MMRF Patient Webinar: Health Equities in Multiple Myeloma

December 20, 2023

Transcript

Mary DeRome: Hello and welcome to the MMRF Patient Webinar Series, brought to you by the Multiple Myeloma Research Foundation. I'm Mary DeRome, senior director of medical communications at the MMRF.

We have with us today two myeloma experts who will be examining the path to improving health equity in the management of multiple myeloma for underserved patient populations. Dr. Sikander Ailawadhi is a professor in the division of hematology-oncology at the Mayo Clinic in Jacksonville, Florida. His focus has been on the treatment of multiple myeloma, Waldenström macroglobulinemia, and chronic lymphocytic leukemia. Dr. Ailawadhi's research has focused on better understanding these disorders and evaluating the benefit of various therapeutic strategies in different populations based on racial, ethnic, and socioeconomic diversity.

Dr. Surbhi Sidana serves as an assistant professor of medicine at Stanford University in California. She specializes in the treatment of multiple myeloma and related disorders and leads the myeloma cellular therapy CAR T program at Stanford University. Dr. Sidana is active in research, leading clinical trials—especially those focusing on CAR T-cell therapy, immunotherapies such as bispecific antibodies, and transplantation in myeloma. We appreciate our speakers taking the time to speak with us today.

Let's get started with our first speaker, Dr. Surbhi Sidana.

Dr. Surbhi Sidana: Thank you very much for the kind introduction and thank you to all of you for taking time from your day to hear about this topic, which is very near and dear to our hearts.

For the first part of my talk, I'll talk about access issues and disparities in care in multiple myeloma. There are several factors that affect health care access and myeloma disease outcomes. These are very complex, and some are interrelated. They can be patient-related factors, they can be access-related factors, and other factors.

When we think about making decisions for a patient with myeloma, whether it's in a newly diagnosed or a relapsed setting, things that come in mind. What is the disease biology and clinical course? Is the disease aggressive in presentation or is it less aggressive? What about prior therapy?

The second part we think about is the patient, their clinical factor and sociodemographics. How old are they? What are their other comorbidities? Do

they have a lot of other medical issues that we need to keep in mind? How fit are they? Because we need to tailor our treatment to patient fitness. We don't want to give very aggressive treatment to someone who's not very fit, because that is not going to help their quality of life. Some of the treatments also require intense caregiver support. So that's something we often consider. What is going to be the financial impact and toxicity and the socioeconomic factors that are in place.

Lastly, of course, we have to look at prior treatment history, what drugs they've been exposed to. If you're already not responding to a certain drug, it's unlikely you're going to respond to it in the future: adding that in combination is likely not going to work. What is the expected effectiveness of a regimen, what are the expected side effects, and how can we tailor that to that particular patient? We also want to involve the patient in treatment decision-making. These are not unilateral decisions, these are bilateral decisions that we talk about with our patients and have an informed discussion.

Regarding risk factors, multiple myeloma is typically a disease that occurs in patients over the age of 60, typically over 65, though I have plenty of younger patients in my practice. Myeloma is more common in men than women, and myeloma is more common if you have a history of myeloma in your first-degree relatives. It is also more common in African Americans and less common in Asians.

Data from the SEER Registry, which is a national registry that evaluates the incidence and outcomes of all cancers in the United States, shows that myeloma is much more common in Black individuals compared to Hispanic and White individuals. This is very well established at this point.

If you are Hispanic or Black, your age of diagnosis is likely going to be lower than if you are White or Asian. Black and Hispanic patients tend to be diagnosed earlier in life, and we know that there are disparities in access to care.

Stem cell transplant is a procedure that has been around for 40 years. It has to be performed at one of the specialized centers dispersed throughout the country. Despite this procedure being around for 40 years and despite several centers doing it, Black patients, even in the last decade, have been less likely to receive transplants than White patients, even after you control for age, sex, socioeconomic status, other medical issues, and insurance providers. That is very striking. Even Hispanic patients have low utilization of stem cell transplants. Several trials have shown that stem cell transplant provides better duration of response and progression-free survival (PFS) in myeloma patients than is seen in patients who do not receive transplants. This is a big disparity, and this is not just the case with transplants.

