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Analyzing Toxicity Trends Post-CAR T-Cell Therapy: Implications for Patient Monitoring

Announcer:
You're listening to *Project Oncology* on ReachMD, and this episode is sponsored by Bristol Myers Squibb. 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 new data and approaches that can improve safety and outcomes post CAR T-cell therapy is Dr. Manali Kamdar. Not only is she an Associate Professor of Medicine in Hematology and the Clinical Director of Lymphoma Services at the University of Colorado, but she also authored a poster on this topic that was presented at the 2025 American Society of Clinical Oncology Annual Meeting. Dr. Kamdar, thanks for being here today.

Dr. Kamdar:
Thank you for having me.

Dr. Turck:
So why don't we start, Dr. Kamdar, by taking a look at the new data. It's my understanding that your study reported the timing of cytokine release syndrome, or CRS for short, and immune effector cell-associated neurotoxicity syndrome, or ICANS, in patients treated with Liso-Cel. But before we dive into the findings, would you explain why you decided to analyze acute toxicity trends and what methods you use to achieve that objective?

Dr. Kamdar:
Absolutely. So as the audience is very well aware, CD19-directed CAR T-cell therapies, like Liso-Cel, have transformed the landscape of B-cell malignancies. They offer deep and durable responses. However, one of the key challenges of all CD19 CAR T-cell therapies is the management of cytokine release syndrome, CRS, and neurotoxicity, also called ICANS, or neurological events.

Currently, patients who receive CAR T-cell therapy are required to be near a certified treatment center for at least 4 weeks after infusion. While this is obviously intended to ensure timely management of adverse events, it creates profound logistical and socioeconomic challenges, thus limiting access to CAR T-cell therapy.

Lisocabtagene maraleucel is a 4-1BB CAR T-cell therapy product that has demonstrated excellent efficacy but also extremely favorable safety profile in relapsed/refractory large B-cell lymphoma, follicular lymphoma, CLL, SLL, and mantle cell lymphoma. And thus, based on multiple pivotal studies, it has expanding indications to be used in these subtypes of lymphoma.

Given these varied indications in different subtypes of lymphoma but also the need to improve patient access, we asked: can we better define when these toxicities actually occur, and can we help personalize, or maybe shorten, post-infusion monitoring without really compromising patient safety? So this was really the reason for why we decided to conduct a huge analysis of toxicity trends, primarily around an analysis of CRS and ICANS for patients who receive Liso-Cel. And this comprehensive analysis of CRS and ICANS timing and severity was gathered from two key data resources. One was basically a conglomeration of five pivotal clinical trials across multiple B-cell malignancies for patients who received Liso-Cel—so patients who had large B-cell lymphoma relapsed/refractory, follicular lymphoma relapsed/refractory, CLL, SLL relapsed/refractory, and mantle cell relapsed/refractory. In these pivotal studies where patients received Liso-cel, we looked at the CRS and ICANS timing. And then, we also looked at the real-world data from the CIBMTR registry in relapsed/refractory large B-cell lymphoma.

Dr. Turck:
So with that background in mind, let's zero in on the results. What stood out to you about the timing and severity of CRS and ICANS events in both the trial and real-world cohorts?

Dr. Kamdar:
So these two data sets, which is the pivotal study as well as the CIBMTR analysis, evaluated a total of 1,500 patients, about 700 in each. And then, we looked at both of these and assessed the timing as well as the severity of both CRS and ICANS.

So let's dive into the results. In the clinical trial subset, 54 percent of patients experienced any-grade CRS, and 98 percent of those events occurred within the first 15 days after infusion. Only 7 patients had CRS that started after Day 15, and all of those were low grade. In the CIBMTR cohort, 49 percent patients experienced CRS, and 97 percent of those cases also occurred within the first 15 days.

Now, let's dive into ICANS. In the clinical trial cohort, 31 percent of patients experienced neurological events, with 88 percent having this by Day 15. In the registry set, 27 percent of patients had ICANS, and 95 percent of those occurred within 15 days.

