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CAR T-Cell vs Bispecific Therapies for R/R Multiple Myeloma: How They Compare

Announcer:
You're listening to *Project Oncology* on ReachMD, and this episode is sponsored by Kite, a Gilead Company. Here's your host, Dr. Charles Turck.

Dr. Turck:
Welcome to *Project Oncology* on ReachMD. I'm Dr. Charles Turck, and joining me today is Dr. Krina Patel, who's a Professor in the Department of Lymphoma and Myeloma at the University of Texas MD Anderson Cancer Center in Houston. She'll be discussing her research that was presented at the 2026 International Myeloma Society Annual Meeting. It used matching-adjusted indirect comparisons to evaluate efficacy and safety outcomes with anitocabtagene autoleucel, or anito-cel for short, teclistamab, and talquetamab in patients with relapsed or refractory multiple myeloma. Dr. Patel, thanks so much for being here.

Dr. Patel:
Oh, thank you so much for having me.

Dr. Turck:
Well, why don't we start, Dr. Patel, by doing some level setting. What prompted you and your colleagues to conduct this analysis of anito-cel, teclistamab, and talquetamab in patients with fourth-line or later relapsed or refractory multiple myeloma?

Dr. Patel:
Yeah, this is a huge question for us. We always joke that when there are five myeloma doctors in a room, you'll probably get 20 different recommendations because we are in a world, thankfully, where we have so many different treatment options. We're learning how the immune system can actually help us kill myeloma. And I think because we have so many options, it's really hard to know which therapy to talk to a patient about or for patients to pick in terms of what they want to do next. And so I think unfortunately, we're probably not going to have any prospective studies or phase three studies where they get randomized to either a bispecific or a CAR T which target BCMA versus GPRC5D.

And so the only way that we can really look at this data and say scientifically, who are those patients that maybe I should be treating with a bispecific first versus who are the patients we should be doing CAR Ts for? For us, efficacy and safety are usually the two biggest reasons. Here, we're actually trying to look at different mechanisms of action. And so I think it makes it even more interesting because they're not drugs from the same category.

Dr. Turck:
And if we look at the analysis design, it's my understanding that you and your team used unanchored matching-adjusted indirect comparisons to evaluate anito-cel, teclistamab, and talquetamab. Would you walk us through how these comparisons were conducted and what factors were considered when adjusting for differences across the patient samples?

Dr. Patel:
Yes, I think this is the most important part of any MAIC: what are we using to compare patients? This is the limitation of the studies we'll talk more about later. But when we're looking at patients who got treatment on different studies at different time points, the eligibility might have been a little bit different. And so the only way we can actually try to compare apples to apples instead of apples to oranges is really looking at the most important factors for our patients that tell us what could make efficacy worse or better versus safety worse or better.

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And so we looked at those two differently. And we looked at other papers that have been done that have established what those important factors are. But we also discussed with some of our colleagues who do myeloma research and see myeloma patients and prioritized, right? We could have so many different categories, and it would be great to look at every little thing and make sure these patients match up. But there's only so much you can do with the number of patients that have been on these studies.

And so we prioritized for efficacy things like extramedullary disease that we know make the disease harder to treat and usually does lead to worse outcomes in terms of response and PFS; cytogenetic risk because if someone's high-risk cytogenetically, we know that those patients don't do as well; refractory status—we have proteasome inhibitors, immunomodulatory drugs, and anti-CD38 antibodies that most patients have had when they've gotten to this type of fourth-line trial, and so we look at if those patients were exposed or how many were actually refractory because we know that if you're refractory, the myeloma tends to be more aggressive and patients tend to have less of a deep response as well as PFS; and the Revised International Staging System. Another big one for immunotherapies, especially, is the percent of bone marrow plasma cells. We know now that patients who have a lot more bone marrow or active disease going into these therapies tend to have not as good of an efficacy in terms of response, depth of response, as well as PFS.

And then we looked at safety. Safety is a little bit different, but for the ECOG performance status in these clinical trials, most patients had to have an ECOG of zero to one. And so we looked at those that had zero versus one; some trials do allow up to two. Age—our older patients tend to be more frail, so we use that as a biomarker even though we do say age is just a number, but we needed a way to look at frailty somehow, and we looked at the sex of patients. And then here, we actually borrowed something from the efficacy, which was the percent of bone marrow plasma cells.