A study done by Dr. Ailawadhi showed that Black patients have lower utilization of novel treatments. Dr. Ailawadhi and his colleagues looked at triplet therapy—

which is now becoming quadruplet therapy—but for a while, that was the standard of care. Fewer Black patients were getting triplet therapy, which is three drugs for the treatment of myeloma. Fewer Black patients were getting a proteasome and immunomodulatory drug (IMiD)-based triplet, which many of us considered the standard of care for the longest time in myeloma, compared to White patients. This study also confirmed that frontline transplant was lower in Black patients than White patients. This is from 2007 to 2013. This data shows that there are disparities in access to care, even for novel agents, for transplants, and so on.

A different study looked at access to clinical trials. Clinical trials bring new treatments to the clinic, and this can give patients access to new treatments before they're available as FDA-approved therapies or for different indications than they're approved for. Black patients make up approximately 20% of the US myeloma population, but in this study Black patients made up less than 5% of the FDA registration trial. Similarly, Hispanic patients make up a larger proportion of the US myeloma population compared to their representation in clinical trials. This is sobering, and this really has been a call to action for many of us. Now we have special cohorts for Black patients so that we can ensure that there is at least equitable representation in trials.

This is so important, because these trials ultimately lead to the approval of new therapies, and if we don't include patients equitably, we will not know there are differences, side effects, differences in efficacy. It's very, very important for the proportion to be equitable.

Another interesting study looked at the question of why is access different in trials? Some of it might be where trials are available. A study published last year that looked at clinical trials of CAR T-cell therapy and bispecific antibodies in multiple myeloma looked at the distribution of trials in different states. In the Southeastern United States, where there are large Black populations, the trials are quite sparse. So the trials are not there where our patients live, which shows that there's a disparity in access—even if patients wanted to be part of a trial, it's not available in their state or even the neighboring state. How do we expect our patients to participate in trials?

There are several barriers associated with clinical trial participation. Some of them are practical issues. Trials require more time commitment from patients, and transportation is a factor, because you often have to go to a tertiary care center and you need transportation. Usually, that's not your center right next door to your house. Trials often require extra studies, extra labs, extra bone marrow biopsies, because the researchers want to dot their i's and cross their t's and have more extensive data. Then there are socioeconomic and demographic issues, with all of this travel going back and forth, that can create a financial

burden for patients and their caregivers who often need to take time off to accompany patients to trial visits.

Some of the limitations are health literacy limitations. If you don't understand what trials are, what interventional studies are, what a control arm is, that can create doubt in patients. If I don't understand it, I don't want to participate in it. For a lot of trials in the U.S., part of the research costs are covered by the trial sponsor, but part of it is billed to insurance. If your insurance is not good about covering trial costs that are considered standard of care, that can create a big access issue.

Then, of course, if you're older and frail, it's harder to go to a center that's further away that requires more visits. There are real barriers to that. There are also cultural issues. Sometimes there's discordance between what patients think trials are and what clinicians think trials bring to the table. Patients are worried about investigational therapy, because they fear the unknown. Sometimes there are big trials that are randomized trials with placebos. Of course, understandably, patients don't want to take placebos. A lot of it is a lack of knowledge about the trial process. It seems very opaque to sit on the other side as a patient. What's a study? What's a phase 3 study? How long do I need to be on it? What happens 6 months from now? A lot of it is needing extra information about the trial and the trial process. It's different for each trial. Trials with CAR T, for example, will be much more involved than trials with a pill for the most part.

A study done by Dr. Ailawadhi and his colleagues looked at the cost of care by patient race and ethnicity. Patients of Hispanic descent had the highest all-cost per patient compared to patients who were White. When you look at multiple myeloma–related costs, this was again the case: Hispanic patients had higher costs than White patients.

What this tells us is that, as clinicians, even though our visit might just be 30 minutes, we really need to be careful. Yes, some of these costs are borne by insurance, but many may not be. We need to be asking patients about financial impact and the financial toxicity of these costs. We need to have social work support available to help cover some of these costs if there are out-of-pocket costs and really have a lower threshold for intervention.

There are disparities here, and these disparities can exist for many reasons. There can be comorbidities that cause increased costs. There can be late diagnoses that cause increased costs. But as health care providers, we need to be aware to intervene.

Racial disparities persist in myeloma-related mortality. Black patients have the highest mortality or risk of dying from myeloma compared to other patients. This is sobering, which means that we need to intervene.

