FAQs on Multiple Myeloma Diagnosis and Prognosis

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Transcript

Mary DeRome (MMRF): Welcome and thank you for joining us for today's Facebook Live session on frequently asked questions on multiple myeloma diagnosis and prognosis. I'm Mary DeRome, Senior Director of Medical Communication and Education at the Multiple Myeloma Research Foundation. Today I'm joined by Dr. Ken Shain and Ms. Christine Simonelli from the H. Lee Moffitt Cancer Center in Tampa, Florida, and also Jackie Whitaker, a patient from Wesley Chapel, Florida.

We've invited them here today to answer some of the frequently asked questions we receive from patients and caregivers when they've received a diagnosis of multiple myeloma.

Dr. Shain, patients and caregivers often want to know what their myeloma stage is. Can you explain what tests are conducted to determine a patient's stage and what the stage means both for the care team and for the patient?

Ken Shain, MD, PhD: Fantastic question. It's one of the things that we all want to know, what stage is my myeloma? I review it with patients by reminding them that myeloma has its own staging system. It's not 1, 2, 3, 4, like lung cancer or breast cancer, because myeloma is already everywhere. We have to come up with our own staging system, and it involves multiple factors. It involves some lab tests. It involves a bone marrow biopsy and getting some genetic testing from that bone marrow biopsy.

Essentially, what we're going to do is put you in categories. We have what we call the revised International Staging System (R-ISS), which puts you in the categories of one, two or three. And that translates from best risk to lower risk or higher risk, meaning patients might not do as well as you want them to do, or patients will do optimally well.

What we're looking for is something called a beta-2 microglobulin (β2M), which is a blood test; something called albumin, which is a blood test; and lactate dehydrogenase (LDH), which is also a blood test. Those things tell us what the myeloma is doing, the β2M. The albumin tells you how well you're doing, and the LDH shows how much inflammation is going on because of your myeloma.

And then we do a bone marrow biopsy. We're going to take some cancer cells out of the bone marrow, which is where myeloma lives. We look for very specific genetic and molecular features that are associated with myeloma. There's a string of them. Some we know are associated with better outcomes than others. Some are high risk. We will talk about deletion 17p and translocation 4:14. These are changes or losses of certain chromosomes that we know are associated with patients who have higher-risk disease. We put all the results together in a scoring system, the R-ISS.

If you have all good things, you're R-ISS-1. If you have bad things, meaning high-risk cytogenetics—those molecular characteristics, high LDH—and you have low lab tests, that means you're going to be R-ISS-3, and it helps guide us in taking care of you. We always want to make sure we give you an idea of how we think you're going to do. Are you going to have a better outcome or not as good an outcome?

But no matter how we look at it, your job is always to do better than whatever that risk says. I always emphasize to patients that those categories are categories of patients. They aren't you. You are an individual. You will carry your own path. You'll have your own story along the way.

We use those as guides, and they also help us in some way dictate what we're going to do with a therapy, mostly long-term, but also short-term. That's where I suggest we think about staging. It's a way for us to categorize how we look at you relative to all the other patients with myeloma: good risk, middle risk, or higher risk.

But, again, you are your own patient. You have your own disease. Regardless of where you fit, we're going to walk you down a path that way. Hopefully, that gives you a general picture.

Mary DeRome (MMRF): When patients are newly diagnosed and they present to their physician, that's an important time to stage a patient. Are patients staged at other times?

Ken Shain, MD, PhD: What I always emphasize to patients is that your stage, how we characterize you at the beginning, is how you walk through the rest of your disease. You will always be R-ISS-1. You always have your para proteins, and that lives with you.

That being said, we have looked at staging. Does it change over time? Yes. Does it work at different stages of disease? It does still put people in categories, but we don't use that to define therapy as much afterwards. You need to have these tests done at the beginning.

A lot of times, we have to make sure we get these tests, because I can tell you more often than not one of those things is missing. It's an incomplete staging. We don't have the full picture of our patients. I always emphasize the importance of making sure—if you have a chance and it's available—you get to a center that does see myeloma, so you get all of those things done appropriately so we can put you in the right category and give you the right therapy.

Mary DeRome (MMRF): Christine, can you tell us what patients have to go through for tests like a bone marrow biopsy or blood draws? For example, do myeloma patients need a port for frequent blood draws?

Christine Simonelli, BSN, RN, OCN: As Dr. Shain mentioned, patients undergo a bone marrow biopsy to confirm a new diagnosis. Bone marrow biopsies at the center that I work at are typically completed under sedation, which often allows for a better sample to be obtained.

For a patient to undergo a marrow biopsy under sedation, he or she must have nothing to eat or drink after midnight the night before. They have to hold all of their blood-thinning medications for 2 to 3 days prior to the procedure. And they're asked to bring a caregiver with them to assist with the drive home for safety, as they've been under sedation.

Once a patient is sedated, a needle is introduced in their posterior iliac crest and a sample of the aspirate inside the marrow is drawn, and a sample of the bone marrow biopsy is taken. The procedure is relatively quick; it's about 20 minutes that they're under sedation. The results of those biopsies are typically back within 1 to 2 weeks.

