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Case Application: Unlocking Relapsed/Refractory Myeloma With CELMoDs

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Dr. Richter:
Hello, this is CME on ReachMD. I'm Dr. Joshua Richter. Here with me today is Dr. Sagar Lonial. Our discussion today is the potential role for CELMoD therapy in relapsed and refractory myeloma, and we'll start with a case.

We have a case of an 83-year-old female with IgG kappa multiple myeloma Durie-Salmon stage IIIA, ISS stage I with a 13q deletion noted. She was started on initial therapy with daratumumab, lenalidomide, and dexamethasone per the MAIA protocol, and was deemed to be transplant ineligible.

At the time of progression, she opted to proceed with the combination of bortezomib, pomalidomide, and dexamethasone in similarity to the OPTIMISM regimen. She is now progressing on VPD. She is a bit older and some comorbidities, so we're really not considering her at the moment for CAR-T cell-type therapy, and this may be a place where CELMoDs have a role.

So with this, Sagar, I'll turn over to you. Any thoughts on options for this patient in third line?

Dr. Lonial:
Yeah. Thank you very much, Josh. And I think you highlighted, really, an important point in the current paradigm of myeloma treatment, which is many of our standard sort of backbone agents will likely have been used or exhausted by the time you get to third-line therapy. And so choices and options, particularly for an older patient, do become a little bit more limited.

I think what we know from the early data with iberdomide as a single agent is that iber/dex in this kind of a patient population has about a 30% to 40% overall response rate. And the upside of iberdomide, again, is that it's well tolerated, it's oral, so the visits to the office are a little less frequent. It is better tolerated than len with much less fatigue, GI toxicity, fewer grade 3/grade 4 non-heme toxicity. So iber/dex certainly would be one potential option based on the expansion cohort from the original phase 1 study.

Alternatives, actually, for this patient, also in the context of a clinical trial, would be mezigdomide in combination with carfilzomib and dexamethasone. And recall in the SUCCESSOR trial, the randomized phase 3 trial, it was mezi/car/dex versus carfilzomib and dexamethasone. And I think if you've got the choice of a potential triplet over a doublet of just KD alone, particularly since in an older, frailer patient, the likelihood of dose reductions for the carfilzomib are pretty high, I think we'd all feel better using that in part of a combination.

And that this is where an agent like mezigdomide, which clearly is probably the most potent even of the CELMoD categories, can partner really nice with a proteasome inhibitor and allow us that synergy that can potentially achieve not only a deep response, but in some cases even MRD negativity.

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So I think that these types of combinations represent opportunities for us to use the CELMoD category, whether it's iberdomide or mezigdomide, in combinations with agents that patients perhaps have not been exposed to in third-line therapy that allows us to deliver a novel combination after they've had highly effective frontline and second-line therapy.

Dr. Richter:
Absolutely, couldn't agree more. And I think particularly, one of the areas that I struggle with is, by the time I get to third line and I'd like to use carfilzomib, some of the options to make that doublet into a triplet are a little more complex. There's been a number of studies that haven't shown a lot of great benefit of adding cyclophosphamide to carfilzomib. There is the STOMP regimen of adding selinexor, although that may be a bit of a more tough therapy to tolerate. So I completely agree, especially at the moment where a patient like this may not be eligible or appropriate for CAR-T. And at the time of this conversation bispecific antibodies are not approved until fourth line plus. So to me, having a regimen like mezi/KD is a really great option, especially academic or community center-based.

Well, listen, this has been a great bite-sized discussion, but our time is up. Thank you so much for listening.

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