

FAQs on Clinical Studies

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Transcript

Mary DeRome (MMRF): Welcome and thank you for joining us for today's session, Frequently Asked Questions on Clinical Studies. I'm Mary DeRome, Senior Director of Medical Communications and Education at the Multiple Myeloma Research Foundation (MMRF). Today, I'm joined by Dr. Noopur Raje and Kathleen Lively from the Massachusetts General Hospital (MGH) in Boston, and their patient, Bob Lupacchino, from East Long Meadow, Massachusetts. They've agreed to answer your questions about this integral part of multiple myeloma care. First, we're going to talk about finding and joining a clinical study. My first question is to you, Dr. Raje. Many patients and their caregivers believe that the option of joining a clinical study is only for patients who have run out of other options. Is that true?

Noopur Raje, MD: I think this is such an important and timely discussion, so I thank the MMRF for spearheading this. I would say that the answer to your question is no. The important thing for everybody to take away from this conversation is that we are where we are, in the context of myeloma, because of clinical trials. We have had unprecedented development in terms of the drugs available. We are in 2023 and we have more than 16 separate drugs that have been approved in the last 15 to 20 years. Even through a pandemic, we've been able to get clinical drug products such as CAR T and bispecifics approved.

Are clinical trials only an option for patients who've run out of other options? The answer to that question is absolutely not. When we do clinical trials in the context of myeloma, we're doing them in all different spaces—from the early precursor disease state when you don't even have symptoms, all the way to when your disease comes back. If you're diagnosed with myeloma, it's really important to talk with your caregivers and say, "Is there a clinical trial option for me?" Because most of the clinical trials that we have in the early precursor disease state are with drugs that have already been used in the context of myeloma. Because we have seen such good results with them, that's why we want to use them earlier. Every patient should be inquiring about a clinical trial option.

Mary DeRome (MMRF): Great. So, there's no specific time in the patient journey that they should consider a clinical study. It really is at any time at all during their journey?

Noopur Raje, MD: I would say so. I would also say that our patients have been amazing and have always agreed to participate. It's been a collaborative effort and that's why we have the success that we have in myeloma.

Mary DeRome (MMRF): I agree. We certainly have an unprecedented set of drugs that are approved in this space, just in the past few years, so it's really been amazing. Kathleen, our patient audience has told us, over the years, that clinical studies are not always offered or discussed between themselves and their doctors. How can patients and their families be more proactive in bringing up the possibility of going on to a clinical study as part of their care?

Kathleen Lively, RN: Thank you for that question. I think knowledge, as well as being comfortable with your caregivers, is power. Whether clinical trials are available also depends on where the patient is receiving care. If the patients isn't being treated at a major medical center that has a myeloma-specific treatment group, maybe they aren't available. One of the best ways that patients and their families can approach this is to have an open discussion about all treatment options and also to educate themselves. Clinicaltrials.gov is a good resource to look at where clinical trials are available. It's a search engine that may give them a little more information going into the appointment themselves. They should also have an open dialogue with their care team and ask, "What are my treatment options?"

In our team, we go through standard-of-care options as well as opportunities to partake in clinical trials. We go through the positive and negatives of each with our patients. We review the options that are available collaboratively as a team. Open that dialogue, because for successful treatment, you need to be part of the team, and feel comfortable in just asking questions. Coming to the appointment prepared and having more than one single discussion sometimes helps. The decisions don't necessarily need to be made all at once. Information can be gathered, thought about, and then questions can be asked and thoroughly explored.

Mary DeRome (MMRF): I agree that communication between the patient and their care team is exceptionally crucial in multiple myeloma. That's one of the things that we hope to demonstrate at events like this by having patients attend with their care teams, and sort of demonstrate how that communication is supposed to work and how it could benefit the patient.

Bob, we're gonna turn to you, now, and ask you a little bit about your myeloma history and how you ended up in a clinical study. I'm going to preface this by saying that we've discussed this previously and we know that you're in the MyDRUG trial, which is one of the trials that is sponsored by the MMRF. It is one of the few, if not the only, precision medicine study ongoing in multiple myeloma right now. Can you tell us about the study and how you decided to participate?