In addition to the bone marrow biopsy, blood samples are also needed, which are drawn from the peripheral vein.

The blood tests include quantitative immunoglobulins looking for excessive heavy chains in the serum. We do a serum protein electrophoresis with the immunofixation looking for a monoclonal M spike as well as kappa lambda free light chains, a β2M, a complete blood count (CBC), and a complete metabolic panel (CMP). Ports are not recommended.

We typically avoid them unless they're absolutely needed, as they can add additional risks for clots and infections.

We also ask the patient to collect, at their first visit, a 24-hour urine collection to see if they have measurable myeloma protein in their urine. Once the diagnosis is confirmed, the blood tests are completed again at the beginning of each new cycle of therapy to confirm that response to therapy is being achieved.

We also perform imaging studies, which may include positron emission tomography (PET) scans, total-body magnetic resonance imaging (MRI), and whole-body computed tomography (CT) scans. Bone marrow biopsies are repeated at different times to assess for disease response. Often, biopsies are completed after induction and immediately prior to transplant, approximately 3 months post-transplant, and at additional time points afterwards to assess minimal residual disease (MRD) status.

Mary DeRome (MMRF): Thank you; that was very comprehensive.

Jackie, I'm going ask you to walk us through when you were diagnosed with multiple myeloma. How did you learn that you had multiple myeloma? What led you to go to the doctor? Did you have a symptom or were you at the doctor for a regular checkup and they found something, which I know happens to a lot of patients? How did it happen for you?

Jackie Whitaker: Let me start off by saying thank you to the medical team and Mary for allowing me to participate today. I couldn't be more excited to be here so others can learn about my experience and my journey through this.

I learned about my myeloma through my dog. I was visiting my daughter in college at Georgia and a dog that never gets out of her harness decided to on this day... and to run towards traffic. She looked back at me to make sure I was following her, which I was, at high speed. I grabbed her just before she hit a big intersection, and I heard my back crunch, but I didn't feel any pain. My daughter and I drove 19 hours to Colorado to have the holidays with my son. And when I got there a couple of days after I arrived, I could no longer stand up straight and went to the emergency room, thinking I had broken a rib or two.

They did an MRI and a CAT scan and said that I had a very complicated situation. Something told me it was much more serious than I could ever have expected. I had what they call a plasmacytoma, and they thought it might be related to multiple myeloma. They were not a cancer clinic, but they wanted me to know this was serious. I had crushed three vertebras in Georgia and drove 19 hours like that. I was very lucky to have caught it very early through my dog.

Mary DeRome (MMRF): That's an amazing story. That darn dog? Oh, maybe it's a good thing. Otherwise, you may have lived a lot longer with myeloma and it wouldn't have been caught so soon.

We're going to go back to you now, Ken. Many patients ask what it means to have certain genetic changes as part of the bone marrow biopsy testing. We've heard terms like "chromosomal deletions," "translocations," and "amplifications." Can you help us understand what those changes are and what they might mean to a patient?

Ken Shain, MD, PhD: Going back to our initial question about staging and the R-ISS; part of that was genetic changes—aberrations in the DNA. Essentially, what we know is that myeloma comes from a plasma cell, which is a normal cell. To do that, it has to acquire some genetic changes, some mutations. We know that there are some mutations that are typical for myeloma. They involve deletions, which is the loss of part of a chromosome and the genes that are on it. When this happens, the cell becomes more aggressive than a normal cell. Or sometimes it involves the combination of two chromosomes at certain spots, which drives the expression of certain genes that again leads to a more aggressive cell. Those things lead to myeloma.

What we've learned in the myeloma world is that it's certain genetic changes that we can equate with better or poor prognosis. That goes back to high-versus-low risk.

Some of those are deletions. Those are not good things, because you're setting yourself up for lacking genes that help you do things—like killing cancerous cells.

Certain things are revealed with translocations that drive oncogenes—things that drive the cancer to grow. Again, those aren't always good, either.

The most common change in myeloma is lots of copies of odd-number chromosomes. Long story short: these are things that we know happen in myeloma—the genetic

changes that happens in myeloma that allow us to characterize what's going on in individual patients.

Based on those changes, you'll behave like X or Y. So far, they've only been prognostic, which means they help us put you into categories: you're going to do better or you're not going to do as well as we want. More recently, we've learned that even certain drugs may be targeted to certain genetic changes. It’s very exciting in the context of multiple myeloma. One of those, just as an example, is the translocation—the putting together of two chromosomes, 11 and 14—called translocation 11;14.

We’re not very inventive in the world of myeloma, but that’s just what it is. We know patients who carry t(11;14) are really sensitive to a drug called venetoclax. We're learning more and more in testing this in clinical trials. This is a new drug that we can utilize in myeloma. Now, it’s not FDA approved for myeloma yet. But it's a drug we use frequently in this disease that's approved for other diseases.

