Real-world tactics to address health inequities in multiple myeloma care

CMEO Podcast Transcript

Joseph Mikhael:

Hello, my name is Dr. Joseph Mikhael. On behalf of CME Outfitters, I'd like to welcome you to today's educational program entitled, “Real-world Tactics to Address Health Inequities in Myeloma Care.” Today's activity is brought to you by CME Outfitters, which is an award-winning, jointly accredited provider of continuing education for clinicians worldwide and is supported by an educational grant from the Johnson and Johnson Institute and the Johnson and Johnson Family of Companies.

So let me start today by introducing our faculty. As I mentioned, my name is Joseph Mikhael. I'm a professor at the Translational Genomics Research Institute in Phoenix, Arizona, and I have the privilege of serving as the Chief Medical Officer of the International Myeloma Foundation. Joining me today is my very good friend and colleague, Dr. Saad Usmani, who is the Chief of the Myeloma Service and a member of the Memorial Sloan Kettering [MSK] Cancer Center and attending physician in myeloma in cellular therapy and adult BMT in New York, New York, and is clearly recognized as one of the leaders in myeloma in the world. So, thank you so much for joining me today, Saad; it’s great to see you.

Saad Usmani:

It’s a pleasure to be here, Joe. Thank you so much for having me.

Joseph Mikhael:

So let’s start by reviewing our learning objective for today’s session. We would expect that after participating in today’s activities, clinicians should be better able to recognize the impact of health inequities on patients with multiple myeloma and develop individual treatment strategies for optimal clinical outcomes.

This is such an important topic that we’re addressing today. We could argue that multiple myeloma, more than any other malignancy actually, demonstrates a very significant health disparity. It accounts, in this last year, for approximately 12,000 deaths across the country and accounts for roughly 1.5% of all malignancies. But we know that the incidence rate of the disease and the death rate of this disease is significantly highest in African American men more than any other ethnic group. And so today, in recognizing the degree of this disparity, we want to discuss these disparities so that we understand them better and understand that part of that disparity is the delay in diagnosis among Black or African American individuals.

Joseph Mikhael:

We'll also be reviewing the disparity, not just in initially making the diagnosis but in access to treatment. And literally all the treatments we have in myeloma we know sadly have a disparity in access. And then we're going to examine the effect that the use of standardized care has had on some of these outcomes and hopefully in a positive way, look at potential strategies to improve these disparities. And I will remind the audience that this is one section of an eight-part series that we are conducting on these health disparities so that we can better understand the problem and indeed come up with some specific solutions. So Saad, I'm going to turn it to you now because I understand that you have a case that you're going to share with us that helps us appreciate some of the significance of these disparities. So I'll turn it to you to share that case with us.

Saad Usmani:

Thanks, Joe. So let me share this case of relatively young gentleman from the myeloma standpoint. Daniel is a 55-year-old gentleman who's overweight. He's got mild, untreated hypertension. He went to his primary care physician with complaints of fatigue, thirst, and frequent urination. He was diagnosed with prediabetes because his A1C was 6.2%, rightly so. He was given instructions on weight control and to exercise. And then he returned six months later with not just the same symptoms. Now he has this lingering sinus infection and increased generalized aches and pains that are not going away. So he's told his prediabetes probably makes him prone to infections and that's been made worse by seasonal allergies. His [prostate specific antigen] PSA is checked, and it appears to be in normal limits. So he's told that this just simply needs to be watched. And that's the issue, if we look at the realities of health care access, much of the disparities and outcomes in myeloma, they come from delayed diagnosis.

We know that Black people have twice the higher incidence and mortality from multiple myeloma compared with White people. And I think having that knowledge gap, that's what we have to try to overcome. And it's not just Black patients. Black and Hispanic patients both are less likely to utilize novel therapies such as proteasome inhibitors and stem cell transplantation compared to White patients. However, when they do receive these treatments, their survival rates tend to be higher than White patients. So making the case that all patients, if they have access to care, they can achieve better survival outcomes than what they've got. What do you think, Joe?

