**FAQs on Multiple Myeloma Following Relapse**

**March 28, 2023**

**Transcript**

**Mary DeRome (MMRF):** Welcome, everyone, and thank you for joining us for today's session, "Frequently Asked Questions on Multiple Myeloma Following Relapse." I'm Mary DeRome, senior director of medical communications and education at the Multiple Myeloma Research Foundation. I'm joined today by Dr. Brandon Blue and Nurse Dana Spiak from the Moffitt Cancer Center in Tampa, Florida, and their patient Natasha Cooper, a myeloma patient who is from West Park, Florida.

They're here to answer your questions about relapsed and refractory multiple myeloma. We're going to talk about what happens when treatment no longer works.

Dr. Blue, is there any way to predict if a patient will experience a relapse, whether it's their first relapse or their fourth relapse? And does having certain cytogenetic abnormalities play a role in relapse?

**Brandon Blue, MD:** The big thing about relapse, especially in multiple myeloma, is that it happens for everyone. We have not, as of March 2023, found the cure. That means, regardless of whatever we do, the disease will come back. For some folks, that's years and years in-between, and some folks it's only months, but it does happen for everyone.

There are a certain group of people who have what we consider high-risk multiple myeloma, which means that the cancer cells actually have mutated in a way that give the cancer cells somewhat of a survival advantage. So, unfortunately that means the remissions are shorter and not as deep as we would've hoped.

While that does happen from time to time, it is not a vast majority of patients.

Each person is individual, but just know that it will happen at some point, but it shouldn't necessarily be something that keeps you up at night or gives you extra anxiety. It should be something that the doctor is ready to follow because you're coming in for regular visits and we'll be able to tackle it the first time we see the disease may be waking up again.

**Mary DeRome (MMRF):** Great. So, Dana, speaking of relapse, what tests should patients follow, to be aware of potential disease reoccurrence? Or to put it another way, which test results would indicate that the patient needs to be on a different therapy?

**Dana Spiak, RN:** We will do blood tests, including blood chemistry, liver function, immunoglobulins, kappa/lambda light chains, the ratio and specifically M-spike. We also look at the bones, with imaging with a PET scan, an MRI or a bone density test. We look at the bone marrow itself, to see how many plasma cells are within the bone marrow.

**Mary DeRome (MMRF):** Great. Natasha, we're going go to you now. Thank you for taking the time to be with us today. We really appreciate your time. Can you tell us how you found out that you had relapsed from your treatment?

**Natasha Cooper:** Those blood tests that Dana spoke about.

**Mary DeRome (MMRF):** You follow your results regularly? When you come to visit the doctor, you always follow your results and you understand what it means when these numbers go up or down or change?

**Natasha Cooper:** Absolutely.

**Mary DeRome (MMRF):** Could you tell, in any way other than the blood tests, that you were having a relapse? Did you experience any physical symptoms that might have told you, you were relapsing?

**Natasha Cooper:** No, and that's the scary part, I didn't.

**Mary DeRome (MMRF):** When you went to the doctor and got your lab results back, it was kind of a shock?

**Natasha Cooper:** Yes. Absolutely.

**Mary DeRome (MMRF):** Dr. Blue, we've been learning, on our webinars, about the importance of achieving the deepest remission possible with initial treatment, and that includes achieving minimal residual disease negativity. I've got a couple of questions for you regarding MRD. Can patients who have relapsed from initial treatment still achieve MRD negativity with their next treatment?

**Brandon Blue, MD:** Yes, that's really one of the exciting things that's happening with myeloma is trying to get not only people's light chains to go down to normal, and not only for people's bone marrow to be clear, but actually to get to what is called MRD negativity. That means, we cannot detect it, even with the most advanced methods. If we can detect it, that means someone is MRD-positive. But there are some people in whom we really can't detect it.

I will give people the caveat, though, to know that even though somebody is MRD-negative, it doesn't mean that they have zero cancer cells. The reason why that is important is because, even if you only have one cancer cell, one will turn

to two, two will turn to four, four will turn to ten, and that's how this cycle starts up again. It just means that it's below our level of detection.

The good thing about it, is that our ability to detect gets better and better every couple years. Right now, we may just be able to detect 1 out of a million cancer cells, but at some point, we hope to detect 1 in 100 million cancer cells. Every couple of years, things are getting a little bit better and better. It's always our goal is to get someone in MRD negativity, and that can happen even in a relapse setting.