We've learned that genetic change is a really important predictive biomarker—meaning that if you have it, you're likely really sensitive to that drug. You have another therapeutic in your armamentarium against your disease. As we learn more about the detailed genetics of myeloma, we may be able to better tailor therapy—that is, better decide what drug you should be getting and when. Those are all things that we're working on at Moffitt and around the world—figuring out how we can better allocate all these cool therapies to the right patients at the right time.

Mary DeRome (MMRF): Christine, what information is important for patients and their caregivers to keep track of once the patient has been diagnosed and the diagnosis has been confirmed?

Christine Simonelli, BSN, RN, OCN: Once a diagnosis is confirmed, a patient should be aware of the type of multiple myeloma he or she has so that they can watch those markers with each cycle of therapy. An example would be Ms. Whitaker. She has IGG kappa multiple myeloma, and so every month she's checking that her IGG level, her kappa light chains, her serum M spike, and urine M spikes are trending downward as opposed to going upward. Along with tracking these disease markers, a patient and his her caregiver always want to make sure they know the drugs that they're currently taking and the most common side effects that may occur with each of them. They will also want to know the telephone number to their teams, so if they run into any problems they can reach out immediately. I also tell my patients to track their cycles on a calendar, as well as appointments, and share times so that they are less likely to miss any of their appointments.

I also think it's a good idea, in case a patient is admitted to a local hospital, to be able to tell the admitting physician that he or she has multiple myeloma, what the drugs are, and where they are in that particular cycle of therapy.

Mary DeRome (MMRF): Jackie, myeloma is such a complicated disease and there really is a lot to it. Can you tell us about how you learned about multiple myeloma so

that you could understand the results of your lab tests, what they meant, and other aspects of your care and your disease?

Jackie Whitaker: It is a very complicated subject, especially for somebody not in the medical field. I research everything. I have been blessed to have a brother who's also a physician who guided me to Moffitt for their care. That's the best fit for me. Also, I researched my medical team and thought I was in good hands with the route that we decided to go with Dr. Shain and Christine's group. I will tell you this: over the years, you see doctors, and you can compare how their bedside manners are and how well they explain things.

When you're given a diagnosis of cancer, everything goes through your mind? It's the end of the world, it's the dark side of the moon. You think the worst, and I did. I was broken from the inside and out. I had crushed vertebras. I'm dealing with cancer. I was 53 at the time, and just didn't know what to expect.

The first time I sat down with my medical team, Dr. Shain took as much time as I needed to answer my questions. I always go in with a list of questions. They probably see me coming. But he takes his time.

It's important really as a patient to write down questions and answers, because it gets to become very overwhelming. You forget everything the minute you walk out the door.

I also keep a calendar, which Christine was wonderful about suggesting. This has every appointment in here. It has all of my markers. It prompts me to write questions the night before I go in, and I have a better understanding coming out of what to expect and what the plan is going forward.

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

Dr. Shain, a lot of patients ask, is there a hereditary component to multiple myeloma or the precursor conditions of myeloma? If you have a member of your family who's been diagnosed with a precursor condition or with multiple myeloma, is it important for everybody in the family to get tested?

Ken Shain, MD, PhD: I'll get to that question in a second.

First I want to emphasize what both Christine and Jackie said: as a patient, you want to take ownership of your disease as much as you can. Jackie trusts me. She brings in 50 questions, and my goal is to answer as many as I can before she actually asks them.

Again, you want to be invested in your care, because that's how you get the best care you can. Know what you've got going on, at least have a list so you can hand to people. It is your safety, your health, and how we take care of you long-term. This isn't a sprint, this is a marathon. That's the biggest thing. I've tried to emphasize to everybody I see that this is going to be years and years, as long as you can make it.

You want to be in involved as much as you can. I just wanted to emphasize those points. I think what Christine mentioned and what Jackie mentioned are really critical for the best care you can get.

Back to your question, which is about genetic predisposition and/or screening.

The way I try to address it with most patients is tell that that it's very rare but not unheard of to have it passed down from generation to generation. There are patients who have brothers, fathers, uncles, and aunts that have myeloma, and there's obviously some genetic component. We don't know what that genetic component is, but it's still a rare phenomenon.

Myeloma is generally a disease that comes on with age; it's spontaneous. It just happens because of how our immune system tries to function, and you get these mutations we talked about earlier that lead to myeloma. Now that doesn't mean there isn't some increased risk for first-degree relatives. There are certain groups in this world that have a higher risk than the normal person for myeloma or MGUS, its precursor condition. For myeloma patients, there's about a twofold increased risk in their first-degree relatives—mothers, fathers, brothers, sisters, sons, and daughters—for developing myeloma. I ask patients to make sure that they inform their first-degree relatives, to let them make it part of their family history, so that their physicians can look for myeloma sooner rather than later, if there's something a little odd going on. That's standard of care.

