lonni a question?

Mary DeRome (MMRF): Sure.

Louise Kraft: Where were you in your myeloma journey at that time?

Lonni McDonough: I was diagnosed in April 2021 with high-risk smoldering, and I am still smoldering. The TRANSFORM trial is for precursor disease.

Louise Kraft: I was diagnosed in 2016, and I had the standard of care, which was RVD and the stem cell transplant, and then maintenance was on Revlimid. I did well for about 3 years, and then I relapsed in July 2019. My husband and I met with the doctor, and Dr. Jasielec said that I'd become refractory to Revlimid, and the standard of care was to have maybe four, five, or six rounds of chemo and then a second stem cell transplant.

My daughter started crying and she says, "I just hate to see you go through that again." Dr. Jasielec said, "We have a clinical trial here at the University of Chicago that Dr. Jakubowiak is running, and you might qualify for that." She checked into it and said I qualified. Then I had a decision to make, and I have to say the first 3 years I went into it like this: I just did whatever the doctor told me to do, and I didn't research a lot. I didn't really want to know too much. I just wanted to do what I had to do to get better, and I did get a lot better for a while. I was asymptomatic even when my numbers started to climb. That's how I found out about it. I qualified and then there were a lot of decisions to make, but we can go into that later.

Mary DeRome (MMRF): Lonni, you might have been the only one who really sought out the trial, whereas for Louise and Tricia, it was actually brought up to you by your doctor. Now for Louise, for example, if they hadn't brought up the fact that there was this trial that you might be eligible for, would you have looked to see if you could find a trial that you might be eligible for?

Louise Kraft: I don't know if I would have. I know when I started researching it at that point, one of the guys in my myeloma networking group was on the trial, and he was proactive like Lonni. He was at Northwestern, and I think he had two stem cell transplants, and it was coming back again. He went on clinicaltrials.gov and found this trial, so he switched over to University of Chicago. I don't know if it would've crossed my mind unless someone had mentioned it to me.

Mary DeRome (MMRF): I think that's actually fairly common. Tricia, if Paul Richardson had not mentioned to you that you could be a member of the DETERMINATION trial, do you think that you would've joined the trial?

Tricia Charamut: If he didn't bring it up, I would've asked him, because like I said, over the years I've looked. The only issue I had was my local oncologist in Connecticut, I think he was against trials. He said, "Oh, you don't want a placebo." He was just against them for some reason. I also think that sometimes trials have the latest and newest, and it's not always 100% better, but with myeloma it has been.

Mary DeRome (MMRF): Sure. Certainly for myeloma patients, it's absolutely an option at almost any stage of disease. There's a lot of studies ongoing to determine what causes some patients to really go for a clinical trial while others do not. And I think that one of the most important pieces there is that most patients, if they're asked if they would like to join a trial, will join a trial. Almost everybody who is asked will join, but often they're in a situation like you, Tricia, where the doctor is either against trials or wouldn't mention a trial, and then you don't even know that you have that option, right?

I think the lesson here is that if your doctor doesn't offer you a clinical trial, then patients should talk to the doctor and say, "Do you think that a clinical trial is an option for me at this time? And do you know of any that are nearby? And if I might be eligible for the trial, do you think it would be a good idea for me to be on that trial?" I think that's a very important lesson for many myeloma patients is if the doctor doesn't mention it, then they should ask.

So, once you're in a trial, what can you tell us about the time commitment or the logistics of being in a clinical study and how that might be a barrier to enrolling? Let's start with you, Lonni, because you're on a trial that's far away.

Lonni McDonough: Mine's probably a little unique in that I understand, in general, it really would be a barrier for me just because of my location. Our nearest myeloma center would be 6 to 7 hours away. Regardless of the type of trial, if I was in a treatment trial, it would be very inconvenient. That's why this particular trial, being observational and only having to travel once a year, [works for me]. By the way, Dr. Landgren is my primary specialist as well, so I see him on a regular basis via Zoom outside of the trial as well.

