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Comparing CAR T-Cell Therapies for R/R Multiple Myeloma

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:
This is *Project Oncology* on ReachMD, and I'm Dr. Charles Turck. Here with me today to discuss findings from a matching-adjusted indirect comparison of anitocabtagene autoleucel and ciltacabtagene autoleucel, also known as anito-cel and cilta-cel, respectively, for relapsed or refractory multiple myeloma, is Dr. Krina Patel. She's a Professor in the Department of Lymphoma and Myeloma at the University of Texas MD Anderson Cancer Center in Houston, and she presented these data at the 2026 International Myeloma Society Annual Meeting. Dr. Patel, welcome to the program.

Dr. Patel:
Thank you so much for having me.

Dr. Turck:
Well, to help set the stage for our discussion, Dr. Patel, what was the rationale for comparing anito-cel and cilta-cel in patients with fourth-line or later relapsed or refractory multiple myeloma?

Dr. Patel:
In myeloma, we are now at a point where we have so many different therapy options. I mean, we're a little spoiled, which is great. It's a great feeling. But a lot of our new treatments are never going to have prospective comparative studies, right? We would love phase III randomized studies to tell us which treatment's the best for which patients. But with some of these therapies, because there's just so many, we're never going to be able to do those. And so what is the next best way to really help me say what the best product is in terms of efficacy and safety? Are there certain patient populations that I should be using one therapy versus the other? And in the end, when you have that discussion about the risk-benefit of any therapy with patients, I would like to have data.

And so we really have been starting to use these MAICs, knowing there are limitations we'll talk about later, but saying, "Hey, how can we compare these to say: will it really help us decide which therapy is the best for the patient that's sitting in front of me that needs something?"

Dr. Turck:
So then to conduct this comparison, you and your team used an unanchored matching-adjusted indirect comparison, drawing on data from two trials: iMMAGINE-1, which assessed anito-cel, and CARTITUDE-1, which evaluated cilta-cel. Would you tell us how you accounted for baseline differences between the patients in the two trial samples?

Dr. Patel:
Yeah. So thankfully, we have two prospective studies that we can look at. But obviously, these were done at different times, and of course, there were different patient populations that were on those studies. So to look at efficacy and safety, we used different categories that we compared between patients in each study. And so it came from other trials and other studies that have already been done that we think are important in myeloma in terms of when we do these MAICs and also just by talking to other expert physician colleagues of ours that do research as well as see myeloma patients and how they read studies and what they're looking for.

And so with efficacy, we really looked at extramedullary disease, knowing that's a high-risk feature for our patients; cytogenetic risk, of

course—standard risk versus high risk; refractory status, or how many therapies in different categories like PIs or proteasome inhibitors, IMiDs or immunomodulatory drugs, or anti-CD38 drugs have patients been exposed to versus refractory to; and the R-ISS staging, or the Revised International Staging System. And then the other big one is the percent bone marrow plasma cells. We know that with these immunotherapies, especially CAR T, the more myeloma there is, the more likely there could be issues with efficacy as well as safety. So for efficacy, those are the categories we put at the top. Of course, there's a lot more, but you can't do everything, so these seem to be the best ones to look at.

And then for safety, we looked at ECOG performance status. Of course, if patients are frail, we want to make sure that they're not getting extra safety issues or adverse events. We did look at bone marrow plasma cells again because I think the amount of myeloma that patients have going into any of these therapies really does make a difference in some of the unique side effects, like CRS but also in terms of infections and inflammation as well as age and sex.

So those were the categories between efficacy and safety that we prioritized.

Dr. Turck:
So zeroing in on efficacy a little bit more, after adjustment, there were no statistically significant differences between anito-cel and cilta-cel in overall response. What else did the analysis show across efficacy endpoints?