Joseph Mikhael:

No, I mean, I think you're already capturing so much of the magnitude of this issue, that so much of it has to do with the diagnosis and indeed access. And thinking about the diagnosis for a minute with you, what I find particularly important about the case that you just shared with us as well is we see this very commonly in all patients with myeloma. In fact, we now have studies that have shown, and then another one was literally coming out this month, that more often than not, patients see a primary care physician three, if not four, times before the diagnosis of myeloma is made with signs and symptoms that could be consistent with myeloma. So there's a delayed diagnosis unfortunately in almost all patients with myeloma. Occasionally it may be detected by a high protein, incidentally, what I call the *incidentaloma*, but more often than not, people have signs and symptoms.

Joseph Mikhael:

And what makes this disparity significant is that within African American patients and Hispanic patients, where, for example, diabetes is much more common, often those signs and symptoms are just immediately attributed to the diabetes. And sometimes that's correct because we know, as you said, the prediabetic condition can put you at risk of an infection, can cause so many overlapping features, right? Anemia, renal insufficiency, proteinuria, neuropathy. So many of the things that we see associated with myeloma can be attributable to the diabetes and very often the diagnosis is even further delayed in these populations than the average population because of those confounding symptoms. And so if we can shorten the time to diagnosis, that's going to be one huge step, I think, towards better equity. And as you commented, a lot of this ultimately comes down to access to therapies as well.

Saad Usmani:

No, I completely agree with you, Joe. And look how far we've come in the last two decades. Myeloma has turned into a chronically managed disease for the vast majority of our patients. There was a time when the average survival of myeloma used to be two to three years, now it's more than 10 years. We have a better understanding of myeloma as a disease and how it progresses from this precancer [monoclonal gammopathy of undetermined significance] MGUS condition to active myeloma. We understand that it's not one disease—there are many different subtypes of multiple myeloma. And the way that the myeloma cells behave also depends on their neighborhood, the bone marrow microenvironment, and the other immune cells. And we are trying to not just put all of those puzzles together; we are recognizing that picking the right strategy for our patients at every step of the way, whether it's at the time of diagnosis to get them to the best depth of response or even if the myeloma returns in the future, each of those steps is so important.

Joseph Mikhael:

I think you've captured it so well. I mean, it's amazing to see. I mean, you and I are myeloma geeks, right? We're living this every day, and we see all the different elements. And sometimes people might think, "Oh, this is more basic research." But pragmatically, myeloma has had more advances in survival and understanding than perhaps any other malignancy. And it's had a real impact and one of those I think themes, if you will, of myeloma has been that we try to intervene earlier, that we've come to recognize let's not wait until the whole crab features are present and people have broken bones and damaged kidneys. We want to intervene earlier, which I think emphasizes the point that you made earlier about how that early diagnosis becomes so important in the care of a patient.

Saad Usmani:

Yes. And this is an anecdote that I share with my patients, that when the conventional, old fashioned chemotherapies were just being discovered and utilized for cancer medicine back in the '40s and '50s, the average life expectancy of the world population at that time was two or three decades less than what it is today. And so if you were diagnosed with myeloma and you lived to be 68 or 69 and you get diagnosed with myeloma, the treatment was to approach it gently and then not a lot of progress was made in therapeutics. But we've seen such an amazing explosion of novel therapies in the last two decades from small molecules and now immune therapies and [chimeric antigen receptor] CAR T-cell therapies, which are so much better tolerated than the old-fashioned drugs. We are trying to find the right recipe for our patients and I think we can do that for majority of our patients today.

Joseph Mikhael:

Oh, it's amazing. When you show me a chart like this, with all the decades and the things that have changed… One, it makes me feel a little bit old because I remember some of these, but it also really floors me as to the progress that's being made. In the context of our discussion today, I do want to emphasize, sadly however, that although we've had huge progress and we brought in all these new therapies, we have sadly also, in some degree, recognized the worsening of the disparity in access to these newer therapies. When I think of them, sometimes I remember them by the letter T, that there are four Ts that have really significantly contributed to the improved survival in multiple myeloma. Triplets, those three-drug combinations. Transplants or the use of autologous stem cell transplant. Clinical trials that we know have had such a positive impact. And then most recently, under your leadership, to much of our benefit, CAR T-cell therapy.