Bob Lupacchino: Thank you, Mary, Dr. Raje, and Kathleen, for including me on today's panel. I'm going to start off with my myeloma history. I'm going to go back a couple months prior to diagnosis, just to provide some context. Back in the spring of 2019, I had gone to a routine dental exam, during which they noticed a white spot on my mandible in a series of x-rays. I was referred to an oral surgeon who saw the same spot on my x-rays. It was left as, "We'll follow up. We'll monitor." In the fall of 2019, I began to experience lower back pain at my primary care physician's office. They ordered x-rays, which were done around three days after that visit. The x-rays showed that I had compression fractures in multiple vertebrae.

I was getting closer to diagnosis, so things started happening pretty quickly and became pretty intense. We were monitoring and following up because we knew something was going on. In December of 2019, I experienced severe muscle spasms and an elevated heart rate. They were muscle spasms in my abdomen that would essentially drop me to my knees, so I knew something was going on at that point. That's when things started moving pretty quickly and I was in and out of the emergency room at the local hospital. On December 18th, I went to get out of bed that morning and experienced an incredible pain in my lower back. At that point in time, I was immobile.

I was taken to another hospital and admitted for 15 days. I would say that halfway through that stay, they were zeroing in on a multiple myeloma diagnosis, but they weren't sure. They ordered a bone marrow biopsy and it came back and confirmed their suspicion. It was during that time that I knew what they were looking at and it was then confirmed, that I had learned about Dr. Raje and the clinic at MGH. When I was in the hospital, we reached out to the clinic to set up an initial consult with Dr. Raje. I would say by early January, I had gone through the consult. I became her patient and was on the first line of treatment by the end of January 2020. Subsequent to that, two years out to February 2022, I entered a clinical trial, and here we are today, 16 months later.

Mary DeRome (MMRF): This is a story that we hear over and over—how people are diagnosed because of bone pain and things that normally happen in their back, so this is quite common. I applaud you for taking the step of reaching out to a multiple myeloma specialist immediately. That was probably the best thing that you could've done for your prognosis, very excellent. After all of this happened, how did you end up on the MyDRUG Study?

Bob Lupacchino: We were looking at the labs during the initial line of treatment that I was on for almost two years. That's when the conversation came up to consider a clinical trial. So, I met with Dr. Raje and Kathleen to review all of it. Of course I was given some time to discuss it with Janet, my wife, and other members of my care team. It's kind of funny because, although I have the final say on everything, you have to rely on the expert, which is what I do, you know?

Mary DeRome (MMRF): Of course.

Bob Lupacchino: So, I was given all the information, spent a couple of days to review it, and I just decided it was the right fit for me at that time.

Mary DeRome (MMRF): That's a really great story. Thank you for sharing that. Dr. Raje, let's talk more about clinical studies. Are there certain conditions that may make joining a clinical study very difficult? For example, any inclusion and exclusion criteria? Clearly, that changes from study to study. Are there things like age limits, or kidney disease, or heart function that have to be taken into account for patients to be able to join a clinical study? Can you tell us about that?

Noopur Raje, MD: Sure, absolutely. When we do clinical trials, we always have certain criteria that determine whether we can include a patient or not. We try our best to be very inclusive. There are certain parameters that are really important to make sure that participating in the trial will be safe and that it's the right fit for our patients. That's why we generally have a portfolio of patients. That's why Kathleen suggested going to a website such as the MMRF or Clinicaltrials.gov. The nice thing about myeloma is there are a lot of resources where you can explore different clinical trial options.

Certainly, myeloma tends to happen in the older patient population, so we have trials that are designed for those patients. I wouldn't say that age necessarily is a cutoff. I would say that there are certain issues, such as heart, kidney, and lung function that need to be adequate from a safety standpoint. We do not want you to have any adverse effects from the clinical trials. We want to be careful that we are doing the right thing by the patient. So those things do play into whether or not a patient can participate in

certain clinical trials. The parameters are different for different trials, based on the drugs that we are using and the side effect profile of those drugs.