Dr. Patel:
Thankfully, we had enough patients between the two subsets of cilta-cel from CARTITUDE-1 and anito-cel from iMMAGINE-1 to look at patients that were similar enough. So I think it was 88 percent for the effective sample size for efficacy. And in general, the analysis overall looked great for overall response and depth of response for both cilta-cel and anito-cel. As you said, statistically, there was no difference in patients.

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 and ciltacabtagene autoleucel, or anito-cel and cilta-cel, respectively, in patients with relapsed or refractory multiple myeloma.

So looking at the safety findings, anito-cel was associated with a significantly lower risk of any-grade cytokine release syndrome and ICANS, as well as grade 3 to 4 infections and non-relapse mortality when compared to cilta-cel. From your vantage point, Dr. Patel, how do you put these safety findings into clinical context?

Dr. Patel:
When we have two therapies that have a similar mechanism of action—they're both CAR Ts—we have an idea of what adverse events we're looking for, especially things like CRS, or cytokine release syndrome, or ICANS with neurotoxicity. And again, in matched patients, we actually see a little bit less of that CRS and ICANS.

And then we of course have some of the other side effects that we want to look at, which are infections, especially in our myeloma patients. These really powerful, effective therapies can lead to some significant infections. And here again, we didn't see any worsening, and actually, we saw statistically significant lower risk of grade three or higher infections as well as non-relapse mortality with anito-cel than with cilta-cel. So it does seem to be a little bit safer in some of those major categories of both acute toxicities and then long-term toxicities.

And then, we didn't know about this with myeloma therapies and CAR Ts in general for lymphoma or leukemia before, but with some of our BCMA therapies and with cilta-cel, as we were using those both in studies and in the real world when it became approved, we started noticing this delayed non-ICANS neurotoxicity. And it was something new for us, and now we know ways to decrease that incidence. And in the iMMAGINE-1 study, we actually haven't seen any delayed neurotox symptoms at all as of yet.

And so I think there is a little bit of a difference in terms of the longer-term side effects as well.

Dr. Turck:
As we wrap up, Dr. Patel, let's consider the efficacy and safety findings together. What do you think are the key takeaways from this analysis of anito-cel and cilta-cel, and what limitations are important to keep in mind when interpreting these indirect comparisons?

Dr. Patel:
This is really important because this is not a prospective study in real time where patients get randomized at the time of enrollment. Unfortunately, here's going to be a lot of data that we just can't compare between these, so you have to be careful of how we look at this.

So I do think in general that this shows that anito-cel does seem to have a favorable toxicity profile when we compare it to cilta-cel. And in terms of efficacy, we don't have the PFS here, so of course that is something we're going to look for long-term. But at least in terms of overall response and depth of response, when patients are matched in terms of high risk or standard risk, it looks pretty similar so far. But again, that data is missing here, so we do need to follow up on that down the road. I think this is really important in today's world when my patients are coming to see me and I have so many different options.

I think the pendulum has been swinging that when cilta-cel had some of these side effects—and some of the patients did get serious side effects—all of a sudden everyone said, "Oh, maybe CAR T's not the right thing to do anymore. Maybe we try bispecifics or other CAR Ts on trials." And so I think this is going to make a big difference. If anito-cel does get approved in the future, I think it opens up more options for patients that maybe would have said no because of that risk with cilta-cel, and now we'll have patients who are wanting to and excited to do CAR T again with anito-cel.

So here, to see that the efficacy is actually comparable and the safety seems to be better, obviously, we want the most efficacious product with the best safety. And so again, I think there'll still be patients that we give different CAR Ts to, but I'm hoping that this will bring more patients access to CAR Ts without them worrying about the toxicity as much.

Dr. Turck:
Great comments for us to think on as we come to the end of today's program. And I want to thank my guest, Dr. Krina Patel, for joining me to share these findings from a matching-adjusted indirect comparison of anitocabtagene autoleucel and ciltacabtagene autoleucel for relapsed or refractory multiple myeloma. Dr. Patel, it was great speaking with you today.

Dr. Patel:
It was a pleasure. Thank you so much.

Announcer:
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