And sadly, we've shown that for each of these four, triplets, transplants, trials, and CAR T-cell therapy, there has been reduced access from African Americans and other groups, including Hispanic and Latinx Americans in having access to these therapies. And so, it's great to see these therapies developed, but we want to make sure that they're accessible to all, especially because of that very important comment you made earlier, that we know with equal access, African Americans cannot only do as well but perhaps better than White Americans whereas, now the average survival is roughly half that of White Americans. It should and could be better, and we have to take an approach, obviously, that points us in that direction.

Saad Usmani:

No, absolutely, Joe. I think you've made an extremely important point. We have to engage and empower those communities to recognize and seek out the best care possible for when they get diagnosed. And I think, again, as geeky myeloma clinicians and researchers, we also appreciate the fact that we are still learning a lot about the disease. Because the myeloma cells live inside the bone marrow factory, we are highly dependent on those biopsies right now to understand the disease biology and that helps us in managing our patients. At the same time, we also have to understand that looking at imaging and trying to find myeloma cells can go out into other tissue and that can have important consequences for treatment planning for patients. We need to understand a lot of what's happening to the disease biology in different subsets of patients and then that will help us in the bigger picture of putting this together and packaging the right treatment for patients. And this is so important from the disparity standpoint because even today we don't understand those racial differences in disease biology.

Joseph Mikhael:

No, you've captured it very well. It's a diagnosis problem, it's an access problem, but it's also a biology, if you will, problem where we haven't fully understood it. And I tell all my patients, and maybe because one of my daughters is pursuing forensic sciences, I say that myeloma is like a crime scene. There isn't one piece of evidence that tells you the whole story. And like you've said, it's one thing to have the blood tests—we need marrow, we need imaging, sometimes we need other advanced imaging. And sadly again, just like access to therapies, we see a disparity in access to the diagnostic testing.

And so the onus is on all of us, that we have to recognize, as we're going to discuss I know shortly, that there are systemic and health care issues that underlie this lack of access—insurance challenges and so many others. But to recognize the significance of that, that if myeloma's the kind of disease where you can't just measure it with one simple test, you really need all these different tests, then it's incumbent on us to make sure those tests are available. And when they're not available, sadly, we're going to see continued disparity in outcomes with our African American and Hispanic and Latinx and other patients.

Saad Usmani:

Yeah. And if we look at the treatment paradigm for newly diagnosed patients with myeloma today, it's so different than what it used to be. Back in the day, we used to not have enough drugs, so we would treat patients for a fixed duration of time and then try to relieve their symptoms. And now it's more of a marathon. We try to pick induction treatment strategies for patients, think about transplant eligibility and whether that has a role to play in their frontline strategy. And once we get patients to a good response or a response plateau, we try to maintain that response.

So it's become more of a marathon, and we manage infections, bone health, pain management, all of those things become important. And then we go through this exercise again if the myeloma comes back. So this is an ongoing management process. We gather the data. We want to make sure that it's a multidisciplinary effort. Myeloma is a team sport, so we are relying on our orthopedic colleagues, our supportive care, palliative management colleagues, nephrologists get involved in the care as well. We develop a treatment plan, we implement it, but then we go back and revisit the plan at every step of the way. And so it's a very dynamic process, which requires a lot of moving parts.

Joseph Mikhael:

Yeah. And I mean you've exemplified this in the multiple centers that you've worked at, and you've built wonderful teams around yourself to do this because it is absolutely a team sport. It's one of the few cancers that really does touch so many different organs in the body literally at the same time. And that, of course, requires a concerted effort within the healthcare system. And we've discussed this in other aspects of this eight-part series and so I don't want to focus too much of it on today, but just as a quick reminder to individuals that a lot of the challenges in accessing health care to hit the nirvana team that you've been discussing, Saad, and everybody working together includes issues like systemic racism, the trust that we have in the healthcare system, clear social determinants of health. I mean, if people don't have food in their bellies, they're not going to get a [positron emission tomography] PET scan.