Data from the SEER registry, which is a national registry, shows that there was no difference by race or ethnicity in both PFS—which is a surrogate for remission—duration, and overall survival. If Black or Hispanic patients actually make it to the treatment and get access to these trials and new treatments, they do just as well. It's not about disease biology, it's a lot about access to treatment.

A study of VA patients—all VA patients get similar access to care—showed that, regardless of age, Black patients do slightly better than White patients. That was particularly the case for patients under 65 years. For patients over 65, the outcomes are very similar for survival. What this again tells me is that if patients have equal access to care, Black myeloma patients can have similar or better outcomes than White patients with equal access to modern therapies. Again, a fact that we need to be aware of and emphasize. It's all about access to the right treatments.

To summarize, outcomes do differ in myeloma based on patient race and ethnicity. Myeloma is twice as common in Black patients than White patients. But the disparities can be due to delayed diagnosis, lower access to transplants, novel agents, and clinical trials. What is very important is that when we see equal access to care, Black patients can have survival outcomes that are equal to or better than what is seen in White patients. Again, telling us that all patients, regardless of race, ethnicity, and age need to have good access to care to have the best outcomes possible. Our good treatments do no benefit if a patient cannot access that treatment.

Mary DeRome: Thank you Dr. Sidana. Pointing out these disparities is so important. It's important that we make sure that when we're doing research, we're including the entire range of patients in the real-world population of multiple myeloma, so that the research we're doing and the outcomes we're seeing are representative of all patients.

We're going to move on now to Dr. Ailawadhi.

Dr. Sikander Ailawadhi: Thanks a lot, Mary.

As Dr. Sidana pointed out, this is an extremely important and urgent issue that needs to be addressed actively, continuously, and persistently, because it's not easy to sort out.

This issue about how to provide appropriate evidence-based treatment to everybody—the right patient at the right time for the right treatment—how do we make that happen? That the benefit of four-drug therapy, minimal residual disease, next-generation sequencing, and all that stuff reach every single patient? How does the benefit of that research come back to every single patient? I'll take you through how can we try to overcome some of these barriers.

Several factors are involved in providing appropriate care to a patient. It is a very complex path, not just understanding the disease but navigating through the process. When does a patient come to an academic center? When do they get a transplant? How deep of response do they need? Which drugs are used first, which drugs are used later?

I was reviewing some data for another presentation around health care disparities, and I came across a reference that about 70% of patients with multiple myeloma are diagnosed in primary care. Does the primary care physician have the appropriate thought process to diagnose the patient in a timely way? When does that primary care physician trigger a consult? When does the patient get diagnostic testing? Are they able to get all that testing in time? Who pays for it? How are those results conveyed to the patient? Timely or not? When does the patient get to a referral, a specialist, and the diagnostic testing at the specialist center? How is that reported to the patient? How is the treatment informed to the patient?

These are all extremely important things, because they will determine how likely it is that the patient gets timely treatment and what support resources are provided to them. A lot of these are things that we need to do better on. How early can the patient be seen? How well are they educated with their caregivers? Because, frankly, this is not a one-person task, we need all these resources to come together. How can we get the patients to stay adherent to the treatment and to the follow-ups? Those are all extremely important factors, and it is incumbent upon us to try to figure out solutions for every one of these steps that may be a barrier for a patient.

An interesting study I came across looked at the social determinants of health that affect how we consume health care. According to the study, approximately 40% are socioeconomic factors, 10% are physical environment of the patient, and 30% are their health behaviors. This is not myeloma specific; this is overall health care-related. Finally, 20% is dependent on health care.

It’s interesting, because these are all factors that could affect access to care. What if the person has, let’s say, a mental health issue—depression or concern or anxiety or fear because of their cancer diagnosis is preventing them from seeking or receiving or continuing with the right care. These are all important questions to think about. We first need to identify the barrier for that patient at that time and then be able to do something to overcome it.

It’s also important not only to identify these social determinants but also to monitor them throughout the patient’s journey with their care. What is their employment status? What is their insurance status? Is their living situation good or appropriate or not? Has that changed? I have a few patients who have mentioned that their caregiver situation changed because along their journey of

the diagnosis, things didn't work out, and their partner, their significant other—they're now separated. It was too much stress for everybody, and the significant other had to move on. Has that changed the living situation? Has that changed the financial situation?