**Mary DeRome (MMRF):** Thank you for that explanation. I know that I was talking to one of our folks that talks to patients, and they said that the patient told them their MRD was 1,000 cells in a million. And they were asking if they were actually positive or negative, and I said, "Well, that's actually pretty positive." So, you have to get down to, one or less to be negative.

My second question is if a patient who achieved MRD negativity after initial treatment becomes MRD positive sometime thereafter, is that considered to be a relapse? If they just go from negative to positive?

**Brandon Blue, MD:** Not necessarily, but that is potentially a sign to say that maybe things are starting to change. Again, these are cancer cells, and cancer cells, as a principle, like to grow. Despite whatever we do, whether that be medications like lenalidomide, pomalidomide, or daratumumab; all these wonderful medicines that we have, those cancer cells would still like to grow. You may notice that you went from undetectable to now detectable, but your bloodwork still looks fine, your bone marrow's still doing fine, and if those things are still intact, it could potentially still be several years before those things become detectable and before it's actually considered a relapse and someone would need to change treatments. So, is it important to know? Yes. But is it a panic mode or something that would necessarily need to change treatment? No, I wouldn't say that.

**Mary DeRome (MMRF):** Is it very common practice at Moffit, and at other academic medical centers, for people's MRD levels to be measured after initial treatment and after subsequent treatments, to see how effective the treatment is? And is it as common for MRD to be measured in the community as it is in a major academic medical center?

**Brandon Blue, MD:** I'll answer the first part. We believe that we're here to help people. As a doctor, it's our goal and our job to really inform the patient as much as possible. As a patient, you may have a question, "All right, you want to do maintenance, but how long will this last?"

We typically need some kind of information to be able to give you, and typically, that's where MRD plays a role. You can tell, if they have 1,000 copies of their

cancer cells, we could expect a certain amount, as opposed to someone who only had 1 copy. There are levels to the depth of disease control, and we expect different levels of remission based off of those depths. It's just something that's an extra tool in our toolbelt, just to help give people more information about what's going on.

The second question you asked is, "Is this done everywhere? Is this something that is readily available at my doctor down the street?" I would say, from our standpoint, we work very closely with the community doctors to let them know the importance of this particular testing.

Is this something that can be available? Yes. Is it something that your doctor has done for you, if you have multiple myeloma, or done for your loved one? Possibly. But you know what, the only way to know is ask. Listening to webinars and things like this information that we're doing here will really be able to educate you and say, "Hey, I heard about this MRD. Have I been tested for that or do I have that?" Those are things that are super important. And if there's ever any concern, we always recommend that if someone is seeing a doctor in the community, it never hurts to get a second opinion, especially from someone who is considered to be a multiple myeloma specialist or at a large academic center.

**Mary DeRome (MMRF):** Absolutely. That's something we try to reinforce in all of our patients. It's especially important because multiple myeloma is such a complicated cancer, and it's really so difficult to keep up with all the new advances and all the information. Unless you're a doctor who really specializes in multiple myeloma then chances are you don't know all the really new stuff, unless you've gone way out of your way to really learn it. We do recommend that patients at least consult with a specialist, every time that they relapse or when they're newly diagnosed.

**Brandon Blue, MD:** The thing that makes it tricky; when people have things like breast cancer, they can feel a lump in their breast and they say, "Hey, this shouldn't be there, make it go away, Doctor." Or, people who are diagnosed with colon cancer, they have blood in their stool, and they say, "Hey." They look back there and they say, "That shouldn't be there, make this go away, Doctor." People who have prostate problems or prostate cancer, they have difficulty urinating.

Those issues don't happen with multiple myeloma. You may have fatigue, you may have back pain, you may have some of these common conditions, and unfortunately things get missed because there's no specific thing to point to any one condition and say, "Oh, aha, this is multiple myeloma." The things Natasha was saying as far as relapse, those are things that as the doctors, we're very in-tune to what necessitates disease relapse. And if you're not in-tune with that, sometimes that's where things get missed. I tell all my patients that I think it's very important for you to be in-tune with your own body. For you to know, "How I feel right now," and when we talk and we have our doctor visits, to say, "Hey, I

don't know what's wrong, but something's off," or, "I feel different," or, "My body is telling me something," because it could be some of those subtle changes that really make the biggest difference. Disease relapse is a scary thing, and again, I'm looking at it from the other side of the table, but Natasha can speak more about that, but just be in-tune with your body and listen to your body; I think that plays such an important role.

