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## Considerations for Dosing Bispecific Antibodies

### 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.

The NCCN panel included bispecific antibodies as preferred therapies for heavily pretreated relapsed myeloma after 4 prior therapies. Do you know the appropriate dosing of these agents?

Dr. Costello, can you help us out?

### Dr. Costello:

Absolutely. So currently, there are 3 bispecific T-cell engagers that are approved and included in the NCCN, as you mentioned. And each of them have subtle, slightly different differences in terms of how to administer these drugs. And like with all drugs that get approved, we all kind of act on a little bit of the art of medicine and make some adjustments. I'm going to go through a little bit of the package insert, but also maybe we can touch on where the art comes into all of this.

So teclistamab, remember, is one of the BCMA-targeted T-cell engagers. It was originally designed with a step-up dosing scheduled to be done per the package insert of day 1, day 4 as the step-up dosing, with the first treatment dose being given on day 7, with weekly dosing thereafter. Now there is a little wiggle room there where you can really give it, they say, give or take a day, where I think many of us in the beginning just for the opportunity to kind of shorten that inpatient stay, were doing it basically every 48 hours. But you have some flexibility on both sides. So let's say for the package insert, it's day 1, day 4, day 7. Really, those patients for the package insert should be in the hospital so that we can be monitored carefully. And I think we'll figure out, and I know we've talked about before, how we could potentially do this outside of the hospital, such that when they finish their first treatment dose, you'd stay in for monitoring for maybe another 48 hours after that treatment dose, be discharged to be able to continue that on a weekly dosing schedule.

Not to be outdone, elranatamab, the second BCMA-targeted T-cell engager, had a somewhat similar target schedule of administration, again, needing those 2 first step-up dosing, and they were designed originally to do it on day 1 and day 4, followed by a day 8 first treatment dose. Now their recommendation was for those first 2 doses to be done in the hospital where you had a 48-hour minimum of observation after that first dose, followed by a minimum of 24-hour observation after that second dose, with the option to discharge these patients and potentially do the first treatment dose as an outpatient. Once the patient had gone through the initial step-up dosing, received their first treatment dose, the package insert has them receiving once-weekly dosing thereafter through at least week 24. Now this was the first time, after seeing teclistamab which first said weekly dosing indefinitely, finally had something in the package insert that said, hey, there's an opportunity to space things out a little bit. So at least that could potentially be moved on to every 2 weeks thereafter.

Now let's touch a little bit on talquetamab. Talquetamab has 2 dosing schedules, where it was designed for one to be given once a week, and one dosing schedule be given every 2 weeks. Now depending on which schedule you chose, that step-up dosing was slightly different. For the weekly dosing, there's 2 step-up doses followed by the first treatment dose on days 1, 4, and 7; they're given weekly thereafter. If you choose to do the biweekly dose, which I think many of us do choose, there are 3 step-up doses, followed by the first treatment dose, and that was designed for days 1, 4, 7, and day 10, with biweekly dosing there afterwards. And these patients, again, are oftentimes administered in the hospital with more opportunities, however, to be receiving them than as an outpatient basis as we figure out how to safely administer them.

**Dr. Lonial:**

Yeah, I mean, I think this is really, really an exciting set of differences between the drugs. Thank you very much, Dr. Costello, for that summary on the dosing strategy.

What I think is really interesting is that what we're seeing is that, particularly for talquetamab, that some of the toxicity may be linked to a peak effect. And so wondering whether every-week, every-other-week, once-a-month dosing, those are all things we're going to have to spend the next few years trying to better understand. And particularly when they're partnered with drugs like the immune modulatory agents, how does that affect our dosing schedule as well? We know the infectious complications are, in fact, linked with the frequency of dosing with the BCMA-directed bispecifics in that, if you go from weekly to every other week, you may reduce the infectious risk by half. So I think understanding what the right way to get this really is an important next step for us. And centers like yours and ours are already preemptively making dose reductions as a standard approach to try and reduce the toxicity that patients may experience.

So this has been a brief but great discussion. I hope you found this information useful, and thank you for tuning in.

**Announcer:**

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