Frankly, something that we don't talk about enough is this whole issue about food insecurity. We mentioned that eating healthy, eating a nutritious diet is important, but does everybody have access? It's easy for me to just say that in my clinic and move on, but how much time do I have to try to figure out what might be affecting that patient? That's exactly what Dr. Sidana was mentioning earlier: that our threshold for identifying or addressing these issues must be different for different patients, because everybody's situation is unique.

There are several screening tools for assessing these social determinants. I understand that in our clinics we are rushed for time, we are moving from patient to patient, but that is exactly where sometimes we put teams that take care of the patient. I may not have time to go over all of this, because I'm addressing the nausea or the diarrhea or the infection for the patient, but that's where one of our nurses, or a clinical assistant, or a social worker comes in and addresses this. There are several tools we can employ or that the patients can think of going through, like a health-related social needs questionnaire. These different tools are actually validated, and we use them to determine what might be the needs for a particular patient.

It's extremely important—I cannot stress it enough—to provide education to patients. We did a study which we've presented at the American Society of Hematology where we surveyed about 550 patients with cancer at Mayo Clinic. We looked at their awareness, their understanding of clinical trials. This was not myeloma specific; this was all cancers. The number one factor that was different between Black patients and everybody else was awareness about clinical trials. I understand in my mind about bias and fear and anxiety, but at least in our study, awareness of clinical trials was significantly different. Black patients were less likely to be aware about clinical trials, and this is all patients who were new to Mayo.

Education is extremely important. Not only at the time when the patient is diagnosed with cancer—when somebody just got a diagnosis of cancer in the clinic, and now they have to figure out the rest of their life—but then ongoing with treatment. How do the patients cope with the side effects? What can they do to mitigate the side effects, manage them, all these social determinants, and then whenever the disease relapses, how to make the right decision? You see a theme that is emerging, that it's teamwork between us as health care providers, our patients, our teams, caregivers, everybody has to come together. In fact, I'll go one step further and say that, between the physician in the academic center

and the physician that might be a community physician for the patient, that interaction is also extremely important and vital.

This patient-centered approach is integral to how we try to make the right decision. As doctors, we need to keep reminding ourselves that 95% of the patients do want to participate in their treatment decisions. I cannot assume that what I'm saying is also what's conforming to what the patient says. In fact, there was a study done out of the MMRF itself a few years ago where the doctor's perspective on disease and treatment in myeloma and the patient's perspective were compared. A lot of times, the doctor's perception about the goals of treatment were very different from the patient's perception.

We have found some of those things in some of our recent studies, where the patient's perspective about—for example, CAR T and bispecific treatments—is very different. They're looking for different things than what I think they might be looking for. It's important, because this back-and-forth discussion between the patient and the health care team will improve confidence and will build that trust. The patients are more likely to stay on treatment and have better quality of life.

I understand that you as a patient are interested in participating in your care, but it may be important to make that fact known to your doctors. Don't assume that they're going to make you participate. They need to know that you are interested and you're willing to participate.

Access to transplant is something Dr. Sidana mentioned very nicely. Access to transplants—to all these complex therapies—is extremely important, because a lot of times a patient is labeled transplant eligible or ineligible right at the beginning when they got diagnosed. Yeah, if somebody had kidney failure from myeloma and a lot of fractures and bone pain and is wheelchair-bound, they may not be transplant eligible. But give them a couple of months of good treatment; things improve, pain gets controlled, get them supportive care, kyphoplasty and orthopedics or interventional radiology or whatever, they feel better, they become transplant eligible. It's important to assess that eligibility in a dynamic fashion rather than as a point decision.

Patients need to be educated about the transplant. A lot of patients are so afraid of it. I actually just this morning had a clinic appointment with a patient who's an international patient from Brazil who gets treated locally but is interested in coming for a transplant. He's a physician himself, and he had so many concerns about the transplant that he was planning to defer it or not go in for it. We spoke for about 30 minutes just trying to address his fears, and now he plans to come in January and start with the workup.

During the transplant process, patients need resources. It's important to connect the patients with advocacy groups—the MMRF, the Leukemia & Lymphoma Society, the American Cancer Society. There are many resources available. It's

important for the patients to be referred to transplant, to CAR T, to these novel complex things, to clinical trials early. Transplant, CAR T, clinical trials—these are not last-resort things. The discussion about these things should happen way earlier and sometimes even at the time of diagnosis.