I will also add that participating in a clinical trial is certainly a commitment in terms of time and travel to the site. It is something that our team here at MGH doesn't take lightly. I'm so fortunate to work with people like Kathleen, our clinical research coordinators (CRCs), and our research support staff. We try and identify trials that are appropriate for the patient, as well. They have to be right for the patient plus they have to fit their lifestyle. A lot goes into thinking about what the right trial should be for the patient.

Mary DeRome (MMRF): In general, patients are really only allowed to be in one clinical study at a time, right? But, just because they've been in and out of one doesn't mean that they're prevented from participating in a different one, correct?

Noopur Raje, MD: Yes, that's so important for people to understand. The other thing for people to understand is the converse of that. Because people think that if you've been in a clinical trial—many of our patients have been in sequential clinical trials—and then you do a standard of care approach, can you go back on a clinical trial? The answer to that is, absolutely, yes. So, any time a clinical trial is right for you and you feel good about it, try and do it. If you decide to do a standard of care option, you can always come back to a clinical trial as well.

Mary DeRome (MMRF): Yes, great. As you mentioned, this is how the myeloma community has come so far with all the new drugs that we have had approved. So, it is very important for patients to consider clinical trials when they can. Kathleen, let's talk about eligibility. How can patients who have active myeloma, or a precursor condition like smoldering myeloma or monoclonal gammopathy of undetermined significance (MGUS), know of studies they might be eligible for, if their doctor doesn't raise the issue with them? Is this where getting a second opinion might be critical? I know we already talked about places that you can go on the Internet like Clinicaltrials.gov or the MMRF website. There are also a number of other organizations that have clinical trial finders that concentrate in the myeloma area, and those are good places to learn things, as well. Talk a little bit about eligibility and the second opinion, and why that's important.

Kathleen Lively, RN: In general, it sort of dovetails with going into the appointment with some knowledge of what is out there, but also discussing, with your physician and the care team, what options might be available to you at that site. If you're being treated at a site that doesn't offer clinical trials, the physician may be aware of and can refer you to a site that might have something available, which a patient could explore to see if it would fit into their life. There are some medical centers or providers that don't participate that heavily in research or their research portfolio might be limited. So, going and getting another opinion at a medical center that may have a more developed program and research profile in multiple myeloma. This may be appropriate to at least explore and consider whether that fits into your life and is an option. The patient should do this with the obligation to take into account that being part of a research study may take more time and effort. Then you know as a patient that you've considered everything that would be right for you and your treatment at that time.

Mary DeRome (MMRF): That's really good advice. Bob, you were being treated somewhere, and then you went to Dr. Raje for a second opinion on your condition, and became her patient? Dr. Raje, can you talk to us a little bit about how that transition of care is handled? For example, if a patient is being seen by a hematologist-oncologist and they've been diagnosed with multiple myeloma. Then they're seen in their community center and they learn about and would be interested in transitioning over to a trial at MGH. Would you talk a little bit about how the transition from one care team to another happens? We did have a number of patients who asked this question at our last webinar about clinical studies. They were afraid to offend their doctor if they got a second opinion, or decided to move from standard of care to participating in a clinical trial. Talk to us a little bit about that and what your experience might be.

Noopur Raje, MD: This is such an important thing that you brought up. I'm sure we'll hear about your perspective on this as well, Bob. I will say that patients have to advocate for themselves. It's really important and in a disease like myeloma, where there is so much incredible research going on, if there is something that is right for the patient they should seek that out and try to pursue that. In terms of if you're offending your treating team by getting a second opinion, I would say that the answer to that is "no". At the end of the day, all of us, including your local hematologist, oncologist, care team, and specialized center want only the best for you.