**Mary DeRome (MMRF):** Yes, I agree.

**Dana Spiak, RN:** As Dr. Blue's primary nurse, I go in and I assess the patients every time they come in, and I need to be listening to what they say. Because it could be the slightest, "Oh, you know, this weird thing happened, I have this pain here," or they're not able to control their bladder or bowels as well. Those can be signs of disease progression, plasmacytomas on the spinal cord, or things like that. It's just listening and keeping an eye out for those things with the patients.

**Mary DeRome (MMRF):** Right, I agree. Patients also need to know that they have to really communicate with their healthcare team in order to get the best care. If they're having some kind of symptom or some kind of side effect, these things need to be communicated to the care team, so that you can help them. Because if you don't know what they're going through, then you really can't help them.

Dana, we talked a little bit about cytogenetic abnormalities, earlier, but if people have those, can the ones that they have change when they relapse? For example, if you are newly diagnosed and your cytogenetics are examined and no abnormalities are found, can you then get an abnormality when you relapse? And is it important for patients to keep track of that information?

**Dana Spiak, RN:** Yes, sometimes with treatment, your cytogenetics can change, but typically, there are two important things that the physician will look for and follow with cytogenetics. The first one being translocation, for example 11;14. The doctor is able to recommend specific treatments. Certain medications only target specific translocations, so that's what the doctor will choose as treatment.

The second item is the cytogenetics, if it's high-risk or not. Again, certain treatment regimens depend on those things, so then that falls back to the doctor to decide what's best for the patient.

**Brandon Blue, MD:** I also think, as a second part of the question: is it something should people keep track of, I always recommend that people are as knowledgeable about their disease as possible. Sometimes, this is a very complicated thing; it's almost like having science class again. Some people, they haven't been to science class in 20, 30, 40 years. Even if you don't know the technical terms you could potentially at least say, "Hey, I know that there was something different about my cancer," or you could put it in whatever terms make

sense to you. But I think to say that, "Do I need to know every specific translocation?" I think that's always ideal, but always to let someone know, "Oh, at least I know I'm high-risk," or, "I know that I have a certain mutation that Dr. Blue told me about." I think those things are very important and that's always something I recommend that people educate about. Because you have to lie there and get these bone marrow biopsies. At least you should know what they say, when the report comes out.

**Mary DeRome (MMRF):** Right that's true. Natasha, once you were on treatment, did you have certain expectations about how long your response would last to the treatment?

**Natasha Cooper:** Initially, I was actually on two lines of treatment and they were not working out. At least, they weren't going in the direction that Dr. Blue wanted them to go in, and so initially, I did have some expectations about how long this would be, not knowing a whole lot about it. But as Dr. Blue said, I quickly started researching and educating myself, because when I looked at what multiple myeloma was, I didn't fit the criteria. So, I'm trying to figure out how I ended up with it, no cancer history in my family or anything like that, and according to what I've read, it definitely shouldn't have happened to me. In educating myself, I started doing a lot of reading; I joined some groups, went on Facebook, because I felt that it was important to know. Because as Dr. Blue said, there is no one thing that happens, and I did not initially feel any things that were happening. I thought it was just age. I'm 52 years old and I was diagnosed almost 4 years ago, so I was in my late-40s. I thought it was coming with age and being overweight.

Some of the things like the backache, the shortness of breath from time to time, I felt like I needed to lose weight and things of that nature. Not knowing that it was brewing, if you will, and by the time that they got to it, I had already failed two lines of therapy. And Dr. Blue said, "Yes, you should try this, I want you to try that," and I had to follow his lead, because he is the expert.

But definitely knowing more about the disease, and I learned more about it on a day-to-day basis, and I know that this is a forever fight for me.

**Mary DeRome (MMRF):** Good for you for going out of your way and doing your research. That's really such an important thing for patients to do.

This is a question we get from a lot of patients. Dr. Blue, since many patients are treated with a three-drug regimen and relapse occurs, if patients are on three drugs and they relapse, how do you know which drug wasn't working that caused the relapse? Or was it just a basic failure of everything at once?

**Brandon Blue, MD:** There are different ways that people relapse. Typically what happens is that, similar to what Natasha was saying, is that people, when they

first get diagnosed, they don't know that they had this. Typically, it's not the first thing on anybody's mind.