But that is an issue, being from a rural state and not having access, I know can be a challenge, but there are so many types of trials like mine that are observational. I think there's something for everyone if you truly look.

Mary DeRome (MMRF): I agree. And for some people, it's easier than others. I know Tricia, you live in the Northeast, and there's certainly a great concentration of amazing multiple myeloma specialists in the Boston and New York areas.

Tricia Charamut: Yeah, I have a 2-hour drive. During the trial there were a lot of visits, especially at the beginning and before the stem cell transplant with the collection and everything else, and all the testing. There was a lot of back and forth, but my family felt strongly that this was the right place for me. I know with a trial you're watched more carefully. Any time my numbers went up or if I got sick, they took care of me immediately, and it was amazing. Some have discounts for hotels that people aren't always aware of. My health insurance reimbursed me for some of that, even gas. I don't think people realized that even though it's a haul, you don't financially have a burden to bear. You can get help.

Mary DeRome (MMRF): And how about you, Louise? Do you live close to the center where you were being treated, and how was that logistically working out for you time-wise?

Louise Kraft: It really wasn't a problem at all. Luckily, we are only about an hour from Chicago, so in the beginning I drove to Hyde Park, which is about an hour away for all my treatments. I did that for the first year or so, and then I found out through my group that the University of Chicago has a cancer center at Silver Cross Hospital in New Lenox, which is only 20 minutes from my house. And it's just been great, 20 minutes is nothing. I would have to go every other Monday and Tuesday, so it was four times a month. The only time that I really complained about that was in summer because it cut into my playtime. I wanted to take little trips and do stuff with my grandkids while they were off. During COVID, they shortened it to three days a month. They doubled up on the carfilzomib into one day. I asked them if we could do that again, so I actually only have to go in twice a month now. It's just been a real big difference. Of course, we were watched to make sure that there were no side effects from doubling up and taking it all in one dose, and there weren't, so that worked out well.

Mary DeRome (MMRF): That's great to really hear. Some patients believe that clinical studies are so inflexible, and if they deviate from the protocol, then it's a big problem. And this could be an issue for people who live a long way from a study center, have difficulty with side effects, or like you were saying, wanted to participate in life events like a vacation, wedding, or visits with family. It's great to know that they were able to accommodate you in that way and make it easier on you. Tricia or Lonni, did you find that your study coordinators were able to

accommodate you when you had some of these events coming up and needed to potentially change something?

Tricia Charamut: At the very beginning, I had an issue with working and all the treatments and running back and forth. I actually had an episode where I fainted at work and spent a couple days in the hospital. They never found anything wrong, but they changed the dates regarding that and lowered the doses. I got all my appointments 6 months in advance. If I had a wedding or something to do, they would work around it. There was quite a bit of leeway because they understand that we want to still live and enjoy our lives and go on with our vacations or whatever we want to do. I never had a hard time, even in snowstorms. If you don't make it, you go the next week or a couple days late, and it was never an issue.

Mary DeRome (MMRF): Getting back to why some patients may not be interested in participating in a trial, there's always the risk of taking some kind of unknown or experimental treatment, or as you mentioned, Tricia, fear of receiving a placebo or concerns about privacy.

Did any of you have concerns when you were joining the study? And do you have advice for other patients who might still be on the fence about whether to join the clinical study? Louise, let's start with you.

Louise Kraft: In my trial, there's no placebo. I'm in the daratumumab group, I know exactly what drugs I'm getting, and I'm identified by a number in the trial documents. Privacy is not an issue for me either. My concerns were what would be the side effects? How often do I have to go in for treatment? How long will I have to be on the trial? And most of those questions were answered in the 39-page document that I had to read over and sign.

Mary DeRome (MMRF): The informed consent form.