At MGH, we communicate really closely with the local care team, because it's really important to have a strong local care team as well. Myeloma is a journey. We have multiple lines of treatment and the patient is going through treatment over years and years. There are times that they would be in a clinical trial and others where they are on regular drugs. The participation of the local oncologist with your specialist is absolutely critical. That's something we've always done, so I think the bottom line is communication. I don't think anybody feels offended. A lot of people come to me and ask for a second opinion. I encourage patients to get a second opinion, because sometimes they need to hear the diagnosis from somebody else. There may be other physicians with better ideas. So, I do think we all need to be able to communicate without being afraid. Seek a diversity of opinions, because that's what's going to make your care better. I'm going to turn this back to you, Bob. Was there fear when you first came to us? How do you think that has been handled over the few years that we've known you?

Bob Lupacchino: You touch on what I consider to probably be the most important decision that I made throughout this entire journey. It was hands down selecting a doctor, because it's that critical.

Mary DeRome (MMRF): Absolutely.

Bob Lupacchino: There were no second thoughts, when I was at the local hospital, about what I was going to do. After all, you have to be your own advocate. When I think of it that way and the resource that I have less than a two-hour drive away to see Dr. Raje at MGH, it's almost a nonissue. I would probably travel to the end of the earth. That's how important that decision is, in all seriousness.

Mary DeRome (MMRF): I don't think that anybody can argue with that. That goes back to how complicated myeloma is as a disease. Unless you're being seen by someone who is a true specialist in myeloma, you may not be getting the most adequate, up-to-date, or powerful treatments that you could possibly be getting. That's why you need to

get these second opinions and, in many cases, you may potentially have to move on from your community center to see a myeloma specialist. If you can't be there in person, at least consult with that person and have that person consult with a doctor that you can see. You're lucky that you live close enough to a place that's not so onerous to travel to where you see Dr. Raje in Boston and have your treatments. I think it's very telling that people go to see Dr. Raje to seek a second opinion. It's guaranteed that the second opinion is going to be different than the first opinion, because that's the way myeloma is. Everybody has their own opinion.

Bob Lupacchino: Right. What I do find is by making that transition from the local hospital to MGH, I feel as though the doors are open to all possibilities. It is true. Whatever is out there for the treatment of this disease, I'm going to find through the clinic. That's a pretty reassuring feeling.

Mary DeRome (MMRF): Yes, I agree. Let's move on to talk about how it is to be involved in the study. Bob, what was the process, when you decided, finally, that you were going to enter this study with Dr. Raje? What was the screening process for the study? You had to take certain tests to ensure that you were eligible for the study. Did you get the results of those tests and discuss them with Dr. Raje? Did that help in making your decision about going into the study?

Bob Lupacchino: Yes, we knew from the time that the study was recommended that it was a good fit. Of course, I went through a battery of tests and imaging to qualify, which we reviewed in Dr. Raje's office. All of that went according to plan. There is a process from the time you agree to enter the study to the time you're actually in it. It can happen overnight or in two nights.

Mary DeRome (MMRF): Sure. When you were being screened for the MyDRUG study, you had to undergo some pretty extensive genomic sequencing, right? They had to take some bone marrow and send it off to the University of Michigan, where they do the sequencing to see which arms of the MyDRUG study you could be placed. That's pretty extensive screening that a lot of patients haven't done before they participate in a clinical trial. Kathleen, from a research nurse perspective, how long does it take from the time a patient agrees to be in an interventional study to when they actually receive treatment? What steps does the care team have to take before the patient starts treatment, to ensure that everything is going smoothly?

Kathleen Lively, RN: That's a great question. Most of our screening periods are 28 days from the time that a patient signs the consent form. We have a 28-day turnaround that we are allowed. Prior to that, there are multiple visits, phone calls, etc. to make sure that information is exchanged and people are in a comfortable place. From the time of signing the consent form there are studies being done that are required to see if the patient is eligible and safe to move forward and then registration happens. We do have a 28-day window, but there are more times than not, that treatment starts in 2 to 3 weeks. It depends on the turnaround time for when we receive the results of the studies and are able to get the patient registered. If patients are greatly in need of treatment because of where they are with their disease, we've been able to compress this to a shorter period of time, if need be.

Mary DeRome (MMRF): That's interesting. If you go beyond the 28-day period, does that have something to do with the date that the consent is signed? Does the patient have to re consent if you go past that deadline? Or is that an arbitrary thing?