Joseph Mikhael:

I mean, we have some basic things that we need to obtain, the types of insurance coverage and what those cover, especially with some of these tests that we've described. And then of course, even just proximity, geographical isolation. When we look at certain populations, within the African American population, over 80% of African Americans live within 18 states in the U.S. and many of those states don't have the kinds of centers of excellence or opportunities that many of the others do. So it is wonderful to see how this management process works, but we also want to recognize how it may exclude others and how we can work towards including those.

Saad Usmani:

All right. So I do want to share with you what happened to this patient and maybe also talk about how we're approaching treatments of such a patient at our center here in New York. And the story may be very similar for most of the myeloma centers. So, Daniel did receive a diagnosis of multiple myeloma. He was characterized as having the IgA lambda protein producing or isotype multiple myeloma. He was deemed standard risk based on the bone marrow biopsy test finding no chromosome abnormalities. He went on to receive [bortezomib, lenalidomide, and dexamethasone] VRd as induction and then he did get a stem cell transplant, but he did not receive any maintenance therapy because he had achieved a complete response. However, two years later he experiences serological progression, so his myeloma protein levels started to rise and then imaging reveals that he has neolithic bone disease. So if you look at this schema that I'm showing on this slide about approaching myeloma treatment, I think, you mentioned the four Ts and how they're making things better for our patients.

And so you see the approach to patients who are standard or high risk is typically a three or a four-drug induction combination, which I think is reasonable for what Daniel got. But then post transplantation, patients who are standard risk received lenalidomide maintenance and this is based off of the large [Cancer and Leukemia Group B] CALGB study that our colleague Phil McCarthy led that actually showed overall survival benefit compared to patients not receiving maintenance. And then many of us, for patients who are high risk, use [immunomodulatory drugs] IMiDs and [proteasome inhibitors] Pis as maintenance. So was this a missed opportunity? I'm not sure. I want to get your take, Joe.

Joseph Mikhael:

Yeah. I think, as you've said, unfortunately there are so many different reasons why access may not be had and sometimes oral therapies paradoxically are the most difficult to access. We think that they should be the easiest because they're easier to administer, there isn't chair time in a cancer center, there isn't a preparation of that infusion, and so on. But with the way the system is built and we don't yet have clear oral parity laws, we know that there tends to be a greater burden on the patient, financially speaking, when it comes to oral therapies. And you've mentioned it, I think we have pretty convincing evidence that almost all patients, even with a deep response… And I'm very thankful that Daniel here had a deep response after his transplant, but it would seem to be appropriate for them to be on some kind of maintenance therapy, likely at least lenalidomide maintenance and it's unfortunate. And so sadly we do see, in this case, roughly a two-year time frame before the disease came back, whereas, as you noted, with lenalidomide maintenance, that's probably double that, at least four years.

Saad Usmani:

Yeah, I agree. And then I'll share other things in this case now. So if you look at the timeline, Daniel is still 58, so he's still a relatively young patient with myeloma. If we go onto the subsequent care, the patient got started on the regimen daratumumab, which is an anti-CD38 monoclonal antibody, along with carfilzomib and dexamethasone. And because his hypertension was worsening, the dose for carfilzomib was adjusted and eventually he was taken off of carfilzomib and continued on that monoclonal antibody. But he had disease progression after 18 months. He then went on to receive pomalidomide along with cyclophosphamide and dexamethasone and, again, had a very short duration of response. And this is where I think things turned around because he was referred to a myeloma center of excellence, and he went on to receive the new [B-cell maturation antigen] BCMA-directed CAR T-cell therapy that had just been approved by the FDA, [ciltacabtagene autoleucel] cilta-cel. And he went on to achieve a complete response, and it's an ongoing response for this patient. So Joe, your thoughts around some of these newer therapies and this patient's journey?

Joseph Mikhael:

I mean, in so many ways this patient exemplifies myeloma in general—that sadly with each treatment, the time in remission gets shorter, the disease becomes more aggressive, but yet hope in that we hope that it goes beyond nine months, that the patient's now in [complete remission] CR. With these newer therapies we're seeing extraordinary results, which again reminds us of how critical these disparities are so that we can provide these to others.