Louise Kraft: Informed consent, exactly. But my greatest concern was, is this the best option for me? So my advice would be to do your research. Of course, I discuss it at length with my doctor. There were two gentlemen in my myeloma group who were already on the trial, and one would get his infusion and then go off to work, and I thought, oh my gosh, I can't believe how well he's doing. One of the fellows, Ian, he's an engineer and a walking encyclopedia about multiple myeloma. I talked to him at length about the trial, and he answered all my questions from his point of view. I also called the nurse at the MMRF. She was great. She even did a little research and told me that they were finding that the quadruplet therapy, which was what I was on, was going to be on daratumumab, carfilzomib, Pomalyst, and dexamethasone. They found that it was more effective than the triplet therapy, which is the standard of care. So I thought, that's another

plus. I called a friend of mine who works with clinical trials, and she went through the document with me page by page.

And then I prayed for guidance. I just prayed that God would guide me to help make the right decision. And when I do that, I have more peace. Dr. Jasielec called me at home one night, and we discussed it further. I asked her what she thought would give me the greatest chance for the longest remission, and she thought for a minute and she said, "I think the trial." So, I've never regretted that decision. And I agree they take really good care of you. My blood is tested every 2 weeks. I see the doctor once a month. The best part is the warm blankets they bring you in the infusion room. I just love those. I just feel so well taken care of. And since then, after about 6 months, my numbers were going down regularly. After about 6 months, there were no plasma cells detectable. And then they sent a sample to Adaptive Biotechnologies out in Seattle where they do a really deep test.

Mary DeRome (MMRF): So you had an MRD (minimal residual disease) test, and they were looking to see how many cells out of a million cells were actually myeloma cells. And were you positive or negative?

Louise Kraft: Negative. Every time I talk to Dr. Jakubowiak, he's my doctor and the author of the trial, I say, "Well, can I get off the trial yet?" And he says, "No, I think you should stay on a little longer and wait until we talk in 3 months." But I'm okay with that because I've relapsed once and really don't have any side effects.

Mary DeRome (MMRF): As long as it's tolerable, right? And I'm sure that's why he's not having you go off of it because he wants to make sure that this doesn't come back. But it's great to hear that you did a lot of pre-work before you decided to do this. And I think that every patient can benefit by talking to other patients who might have gone through clinical studies, talking to people in their support group, certainly talking at length to the doctor about what the study will entail and just knowing that you're not going to get a placebo and that you will be watched much more closely than a patient normally would be. If I was a patient, that would certainly give me a feeling of relief. Louise, are you considered high risk?

Louise Kraft: That's funny that you should ask because that's not something we ever discussed at the University of Chicago. They don't tell you what stage you're at because they feel that that's not a good indicator of your prognosis, and they never told me what my risk was. So I asked Dr. Jakubowiak once, "Am I high risk or low risk?" And he said, "You're at the low end of high risk."

Mary DeRome (MMRF): So, it's really just trying to think about what might stop other patients from participating in a clinical study. Are they afraid of having some kind of unknown treatment? Afraid of having a placebo? They might have a

concern about privacy. Tricia, did you have any of these fears when you were talking to your doctor about the study?

Tricia Charamut: I was never worried about privacy because, as Louise stated, you are a number on the trial. Your name and date of birth are obscured from anybody else researching it. The people who are running the trial look carefully at all your numbers and you as a person about how healthy you are and the type of myeloma. You have a team of people behind the scenes watching everything about you, which to me is comforting because it's not like you're just another number or another patient that comes and goes. That was really comforting to me to know that there were always people watching out, and even now that I'm off the trial, my doctor said I would be watched very carefully.

