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# Case Study: How Do You Manage First Relapse Multiple Myeloma Following Daratumumab/Lenalidomide/Dexamethasone (DRd)?

**Announcer:**
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**Dr. Biran:**
Hi, my name is Noa Biran. I'm one of the Myeloma Physicians at Hackensack Meridian Medical Center in New Jersey. I'm here today with my colleague, Dr. Joseph Mikhael from the Translational Genomics Research Institute. And today we're going to be discussing a case about managing first relapse myeloma following daratumumab, lenalidomide, and dex.

So we have an 83-year-old woman with a history of controlled hypertension stage 3 chronic kidney disease, initially found to have anemia and lytic bone disease, IgA lambda subtype myeloma, R-ISS stage 3. Her initial bone marrow evaluation had 40 to 50% plasma cells, no evidence of amyloidosis and her FISH exam showed high-risk disease 17p deletion 1q gain and 13q deletion. She was started on daratumumab, lenalidomide, and dex, achieved a VGPR after her first 2 cycles, and unfortunately, she experienced the biochemical relapse after 19 cycles. She did not have any end-organ symptoms upon relapse and has a good performance status.

So I'll start with, Dr. Mikhael, how would you treat this patient?

**Dr. Mikhael:**
Well, thanks, Dr. Biran. Always good to be with you. This is a challenging situation because unfortunately, the patient is demonstrating her high-risk status by the fact that a year and a half into treatment, she's already relapsing. And we know with patients on DRd, very often, the median progression-free survival is not till over 4 years. And so it's unfortunate that this is happening.

So as I think about how I would treat her sort of two really important phenomenon come to mind; number one, she has not seen a proteasome inhibitor and we do have some evidence of proteasome inhibition may be preferable in a high-risk situation, but also that I really want to be careful the fact that she is 83 years old, she has chronic kidney disease. I don't want to - if you will overtreat her, I want to make sure I match the treatment, which she has. And thankfully, we have several options based on this. So with the proteasome inhibitor desire, I probably want to give her bortezomib, which is typically our first proteasome inhibitor used. Also want to give her another class of drug with it, so likely pomalidomide. So I'd likely lean towards bortezomib, pomalidomide, and dexamethasone where I would use weekly, subcutaneous bortezomib and a lower dose of pomalidomide at 2 mg, especially considering her chronic kidney disease.

But there are other options. We could go to carfilzomib, especially with the higher-risk status, where again, I would use it once weekly with - in combination, either with pomalidomide, or maybe even with selinexor. But either way, I would want to be very careful in having a conversation with her about the frequency of these visits, but also watching for any signs and symptoms of toxicity with these regimens, and making sure that we assess on a regular basis, because these are potent drugs. I think they will give her benefit, but we want to make sure that she doesn't experience too much toxicity.

**Dr. Biran:**
I agree with you. I think you brought up a lot of really good points. In our older or more frail patients, especially those with high risk, can be some of the most challenging patients that we have, not only because of response, but because of toxicity as you said. And I think although carfilzomib is an excellent choice in high-risk disease, in patients over 75, we can see slightly higher risk of cardiac events.

I also want to bring up another proteasome inhibitor that may be appropriate in this setting. And that would be ixazomib. It does have slightly lower risk of grade 3 or above peripheral neuropathy. And so certainly, if we do see peripheral neuropathy with a bortezomib-based regimen, we could consider switching it to the oral proteasome inhibitor, ixazomib. And I do agree with you that with the

Pomalidomide, a lower dose would be more appropriate, both in terms of renal dysfunction and in terms of cytopenias.

**Dr. Mikhael:**
I agree. You know, in fact, we did a study years ago comparing 4 and 2 mg of pom, and the efficacy differences is minimal. And I also agree with you that we do have some now community-based evidence that, whether patients are experiencing neuropathy or not, that there can potentially be a switch from bortezomib to ixazomib to reduce that risk of neuropathy and even make it more convenient for a patient by being an oral agent.

So, again, I think this is a fascinating case and a really important one that highlights so many of the critical areas of what we do in relapsed myeloma.

**Dr. Biran:**
Excellent. Well, thank you very much, Dr. Mikhael, for joining me and thank you to the audience. And hope you learned something today.

**Announcer:**
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