Now, that being said, we're in a world today where we have really good drugs. We have really good ways of testing for myeloma. We're changing outcomes to a better place every single year we're here. We need to start embracing ways to find myeloma sooner. Again, we know everybody with myeloma had a precursor condition called MGUS for years, if not decades beforehand. So, though there is no screening today at your primary care physician for these antibodies, we can measure these proteins in your blood.

There's a huge endeavor called the PROMISE study. We're trying to screen 30,000 people at higher risk for having MGUS. Those are people who are first-degree relatives of patients with myeloma—again, mom, dad, brother, sister, sons, and daughters. Or if you're African-American, you actually would have a higher risk of having MGUS or myeloma. So those two groups of high risks, we're trying to screen those and it's all online.

But the goal of that is to get enough people to be screened to figure out who has it. By screening, we hope to identify people who are at higher risk for developing myeloma so we can better treat our patients ahead of time. Can we get people in clinics faster, have better outcomes—we have to learn and test, is that a good thing to do?

But right now, there's no active screening for myeloma as a standard of care. It's something we all recommend. We're testing that out right now. I think the answer is, we need to test for it, but we haven't proven how important it is yet.

Mary DeRome (MMRF): I'm glad you brought up the PROMISE study. That's something that patients often ask about, how to get screened. And, actually, you can get screened for free if you are in those categories that Dr. Shain mentioned, first degree relatives or African-American.

You can look up the PROMISE study online. It's at the Dana-Farber Cancer Institute in Boston. You can just join directly online, and they'll send you a blood test. You go and have your blood drawn, you send it in, and they will screen it.

Ken Shain, MD, PhD: They'll send it to the myeloma center that you're local to. Patients don't have to drive to Massachusetts. It's a way to make it easy for you to get it taken care of.

Mary DeRome (MMRF): We're going to talk to Christine about precursor conditions. If a patient is found to have smoldering multiple myeloma rather than multiple myeloma, is seeing a myeloma specialist still important?

Christine Simonelli, BSN, RN, OCN: Absolutely. Any patient with MGUS, smoldering myeloma, or multiple myeloma should absolutely be seen by a multiple myeloma specialist for a second opinion and to confirm the diagnosis. Once the diagnosis of smoldering myeloma is confirmed, patients should typically be followed every 3 months with multiple myeloma labs to watch for any CRAB criteria or progression to active disease.

Typically, for patients with smoldering myeloma, the standard of care is observation. However, by seeing a myeloma specialist, a patient with smoldering myeloma may get earlier access to clinical trials.

Mary DeRome (MMRF): I want to reinforce that one of the reasons it's important to see a specialist if you've been diagnosed with myeloma or a myeloma precursor condition is that myeloma is not that prevalent. It's only 1.8% of all cancers. Your regular community physician may see one or two myeloma patients a year; they would not be aware of all the newest treatments or tests that a specialist would be aware of.

Ken Shain, MD, PhD: Also, when you have MGUS or smoldering myeloma, there are significant clinical issues associated with it. It's important for you to be seen by a myeloma specialist who can make sure that it's not involving other organs. It's really important to make sure that this is all you have going on, and that you are treated or not treated for the right reasons.

Mary DeRome (MMRF): We're going to move on and talk about initial treatment for patients.

Christine, how long is a typical course of therapy for a newly diagnosed patient?

Christine Simonelli, BSN, RN, OCN: A typical course of therapy or a cycle—I want to start with a cycle—is usually 28 days long. Often included in that 28-day cycle is a week off of therapy. Induction courses differ from patient to patient.

An example would be if a patient is transplant-eligible, the induction course is usually four to six cycles or 4 to 6 months of therapy prior to the transplant. Patients that are not eligible for transplant will have a longer course of therapy, maybe approximately 9 to 12 months or cycles before transitioning to a maintenance regimen.

Mary DeRome (MMRF): Dr. Shain, in our webinar last week on newly diagnosed multiple myeloma, some of our speakers summarized regimens highlighted by the National Comprehensive Cancer Network (NCCN) as either preferred regimens or recommended regimens for patients in certain circumstances. Can you explain the differences between those categories of treatment for newly diagnosed patients?

Ken Shain, MD, PhD: The NCCN works to determine, what is the best data? Where are these studies? What has been looked at? Essentially, you have a grading system from 1, 2A, 2B, 3.

If we have lots of good clinical data suggesting that a new regimen is better than whatever the standard of care was, and everybody agrees, that would be graded a 1. That'd be your preferred regimen.

Then you go down to a 2A, which means that there's really good data and there's good consensus, meaning most of us agree that this is a really good therapy.

Then down a little further there's consensus (2B). We all agreed the data might be not quite as strong.

Grade 3 means that there's of controversy on how much we want to think about that regimen.

When you think of a preferred regimen, it really means that these are drug combinations that work really well, and they have really good data behind them. Recommended regiments are a similar concept, just a little less, but again still recommend, still highly effective, just maybe a little less data. that's how I think about it.

Now that doesn't mean we all use exactly that when we make decisions about therapy, because we all are pushing the envelope of what's right for myeloma using therapies that are our standard of care; our individual-preferred or institutional-preferred regimens might be a little ahead of that, might not have quite all the data yet, but we know how good they are. We want to push those going forward.