Kathleen Lively, RN: Well, that's just what is usual. Every protocol has its own rules. If we would go past that time, we would need to get special permission. The protocol might require re consent and permission to move forward, but each protocol has its own set of rules and guidelines that we follow.

Mary DeRome (MMRF): Okay, great. Dr. Raje, considering the time necessary to enroll the patients, how do patients who are relapsed or refractory participate, when some of them may need to receive their next treatment relatively quickly? I know this always comes into play when patients are four or five lines in and they're considering having, for example, a CAR T therapy. Then they have to wait for the manufacturing of that particular therapy before they can get it, so they need to have some kind of bridging therapy. In a case like that, can a clinical study be lined up for a patient before they really need it?

Noopur Raje, MD: This is really important in the case of myeloma. What Kathleen highlighted is really important. I think 28 days is the outer limit. I will tell you, for most of our clinical trials, the turnaround time is about two weeks or so because patients need treatment. We are not just putting people on clinical trials for the sake of putting them on trials, right? It takes a village to get everything lined up, so people can actually go onto the trial. We have to take how quickly the disease is progressing into account, and we have to intervene quickly sometimes. In the studies with CAR T cells, we know that there is a waiting time, so the protocols are written to include things like bridging therapy. We know that patients need these treatments, so we've preempted that and included bridging therapy in the trial. Even the regulators have allowed us to use the bridging therapy. So, thinking about clinical trials early is important, because it requires planning for things like the waiting period for CAR T. Some of the interventional studies, we can do a lot quicker and patients can go on treatment without needing bridging. It's really important, while they are waiting, for us to make sure that they don't run into problems like kidney, heart, and blood count issues. All of those are really critical, which is why we have the whole research team trying to turn this around quickly.

Mary DeRome (MMRF): That makes perfect sense. Bob, let's go back to you and your treatment on this study. What is your treatment like on the study, compared to how it was when you were first diagnosed? As far as I can recall, the backbone therapy in the MyDRUG protocol, is all oral, so you're just taking pills and not necessarily being infused with anything. That makes it somewhat easier, right?

Bob Lupacchino: Yes, that's correct.

Mary DeRome (MMRF): Good. I know that there are a number of different arms that you can go on in the MyDRUG study, based on the genomic profiling. Did they tell you what arm you were in?

Bob Lupacchino: They did. Dr. Raje could probably explain that a little better than I could as far as the arm I'm in.

Noopur Raje, MD: Mary, in the interest of time, I'm not sure that we need to discuss the MyDRUG trial in detail. Bob is in one of the arms. It's one of the few genomically driven trials. If you have a certain genetic signature, you use a very targeted drug. The beauty of this trial is it's all oral, and if you know what your genome is, it helps with going in the trial. We did discuss all of this with Bob. We would not have been able to put him on the trial otherwise. But, so far, so good. Bob's doing really well, so we are happy about that.

Mary DeRome (MMRF): Excellent. Good results are always the best.

Bob Lupacchino: Absolutely.

Mary DeRome (MMRF): Okay. I know that when we had our clinical studies webinar, there were always patients who asked about a placebo. Dr. Raje, can you tell us about the role of the placebo in myeloma clinical studies? Talk a little bit about the difference between the control arm and the experimental arm of a myeloma study.

Noopur Raje, MD: I think this is an important discussion, because people are afraid that they're going to go into the trial and they won't get a treatment that is effective. So, what is a placebo? A placebo is when you're not getting the experimental drug, instead you're given a "dummy drug." In myeloma, and in oncology in general, we do not use placebos. There are placebo-controlled trials even in myeloma, but they will have the standard of care versus a "dummy drug." You're still getting active treatment for your disease even if you are receiving the placebo. If we feel that you need treatment, you are always going to get active therapy. We do have randomized trials in which we're using an experimental approach versus what we consider standard of care.