We know that efficacy matters in terms of how much myeloma you have. But with immunotherapy, safety is different as well, which is a little bit different than most of our other chemotherapies and other therapies we think about. So some of our acute safety issues like CRS, or cytokine release syndrome, or neurotoxicity can be linked to how much myeloma there is. We added that as part of the safety profile and category when we were comparing these patients on different trials.

Dr. Turck:
So with all that in mind, let's turn now to the efficacy findings. What did you see in terms of overall response after adjusting for differences across the study populations?

Dr. Patel:
Yeah. So thankfully, we were able to get enough patients. That's always an issue if you have too many categories that you're trying to compare because sometimes, you can't get enough patients. So we did get the effective sample size for both efficacy and safety that was actually a good proportion.

So for efficacy, about 90 patients or 77 percent were able to be compared and included in this analysis. And what we were able to show is that anito-cel had significantly improved response compared to teclistamab. Remember, we compared it to two different bispecifics. So with anito-cel, we used iMMagine-1 as the study, and with teclistamab, we used MajesTEC-1. And then we also compared it to the GPRC5D bispecific, which is different than BCMA, which both anito-cel and teclistamab go after. And talquetamab is in MonumenTAL-1.

And so we'll start with teclistamab first. So again, anito-cel had significantly improved response compared to teclistamab. And of course, we're looking at odds ratios for all of this. But again, there were improved outcomes in terms of response, overall response, and depth of response. So in terms of CR or better as well as VGPR or better, some MRD data that we had did show that anito-cel was better for all of those compared to teclistamab in this late-line patient population.

And then looking at efficacy for talquetamab, 78 patients were similar enough that we could compare. And it makes it a little bit more complicated in this one because there's different dosing. There's a .4 milligram per kilogram dosing as well as a .8 milligram per kilogram dosing, and we went ahead and compared to both. However, we were able to find those patients, and anito-cel had significantly improved response versus both the cohorts of talquetamab in dosing. And so overall response rates were much better with and favored anito-cel, as well as the depth of VGPR or better and CR or better. And the MRD data that we did have also favors anito-cel in terms of depth of response.

Dr. Turck:
For those just tuning in, you're listening to *Project Oncology* on ReachMD. I'm Dr. Charles Turck, and I'm speaking with Dr. Krina Patel about her research evaluating anitocabtagene autoleucel, or anito-cel for short, teclistamab, and talquetamab in patients with relapsed or refractory multiple myeloma.

Now, Dr. Patel, you also looked at more stringent response outcomes and overall minimal residual disease negativity. What did the

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analysis show for those endpoints?

Dr. Patel:
This was actually great that we had data because it's sometimes hard to find that data. But we did have a lot of papers as well as conferences where some of this data was presented. And so specifically with teclistamab, again, we're using odds ratios, right? Of all the responses we have between iMMagine-1, everything that's been presented for teclistamab for MonumenTAL-1, and then with talquetamab—again, we have the .4 milligram dose versus the .8 milligram dose—the MRD was ten to the minus fifth. We do look at both ten to the minus fifth and ten to the minus sixth. But it's usually easier for us to get data from ten to the minus fifth when these trials are being done at all different centers.

Dr. Turck:
And when it came to safety, the analysis looked at outcomes including CRS, ICANS, infections, and non-relapse mortality. Would you take us through what you observed across those endpoints?

Dr. Patel:
So yeah, I think the safety is really important here because these are different mechanisms of action, and with anito-cel being a CAR T-cell therapy—really a one and done—that does require lymphodepletion chemo. You might see increased risk of CRS and ICANS in that acute phase compared to a bispecific like teclistamab where we do step-up dosing so that we're engaging those T-cells at a slower pace that are already within a patient rather than making these cells with CAR T and increasing the numbers and giving them all at once.

So we hypothesize and see that CAR Ts in general tend to have higher rates of CRS and ICANS. So we looked at that against both teclistamab and talquetamab, and then we also looked at some of the other big side effects like infection risk, which again, when bispecifics are given continuously, that is something we've seen; the grade three or higher infection risks have been much higher with bispecifics relative to other therapies, including CAR T. And so we wanted to look at all of that. And again, there are a lot of other side effects and toxicities based on the antigen that we will see between BCMA or GPRC5D. We didn't look at all of those things in this evaluation, but I think it's something we could do in the future.