That's how I think about the NCCN and how we think about those guidelines, but, really, anything on the top is really well documented: we’re all in agreement, this is a really great regimen for our patients—meaning safe and effective.

Mary DeRome (MMRF): Whether or not a patient gets a particular regimen is a decision based on whether he or she is high-risk patient or not?

Ken Shain, MD, PhD: Absolutely. The patient in front of you is going to dictate a lot of what you're going to recommend.

Again, we all have guides that help us decide who those patients are, but no matter who you are, the drugs you get as an induction starting therapy, or even later in relapse, is based on who you are, what your disease state looks like at that time, what the risk level is, how you are, your strength, and what else is going on at the time.

Thankfully, we have a number of these regimens, so we're allowed to tell the regimens and also the doses within the regimens that fit the patients sitting across from us.

The most important thing is getting patients on the right drugs, but also the right doses so they can stay on therapy. Putting them on drugs that are too toxic is not something you want to do. You want to look at that patient, get him or her on therapy because that's how you can control disease, and that's our goal. Our goal is long-term control of disease.

Mary DeRome (MMRF): Jackie, we're going to go to you and ask about your initial treatment. Which initial treatment did you receive and did you learn of any reasons why that particular regimen was chosen for your first line of therapy?

Jackie Whitaker: Going back to how individualized myeloma is for each patient, that's where you really have to have an open communication with your medical team. Dr. Shain always gives me options. It's not just black and white. He'd tell me what to expect from this option versus this option, and then I could decide for myself which was a better fit for me with his guidance. As reluctant as I was to jump into therapies, I knew I had to do something.

I'm not a medication-type person, so it was very hard for me to wrap my head around. But I've got to say—and I don't mean to keep tooting your horn, Dr. Shain—you put me at ease, because I was afraid. I'm dealing with cancer and all this other stuff. My back was still broken, and I was healing from that, and he gave me some options that I could feel comfortable taking. That was the path we took initially.

I believe it was a seven-cycle series. We didn't quite get my numbers down to exactly where he was hoping. I had almost a partial response, but not quite there yet. We went into another cycle of a different therapy, which actually got me there. My medical team helped me decide which would be the best route for me to go based on my numbers.

Mary DeRome (MMRF): You guys sound like you're a textbook case of the perfect communication between the care team and the patient.

Ken Shain, MD, PhD: I'd also add that Christine probably does most of the communicating, because she keeps us online.

Mary DeRome (MMRF): Christine, at what point do you discuss with the patient the option of undergoing a stem cell transplant?

Christine Simonelli, BSN, RN, OCN: Generally speaking, if a patient is felt to be a candidate for transplant, it's brought up briefly at the first visit. Dr. Shain wants to give our patients an idea of what the standard of care is after induction therapy, which

includes transplant followed by maintenance. At each visit we give our patients a little more education on the transplant. I often give them, the first time I meet them, a brochure on what stem cell transplant entails, so they can read up on it.

At each visit, we delve deeper into those transplant discussions. This way, once we place a consult for them to meet the transplant team, they have a better understanding and their questions are certainly more in depth for the transplant team to answer. Sometimes it takes them a while to get there, but I think it's important to give that information up front to patients.

Mary DeRome (MMRF): Often, patients will collect stem cells and then elect not to have a transplant until later. If patients make that decision, is it important to advise them to freeze their stem cells when they can, so if they don't want to have the transplant right now, they could have it in the future?

Christine Simonelli, BSN, RN, OCN: Yes. With regards to collecting and storing, the patients always meet our transplant team to have those discussions. We certainly recommend that all transplant-eligible patients collect and store their cells. The big problem that is often found is that insurance coverage may not be there. Some insurance plans do not allow for collection and storage up front, making it an option that's not available to the patients. That becomes a difficult discussion, which is certainly a discussion that happens with the transplant team.

Mary DeRome (MMRF): Dr. Shain, some patients note that their care teams focus on the M spike value as a measure to determine whether or not the patient has responded to the treatment that they've been given. Is the reduction in M spike how response is measured, and how low do those levels have to go?

Ken Shain, MD, PhD: We follow these abnormal protein levels, these M spikes in your serum—myeloma proteins, bad proteins, whatever you want to call them—through an M spike, through your IgG, through your IgA, as well as your serum free light chains, and then we should be measuring them though less and less these days, even in your urine protein electrophoresis, so a urine M spike.

The point is, we're tracking those numbers because that number when you're diagnosed equals the number of bad guys you have in your marrow. As you kill bad guys in your marrow, those numbers get lower and closer and closer to normal. For an M spike that’s zero. For serum free light chain, it means your ratio is normalized, and that's what we can test.

We can test those every month. Every cycle you come in, we check those numbers and watch them go down. We have really inventive phrases like partial response, meaning 50% decrease in those numbers, a very good partial response being a 90%. Then we have complete response (CR), stringent complete response (sCR). All those things mean is that we can't measure those proteins anymore. Once you get to that CR date, we have to do another bone marrow biopsy and imaging to make sure there's nothing that we can see in either of those places.