The other disparity we didn't really cover, but just to quickly mention that Daniel fits in the picture is that the average age of diagnosis in myeloma in this country somewhere around 70, but it's about five to six years younger in Hispanic Americans and about five years younger in African Americans. And so that also has to factor into our thinking around not only the diagnosis but ultimately access that these generally are younger patients. But I really hope that he continues to do well after his CAR T, but this is textbook myeloma, but obviously with our spin today of having to understand the implications for health inequities.

Saad Usmani:

No, I agree with you. And the fact that his fourth response or remission is actually longer than his third one—what he had with pomalidomide, cyclophosphamide, dexamethasone—speaks volumes to what we can accomplish with the newer therapies. Now I do want to share, what if Daniel was in his mid-seventies? I think that the appropriate treatment for that kind of patient, people still give a three-drug combination. Are we the right when I say people? It's the myeloma experts and our hepatology and oncology colleagues. Many of us feel comfortable utilizing that proteasome inhibitor, ImiD regimen, especially for our patients who are high risk. But then the MAIA trial showed us that the combination of daratumumab blend X is a very reasonable choice for that older patient population. So the bottom line from this slide is the approach that we take is similar. We are trying to get to that best response for our patients, even at the older age. That goal doesn't change. It's the tools that we utilize that get modified a bit. What do you think, Joe?

Joseph Mikhael:

Yeah, you're absolutely correct. I mean, this is where there has been such an unmet need, hasn't there? In myeloma in older patients because so many patients... And the average age of diagnosis is going up a little bit as we are living longer in general and as we're getting better to detect the disease. So I think the strategy that you've mentioned here, obviously what you do at MSK is very much replicated elsewhere, where we have this idea of now being able to treat people for longer. Which again, I know I sound like a bit of a broken record, but it becomes important in health disparities that if you have a strategy that depends on people being on long-term therapy, how have we ensured that it is accessible to all? Not just getting it at the start, but being able to continue on it, even if it is a regimen where they may only have to come in once a month for that CD38 antibody.

Saad Usmani:

And then Joe, I do want to make a couple of very important points. There was a time when the word cure for myeloma was a taboo because of all we saw in our clinics, but it's becoming an important goal to explore for us as clinicians and researchers. And I can geek out on this slide with the points I'm trying to make, but the bottom line is we are trying to understand the disease biology and what's happening to the immune system in patients with myeloma and picking up signatures where we can define duration of treatment, of how long do we treat patients... And we are trying to marry that information with the depth of response that we are able to achieve with treatment. And eventually the goal would be that those signatures actually help us guide how we manage different types of patients. And then eventually we also want to sequence these therapies in a way that we get our patients to the longest duration of survival possible. And participation in clinical trials becomes very important, and we have to do a lot of groundwork to remove those barriers.

Joseph Mikhael:

You're absolutely right. I hope, my friend, within our lifespan... I mean we're not that old yet, but we still have hopefully a little time that we are going to be able to realize at least a fraction of patients with significant cure with myeloma. Which leads me to ask you to bring us towards the end here, but to think about what's coming in the future. I mean, if we look at that slide you showed earlier that showed every decade's change. And I mean, I've been doing myeloma for 25 years. I don't know if I have ever seen a year as exciting as right now in terms of what's coming down the pike in the future. So maybe you can walk us through some of this. What do you see as really changing even in the near and maybe more distant future in myeloma?

Saad Usmani:

I think the most near-term thing is the use of four-drug combinations to treat our patients and in the frontline setting. I think that's becoming an accepted standard of care for the majority of patients. And then we do have trials in older patients looking at those four-drug combinations that will come to fruition. But further down the road, we have very exciting small molecules that are being combined with each other for certain subsets of patients. We have combinations with antibody drug conjugates that deliver a specific chemotherapy payload to cancer cells. And perhaps the most exciting thing are the bi-specific antibodies and the CAR T-cell therapies. And we are starting to now use them in clinical trials, even in early relapse or even in the frontline setting. And I think that's the most exciting part for me as a clinician to see us moving away from more old fashioned chemotherapy to more novel immunotherapies that we can potentially utilize for patients—highly effective and with less side effects.