The stories of how people got diagnosed with myeloma, can be very complex. By the time it gets to us, it's typically, like, "Hey, there's a good amount of cancer there, and we need to get this under control." In order to do that, we try not to just hit the cancer one way. We hit it from the left, the right, the up, the down, so the cancer does not have any way of moving. It has no way to go but down. We use drugs with different mechanisms of action, meaning each drug actually kills cancer a different way. You don't know which one will fit like a lock and key and actually be the magical one that basically does most of the heavy lifting. At that point, it doesn't matter, because you need the cancer to go away. That's why we do that.

It's probably not really one drug, but it's the combination, because they, to some degree, help each other. The cancer goes away. Sometimes people do what they consider to be a stem cell or bone marrow transplant, and then we say, "Well, the cancer's gone, now. Let's put you on some type of maintenance program." Then we choose some very low level of treatment to keep people on, but then, there's two ways that the disease shows itself. The disease could have what we call a biochemical relapse, meaning that we see the M-spike go from 0 to 0.1 to 0.5 to 0.9, and we notice that the kappa and lambda light chains may go from 10 to 20 to 50, and things are slowly happening.

However, there's also people who say, "Hey, Doc you know, my back is hurting and I've never had back pain before, even with the first treatment." We look and do an MRI or an x-ray or something, and they have a new fracture or they have what we consider to be a lytic lesion or some type of bone involvement that was not there before. That's a big problem, because the way that we treat those two scenarios is very different. If someone has slow progression, meaning that the numbers are just ticking up and up and up, we have time. We have time to figure it out; we may even repeat the bone marrow biopsy. We need to figure out the best course of action, and we have time to do that.

If someone is coming to you because they're in significant pain from a new fracture caused by the cancer, you need to help that person relatively immediately, and how you treat that person is very different. The type of relapse typically dictates what we do, how fast we do it, and the sense of urgency.

**Mary DeRome (MMRF):** That's great. Dana, Dr. Blue was referring to lines of therapy, and this is another common question that we get from patients. Can you define what a line of therapy is?

**Dana Spiak, RN:** A line of therapy simply is just the treatment regimen you're currently on. Sometimes patients see multiple lines of therapy. They see multiple different treatment regimens. When a patient relapses, the disease is no longer

under control, and starting to progress. The treatment regimen, the line of therapy that they're receiving, is going to change, and maybe a new medication is added or everything's changed completely.

**Mary DeRome (MMRF):** Natasha, what can you tell us about the treatments that you've been on, and what responses did you achieve, and what side effects have you experienced?

**Natasha Cooper:** I think, the first line of treatment, I started out with Velcade and – Dr. Blue, you can help me – Velcade and – two others. Then I went from that to Velcade, Kyprolis, and something else. The second line of treatment, I had the – what was it?

**Brandon Blue, MD:** Revlimid.

**Natasha Cooper:** Yes, Revlimid, and I didn't really get any side effects. When I got to Dr. Blue, I'll just preface by saying that I was already at stage three, right, Dr. Blue?

**Brandon Blue, MD:** Yes.

**Natasha Cooper:** I don't even know how long it had been brewing. Seventy percent of my bone had lytic lesions. Dr. Blue said I was already at stage three.

Those first two lines of therapy, they did a little, but then my numbers would come down and then they would go back up, so it was doing that yoyo kind of thing. After that second line, I was kind of stagnant for a while, and he mentioned the clinical trial. I got in the clinical trial. But honestly, I don't recall having many – besides the fractures that I did not know that I had, until I had MRIs and PET scans, bone density scans, I did not know. That would be the only thing that I really remember complaining about, I had a lot of rib fractures. I could sneeze and break a rib or fracture something.

As far as any other thing, I really didn't have any side effects or anything like that.

**Brandon Blue, MD:** Natasha, your case was a little bit different, and you can tell people about it, because one of the things that Natasha got was something called CAR T cells.

**Mary DeRome (MMRF):** Oh, you had a CAR T?

**Natasha Cooper:** Right.

**Mary DeRome (MMRF):** Wow, amazing.

**Natasha Cooper:** Yes.

**Brandon Blue, MD:** She had it in a clinical trial before it got approved by the government, so she was one of the ones that the government used to approve and basically say, "Wow, this works so well for people, let's make it available for everyone else." You can tell them about the CAR T process and if you had any side effects or what your experience was with that, because I imagine a lot of people listening may have not had that done, yet, and they're probably curious on how you felt during that process.

