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# Efficacy Data for Bispecific Antibodies in RRMM

**Announcer:**
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**Dr. Lonial:**
This is CME on ReachMD, and I'm Dr. Sagar Lonial. Today, I'll review the efficacy data of the bispecific antibodies for multiple myeloma. So let's start off talking about the BCMA CD3-directed bispecific antibodies. And those include teclistamab, which was the first kid on the block, and elranatamab, which was the second kid on the block.

From a mechanism of action perspective, what we know about this is that what it reallydoes is hook both a T cell and a myeloma cell that expresses BCMA at the same time, brings them into close proximity, and then subsequently activates that T cell to ultimately kill the myeloma cell. And it is, to me, fascinating that something as simple as bringing a T cell in close proximity to a myeloma cell is able to have such high efficacy. And in fact, when I had discussed some of these targets years ago, I was skeptical that in a patient with refractory myeloma, you'd be able to get much benefit out of what I would have expected were highly exhausted or ineffective T cells.

And yet, what we see in the MajestTEC-1 clinical trial of teclistamab, in both the phase 1 and the phase 2 proportion, is that a very high percentage of patients, over 60% of patients, can achieve a deep response, with about half of those patients achieving a complete remission, many of those patients achieving MRD [minimal residual disease] negativity. And in fact, if you achieve a complete remission or better, the median duration of response is well beyond 18 months. And this to me, again, in a median of 6 to 7 prior lines of therapy, is really quite striking.

Now in the early-phase trial of teclistamab, it was initially given as an intravenous injection. And what we saw subsequent to the initial phase 1 experience is that it was switched to a subcutaneous injection. And what we know about that sub-q injection is that it did not impact the efficacy at all. It did, however, reduce some of the adverse events, particularly infusion-related reactions did drop a little bit with the subcutaneous injection, and that most patients did quite well with that and the efficacy was maintained, both in terms of depth of response and durability of response.

Now the next BCMA agent that was approved was elranatamab, and that was based on the back of the MagnetisMM-3 trial, which again, was a heavily pretreated group of patients, 6 to 7 prior lines of therapy. And what we saw in that trial was not only good safety and efficacy, response rates over 60%, but we saw similarly median progression-free survival at or above a year, with duration of response not met, and a median follow-up of over 18 months. And this, to me, again reiterates, A, the validity of BCMA as a target and, B, the importance and activity of a BCMA-targeted T-cell engager in the context of relapsed and refractory myeloma.

Now the last target that I'm going to talk about is GPRC5D, and this is also a bispecific, so it targets both GPRC5D and CD3, and this is called talquetamab. And what we know about talquetamab is that GPRC5D is, in fact, expressed on almost all myeloma cells and normal plasma cells. And the mechanism of action is not appreciably different than what I told you about a BCMA-directed bispecific.

What we do, however, know from the MonumenTAL-1 trial is that the overall response rate was between 60% and 70%, that the median PFS for that trial was close to a year, and again, the median duration of response was over 18 months for patients who achieved a CR or better. And this really high activity and efficacy mimics what we saw with BCMA, but we have a brand-new and different target.

Now there are many other bispecifics that are on the heels of these, including AMG 420, AMG 701, and alnuctamab, CC-[93]269. And these are all agents that have similar high efficacy, high durability, and similar adverse event profiles, including CRS as well as neurotoxicity.

Well, my time is up. I hope you've gotten something to think about now and thank you again for listening.

**Announcer:**
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