Joseph Mikhael:

I couldn't agree with you more. I mean, I think you made the comment about Daniel's case, that his most recent therapy lasted longer than his previous one. And I hope we can break that concept of shortening and shortening of remissions with time as we introduce these great therapies and as we bring them earlier into the disease course. So, this has been a great review of myeloma. Thank you, Saad, for your insight and your input. I do also just want to remind our audience and the spirit of what we're looking at today that it's one thing to understand myeloma and the treatments, but at the same time we need to address the disparities. And many of them are mentioned here that we understand that there are disparities. That we build trust, both as a corporate phenomenon and as an individual phenomenon.

Am I working on inherently building trust with my patients on a daily basis? Am I engaging the community? Am I truly involved in what's been called many things, culturally competent, culturally sensitive, culturally humble? All these aspects of care where the focus really is listening to our patients, understanding where they're coming from, what's valuable to them, what's important to them, what barriers they have and helping overcome the barriers. Which involves not just us as the clinicians, but the whole health care team. We know that many populations, including the African American population, has tremendous trust in nurses, in social workers, and pharmacists. And we should be working together as a team, as Dr. Usmani mentioned earlier, so that we can make sure that patients do have access to therapies, that we can overcome these insurance barriers and others.

One of the programs that I'm of course very much involved with in the IMF is the M-Power Program. It's M-Power, a bit of a play on words, and Dr. Usmani's been a centerpiece of this, where we're empowering patients and communities to change the course of myeloma and trying to give very practical advice both within the community and within the medical community to understand these disparities and improve outcomes for patients with myeloma. And you can of course read more about it there. So I do want to thank Dr. Usmani for this great discussion, we'll just summarize a couple of key things that we've said from the start.

Joseph Mikhael:

Early detection of myeloma is critical and discriminating it from other potential diagnoses becomes really important. Knowing that African American and Black patients typically have a later diagnosis, that there's a prolonged period of time between their symptom onset and their diagnosis. Sadly, we also see a significant disparity in survival overall, partly reflected by that diagnosis, but also reflected by the access issue that we discussed, including those four Ts: triplets, transplants, trials, and CAR T-cell therapies. But we do know, and really what is the shining light of hope in all of this discussion is that when given similar access to therapies, as we've seen through large VA studies and others, we know that Black patients can do as well, if not even better.

So I'm going to close out the program today with what we think of as SMART goals, which refers to Smart, Measurable, Attainable, Relevant, and Timely. And a few key points to take home. Don't discount those symptoms that may be consistent with another diagnosis but that are truly consistent with multiple myeloma. Those things we've mentioned—the anemia, the renal insufficiency, the infections, the approaching area, those things that sometimes can be passed off as another diagnosis. Adhere to these treatment guideline recommendations that we have, where, as we could see in the case that we saw, that maybe that patient had, had lenalidomide maintenance, it might have been able to produce a better outcome. And encourage when we can, clinical trial participation and participation in these novel therapies.

Well, I'm going to close off by reminding us that to receive your CME or CE credit for today's program, please complete the post-test and the evaluation. It always gives us good feedback. It's always a pleasure to do programs with the CME Outfitters, so please give us feedback on the program and you'll then be able to download and print your certificate immediately upon completion.

And then lastly, today, as I mentioned a couple of times, we have an eight-part series here of which this is just one today with Dr. Usmani, but please visit the CME Outfitters Oncology Hub, where you can access a whole host of activities that are related to oncology, and the issues of diversity and inclusion in that hub as described here, where you can learn much more about these topics that we've discussed today. You can also follow CME Outfitters on Twitter at @CMEoutfitters. So again, Saad, thank you so much for your contribution today. It's always a pleasure to talk to you, my friend, and I always learn from you every time we have this discussion and it was great to spend some time with you. And thank you to our audience for joining us today.