The DETERMINATION trial has been on for 13 years, and I had to stop it because I had chronic strokes. We decided it was best, and my numbers were fine. But he is still watching to see the outcome in the long period. So it's not, "You're done, see you later, bye." But the only issue is with people who are on certain medications for the first time. The doctor would joke about some of the first people who tried Revlimid, because they used to hospitalize them to see if there was any kind of reactions. If you are trying on a phase 1 trial where it might be new medications, you may have a hospitalization just to see how your body handles it until they look at all the numbers and start using it more frequently. So, the phase 1 trial might be a little more nerve-racking for some people, but it depends on your risk. I had a woman in my support group, she's on her third trial, and I just thank God for people like her who do this because when I started in 2005, there really was nothing. That was scary for me.

Mary DeRome (MMRF): I think that no new drugs would be approved without people who actually participated in trials. It's a great thing that all of you are doing that. And even Lonni, the type of trial that you're in, which is an observational trial, that certainly still has value to the myeloma community. Tell us about anything that might have made you a little nervous about going on the trial and how you dealt with that?

Lonni McDonough: For my particular trial, I wasn't really nervous. Dr. Landgren does such an excellent job of explaining the purpose and what it entails, so I really wasn't nervous about that. The great thing about my particular trial is that hopefully the outcome is going to be that he develops a molecular test in the future for smoldering or precursor disease that really helps determine if somebody's high risk of progression or not. That's the big lingering question. Should someone be treated or should they not? I feel really good about participating in that because I know he's going to be successful, and I know this is going to have a really good outcome. But I understand people's concerns about treatments. If I am found on this trial to have the progression signature,

then I will be offered a follow-up trial to start bispecific antibodies. So that's another trial that will be coming out that does not exist right now for smoldering.

Of course, I'll have concerns like these ladies have mentioned as well. I plan on doing all of my research, but I think my biggest advice would be to make sure that you are connected with a myeloma specialist who you trust and who really can help guide you and answer all of your questions. And then secondly, the people who run the trials, they've been amazing. If I have any questions, it's so easy to talk to the team, but everybody has their own journey. This is definitely not an easy path for anyone, but there are so many great resources for us, like the MMRF and other foundations, that offer assistance with clinical studies. Like I said earlier, I think everyone can participate in something, even if it's just surveys.

Mary DeRome (MMRF): And even the trial that you're on, which is observational, that's also so valuable. All research is valuable to you and also to many other patients. And I think it's really fascinating that you're going to be going on to a bispecific trial for smoldering patients if you progress. I don't think I've actually heard of that. So, that's using bispecific antibodies up front as opposed to utilizing them after a patient has had three or more lines of therapy, right? Which is what they're basing the approval of this new one on, which could be approved within a few days.

Louise, when you were talking about your experience, you talked about how you asked many people, including your doctor and your support group folks, about how they felt about being in a clinical study, what that meant to them, and what gave you peace of mind when you were making your decision. That's such valuable advice to other patients to determine what gives you peace of mind when you're thinking about these things. How would you suggest other people find their own peace of mind when they're pondering whether they should participate in a study?

Louise Kraft: Read through the documents thoroughly. It takes a while, but I would do that. Definitely talk to your doctor. Find out if this is the best choice for you at the point that you're at in your myeloma journey. If you can find other people who have taken part in the trial, talk to them and see how it's affected them. I really enjoyed talking to the nurse at the MMRF. It's just another point of view. It's just more information. Do your homework and collect all the information you can, put it all together, discuss it with your family and your doctor, of course, and make that decision based on all that information.

Mary DeRome (MMRF): All information is good when you're walking into something like this. Tricia, I know that you talked about the trial and how it gave you peace of mind because the study was what you would've been on anyway, and you knew you weren't going to get a placebo. Was there anything else about

the study that gave you peace of mind when you were thinking and considering whether you wanted to go on it?

Tricia Charamut: The comforting feeling I had from my doctor. The Dana-Farber Cancer Institute in general, Dr. Richardson, and his team were just willing to spend as much time as necessary and explain everything. I always had my husband and one other person come with us so that we had another person to actually understand. They weren't as vested or stressed out as we were. The main thing was I felt very comfortable having a myeloma specialist at my hands, whereas my local doctor was not. I would've had the same treatment, but I probably would have just been another patient.