**Mary DeRome (MMRF):** Yes, that would be really helpful, Natasha.

**Natasha Cooper:** Once I got in the clinical trial for the CAR T; Dr. Blue will say that I'm their posterchild, because I came in full stage three, and then I got in the CAR T clinical trial, and I was worked up for everything, and then I got Covid. I got Covid right when I was supposed to get my cells back, and I actually tested positive from March until August. I couldn't really get any treatment. I had no symptoms, but I was testing positive.

From March to August, it was kind of a slow pace, I couldn't get any chemo, and they couldn't move forward with the CAR T. Finally, I got a negative result, two negative results, and then they rushed me in and the process went really quick. I got my cells back and that was an experience, because I did go through C – is it CRS, Dr. Blue?

**Brandon Blue, MD:** Cytokine release syndrome but sometimes we use the abbreviation CRS.

**Natasha Cooper:** I experienced that, I was running a fever right after, for maybe two days, and then I got the tusuluba – you know what I'm saying, the medication.

**Mary DeRome (MMRF):** Tocilizumab.

**Brandon Blue, MD:** Yes, tocilizumab, it worked very well.

**Natasha Cooper:** Yes, that one, yes. That's probably the only side effect that I did have. I will say that, for whatever reason, divine intervention, whatever, I did not experience a whole lot of bad things with this disease, thus far, besides being let down by the relapse, the two lines of therapy not working. Since I got CAR T, and I followed Dr. Blue's rules, and stayed in the home and things of that nature.

I followed the rules of the trial. I think that I was MRD-negative when they did my first follow up. I had a deep response and it'll be three years that I've been in remission, in August.

**Mary DeRome (MMRF):** That's great, and you're not on any other treatment?

**Natasha Cooper:** No, I'm not, no maintenance.

**Mary DeRome (MMRF):** Wow, you are a posterchild. That's amazing.

**Natasha Cooper:** Yes. The clinical trial was the best thing that Dr. Blue could've done for me, suggested, recommended, and I was definitely just going to follow his lead, because he's the expert.

**Brandon Blue, MD:** I'm glad things are working out, you're doing so well.

**Natasha Cooper:** Thank you.

**Mary DeRome (MMRF):** That is great. You hear a lot of stories from people who have CAR T, for some people it works great, for some people it kind of works, and then for some people it doesn't really work at all. It's not the easiest treatment to get, because there's just not that much availability. Although, if you're in a clinical trial, that's not as bad, but then you have to put up with a lot of monitoring, but that's okay, too.

Dana, we cover a lot about the efficacy of drugs, on our webinars, and we also cover side effects, which are many. Considering that some patients may experience multiple relapses and be exposed to many different drugs, what can be done to minimize the overall impact of drug side effects on patients?

**Dana Spiak, RN:** That's part of my job, educating the patient, when they're about to start a new drug regimen. Educating them about the drug, the possible side effects, how they're managed, what to do if they arise. We always say call us, so that we can assess and determine what to do next.

Another thing is more prophylactic treatment. There are certain drugs that we know have side effects, such as, Revlimid. It has a risk of blood clots (deep vein thrombosis [DVT]). Patients are put on blood thinners such as aspirin. Velcade can cause shingles, so patients are put on acyclovir, an antiviral medication, to help prevent that from happening. There are certain things we know are possible side effects, so we treat those preemptively, but other than that, just through education and following up with our patients.

We do what are called, coping calls, after we prescribe Revlimid. We make sure that it doesn't cost a lot for the patient; we don't want them to ever have to pay too much. Also, we ask about the side effects. Rash is a big side effect of Revlimid, and sometimes patients say "Oh, yeah, this thing on my arm, it's really itchy," or, "My scalp started itching," and that's one of the main side effects. Through that, we educate, tell them to take Zyrtec, Benadryl, or an antihistamine, something like that.

**Mary DeRome (MMRF):** Natasha, you talked about the clinical trial that you're on with the CAR T, can you talk a little bit about what your spouse or caregiver did for you during that time? It's a pretty intense process to go through that, can you tell us a little bit about that?

**Natasha Cooper:** My caregiver was my oldest son, and unfortunately, it was a time when Covid had just hit the scene, and I did the majority of it by myself. I was in the hospital by myself; I had my tablet where I could see them, video call, and things of that nature, but I was in the hospital, for the two weeks, alone. I basically was on my own.