The best response we could've gotten 5 years ago was an sCR. No proteins are abnormal, we don't see any bad guys, and your PET scan is negative. Today we can actually test even deeper than that. We can check to see if there are as few as less than one in 1 million cells in your bone marrow. We call that minimal residual disease (MRD) testing, and we do it mostly by next-generation sequencing. There's a lot of multi-parameter flow cytometry or high-definition flow cytometry ways of measuring it, as well.

We can measure deeper than we ever have before. Essentially, what we're doing is assessing how well our drugs have worked for individual patients. Generally, the deeper you are—generally, not for everybody—translates to better outcomes, which is why we want to know all these things.

Those are the ways we assess response. What we all want is to be CR, sCR, and MRD negative. That's great. Not everybody gets there. It's still not the majority of patients.

It's not the end-all be-all, but it helps us put a goal in there, helps think about how we want to be giving you therapy, adding drugs to maybe get you a little further. We hope one day that that assessment will help us make decisions about whether you need transplant or don't, maybe when we can stop maintenance therapy because maintenance therapy goes on forever. Someday we can learn about these things, but today we're just using them to tell you how awesome you did with the response to therapy, but hopefully it'll translate into something we can do in terms of operationally: let's get you off therapy or no, we really need to do this or don't need to do that.

Those are the things we're all working on in clinical trials to help figure that out. It’s why clinical trials are so important. Every step in myeloma, not just newly diagnosed, not just relapse, but every step of myeloma needs to figure out how we can better take care of you guys, both short-term, long-term, and the next generation of myeloma patients as well.

Mary DeRome (MMRF): Jackie, let's hear about your experience. What was your response to treatment?

I think that you mentioned earlier that you needed to have one extra round of therapy to get to your partial response or very good partial response. Did you opt to have a stem cell transplant? Did you have MRD testing, as well?

Jackie Whitaker: I was given the option to have the stem cell transplant. I held off a little longer. I was one of the lucky ones that was diagnosed very early, so I did not have to go through a lot of failed therapies to get to where I was. I held off on the stem cell transplant when I was lucky enough to get one of the last seats for a CAR T-cell transplant. It was the best decision I ever made with the team.

It really was the best thing I ever did. I'm here today to tell you I'm in complete response right now. I think there was a reason I held off on the stem cell transplant, because CAR T was gone and I just didn't know it, but it was really a wonderful decision that I made for myself.

The MRD testing, yes, they tested. The first time I finally tested negative, which was just a few months after my transplant, and I have remained negative ever since.

Mary DeRome (MMRF): You may be the first patient that I've spoken with that's had a CAR T after your first line of therapy.

Jackie Whitaker: It was second line, but yes.

Ken Shain, MD, PhD: She did great.

You have to personalize therapy. A transplant is a real decision people need to make. The best way to take care of myeloma today is still induction, transplant, and maintenance therapy.

Transplant is not for everybody. There may be organ problems, the patient can't get it, or sometimes just where the patient is in life—maybe they can't sacrifice that amount of time or just can't wrap their head around that amount of toxicity and what it really means.

You have that right to collect and store cells, as we all talked about in our transplant group. With Jackie, I said, “Here’s what I want you to do, but here's a path if this is not really for you.” She said, “Let’s wait.” We got a response really nice, and then CAR T rolled around just at the right time for her. The study opened up, and I said, “I have the perfect person for you because she doesn't like seeing me at all. She doesn't want to come in every month.” She got CAR T, she’s been CR/MRD-negative since. Let’s keep it that way.

Jackie Whitaker: Yes.

Ken Shain, MD, PhD: No therapy, just watching her. She’s come to get labs every 3 months.

Mary DeRome (MMRF): Dr. Shain, let's talk about the statistics on survival and multiple myeloma. What percentage of people who are diagnosed with myeloma live beyond 5 years, 10 years, or 20 years?

Ken Shain, MD, PhD: I'm going to answer that in several different ways. First, I hate statistics. Where you get the statistics tells you a lot about when the statistics were done. I have patients coming in and saying, “Oh, I'm going to live 5 years. That's all I'm going to live,” because they use statistics from a long time ago. That's not the expectation today.

Even modern statistics that we have in myeloma probably aren't all that realistic, because they're from 5 years ago, because it took us so long to figure out what's going on. Thankfully, in myeloma today, every half decade, we're making huge strides in how we take care of patients.

Look at Jackie, she had CAR T as second-line therapy. That's going to change. You can plug in drug X, Y, or Z, or combination, or keep pushing that.

For patients with transplant and risk-adapted therapy, the expectation should be on average 10 years. That's my expectation when I see somebody, that's average.

Your risk divides you into different categories, too—better if you're standard, a little less if you're high. But again, long story short is you are your own myeloma. You're different than anybody else, and that path is going to be different for you than it is in that statistic.