Mary DeRome (MMRF): It sounds like you all had positive experiences on these clinical studies, and you're glad that you took part in them and think they really benefited you as a patient to participate in them. Tricia, when you were on the study, did you ever feel like you were a guinea pig being experimented on since they were watching you more closely than normal?

Tricia Charamut: I never felt that way at all. He explained at the very beginning that there would be a few extra blood tests and an extra bone marrow biopsy, because they needed to look at different things as they're researching it. I never felt that anything was done as experimental. It was a well-thought-out clinical trial and very well organized. And, like Louise said, a ton of paperwork and signatures was very well explained.

Mary DeRome (MMRF): Louise, how about you? The regimen that you're on is pretty stringent. Did you ever feel like you were some type of experimental subject, or were you comfortable with it because you knew other people who were already on it?

Louise Kraft: No, I never felt like a guinea pig or that they were doing experiments on me. I felt very comfortable just in reading the trial. Basically, it was just adding an extra drug to the standard of care, and they'd already used daratumumab and found that it was effective. It was very well explained and wasn't scary at all. They were really good about side effects. They had to reduce my dose of Pomalyst. I think I started out at 4 mg daily. It's just like Revlimid. You take it 21 days on, 7 days off. I had some issues with constipation, so we reduced that to 3 mg. And then Dr. Jakubowiak suggested that I take two Senokot every day. It is very well controlled now. The other deviation would be the dexamethasone. I think they had me on 20 mg a week, and I was just shaky. My heart rate was beating real fast, and I couldn't sleep to save my life. We kept lowering the dose, and now I'm on 8 mg a week. I take 4 mg one day and 4 mg the next, and that's very tolerable. I take something to help me sleep and drink some Yogi Bedtime tea and that's my regimen. I don't get 8 hours, but I can get

a good 5 or 6, which, as long as it's continuous, allows me to function the next day.

Mary DeRome (MMRF): It's really great to know that. It's so important to communicate with your healthcare team just to say, this is how I'm feeling. Maybe you didn't know that it was the dexamethasone that was causing those symptoms, but you could say to your team, "I'm feeling pretty uncomfortable. Is there anything that you can do for me that will make me feel better?" Because nobody wants the people who are in the study to go off the study because of side effects. They will often accommodate you as much as possible to make sure that people stay in the study and the treatment is tolerable, so they can stay on until the study reaches the end point.

Louise Kraft: That's such a good point, Mary. [It's important to] communicate with your doctor and your team about any side effects. Knowing they can make adjustments, if it's necessary. They document everything that they do. I have a diary that I write down, like the time I take the Pomalyst every night, and then it's got a section for comments. I really don't write much anymore, but if I was having issues I would just write down what was going on at that time, and then it's a good record for me and for the doctor, and we can look that over and make any adjustments. So, definitely communicate with your team, and don't be afraid to speak up.

Mary DeRome (MMRF): I think that is the case with many people. They think that the doctor says this is the dose, and they have to take it. And if it makes them sick, they just have to keep taking it instead of communicating. I don't think that a doctor would say, "Well, I'm sorry that you're having side effects from this drug, but we can't do anything about that." That would never be something that would come out of a doctor's mouth. They want to accommodate people who are taking these studies, because these studies are so important to other multiple myeloma patients to find new drugs, new therapies, new combinations, and to make it tolerable to patients so they stay on the study until they get to the end point of the study, which is so incredibly important.

Lonni, what you may be coming up against if your smoldering myeloma becomes active myeloma, or if you begin to progress in your smoldering, is you might go on a bispecific antibody [study], which could be quite interesting. How do you feel about being maybe one of the first people to undergo that kind of a treatment in smoldering?

Lonni McDonough: I've already started doing research and, of course, it is a little nerve racking. There's quite a bit of cytokine storm. The theory is if it works for somebody who's relapsed and refractory, what's it going to do for somebody who has very low disease burden? He said, "I don't like to use the word 'cure,' but it could possibly be a potential cure, and we could eradicate it early on."