We really don't have control of which arm you end up going into, but you are always going to get an active drug. Whether or not you get the experimental drug is a computer-generated thing. We're not doing you any harm and you're getting what you would get otherwise; however, there is the possible benefit that you could be assigned to the experimental arm which may be a more effective strategy, but that hasn't quite been proven yet. In general, even if you have a placebo-controlled trial, it is piggybacked onto whatever the standard of care is. We do not use the "dummy drug" alone in myeloma and you will always be getting active therapy for your disease. There are first-in-human trials as well.

We are so fortunate in the myeloma world that our patients will participate in the first-in-human studies as well. The beauty of myeloma is you have a biomarker and a blood test that will tell us within a month whether or not you are responding to treatment. We will never keep a patient on a clinical trial where the treatment is not working. We will take you off of it. So, in early trials, there is the potential possibility of things not working, but we know that very quickly, and we can get you off that study.

Mary DeRome (MMRF): It is fortunate that we have so many biomarkers in the myeloma space and it doesn't take too much effort to find out whether things are working or not. That's really great for patients. Kathleen, some patients believe that clinical studies are a little bit inflexible as far as certain life circumstances they may need to take into account, such as vacations, weddings, or other family events. Do patients have any leeway when they're participating in the study to take a drug holiday or dose based on one of these life changes? Does that mean that the patient has to withdraw from the study, if they can't get their dose at the exact prescribed time?

Kathleen Lively, RN: Mary, that's another great question. I'm smiling because we at MGH get very creative and do our best, because we want our patients to be able to live with myeloma. In the beginning, especially in the phase 1 studies, if the treatment is very intense, usually most of them are designed so that the treatment is dialed back and the obligations are a big less. That said, we do have treatment windows for different reasons. As the patient gets further along in treatment and their disease is controlled, it would then be safe for them since they're in a good place to participate. It wouldn't really be a treatment holiday per se. But, while they're on a research protocol, we try to utilize those windows to the best of our ability. If someone has something important coming up we do proactively reach out to the sponsors, ask for permission in advance, and really work hard to make that happen. The treatment usually does roll back by design and the commitment does usually become less. If the patient is in a good place in treatment, we do our best to make it work. As a care team, we're pretty successful. We haven't had too much sponsor pushback in these situations, because they understand that patients are working hard to live a good life with myeloma.

Mary DeRome (MMRF): Right. Having patients withdraw from studies for things like this is not really in the best interest of the study. But, it's possible that everyone can be flexible and make everything work out with the permission of the sponsors and improve the quality of life for patients while they're on these studies.

Kathleen Lively, RN: Correct. We don't want patients to feel like they're imprisoned because they feel an obligation to the study. There is extra commitment and extra time that is required, and we realize and honor that. I would say our care team at MGH, does our best to allow patients to take part in and still live their lives. One of my goals is that I want the patient to get up in the morning and not think "I have myeloma" as the first thought in their mind. I want them to be able to move forward through their day with an optimal level of life and participation. I would say that carries through to our approach to clinical trial participation.

Mary DeRome (MMRF): Great. Bob, let's talk a little bit about your quality of life on the study. Have you had to deal with any side effects from being in the clinical study that you're in?

Bob Lupacchino: It's interesting because pretty much from day one of my first line of treatment, the two side effects that I experienced then and continue to experience today are fatigue and aches and pains. On average, I would say they're at a level of three to four on their respective scales. Those are the most notable, but other than that, there aren't many side effects.

Mary DeRome (MMRF): With fatigue being a major player here, how do you deal with that side effect?

Bob Lupacchino: I'm an early riser, so I'm up by 6:00 AM, sometimes earlier. Depending on what I'm doing that day and in my life now, compared to where I was three years ago, I can do everything I did premyeloma. Maybe not at the same intensity, but I go for it. I'm a bike rider, so I go for rides on my bike. I ride 15–20 miles. I'll walk or workout in the yard. There's really nothing I can't do that I was doing before. Of course, the quality of life has changed, but I can still do the things that I was doing prior to all of this, which is important.