This is also true for CAR T. There are many steps involved in the CAR T process, where there's a primary oncologist and their team, academic oncologist and their team, insurance, and a benefits manager—somebody confirming that the patient actually can come insurance-wise. There are certain patients who are required to go for transplants to certain institutions because of the contracts with their insurance.

Then, where the patient goes, what is done? A lot of testing. The patient has to stay close to the CAR T center for about a month or so. That's important. Initially in 2021, when CAR T cells came about, about a third of patients died while on the waiting list, not being able to get to CAR T. Things have improved quite a bit since then, slots have increased, centers have increased, more patients are getting CAR T. But it is important to keep in mind that these are complex treatments, so we cannot wait until the last moment to get the ball rolling. Planning needs to be done ahead of time.

Similarly, facilitating access to clinical trials, clinical trial development, and protocol development requires a lot of planning, and we spend tons of time opening a clinical trial. Typically, for example, in my clinic, when a clinical trial is getting close to its activation, we start maintaining almost like a wait-list internally to try and figure out who should be going on a certain clinical trial appropriately. When the trial activates, we are able to get the patients in. But when we do clinical trials, it's important that we have a very patient-centric approach and try to figure the eligibility criteria that is broader so that, for example, more Black patients, more Hispanic patients, patients who may have more disease burden, can come into the trials. It's also important to involve patient advocates and always keep in mind the financial impact and the quality-of-life impact of these trials.

If I'm presenting a trial to a patient and the patient does not relate to me culturally, it'll be difficult for them to understand or like what I'm saying. In fact, our trial staff group includes people who are Black, Hispanic, Asian, and White. We have seen this happen, time and again, that a Black patient is more likely to digest the information and be more receptive to it when it's presented by a Black individual.

Similarly, when a patient is on a trial, we want to make sure that they're they're informed or managed by individuals who are providing the care in a very culturally appropriate manner. When trials are closed, we are also talking about how we can generate data in Black and Hispanic patients separately, so that we

fully understand how the drugs work and where they do not work. For example, when patients are on treatment, the general idea is that once a patient starts on treatment, he or she stays on treatment for as long as it works. It becomes a struggle, sometimes, to stay on treatment with chronic side effects.

In fact, the number one thing that we hear from patients for CAR T is, well, after CAR T, if I'm not on treatment and my treatment has worked, then it's almost like I've gotten my life back. I can start living life. I'm not tethered to the institute or the cancer center. It's important that we address adherence of treatment with the patients and give the patients those tools to address their social determinants, to address their stress, to figure out caregiver and caregiver fatigue so that they can continue to care for patients.

Several tools are available. For example, at MMRF's patient Navigation Center, patients can get access to a lot of information, resources, and support; several of my patients have utilized it and have benefited from it. No matter what the disease state is—whether it's smoldering myeloma, newly diagnosed, or relapsed—it's good to try to connect to this Patient Navigation Center.

There are so many resources that are available. As a doctor, I don't talk to my patients about them, because we don't have time and because I may not be fully aware of all the options. I'm much more focused on finding out what's the right treatment for that patient at that time, which is the right clinical trial to choose. Are the guidelines changing? How do I change the guidelines at our institution? What is applicable to our catchment area?

We depend on foundations like MMRF to take some of that burden and some of that work; we don't want to ignore that. We don't want to neglect these questions. Similarly, MMRF does have, for example, myeloma mentors. This is where patients and caregivers have the opportunity to connect with trained mentors via a phone-based program. I've had at least two patients who've gone through this and have benefited. A lot of times, those one-on-one interactions with a trained patient or a caregiver mentor helps the patient convey their concerns and understand. One of my patients has served as a myeloma mentor, and he said that he tremendously benefited from those interactions.

Similarly, there are also several options for financial and transportation support. Sometimes all that is standing between you and your treatment, or you and a transplant, is how to get to the center. For some of these clinical trials, there are extra tests, extra visits, et cetera. Sometimes there is support available that you may not be aware of. It's good to ask.