Although statistics are great for guidelines, they're terrible for making people feel good about themselves. Because when you have myeloma today, hope is the answer. The reality is you have it, but we have lots of hope.

Myeloma patients want statistics. I have trials they go look at, and I can prepare them all and see how these patients do. And there's the MMRF. It has really good data on its website. There are all kinds of legitimate places to get information about myeloma. They're updated, but always take them with a grain of salt; always understand what's going on and recognize that you have your own path.

Mary DeRome (MMRF): What about patients who have other medical conditions besides myeloma? What you would call comorbidities? How are those patients treated, and do those comorbidities affect the outcome from their myeloma?

Ken Shain, MD, PhD: The comorbidities aspect is probably one of the most important things you have to balance with the therapies we have. Most therapies can be relatively agnostic, meaning that they can be treated through most other medications you might be on for any other issue. But one of the things we treat a lot of patients with, I'd say everybody with, is called dexamethasone. We love steroids because they kill bad guys really well, but they're not the most fun if people have diabetes or have other issues. They cause your sugars to go up, even though they're killing bad guys. We have to tailor our therapies to those kinds of things. If you have diabetes, we have to have help from your endocrinologist or your primary care physician to make sure you're on top of your sugar, or if we drive sugars up and we make you induce a diabetic state, we need some help there, as well. Heart issues, when you think about certain drugs, may be a little safer than other drugs when it comes to having cardiovascular risk, but even patients who have cardiovascular risk, there are drugs we're going to use regardless of that risk.

We just need up temporize that, have a conversation. Here are the risks, here are the benefits. Our eyes are open. We need this now. But we're always going to maximize and ask patients to make sure they stay on top of these things, Because the healthier you are from another perspective, comorbidities meaning other things you have, the better off you're going to be.

COPD is another thing we have to be a little careful with, pulmonary issues. These are all things we have to balance with the therapies we're doing, but picking the right drugs and the right doses are just as important, and the right supportive care medications, but it takes a team.

Jackie, although she doesn't have a lot of other comorbidities, came in with back issues. We need neurosurgery. We need XRT. We need radiation. it's a team no matter how you look at it, if it's all myeloma or if it's myeloma plus those things you brought before you had myeloma. It takes a team to do it.

Mary DeRome (MMRF): Speaking of bones, Christine, how can you help patients who have bone issues like compression fractures or vertebrate problems?

Christine Simonelli, BSN, RN, OCN: When patients have compression fractures, pain is often associated with them and we certainly do our best to keep patients' pain controlled. Sometimes that's with narcotic usage, sometimes radiation therapy. We also refer to our neurosurgeons to assess if kyphoplasty may be an option for them for support and pain reduction.

Kyphoplasty can often decrease the pain the patient is experiencing and decrease the risk of additional fractures. We also typically recommend calcium and vitamin D supplementation and bisphosphonates with Xgeva or Zometa to help prevent any new fractures and worsening of bone symptoms.

Mary DeRome (MMRF): Dr. Shain, we did have a couple of patients ask, if they have problems with their bone or problems with their back, do you ever recommend seeing a chiropractor?

Ken Shain, MD, PhD: We don't like chiropractors too much because when they manipulate things, they can break things, and our bones aren't always as strong as we want them to be.

Again, most chiropractors are going to be good. They're going to make sure they get imaging first. They might find a myeloma for that matter. With back pain, myeloma is not the first thing anybody thinks of. They think they hurt something. Ask Jackie! She didn't think she had myeloma, I guarantee it. She probably never heard of myeloma before.

Chiropractors are not our favorite folks to be helping with pain, unless we know that it's going to be massage and more subtle interventions that they can do. I have lots of patients who insist that's all they do. Then I insist back: just make sure they don't manipulate you, because we don't need broken bones, too.

Mary DeRome (MMRF): What about osteonecrosis of the jaw (ONJ), which is another thing that can happen with myeloma treatment? What causes that? How are patients evaluated for it? Can it get taken care of by a dentist or oral surgeon? What are the things patients need to watch out for?

Ken Shain, MD, PhD: We provide a lot of supportive care, and supportive care involves protecting from the drugs we're giving you and also protecting your bones. Zometa as a bisphosphate or Xgeva can build up the bones that are left and reduce fractures in the future.

But one of the risks that both Zometa and Xgeva or drugs in their class have is that they can make what's called a healing ulcer in your jaw. Essentially, because of the environment of your gums in your mouth, you can get an ulcer and it impedes the formation of healing of that bone there. That's called ONJ.

There are certain things that are risk factors, like poor dentition and extractions. Those are things that really can drive an increased risk for getting ONJ.

To manage the risk, what we do is have people get a dentist appointment and make sure that their teeth are okay: they don't need extractions; they all have good dentition before we start long-term use of either of these drugs. That's one way to prevent ONJ.

For some people, it's important to bring calcium down regardless, but one dose of a bone strengthening medication is not going to be harmful. Long-term, if you develop ONJ, it can be fixed with some antibiotics, some mouth rinses, etc., but it does in some cases require an oral surgeon.