So when we look at patients who had the late-onset events, which were basically very, very few patients, it was extremely important to find out—and very assuring, to say the least—that they were very rare, mild, and usually resolved with steroids or tocilizumab. Neither of these patients who had late-onset events, with regards to CRS and ICANS, needed ICU-level care.

So these findings basically underline that after Liso-Cel cell infusion, if patients were to develop CRS and ICANS, 96 percent of CRS and ICANS happens within the first 2 weeks, which basically supports rethinking the 4-week monitoring window, which was previously mandated by the FDA. Since nearly all events occurred by Day 15 and because they are so predictable, we obviously suggested a more tailored monitoring approach, which is absolutely safe and feasible.

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. Manali Kamdar about new data on acute toxicity following CAR T-cell therapy.

So, Dr. Kamdar, now that we've reviewed the findings, let's focus on their implications. What do these data suggest about the potential for reduced monitoring intensity after the first 2 weeks following the infusion?

Dr. Kamdar:
The implications are huge. I do believe that this data basically suggests rethinking the discussion around the mandate, which is 4 weeks, of patients having to be in the proximity of the CAR T treating site. Fortunately, we have good news that we received from the FDA wherein there have been label changes for Liso-Cel. After examining this data set, the FDA now says, for Liso-Cel, that the requirement to stay within the proximity of a healthcare facility no longer has to be 4 weeks; it's now reduced to 2 weeks. The driving restrictions, which is huge, previously used to be 8 weeks, and now it's 2 weeks.

So I do believe from a patient-level perspective, it is extremely important that every single patient—barring socioeconomic and logistical barriers—gets the opportunity to get a curative intent treatment like Liso-Cel, especially in large B-cell lymphoma. And we know that, in reality, that is not true because a lot of patients sometimes are just not able to finagle relocation for a month. Maybe their caregivers are not available for a month. So I do believe at the patient level, there is a huge implication here that there is going to be more access, where patients may be more willing to do this, and then we are likely going to be able to see more people being cured. And from a larger systems perspective, I think it's really going to positively affect the economic implications downstream.

Dr. Turck:
And if we continue to look at this topic from a systems-level perspective, how else could updated safety expectations influence CAR T program designs, including patient flow, staffing, and cost considerations?

Dr. Kamdar:
I think the next steps, based on the study results and thankfully, the FDA's label changes, would be that every CAR T treating site would have to come up with a new operational algorithm for patients, wherein we really have to figure out how to now change our programmatic approach, which used to be 30 days at the treatment site to 14 days. We have had this programmatic approach in place for years, ever since CAR T got approved. I can tell you from my site, we are beginning to have leadership meetings to figure out a streamlined way wherein we can administer CAR T-cell therapy.

The big question now, given the excellent safety profile for Liso-Cel, is if we should just start doing outpatient CAR T-cell therapy for all. And I will say that barring a few patients who have extremely high tumor burden, who have absolutely no caregiver, or who are very old

in terms of their age or frailty status—because none of these are barriers to CAR T—we typically have been doing Liso-Cel treatments outpatient.

So I think with the reduced monitoring, it pretty much allows us to streamline it even more and basically administer the infusion outpatient. We'll have to come up with algorithms in terms of how often patients get seen in clinic and in terms of daily visits along with our nurse practitioner, physician assistant, and pharmacy support. So there's a little bit of revamping that needs to be done, but it's a revamping that's going to really help everybody in the healthcare system and, more importantly, patients. And then downstream, I do believe that if you reduce the patient stay from 4 weeks to 2 weeks, it would have huge ramifications on the economic aspect of CAR T-cell therapy, as well.

Dr. Turck:
Well, with those potential future impacts in mind, I want to thank my guest, Dr. Manali Kamdar, for joining me to share her insights on the potential impact of new data on the way we use CAR T-cell therapy. Dr. Kamdar, it was great having you on the program.

Dr. Kamdar:
Thank you so much.

Announcer:
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