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Clinical Challenges With Triple-Class or Penta-Refractory MM

Announcer:
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Dr. Lonial:
This is CME on ReachMD, and I'm Dr. Sagar Lonial. Here with me today is Dr. Caitlin Costello.

Let's start with triple-class or penta-refractory multiple myeloma. Dr. Costello, what are some of the challenges in treating patients in this setting?

Dr. Costello:
Thank you, Dr. Lonial, I'm delighted to be with you today. This is such an exciting area for our relapsed/refractory multiple myeloma patients. I think we both can say that over the course of the last several years, we've seen this real boon in opportunities and options for these patients that we've never really had before.

The reality of our multiple myeloma patients is that we have such wonderful treatments that are very successful, can achieve deep and very durable remissions in the early stages of their diagnosis and in early lines of therapy. But what's become more tricky over the years is what do we do with those patients when they've had multiple relapses and you've really used up some of your, let's say, more common suspects, if you will, in terms of your immunomodulatory agents, your proteasome inhibitors, your monoclonal antibodies. These patients who we call triple exposed or, if they're refractory to all of these drugs, those 5 drugs in particular, we think of them as being called penta-refractory. Now these patients, we have multiple studies that have shown us that they really have a poor prognosis associated with refractory disease, where really whatever usual suspects we have left over are really not felt to be terribly active, may not last very long, and sadly, the overall survival for these patients can be less than a year.

It's really only been in the course of the past 18 months or so that we've seen new drugs offer new opportunities for these triple-class and penta-refractory myeloma patients. And that came with the introduction of chimeric antigen receptor T-cell therapies or bispecific T-cell therapies. These are 2 classes of drugs that have finally made their way into multiple myeloma. You know, something that we've seen and had our lymphoma and leukemia colleagues really enjoy for their relapsed/refractory diseases, finally, we have them in multiple myeloma.

Now bispecific T-cell engagers, CAR T-cell therapies, these are now approved and are in the NCCN [National Comprehensive Cancer Network] guidelines as preferred regimens for patients who have had 4 or more prior lines of therapies. And again, to be specific, these are patients who have had 2 different immunomodulatory agents, such as lenalidomide, pomalidomide; 2 different proteasome inhibitors, such as bortezomib and carfilzomib; and then those monoclonal antibodies that target CD38, so isatuximab, daratumumab, as examples.

A lot of times in the past, we've tried to recombine those therapies and try and see if we can come up with recycling combinations, if you

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will, hoping we could kind of squeeze out a little extra juice out of any of those drugs and novel combinations, and we don't have to do that anymore. Now we can really look towards opportunities with patients to get CAR T-cell therapy or bispecific therapies. We'll talk a lot further about these different classes of drugs, but really, we've seen in the course of, gosh, in the middle of COVID, if you remember, the first CAR T-cell therapies were approved. More recently, in the last 18 months or so, we've had bispecifics. And these are 2 different classes of drugs that are really designed to traffic those T cells to a very specific target. The 2 most specific targets we know are BCMA and GPRC5D, and we'll talk about those quite a bit. Very exciting on how we can improve upon some of the outcomes that have been rather poor in the last many years and see if we can have those improved, deep and durable responses so that we can really help our patients that have relapsed/refractory disease.

Dr. Lonial:
Yeah, thank you. That's a great discussion on what I know remains a really challenging situation. But as you described, really exciting new options for many of our patients. I think some of the take-home messages that we need to be aware of are that we need to recognize who these patients are. They're getting triple-class exposed earlier and earlier in their patient journey, and recycling the old drugs that we have – and many of the drugs I know that we have we don't consider old, but they're certainly older compared to this new generation; that's not the answer for many of these patients. And that not only do we have new types of drugs, the bispecifics or the CAR T cells, but we have 2 new targets as you nicely described, in BCMA and GPRC5D. So I think these are really on the verge of making a pretty major revolution in the late-stage myeloma and likely will help us to get to a curative endpoint for many of these patients in the future.

Well, thank you very much, Dr. Costello. This has been a great bite-sized discussion. Our time is up. Thanks for listening.

Announcer:
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