Now, after I was discharged and I went home, my son made sure that I went for my appointments, my follow-ups, and things of that nature. They give you this information packet about the CAR T and things that I needed to do afterwards, and I pretty much followed it to a T, with the help of my son. It wasn't as difficult, because I was a good patient, I mean, I really wanted to kick this cancer's butt.

I did everything that I was supposed to or that I was asked to do.

**Mary DeRome (MMRF):** It's great that your son was there for you like that, good job.

**Brandon Blue, MD:** He loves his mama, that's why.

**Mary DeRome (MMRF):** Aw that's great. Let's talk a little bit more about some of the common questions that we get from patients. Dr. Blue, is maintenance therapy used as a part of treatment for disease, or for relapse, rather?

**Brandon Blue, MD:** Each time the disease turns active, then the first goal is to get it back under control. I always think about it as if you have a pot that's overspilling, the first thing is to do is you have to get the lid back on. Typically, for maintenance, we use a low dose, and maybe only one type of treatment, but we don't do that to put the lid back on. Typically, that's just not the best approach. We typically use multidrug therapy, to be able to contain the disease and likely get that person back into remission. But once the lid is on, then you have options, then you can say, "Hey, things are back to a simmer. How do we keep it simmering for the next foreseeable future?"

When it comes to things like CAR T, then the lid itself will typically do the job. CAR T is also in its infancy, meaning that it's only been approved for a very short period of time. We don't really know how well maintenance will improve the amount of time that the disease is under control. Outside of that, almost every other disease relapse and treatment typically means some type of help to keep it under control, and that's where maintenance comes in.

But it gets tricky, because not everybody's disease is the same. Meaning, that there's some people who have such aggressive myeloma that you are nervous, as the doctor and even as the patient, about stopping some of the treatment. We're, like, "Wait, wait, wait, we just got it under control; how do we back off ?" But then, there's other people who are begging you saying, "How much longer do we have this treatment? I'm ready to dial it down." And I think that's where the conversation happens between the doctor and the patient, because sometimes if you do it too soon, unfortunately, the disease basically isn't low enough to continue to simmer, and unfortunately, you may see a rise again. And sometimes, you hold on to too many medicines too long, and unfortunately you beat the patient up in the meantime. Where it was too many drugs for too long a period of time, and that's not good for quality of life, either.

There's not one cookie-cutter recipe to say, "Hey, this is what you need to do," but to know that, really, maintenance is a part of myeloma treatment. Even after your doctor, you guys high-five or you ring the little cancer bell, just know that there's likely going to be some type of treatment that's still coming, because that's just how myeloma is controlled. Some type of maintenance typically keeps it under control longer than without.

**Mary DeRome (MMRF):** Is maintenance therapy given to people who are on a CAR T, like Natasha after she had the treatment? And do patients who go on to bispecifics, which is another newly-approved therapy, do they have maintenance therapy?

**Brandon Blue, MD:** Right now, it's typically under investigation, so the people who are getting maintenance after CAR T are typically on a clinical trial. There's no maintenance that right now is currently approved by the government to say, "Hey, this is what we consider standard of care." CAR T itself is almost like a replicating way, because these cells are alive and these T cells recruit other T cells to basically do somewhat of a surveillance. We don't know if adding maintenance to CAR T helps. That's an unknown question, but something that's being answered with clinical trials. Outside of the clinical trial, that's not standard practice. As far as the bispecifics, these bispecifics really just got approved at Thanksgiving 2022, so we're talking about just a couple of months of approval. And right now, the way that they're given is until disease progression.

So, you can continue on them, just getting them and getting them and getting them, so that they continue to fight until, unfortunately, the disease grows despite your best efforts of giving the treatment. Some of these newer treatments, again, the jury's still out on how to best control them, but there was a period of time we didn't know to give maintenance after transplant. Technology and modern information and medical knowledge had to grow to understand and realize, "Oh, what if we actually gave them something after this? They actually do much better." We may see things like that down the road for CAR T. We're learning more about it, but, the jury's still out.

That's why I think it's important to, again, go to a myeloma specialist, because there are so many things that change so quickly in this disease that you need to be on top of whatever is considered the latest and greatest.