But for CRS and ICANS in anito-cel versus teclistamab, we did actually see favoring most AEs with anito-cel. And CRS actually did favor teclistamab. Again, when you're giving all these CAR T-cells at once after lymphodepletion chemo versus doing a step-up dosing and then slowly increasing T-cell activity for a patient, we expected that. But when you look at grade three plus, we actually didn't see a statistical difference between them. And when you look at ICANS—any grade—we didn't see any statistical difference between teclistamab or anito-cel. And then with infections where we predict that it's going to be higher for teclistamab, we actually saw grade three or four infections favoring anito-cel even more. And then looking at non-relapse mortality—so patients who were still in remission or some kind of response but unfortunately died from usually AEs or something else—it actually favored anito-cel. Odds ratio for that was .18.

And then looking at talquetamab, again, we looked at the .4 versus the .8 dosing, and it was actually similar between the two. There were little differences, but for the most part, big picture was that AEs in general favored talquetamab, but the odds ratio was statistically not significant. Same thing with any-grade CRS. And then grade three or four CRS was also not significant for either one of these. And then ICANS was actually favoring anito-cel, which was interesting to see. And then grade three or four ICANS was actually a wash as well between both talquetamab and anito-cel.

And then with infections, interestingly with GPRC5D being a target, we actually don't think of infections as big of a problem as we do with teclistamab because GPRC5D doesn't tend to be on mature B-cells, and patients actually can keep their IgG levels normal so they don't get as much hypogammaglobulinemia as we see with BCMA therapies. But here, we actually still saw that grade three or four infections favored anito-cel for at least the .4 milligram dosing—again, that continuous dosing of taking those T-cells and redirecting them again and again probably does increase that risk of high-grade infections a little bit more, is what I'm hypothesizing. And then the non-relapse mortality was interesting here. It did look to be significant in the .4 milligram dosing at an odds ratio of .25.

Dr. Turck:
In bringing all these findings together before we close, Dr. Patel, what are the main takeaways from this analysis, and what limitations should we keep in mind when interpreting these indirect comparisons?

Dr. Patel:
I think the devil is in the details sometimes. Looking at it in terms of that .4 milligram versus .8 milligram dosing, it gets a little bit harder. But the big picture here really is that anito-cel, as a CAR T-cell therapy, did have both increased efficacy when we look at either teclistamab or talquetamab as bispecific therapies, with that depth of response and MRD being such a significant difference between all these groups and anito-cel having the best MRD negativity. But of course, we don't have that PFS data, so one of the limitations is we

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don't have that to directly compare as of right now.

And then safety, of course, is one of the biggest things that sometimes we say something that might have a little bit less efficacy as long as it's safer, maybe there is going to be a patient population that this is better for. But here I will say that, for the most part, for infections, we actually see that all of our evaluations and analyses show that anito-cel actually had less grade three or four infections compared to our bispecifics. And I think CRS is the one thing that we just have to look at and say, "Yep, CAR T makes sense that maybe in some of the analyses that CRS is a little bit higher," but grade three or four statistically was not different between the two. In the world of: Are we going to give prophylactic tocilizumab for decreasing CRS to make all of these things more applicable to outpatient? Those are really important, but I think this was really surprising that even some of the things like CRS was not actually very different between the two.

I think one of the big limitations though is when we did the studies for anito-cel, we had already had experience with other CAR Ts as well as bispecifics. So the timing of when these studies were done was different. And so I think if you look at studies today with bispecifics, patients are getting prophylactic toci and they are getting IVIG regularly and maybe those infection risks will be different based on that.

I think in the future, having prospective studies would be the best, but knowing that's probably not going to happen with so many different options that we have in myeloma, some of the real-world data hopefully will help us really decide all of this.

Dr. Turck:
Well, with those final comments in mind, I want to thank my guest, Dr. Krina Patel, for joining me to share the key findings from her research on anitocabtagene autoleucel, teclistamab, and talquetamab in patients with relapsed or refractory multiple myeloma. Dr. Patel, it was great having you on the program.

Dr. Patel:
Thank you so much.

Announcer:
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