For example, for patients going into a clinical trial, the thought may be, well, if I'm on a clinical trial, the clinical trial will take care of it. But a lot of trials don't take care of the transport back and forth; the majority don't. That's where efforts like MMRF's collaboration with the Lazarex Cancer Foundation to provide resources

so that patients can get to that treatment—to make sure that transportation is not a barrier for the patient, and also lodging.

I'll give you a quick example from a recent clinical trial with four newly diagnosed multiple myeloma patients. We fitted this trial with several features so that it becomes very user-friendly, real-world, and for patients who are seen in clinics across the country. The idea is that if a patient needs treatment for myeloma, we have to make our trial so that the patient is able to get it on the trial. Typically, our clinical trials are very drug-centric. The purpose is to get the drug approved. But with this trial, we have tried to change that lens and said, our trials need to be more patient-centric because, remember, this drug is helping the patient. What can I do to make sure that my patient actually gets on the trial? We are allowing transfusions, we're allowing growth factors, we are allowing any degree of kidney dysfunction. You've got myeloma, you need to be treated; if you need to be treated, we've got to make sure there's a way to access the trial. It's important for us to keep modifying the status quo.

There are many disparities that we have talked about. They're difficult to address but not impossible. We do need all of this to come together so that we can provide, like I said, the right care to the right patient at the right time. Again, it's difficult, but it's not impossible.

Mary DeRome: Thank you very much, Dr. Ailawadhi.

We're going to move on now to Q&A.

One of the things we talked was the difficulty of patients to have a timely diagnosis, and a couple of patients asked about that. What are the early symptoms of multiple myeloma that a patient can bring up to their doctor and say, I have this symptom, do you think it might be multiple myeloma?

Dr. Sidana, I'll start with you.

Dr. Surbhi Sidana: This is always challenging, because many symptoms of myeloma can be nonspecific, meaning they can be present in a hundred different conditions. Common symptoms are fatigue, bone pain, and related issues with high calcium, et cetera. What I would encourage people to do is if you are not feeling well, please pursue those symptoms. Fatigue can be many things, it can be low thyroid, it could just be having a lot of stress at work. But don't ignore your symptoms, go to your primary care doctor.

I tell people, even my family and friends, you have to be an advocate for your health. You know yourself the best, if you feel something's not right, you need to go, you need to persist. Your doctor can find things that can be clues for myeloma. If they do a blood count and you're anemic, that can be a clue for many things; myeloma is one of them. If they do a simple blood chemistry test, high calcium levels or bad kidney numbers can be a clue to myeloma. If they do

a urine test, more protein in the urine can be a clue. If you have a lot of pain, if you get a scan done, we can find bone lesions, which is most of the time punched out holes in the bone. Be an advocate for your health, reach out to your primary care doctor, and if you think something's wrong, keep pushing.

Dr. Ailawadhi, anything from your side?

Dr. Sikander Ailawadhi: The only thing I'll add is that in one of our studies we looked at data between diagnosis and treatment—so not just getting to the right diagnosis but also getting to the right treatment—and saw that Black patients had an average of about 5.76 months even after diagnosis to get to the right treatment. For White patients, on the other hand, it was about 2.5 months.

Knowing these symptoms, being persistent about these symptoms, getting to the right answer—it's said that patients should be their own advocates, but patients also need to know what to ask for before being their own advocate.

Mary DeRome: Speaking about treatment, the issue that we discussed is the lack of application of standard of care to certain patient populations. Can you talk, Dr. Ailawadhi, about what actually is the standard of care that patients should be asking for? Is it two drugs, three drugs, four drugs? I know it can vary based on the diagnosis and the patient, but there definitely are standards of care that should be applied to all patients.

Dr. Sikander Ailawadhi: That's an extremely important question. There is no one-size-fits-all treatment, so we cannot say that every patient who walks through the door should get exactly the same thing. There are lots of factors that are taken into consideration, but there are some very broad guidelines that we do adhere to. In this day and age, a newly diagnosed myeloma patient should be treated with a three- or four-drug combination. There are different settings for where three would be used, four would be used, but the world is moving very fast towards a four-drug combination. Every patient, we should at least have in mind, should they be getting to a transplant or not? It's important for a patient to question, why am I not a transplant candidate? At least right now, these are basic starting points of triplet or quadruplet therapy.

