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Next-Generation Innovations: The Future of CELMoDs in Myeloma

Announcer:
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Dr. Raje:
This is CME on ReachMD, and I'm Dr. Noopur Raje. In this brief discussion, I'll review ongoing trials with novel CELMoD approaches.

Before we get started, just let me give you an overview of what these new CELMoDs are. These are the most novel, newest class of immunomodulatory drugs, which are a lot more potent than both lenalidomide and pomalidomide. They target a protein called cereblon, which is really important to the survival and proliferation of myeloma cells. And really importantly, what we've seen with these CELMoDs is that they work well with targeting our T cell compartment, so that if you have an exhausted T cell phenotype, these CELMoDs actually help reverse this T cell exhaustion and augment T cell function. They also augment certain other immune cells, such as the natural killer cells, and by doing so, they improve upon the anti-myeloma activity of these.

Now, these CELMoDs, we have 2 of them. You have a drug called iberdomide and another one called mezigdomide. And both of these are orally available, so they're given as a pill form to patients, and they are being studied in different phases of treatment for multiple myeloma. The fact that these drugs are given by mouth, they're easy to combine with some of our other drug products like the proteasome inhibitors and anti-CD38 monoclonal antibodies. And with that combination, we are seeing very high response rates with some of the trials that I'm going to briefly describe to you.

So let's get started with iberdomide. Iberdomide is one of the CELMoDs, again, given orally. It is a drug product which is going to be developed mostly to try and use in the maintenance setting. And those of us who are familiar with the use of lenalidomide in the maintenance setting do understand and realize and appreciate the challenges of using lenalidomide in the maintenance. It can have an impact on your blood counts. It can result in untoward toxicity, specifically with the GI tract with ongoing diarrhea.

Iberdomide is a CELMoD which has very little in the way of myelotoxicity or low blood counts, and it really does not have a whole lot of GI toxicity. It is being studied in a study called EXCALIBER. There are 2 studies. One, it's being studied in the combination with some of these other drug products that I've talked about in the relapsed refractory setting. And the second study is where it is being studied posttransplant as a maintenance trial.

In the maintenance setting, it is also being studied in some of our other trials, such as the MIDAS trial, which was very recently presented at this year's ASCO, so we are looking forward to incorporating iberdomide in our standard of care treatment options and hoping to see it deepen responses in our patients. It's also being used in the EMN26 study in the context of maintenance.

The second CELMoD, which is also very exciting, is mezigdomide. Mezigdomide is in fact even more potent than iberdomide, and there are 2 ongoing trials looking at this in combination with the proteasome inhibitors. We have SUCCESSOR-1 and we have SUCCESSOR-2. Both of them are being combined either with bortezomib, as in SUCCESSOR-1, or with carfilzomib in SUCCESSOR-2. And what is

really notable out here is as we move these drugs earlier on in lines of treatment, we're seeing very deep responses in our patients to the extent of even MRD negativity, and this is translating into durability of responses and really robust progression-free survivals in our patients.

Now, both of these are being developed, one more in the maintenance, the other one in combination with some of our other drug products. Very generally, easy to tolerate and given by mouth, which I think is something which is of benefit with these new CELMoD class of drugs. So we are looking forward to their approvals in early lines of treatment as well as in the maintenance setting.

To me, what's actually very exciting, and I think where the future is really going, in the last 4 or 5 years, we've really seen the field move towards immunotherapies. And when I started off, I started talking to you about the immunomodulatory effects of these CELMoDs. And to me, combining these CELMoDs with our bispecific T cell engages or using them in concert with CAR-T cells to augment T cell function is really where the future lies, and I'm so looking forward to combining it with some of our T cell redirected treatments.

We have a lot of ongoing trials. We're looking forward to looking at the results of some of these, such as SUCCESSOR-1, MIDAS, there's a COMMANDER study. And with all of this, I do believe we, in the future, are going to see very deep, deep responses and very durable responses with the CELMoDs being a key part of these high response rates and increased durability of responses.

With that, thank you so much for listening. I hope this was informative for your practice.

Announcer:
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