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# Bispecific Antibodies: The Newest Immunotherapy on the Block for RRMM

**Announcer:**
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**Dr. Lonial:**
This is CME on ReachMD, and I'm Dr. Sagar Lonial, and here with me today is Dr. Caitlin Costello. Bispecific antibodies are recent additions to the treatment paradigm for multiple myeloma.

Dr. Costello, what exactly are these agents, and what's the rationale for their use in relapsed and refractory disease?

**Dr. Costello:**
Thank you, Dr. Lonial. You know, what an exciting time. We see these bispecific T-cell engagers be introduced into our arsenal of drugs. So let's talk about what they are. We've learned a lot about CAR T cells over the course of the last many years as well, which is an opportunity for patients to, let's call, harvest, or remove their own T cells, send them off to a manufacturer where they are kind of reengineered, if you will, or taught how to target a specific antigen on the myeloma cell surface. That is a process that takes some time, during which patients must require bridging therapy that we talk about in order to keep their disease under control. After which the T cells that are being manufactured are then sent back and can be administered to the patient. A very exciting opportunity, but it does come with a lot of logistical constraints and can be challenging for some of our patients that have more aggressive disease that may be relapsing sooner and may have some difficulty waiting.

So those bispecific T-cell engagers offer an opportunity to do a similar approach to treatment by trafficking those T cells towards a specific target. And there are bispecific antibodies that have been approved over the course of the last 1 or 2 years now that offer us this opportunity to use them. So it offers an off-the-shelf therapy for these patients instead of having to wait. And these are specifically approved for patients who have had 4 or more prior lines of therapy. There are 2 specific bispecific T-cell engagers that are available now for targeting BCMA. There is a third one that's available that is targeting GPRC5D. Let's talk a little bit about each of them.

So teclistamab and elranatamab were the 2 initial BCMA-targeting T-cell engagers. They were based on early-phase data. Let's start with teclistamab.

So teclistamab received accelerated approval in 2022. Now this was based on the phase 2 MajesTEC-1 study. These were patients that are relapsed/refractory that had at least 3 prior lines of therapy that had to include those IMiDs [immunomodulatory drugs], those proteasome inhibitors, the CD38 monoclonal antibodies, and these patients were treated with weekly subcutaneous teclistamab. Now the response rates of these patients were about 60%-63%, which was very exciting for what our bar had been historically for single agents, about the 30% or so range. These responses were durable. We were seeing median durations of 18 months with PFS [progression-free survival] of pushing a year and overall survival of 18 months. So very exciting initial data that came out with teclistamab, the first BCMA-targeted T-cell engager.

A quick note on elranatamab, the second BCMA-targeting T-cell engager. This received accelerated approval based on the MagnetisMM-3 trial. It was similarly designed for those same heavily relapsed/refractory patients, seeing very similar response rates and, again, durable remissions, with updates recently showing maybe a median of about 18 months or so on the median PFS. So BCMA-targeted T-cell engagers that are a very important part of our arsenal now for treating.

Talquetamab, I want to touch briefly on as well, is targeting a different antigen, GPRC5D, which is overexpressed on the myeloma cells, less likely to be expressed on normal cells, which makes it a good opportunity to target these kind of on-target, off-tumor side effects. Very similar overall high response rates. Maybe a little different on the dosing where you're seeing every-2-week dosing opportunities, perhaps with lower infection risk, less neutropenia.

These are 3 different bispecific T-cell engagers that have been approved that are great opportunities for high response and durable response remission times for our relapsed/refractory patients.

**Dr. Lonial:**
Thank you, Dr. Costello. And I think it really is, as you described, a very exciting time with a series of new drugs and targets. What I think is really quite interesting is, had I predicted years ago that with all the T cell exhaustion in refractory myeloma that these would have been effective, I would have guessed no. I didn't expect these to be as good as they are, and yet, clearly, they're off the shelf as you described, ready to go, and the adverse events are different for the targets, but certainly, in many ways provide new options for patients with limited treatment approaches.

I think the difference in adverse events is really quite key: infections, really, for BCMA and the skin and GI toxicity for talquetamab. But in general, I think it's really an exciting set of new options. And as we do with every drug that gets approved, we spend the next 5 years figuring out how to optimize its use and how to combine it. And I'm sure that's coming in the near future as well.

And with that, our time is up. We hope you found our perspectives useful and thank you again for listening.

**Announcer:**
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