We have to relocate to Miami because I will be treated every 2 weeks, and I have to be at the Sylvester Comprehensive Cancer Center. But if you're using the "cure" word, it's worth it. One thing I did want to say about the observational arm that I'm on right now is I feel really fortunate because I'm receiving whole genome sequencing that I would not be able to get at other locations. Plus, it'd be very expensive. To be able to get this advanced testing to learn more about my particular disease is really a gift.

Mary DeRome (MMRF): It is. I completely agree. This is something that patients also need to know about clinical studies: that you'll often have benefits like this, where it's part of the study to undergo this sequencing, which will tell you a lot about the type of myeloma that you have. This can be very illuminating when it comes time to start a new therapy if they know what types of translocations, what kind of gene amplifications or deletions are present, or any mutations that might be present. This is so valuable to know these things. If you're on a clinical study that includes that type of test, then you get the test and know the results. You don't normally have to pay for it. It's just a real bonus. [This is an example of the] extras that are present in clinical studies that you wouldn't normally get from just going to the doctor and having them put you on a certain combination therapy.

Lonni McDonough: Absolutely. And one thing Tricia mentioned as well is we're working with my insurance company and probably going to have our flights covered for travel, so that's a really good point to make sure that people are contacting their insurance and seeing if some of these expenses might be covered.

Mary DeRome (MMRF): That's really interesting. I didn't know that insurance would cover those types of expenses. That's really a really great point that you and Tricia made.

Louise Kraft: Lonni, if you're still smoldering, why will you be getting treatment every 2 weeks?

Lonni McDonough: I have the progression signature. I flew down and had a bone marrow biopsy, and they're doing genome sequencing. They're looking for a molecular marker that Dr. Landgren has studied previously. If I am one of the people who has it in this first batch of 50 people, he's opening a secondary trial called REVIVE, and that will be open to people that are on this first trial that have the signature. And it's only 25 people, so it's not very many people out of the thousand that are in the TRANSFORM trial. I feel very fortunate. I told him I want one of those spots if I have this.

Mary DeRome (MMRF): Do you know, Lonni, what the signature is that he's looking for?

Lonni McDonough: It's really complicated. There's about six or seven genomic markers. I don't know exactly. I couldn't rattle them off. I've read the paper that he had published, but there's about five or six markers that they look for. Let's say hypothetically that I don't have it right now, if I fly down next year and have my bone marrow biopsy, they'll look for it again. This disease changes, so you can develop it.

Mary DeRome (MMRF): It sounds like they're looking at the certain set of genomic markers, like these certain translocations and amplifications, that would confer you to be a high-risk smoldering patient, which would then allow you to move into a clinical trial. They're doing some amazing work in smoldering down at that center, and there's a lot of really amazing work in clinical trials going on in smoldering right now, mostly for patients who have the high-risk signature because they're the ones who seem to benefit the most from these treatments. And there are many treatments and many trials for high-risk smoldering patients, which was not the case even 3 or 4 years ago. There was nothing. It's brand new stuff.

I just really want to thank all of you, Tricia, Louise, and Lonnie, for sharing your stories about clinical studies with me and our audience. You've given us some great pearls of wisdom. I wish you all the best of luck in your trials that you're on. Again, thank you so much for being with us today.

Narrator: Thank you for listening to this episode of the *Myeloma Matters* podcast on clinical studies in multiple myeloma, hosted by the Multiple Myeloma Research Foundation. The MMRF would like to thank Lonni McDonough, Louise Kraft, and Tricia Charamut for sharing their stories and unique perspectives on participating in a clinical study. You can hear additional clinical study experiences in Episode 2 of the *Myeloma Matters* podcast on Targeted Immunotherapy. The MMRF also thanks AbbVie, Adaptive Biotechnologies, 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.