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Case Study: How Do You Manage First Relapse Multiple Myeloma Following Upfront ASCT and Lenalidomide Maintenance?

Announcer:
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Dr. Mikhael:
Hello, my name is Dr. Joseph Mikhael, from the Translational Genomics Research Institute in Phoenix, Arizona. And with me today is myeloma expert, and friend and colleague, Dr. Noa Biran, who's an Associate Professor at Hackensack in New Jersey. Noa, always good to see you. Thank you for joining me today.

Dr. Biran:
Thank you for inviting me.

Dr. Mikhael:
So we're going to quickly talk about a case where we think about how are we managing first relapse in patients that have had autologous stem cell transplant and lenalidomide maintenance. Now, this is not, of course, all patients, but I would argue a significant fraction of our patients are still undergoing stem cell transplant, due to the evidence for it. Many are still undergoing lenalidomide maintenance. And now that we have so many choices at first relapse, it's worth having a discussion around it. So let me share a case with you, Noa, and maybe you can give me some insight as to how you'd think and approach it.

So this is a 64-year-old, African American gentleman, we know myeloma is twice as common in individuals of African descent, who had standard-risk myeloma, and he was treated about 4 years ago, with VRD, bortezomib, lenalidomide, dex, achieved a very good partial remission, underwent a transplant, achieved a complete remission. So I would say pretty standard for that to occur. And then we placed them on lenalidomide maintenance, 10 mg, 3 weeks out of 4, in January of 2020. And about 3 years later, so just over 3 years later, in March of 2023, he now starts to have a climbing M spike, which when fully evaluated, he has 30% plasma cells, but no high-risk features yet, his biochemistry is essentially normal as his CBC although there's a little bit of a blip in his creatinine. And now his M spike is 1.7 and his light chains are climbing such that his ratio is up to 18. So, Noa, you see this person in clinic, what's your sort of initial approach and thought about how you would treat this patient?

Dr. Biran:
Yeah, so this is a very typical case in many ways. But I think this case is important because it brings up many points. I think the first is risk stratification in our patients. And although this patient was initially characterized as standard risk, our methods of characterization are not always perfect. And it turns out that about a 3 year and change remission with lenalidomide maintenance after transplant is less than we would expect in a standard-risk patient. And so, I would consider him to be functionally high risk. So we have to take those considerations in mind when we think about our next treatment. We also have to look at is he developing end-organ symptoms, and it looks like this is more of a biochemical relapse. So we do have some luxury in terms of time on our side in determining our next course of treatment.

So certainly, we want to present this patient with a few options. I think I would change him away from an IMiD-based regimen. So I would consider probably carfilzomib with a monoclonal antibody, such as daratumumab or isatuximab as an excellent choice. I think the downside of this option is that it does require frequent visits. And remember, this is chronic therapy, this is not going to be short-term therapy. So we have to incorporate whatever we choose into this patient's life. He's 64, he's relatively young. Is he going to be amenable to coming on a weekly basis or sometimes even more for infusions for the relatively long term?

Another option is to use a monoclonal antibody with pomalidomide. So I think we don't really have head-to-head data on which regimen is better. I think if we look at just hazard ratio alone across studies, the combination of carfilzomib with a monoclonal antibody would be probably better, but I would give that patient the choice.

Dr. Mikhael:
Yeah, no, I agree with you. I mean, you've raised all the key points, right? Biochemical versus rapid progression, risk status, class switching. And the good news is we have choice for this person. I totally agree with you, I think I tend to prefer a carfilzomib-based regimen in this context. One of the ways that I tried to make it a little bit more amenable to the patient is I'll try to use carfilzomib weekly. And then after several months, especially if they've had a deep response, which we expect, instead of just giving it, you know, weekly, 3 weeks on, 1 week off, I may even drop the week 2 and give it every other week. And that's actually what we ended up doing with this patient with a monoclonal antibody. In this case, we used daratumumab, but now, based on the IKEMA data, I'm using a lot of isatuximab.

So I think we're very aligned in this thinking. And I really love, in conclusion, the way you said that we really want to give the patient choice. We don't just come in with a final decision. I think we have lots of choices with this patient. But thankfully he's done very well on the DKd regimen.

Thanks very much for your input, Dr. Biran. And thanks very much of the audience for listening.

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