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## The Evolving Treatment Paradigm for RRMM: The Role of Bispecific Antibodies

### Announcer:

Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

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### Dr. Lonial:

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

Bispecific antibodies are some of the newer therapies we have available for multiple myeloma. Dr. Costello, what's the role of these agents in the current treatment algorithm for relapsed and refractory myeloma?

### Dr. Costello:

Thank you, Dr. Lonial. Bispecific T-cell engagers have really offered just a wonderful new treatment option for our arsenal for patients with multiply relapsed/refractory myeloma. Historically, we've really had our IMiDs, our proteasome inhibitors, and our monoclonal antibodies, and we've used them in various combinations, sometimes even recycling some old drugs with some new drugs and hoping for the best. But unfortunately, really had very limited success with some of our response rates for those patients, which in turn led to poor outcomes for these patients. And so the introduction of bispecific T-cell engagers has really changed our treatment approach when it comes to these patients. Especially now that we've seen these drugs really be used in earlier lines of therapy, we really need to have, ready to go, the next treatment opportunities.

So bispecific T-cell engagers have really offered, at least to start with now, single-agent drug treatments. Now remember, a lot of the drug approvals in the past, including our monoclonal antibodies and our IMiDs, have been associated with overall response rates of about 30% or so. When the bispecific T-cell engagers were approved based on some pivotal data leading to accelerated approvals, we found that their overall response rate is about 60% to 70% for – at least let's say for the 3 currently approved bispecific T-cell engagers. Doubling of response rates made such dramatic changes here where these patients had such limited opportunities at that point. So we were seeing high response rate here now that can be used, again, for patients who have had 4 or more prior lines of therapy and have been at least exposed to all 3 classes of drugs.

What we are now seeing between teclistamab, the BCMA-targeted bispecific T-cell engager, elranatamab, also targeting BCMA, we can see that these T-cell engagers are allowing for high response rates, as mentioned, and allowing for very durable responses as well. We were seeing sometimes PFS of a year or more, with sometimes median duration of response not having been met yet. This is, in turn, turning into improved survival. So with just 1 class of drug, just like we saw with CAR T, we are improving progression-free survival and overall survival.

It's important that we've all had to learn a little bit about how to take care of these patients because with new drugs come new toxicities. And while we are well equipped to manage cytopenias and infections, some of these new drugs, based on their targets, are really being seen to have GI toxicity, skin toxicity, nail toxicity in addition to infections, as many of these trials were happening in the midst of COVID. So it's been a little bit of a learning curve for all of us to try and understand how we can introduce these drugs that have been so

successful and keep patients safe. And we've been able to successfully do it. I think this has really changed the way we will approach our relapsed/refractory multiple myeloma patients moving forward.

**Dr. Lonial:**

Yeah, no, I think it's a great summary, Dr. Costello. And I think, from my perspective, hearing about not only the high overall response rate, but if you achieve a deep response, like a CR [complete response], it looks like even at 2-year follow-up, many of those patients are ongoing in remission. And so seeing that kind of, A, high overall response rate and, B, high CR rates in fifth- and sixth-line myeloma is really unprecedented for us in our field and a great opportunity for many, many patients.

I think one of the things that often people are a little concerned about is the complications with the first few doses of administration. I know we're going to touch on that in other episodes, but I think there is now established published data suggesting, even at the outset, this can be given as an outpatient. And our center, and many others, is already beginning to do that. So I think in this context, preparing for what the future is going to look like is going to be really important because it's not going to be the same kinds of things that we're doing now. So I think the future is very bright.

Again, trying to understand how to combine these drugs is really an important next step. Does that allow us to perhaps give less of the drug or give lower doses to reduce some of those on-target, off-tumor effects like infections or skin or gut or nail toxicity? I think that's what we're going to hear about in the future, and I think it really is quite exciting.

Well, this has been a great micro-discussion. Thank you once again for listening.

**Announcer:**

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