Mary DeRome (MMRF): Yes, very important. That's great to hear. Kathleen, if you have a patient who's on a study and they begin experiencing more serious side effects, what happens then? If the patient needs extra care because of the side effects that they're experiencing, does the study pay for that? Does the patient's insurance normally help pick up the tab for extra care, based on their being on the study?

Kathleen Lively, RN: If you're talking about side effects that are not expected and require additional care, the hospital will offer the care that's needed. Insurance would be a part of any care, just like for any standard-of-care or supportive care treatment. We review everything. I know that our consent process is very thorough in going through each thing. The hospital is totally behind the patient. We are always here to take care of any side effects, whether they are small ones or something larger, the care will be given. Just as for any standard-of-care treatments, some go through insurance, but, if there is any harm, that's a different level. If there was considered to be any harm for any reason, which is a scenario that I've not been in or seen in any of my patients, that would be another conversation. The hospital would still offer the care and follow through. Everything is outlined and reviewed very thoroughly in each study protocol and addressed in that manner. Dr. Raje, do you have anything more to add to that?

Noopur Raje, MD: I would just say whether you're on a clinical trial or not, the care you receive is for whatever clinical symptoms you develop. I don't think how that gets covered should be your concern or worry. Your care team is 110% behind you and is gonna get you through it. Who pays for what doesn't matter, at end of the day as long as you're getting the care you need. Some of the cost is submitted to your insurance and some is covered by the clinical trial, but I don't think you ever need to worry about this. Whatever care it is that you need, will be offered.

One thing I also want to add is about living while you are on a clinical trial. I cannot speak enough about my team here. They will do anything and everything for you to go on vacation or be able to visit with family for weddings and things like that. I can say that Kathleen is one of the most resourceful people. We have an incredible group and everybody is committed to your success, including your success of living your life, not just being in the trial. I think that's the takeaway.

Bob Lupacchino: That's 100% correct.

Kathleen Lively, RN: I can echo that a little bit. It does take a team. One of the things that you do have as a resource when you are in a clinical trial is a team of people that are there to support you, whether it concerns scheduling, side effects, or contacting them to answer your questions. I will say at MGH and what I am accustomed to is that we, as a team, are very supportive. Each person in the team is equally as important, because otherwise, the care is not delivered according to the standard that we hold for ourselves and want for our patients.

Mary DeRome (MMRF): That's a really good point. I think it's great for patients to hear how dedicated everyone is to making this a positive experience. It's very meaningful. Along those same lines, Dr. Raje, can you give us an idea of what the goals are for clinical studies? It's a broad question and it depends on the type of trial. Basically, are they designed to lower M-spike or free light chain values, achieve minimal residual disease (MRD) negativity, or prolong time until relapse?

All of those things are probably goals of clinical trials, as well as finding better drugs than what are currently available. We have some great drugs available, but there's always something better around the corner, and we'll never get there unless we do these clinical studies.

Noopur Raje, MD: Absolutely. Questions about endpoints are tough to answer. Every trial has a different endpoint, but I will tell you that as a myeloma community, we work very closely with our patient community, industry partners, and the regulators (including the FDA and the EMEA in Europe). With that, we've been able to accomplish a lot. It's not just about finding newer treatments, but how to give these new drugs in a better way and how to minimize toxicity. We've been fortunate to get so many of these drugs approved. Even with the approved drugs, we go back to study if giving them a little bit differently reduces certain toxicities we saw when we first pushed to get them approved so that more people could access them. Regarding MRD, we've been able to get to a molecular level of negative disease by bone marrow testing, so we have such effective treatment strategies. For most patients who have started a treatment, they're on it for protracted periods of time. As researchers, we're beginning to ask whether we can stop the treatment. That's where we have some of these other endpoints. So, any study you're thinking about, talk to your caregivers and research team at length and figure out whether or not it makes sense.

Mary DeRome (MMRF): That's a very important point. The final question for all of you is, what would you tell a patient who is on the fence about whether or not to participate in a clinical study? Bob, I'm gonna start with you, what would you tell that patient?