**Mary DeRome (MMRF):** Yes, it's kind of interesting, lately, I've seen some commercials with patients who have breast cancer and now they're developing drugs which we would call maintenance drugs for patients who have breast cancer. In the commercial, they talk about taking a medication to keep their breast cancer from coming back, which is basically what maintenance is. I don't know if that was something that was actually started in myeloma and has gone to other cancers, or if it started in another cancer and the same idea came to myeloma.

**Brandon Blue, MD:** Well, it's actually a lot of cancers that do maintenance programs. Because, for someone to look you across the table and say, "Your cancer is cured," we need to be confident that this disease is not coming back. If somebody were to look at you across the table and say, "This is an incurable cancer." The next question your brain is going to say is, "Well, how long can it stay away? And is there anything to do about it?" And we want to make sure that if there's something that we can do, that we do that. Now, sometimes that's contrary to what people's intuitive brain thinks, because they're, like, "Doc, we were successful; we rang the cancer bell; the cancer's gone."

Again, that kind of goes back to my original discussion of undetectable doesn't mean gone. We do the best that we can to try to, again, keep the lid on the myeloma, and maintenance plays a big role in that.

**Mary DeRome (MMRF):** Another common question that we get, Dana, is that now that we have two CAR T cell therapies approved and a bispecific antibody therapy approved, and they all target the same target on myeloma cells, which is the B cell maturation antigen, or BCMA. What is the difference between a CAR T and a bispecific? How should patients decide which one would be the best for them to get, along with their care team?

**Dana Spiak, RN:** First thing, first off, it's the patient with the care team, the doctor, discussing this. With CAR T, there are two different ones that are used, here specifically at Moffitt, the Abecma and Carvykti. Both can be an intense process. There's a lot of pretesting that you have to go through. As Natasha mentioned, she had her son, but you need a caregiver, typically, for about 30 days. You are inpatient; some can be outpatient, but mostly inpatient. And there is risk of side effects. Some can be very intense, some patients just aren't physically fit for that, their functional status is poor, even age is a factor. Those things come into consideration.

The bispecific is new, but it's not as harsh. You can have CRS; it's flu symptoms, but a little bit stronger, body aches, fever, chills, nausea, vomiting, things like that. With CAR T, it is a one-time treatment regimen, and then once completed, you're not in any therapy. Some patients like that; they don't want to be in therapy. They want a break. But the bispecific, it's continuous. As Dr. Blue mentioned, it's until disease progression, so, it's a weekly treatment, so you'd have to come in here, or your local physician's office, and get treatment every single week, so it's different. With those factors, you just have to speak with the care team.

**Mary DeRome (MMRF):** And decide which therapy really is best for you, based on your disease and your quality-of-life issues, things like that, so it's a complicated discussion.

And considering, Dr. Blue, that these therapies are basically attacking the same molecule, the same cell surface antigen that's on the myeloma cell, if a patient is taking Abecma and they relapse from that, would they be able to respond to Carvykti and/or a bispecific that's against BCMA?

**Brandon Blue, MD:** Yes, that's a good question, and again, because these therapies are new, a lot of these things are done under investigation or for research purposes. There's a lot of people and a long list of people who are still trying to get their first CAR T, so sometimes it makes it difficult to give someone even a second CAR T when a lot of people haven't even gotten the first. That's one thing, as you mentioned earlier, availability is the big issue with CAR T. But I'll say that that's where the research is going; trying to understand that.

At Moffitt, one of the big things that we're trying to understand is what happens to the people who still have BCMA, or B-cell maturating antigen, still present on their myeloma cells. So, you say, well, if they have it, that's still a target, and we have a medicine that could potentially target it. I would say that, right now, that's definitely where the research is going, and we're definitely trying to answer those questions, and I would imagine probably within the next short period of time, we should have some of those answers.

**Mary DeRome (MMRF):** Yes. A lot of presentations that we see now at, American Society of Hematology (ASH) or whatever, talk about sequencing of these therapies, and how effective they are if they're the first one, and then how effective they are if they're maybe the second one after the original BCMA targeting agent. Some of that data is pretty interesting. I'm sure that we'll get those answers pretty soon, with a lot of trials ongoing there.

**Brandon Blue, MD:** I agree.

**Mary DeRome (MMRF):** Okay, great. I have one question left for all of you. What can patients or their caregivers do to prepare themselves for the inevitability of relapse? Natasha, I'll let you answer first.