Everybody should be considered for transplant, at least while things are getting better. Every patient must be provided with supportive care. When I say supportive care, in my clinic, the newly diagnosed myeloma patient, there is an initial phase of just educating them about what's the diagnosis, what's the treatment, why is this the treatment, how we're going to do it. The next phases within the first 2 months is managing side effects, providing pain control, strengthening their bones, preventing infections, sending them to IR for kyphoplasty, et cetera. Then the next phase is when we are through about two thirds, or almost four months of induction, is talking about transplant. These are some basics for the initial management of myeloma.

In a relapse setting, again, one size doesn't fit all. It's important to ask the physician why a certain regimen is being chosen. Not just what it is, but why it's the right regimen for that patient. One thing I keep telling patients is, please seek an opinion with a myeloma specialist anywhere along the journey. That's extremely important. Dr. Sidana, do you want to add anything?

Dr. Surbhi Sidana: No, you put it very well, and I cannot emphasize how important it is. Even if you're not getting treatment at a specialized center, maybe touching base once or twice, especially at major decision points, is so important.

Mary DeRome: Okay, so I know you mentioned, Dr. Ailawadhi, relapsing myeloma. That is another area where patients need to be diagnosed by their doctor. What would be the guidepost for a patient that their myeloma is beginning to relapse and that they should talk to their doctor and consider what care to have next? How do patients know when they're relapsing?

Dr. Sikander Ailawadhi: We've both said, time and again, that educating our patients and making them aware about the disease is so important, to the point I mentioned that with a newly diagnosed patient, we spend a lot of time just educating them. What is the disease? What are the numbers? What are the labs to look at?

Relapses or progression in myeloma are typically classified in two categories. One is what's called biochemical progression or progression based on labs. This could be when the patient's myeloma markers, immunoglobulins, free light chains, or monoclonal protein based on blood or urine—M spike—are going up. I tell patients, don't think that the ratio change is progression. It is these proteins that have to contribute whatever's that monoclonal protein. M protein in the blood, M protein in the urine, light change immunoglobulins—they constitute biochemical progression.

The second category is clinical progression. Somebody was doing fine and suddenly, while just doing some routine yard work or walking on the street, they slipped and they broke a bone. That is clinical progression, because there was a new lesion somewhere. Or suddenly kidneys started deteriorating. Biochemical is just a lab progression. Clinical progression is some new symptoms showed up.

Patients should be aware of what are the symptoms so that they keep thinking about them, and patients should be aware of what labs to follow. I would say, it's not just patients, it's patients and caregivers. Both should be aware of what labs what symptoms to follow. If any of that happens, ask the question. If you're not getting the right answer, ask, for example, the helpline at MMRF, or if you at that point you want to seek a consult or an opinion, seek an opinion.

Mary DeRome: Dr. Sidana, can you comment a bit on the impact of stress on a patient's health?

Dr. Surbhi Sidana: This is my opinion, because we don't have a lot of data on what stress does to myeloma, but in general, stress is not good for your health. Stress increases your cortisol levels, which is your own steroid level. It's generally not good for quality of life or tolerability of treatment. If there are things that you can do to improve stress in your life, that's helpful. But it's important to know where stress is coming from. Is it coming from going to a treatment center and getting that treatment? Is it the side effect of the steroids that you're getting? Because many times our patients get a lot of side effects from steroids. We give a lot of high-dose steroids in the beginning, and I'm very quick to cut back on steroids. It's important to realize where stress is coming from and talk with your doctor. Is it financial toxicity? Is it treatment time in the clinic? Is it drug-related side effects that we can help you deal with?

Mary DeRome: We've had a couple of questions from patients with smoldering myeloma. Many primary care physicians, and even specialists, take a watchful waiting approach to patients with smoldering myeloma. The science and the research on smoldering myeloma is really accelerating, but there isn't much in the way of treatment for smoldering myeloma unless you're a high-risk patient on a clinical trial.

What advice would you give, Dr. Ailawadhi, for a smoldering myeloma patient who is not high risk and is not on a clinical trial?

Dr. Sikander Ailawadhi: As Dr. Sidana was mentioning, even a stress-provoking situation for a patient is to know they have cancer—they've been diagnosed with an incurable cancer—but we're not going to do anything about it. Just go home, come back in 6 months. That is scary, and I get that. That's one of the reasons I appreciate these questions, because this is telling us, as clinicians, where there are awareness and knowledge gaps, so we can keep educating and talking about this to our patients.