Bob Lupacchino: Well, regarding the way I looked at the clinical trial, one word that comes to mind is "risk." The day I was diagnosed with myeloma is the day that the ultimate risk was presented to me. Based on that, you learn quickly that risk is going to become an everyday part of your life to some degree. I have to look at the ultimate risk, and set out to do whatever I need to do to mitigate that risk. Just to be clear, the risk I refer to is calculated risk. These aren't risks that I take lightly. I spend a lot of time thinking about them, but the fact remains that the risks are out there. I would never preclude any treatment, clinical trials or otherwise. It's that critical because at the end of the day, all of this comes down to managing the myeloma. We often talk about treatments and therapies as tools in our toolbox and that's true. I use the analogy that you're looking at two toolboxes. One has a few tools in it, but they can't really solve all the problems or address all the needs. The other toolbox is akin to your local home center. They have racks of tools from the floor to the rafters, tools for every need. That's our toolbox. That's the toolbox we share.

Mary DeRome (MMRF): That's a great way to think about it.

Noopur Raje, MD: That's a nice description, Bob.

Mary DeRome (MMRF): Kathleen, I'm going to echo that question to you. When you're talking to patients about the possibility of a clinical study, how do you couch that to them? Do you do it in a way that they can understand its importance and the risks?

Kathleen Lively, RN: Whether on the phone or usually in the clinic face-to-face, our care team does present standard-of-care and research options in a very even fashion.

Then, my job, as the research nurse, is to educate the patient about what participating in the protocol would look like—the obligations, the possible risks and benefits. This conversation has already been started by the physician. I point out the obligations, the scheduling, the things that could happen. I also tell them about the aim of the study to reinforce the information that they've been provided. I remind them that they do have a care team with them and they are ultimately in the driver's seat. Also, that we do watch, first of all, to see if the study treatment is working, and that participating in the research study doesn't mean that they will stay on the study treatment even if it is not working. It empowers them to know that they are always in the driver's seat.

If the patient ever decides to come off the treatment for whatever reason, our obligation is to take them off safely and then offer alternatives. We let them know what the care team that is behind them looks like, the benefits and the obligations of research. We let them weigh their options evenly, go through them with them, and stay available to continue those conversations. We make sure that if someone decides to take part in a clinical trial, that they are comfortable moving forward. That it is really what they want to do at that moment in time. With clinical trial participation, there are certain times this will fit into someone's life, and certain times where maybe it won't. There are also certain times where it will fit into what they need as far as treatment goes, and sometimes not.

Mary DeRome (MMRF): Sure. Dr. Raje, we'll give you the last word on this.

Noopur Raje, MD: I'm going to echo what has been so nicely highlighted already. I'm going to start out by thanking everybody. We are where we are with myeloma, because of the incredible support that we have from patients. Patients have been willing to participate, and that's why we've made this progress. Without that, we would have never come this far.

I will say that when we present options to patients, it's always about what's right for that patient. Like Kathleen said, there may be a time when a trial is right or there may be a time when it isn't. The way I present a trial to a patient is by asking them about what the downside is for them and things that will prevent them from being in a clinical trial. I start my conversation by saying, "Here are the two things you need to know which will be the downsides." Most of that downside is generally scheduling or traveling to the study site. If this isn't a downside to them and they are willing to do that, then over time, it gets easier. This approach helps patients decide whether this is a right fit or not.

I think the other biggest thing is for a patient to speak their mind, because we're here to listen. Nobody is trying to push people to go into a clinical trial right away. If you don't think you're ready for it, there are a lot of other options that are okay as well. Make sure that you've investigated all of those possibilities. It's also important to acknowledge the many drugs that have been approved because of patients' willingness to participate and be a part of the whole research endeavor, so thank you.

Mary DeRome (MMRF): Yes, sure. No one can argue with the fact that this field has come an incredibly long way in a very short period of time. That's due to the dedication of patients to join clinical studies and help make this progress possible as we move forward, hopefully toward a cure for this disease at some point. At this time, on behalf of the MMRF, I'd like to thank our panelists, Dr. Noopur Raje, Kathleen Lively, and Bob Lupacchino for joining me today.