Those are all things we're working out, but it's important to find someone who's adept and has experience dealing with ONJ from an old surgeon perspective. Part of the reason getting to a myeloma center is important is that we have folks in our circle that can help with issues like ONJ. It is something that can become pretty debilitating if we don't catch it early. We're always trying to mitigate the risk.

Mary DeRome (MMRF): Christine, if a patient has to miss a treatment because of a side effect, such as if they have a low platelet count or some other low blood count, what impact can that have on their response to treatment?

Christine Simonelli, BSN, RN, OCN: We always want patients to stay on schedule with therapy, if at all possible, for the best outcome. Certainly, if the patient needs to hold therapy for a side effect, such as a low count, we will try to continue to support them with growth factors to increase their white blood cells or transfusions to increase their red cells if necessary, in hopes that we can continue on therapy. Our goal is to keep patients on particular therapies as long as they continue to have a response and that their quality of life is not adversely impacted.

However, if a side effect continues, a dose reduction may be warranted—or even a new treatment plan might be necessary.

Mary DeRome (MMRF): Jackie, can you tell us about whether you had any side effects when you were on therapy?

Jackie Whitaker: I was a little nervous, of course, getting started on some of the medications that might cause blood clots or something similar. They're just things that they had to disclose, but they weren't very common. But I worry about everything. Again, my medical team was willing to start me off slow and progressively see how I react to the medication.

The only side effect I really had from the steroids was a little weight gain, but the weight came off right after. It wasn't bad at all.

Ken Shain, MD, PhD: As long as you had your cycle going…

Jackie Whitaker: As long as I had my cycles going, yes.

Ken Shain, MD, PhD: I think the key is reviewing the common side effects that people have. Like I always tell patients—and I'm sure Jackie can attest to this—drugs are really smart. They're pretty good, but here are the side effects we need to worry about. Please let us know if you experience these so we can dose reduce, adjust, etc., so we can make the side effects as manageable as possible so you can stay on therapy.

Christine Simonelli, BSN, RN, OCN: That's another reason why it's very important that you find a myeloma specialist, because they can react to myeloma so quickly versus a general physician that may or may not know a whole lot about it.

Mary DeRome (MMRF): For everyone, the final question is what advice would you give a myeloma patient who just learned about their diagnosis?

Jackie, I'm going to start with you.

Jackie Whitaker: I've run into a few people who were recently diagnosed, and I have to say, I shouted out from the mountaintop. I don't know if anyone's heard me. There's hope. There's not just hope. There's promise, too, that it's not a death sentence. If I was to get any cancer, if I had to pick one, this would probably be the one I would pick just because there're so many options out there. It's definitely not the end of the world.

Mary DeRome (MMRF): There's so much work going on in myeloma—it's hard to keep up—with new therapies, how they work, how well they work, and who would be the best patients to take them. There is just so much work going on in myeloma. The story of hope is a great story. It really is.

Christine Simonelli, BSN, RN, OCN: To add to Jackie's comments, I always make sure to recommend support groups for patients. It's important for patients to see other patients that may have been doing this for 10, 15 years. That provides hope for patients that are just getting started.

Ken Shain, MD, PhD: Listen to Jackie and Christine. I've said it before: when you walk in to see me for the first time, no one wants to see me. The reality is you don't want cancer. You don't want myeloma.

I try to make sure patients understand that, one, if you have to have myeloma, this is the best time in history to have this disease. It will be better in 5 years. But right now, we have the best options we've ever had. I want to make sure that patients walk out of the clinic knowing that, yes, we have myeloma—that's the reality.

But the expectation that is we have lots and lots of hope. Our job is to get you on the right drugs, the right path, the right doses, and for you to get the best out of it that we can. We're going to figure out what it is for you as we go. But really, it's a hope. We've

got to balance that hope in reality, but right now, when you're diagnosed, our expectation for you is a good, effective therapy.

Everybody is an individual as you said. Not everybody responds to the drugs as well as you want. Not everybody tolerates the drugs as you want. But again, hope is what we should focus on. The reality is we're going to take care of it for a period of time and we're going to walk that path with you, and that's the most important part.

It's not just us. It's your family. It's the team of people that are helping you. It's a journey. I always say it's a marathon or a steeplechase depending on how you want to look at it. Sometimes there's a little hiccup here and there.

Mary DeRome (MMRF): I would like to say that this gathering of patient, nurse, and doctor is probably the best example of an involved and compassionate care team that I've ever spoken to.

Every patient out there should look for this type of relationship with their care team and this type of communication. This is how you get the best care and the best outcomes… by having this communication, making sure that your care team knows what you're feeling and what your goals are in therapy.

If you're part of the care team… making sure that the patients know what options are available, going over the pros and cons, then making a collective decision together as far as what the best path is to take and clearly including the patient and the patient's family in that decision. That's really, really important.

On behalf of the MMRF, I would like to thank our panelists today, Dr. Shain, Christine Simonelli, and our patient, Jackie Whitaker for taking the time to join us today.