Smoldering myeloma is managed in a lot of different ways. There have been large clinical trials of patients with high-risk smoldering myeloma—and generally high risk is defined based on cytogenetic abnormalities or mutations in the plasma cells. But there is also a criteria out of Mayo Clinic talking about clinical high risk and smoldering myeloma. Patients with high-risk smoldering myeloma, when treated with myeloma drugs, have shown a delay in progression to true myeloma.

Generally, that treatment does not burn any bridges for future treatment. But now we are starting to treat active myeloma even before patients notice any symptoms of kidney failure, bone lesions, etc. We actually treat patients sooner, before they show any symptoms. A lot of times the thought process is this informed discussion with the patient saying, do I need to get exposed to a drug

sooner where side effects, financial impact, more frequent visits, and all of that comes in?

That PFS benefit or delay in progression benefit has been shown in high-risk smoldering myeloma, and that's where treatment is offered frequently to patients. But I have some patients who have considered, well, I don't really want treatment right now. Could you just monitor me more closely? Could I do labs every 4 or 6 weeks instead of every 3 months just to get that peace of mind that I'm doing okay? There is no one size that fits all. Certainly, I'd love for you to add to that, because there's beyond just data, there is also physician and patient preference that comes into this decision.

Dr. Surbhi Sidana: I 100% agree. Smoldering myeloma is where the art of medicine really comes in, identifying priorities, what the patient prioritizes, and what the evidence is. As you pointed out very correctly, we have clinical trials showing that very, very high-risk patients with smoldering myeloma should be treated. I recommend clinical trials for those patients, but for the rest of the patients, unless someone really wants treatment and they're high risk, I recommend observation, usually at least every 2 to 3 months.

But more often I don't have any concerns. If somebody wants to get their labs checked more often, it should not just be once a year, that's fine for another stage called MGUS, which is another myeloma precursor condition. But for smoldering myeloma, they need to get their labs at least in the beginning, the first 2 years, check more often, because that's a time when most people will progress. Your myeloma will declare itself—is it going to stay steady or is it going to rapidly change?—which is an indicator for progression, as well. In the early stages of diagnosis, check more frequently. Later, as things stabilize, you can decrease the frequency of checks.

Mary DeRome: I've got one last question. One patient says that he was ill for at least 2 years prior to diagnosis with multiple myeloma, which is common, because myeloma is rare—only 1% of all cancers—but also because, when they go to their primary care physician and are found to have, say, anemia, the first thing that pops into the doctor's mind is not this patient might have myeloma.

The question is, what conversation should we be having with our local clinicians and health departments to address multiple myeloma education in the future? This is a very expensive cancer; what is being done about getting this information to the Black community?

I can speak to that on behalf of the MMRF. We are doing our best to get this information out into the community. The issue of health equity has come to the fore. This information is important to get out into the community.

Dr. Sikander Ailawadhi: We as clinicians are very cognizant of the financial toxicity to the patients, to the health care system. We don't think it is sustainable

this way. That's where future and current ongoing clinical trials are actually addressing questions of when to stop treatment.

Most clinical trials are working on a discontinuation strategy of treatment so that we use the drugs when they're really needed and have the highest impact rather than everybody getting treated all through. But as far as addressing all these social determinants, it's important for patients to be aware and ask for help. For us, it's important to also educate our fellow clinicians so that they know how to intervene and when to act.

Dr. Surbhi Sidana: The only thing I would add is that we are educating our clinical partners in primary care, but some of this education is now also starting in medical schools for getting myeloma and MGUS and smoldering myeloma as part of their curriculum. Because they may not hear about it anywhere else except that Hematology 101 course. Along with educating the ones that are currently practicing, also educating our medical students and also educating patients, which MMRF is doing a wonderful job of, especially in the Black community.

If you have somebody in your family who has myeloma or smoldering myeloma, MGUS, you might be at higher risk. Just knowing that and education about that can be very helpful. You can actually educate your own health care providers.

Mary DeRome: We do advocate for patients to do that, as well. Certainly, getting a second opinion from a myeloma specialist is key to having the best outcomes for your disease.

That is all the time we have for questions. I would like to thank our faculty, Dr. Surbhi Sidana and Dr. Sikander Ailawadhi, for this enlightening conversation about health equity. Thank you.