**Natasha Cooper:** I'm thinking, I'm thinking, I'm thinking. To prepare for a possible relapse, what can I do or my family or whoever my caregiver will be. I really, I don't think you can prepare, because I think at the three-year mark for me, I'm just starting to try to live or be what I consider normal, as I was before this whole thing started, I'm just starting to get back to that. I don't think you can ever prepare, but I know that communicating with my son, even now, my son doesn't even live in Florida. I call him, when I go to see Dr. Blue; we get him on the video, so that he's involved and he knows what's going on.

**Mary DeRome (MMRF):** Oh, nice, nice.

**Natasha Cooper:** My thing is being open and communicating with my son and with Dr. Blue about what's going on. I ask a lot of questions, I really do, because, like I said, I never know when.

The thing that hit me the most, my last visit in the BMT clinic, before I went back to you, Dr. Blue, and I had a port, and I questioned, since I was still in remission, I said, "Can I get this thing taken out, this port?" And that was the biggest wakeup call for me, to know that this is an ongoing thing and it's not going anywhere. And reality kind of socked me in the gut and said, "No, no, no, there is no cure." I'm on borrowed time, and the inevitable will happen. I can't say that I'm prepared. In the back of my mind, I keep that thought that, okay, at some point, it could happen. I don't know when, but in the meantime I'm just living my life to the fullest, if I can.

I think that just by being very open with my loved ones, and communicating, is the best way to prepare. And not being in denial. Which I've never been, and I don't have these great expectations of, "Oh, these doctors are miracle-workers," things of that nature. I'm a very spiritual person and I have my faith and that I lean on as well. The thing that I say is, just be open, and I communicate what's going on.

**Mary DeRome (MMRF):** Dr. Blue and Dana, how do you prepare for or prepare your patients or even think about what you might do when patients come to you and they do their labs and you see that they're relapsing? What is your thought process and how do you include the patient as part of the care team and thinking about what to do next? Or do you really anticipate, "Well, you know, someday, Natasha is going to relapse and we'll have to think about what to do after that." Is that something that you really think about and plan for, for your patients?

**Dana Spiak, RN:** Well, I would say, if patients are relapsing and they're coming in, we're discussing possible new treatment regimen, being hopeful. There are

multiple lines of therapy. I know it's scary to hear "I'm relapsing," but there are so many options out there and different treatments that we can use. The patient just needs to continue to be hopeful and optimistic that, "Okay, this line of therapy is going to work, and it's going to keep my disease under control for a long time." I'd just say optimism.

This disease is incurable right now, but they're making strides and new treatments come out all the time, so I just think remain hopeful and optimistic.

**Brandon Blue, MD:** Yeah, I would tell anybody who is trying to answer the question, "How do I prepare for relapse?" I would say three things. Number one, I would say make sure that you are going to continue to get your myeloma numbers checked. I think that's something that people sometimes get very comfortable; sometimes too long goes by without the myeloma numbers getting checked and things happen. I would say that's number one, making sure that, whatever is happening, you at least are getting those checked on some type of regular basis.

I would say number two, make sure, again, that you're listening to your body. There are things that happen that you need to tell somebody about and not dismiss. If your body's telling you something especially if that thing just kind of won't go away, you need to make sure your care team knows about it. Sometimes people, their brain almost doesn't allow them to think that way, or they think it's a negative thought. But no, we need to know, because that's the only way that we're going to be able to help. I would say that's number two.

Then I would say number three, what Natasha was saying, I think you have to remember to live life. When the disease is in remission, you should be, whatever your thing is to do, you should be living. Because there will come a time when you will be back, so connected to the medical system, if not weekly or every-other-week, you'll be here very frequently for treatment. So, there is a time that you get to kind of be disconnected from the medical system, typically when the disease is in remission. Use that time to travel, use that time to, whatever you enjoy. Those would be the three things that I would tell people to always remember because, again, we are making progress with this disease. We just haven't reached that point, yet, where that, once it's down, it stays down forever. But we're optimistic, like Dana said, that it's coming.

**Mary DeRome (MMRF):** Yes, agreed. I think that in this field, in the myeloma community, we're very fortunate with the number of new drugs that have been approved just over the past few years, and the upcoming approvals, which are pretty amazing. There's some amazing stuff in the pipeline, so I think it's really something for patients to keep in mind, like you said, to continue to live their life and realize that there is hope.

On behalf of the MMRF, I'd like to thank Dr. Brandon Blue and Dana Spiak and

Natasha Cooper for joining me today. I'd also like to thank everyone for taking time out of their day to watch this broadcast.