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Examining Key Data on CAR T-Cell Therapy for Relapsed/Refractory MCL

Announcer:
You're listening to *Project Oncology* on ReachMD, and this episode is sponsored by Kite Pharma. Here's your host, Dr. Jennifer Caudle.

Dr. Caudle:
This is *Project Oncology* on ReachMD. I am your host, Dr. Jennifer Caudle, and joining me to share real-world evidence and long-term follow-up data on CAR T-cell therapy for relapsed/refractory mantle cell lymphoma is Dr. Matthew Matasar. Not only is Dr. Matasar the Chief in the Division of Blood Disorders at Rutgers Cancer Institute, but he's also a Professor of Medicine at Rutgers Robert Wood Johnson Medical School. Dr. Matasar, thank you for being here today.

Dr. Matasar:
Thank you for the invitation.

Dr. Caudle:
Of course. So let's just jump right in. How effective is CAR T-cell therapy for relapsed/refractory mantle cell lymphoma based on real-world evidence from various countries?

Dr. Matasar:
So looking broadly at the landscape for relapsed or refractory mantle cell lymphoma, we do have a number of tools available to us. Increasingly, we leaned into this relapsed/refractory setting on BTK inhibitors in the second-line or even in the third-line with both covalent and non-covalent drugs approved in this context. Nonetheless, we understand that outcomes for relapsed/refractory mantle cell lymphoma remain poor and there's a clear clinical need for more potent therapies.

And it's in this light that we look at the availability of CAR T-cell therapy for patients with relapsed/refractory mantle cell lymphoma, particularly after failure of BTK inhibition. In that setting, CAR is very active and effective. We understand that the majority of patients will respond to one of the two approved CAR T-cell agents. So in terms of an overall response rate, the response rates are very high.

The durability of response to these drugs remains, I would say, suboptimal. Compared to the other available treatments, they're clearly a game changer. And yet unlike in other context where CAR T-cell therapy may be looked at as holding curative potential, for mantle cell lymphoma, they should best be understood as palliative treatments, although highly effective ones. Median durations of response of between 12 and 18 months is very potent but is not the durability that we see in either follicular lymphoma or, in contrast, large-cell lymphoma where CAR T-cell therapy may indeed hold curative potential.

Dr. Caudle:
Thank you for that. And how about the safety of this treatment approach? I mean, what do we learn from the real-world evidence about this?

Dr. Matasar:
The good news is that when we contrast the clinical trial data for CAR T-cell therapy to accumulating real-world evidence, oftentimes that contrast can be quite striking in oncology and certainly in lymphoma, where real-world treatments fail to clear the bar set for them by the clinical trial data.

This has thankfully not been the case for CAR T-cell therapy in mantle cell lymphoma, where the accumulating real-world evidence does indeed look a lot like our clinical trial data, much to its credit. And that's both in terms of activity as well as you highlight the safety profile of these drugs. We understand that CAR T-cell therapy for mantle cell lymphoma does come with toxicities.

They generally are lumped into different categories: those being cytokine release syndrome, or CRS, neurological toxicities, or ICANS, and then the myelosuppression and immunosuppression that can come from CAR T-cell therapy.

All of these are indeed a problem for patients being treated for mantle cell lymphoma with CAR T-cell therapy, but what we've learned so far, both from clinical trials as well as real-world evidence, is that the incidence and severity of these toxicities is manageable.

Dr. Caudle:
Excellent. Thank you. And now if we switch gears a bit and focus on the available long-term follow-up data, what has that shown us regarding the durability of response and the potential for extended survival benefits?

Dr. Matasar:
I think this is where there remains to be progress in the field of leveraging CAR T-cell therapy for patients with relapsed or refractory mantle cell lymphoma: very high response rates, very predictable responses, and a very well-characterized toxicity profile, but durability remains suboptimal in my opinion, where we do not look at CARs holding curative potential, and the relapse curve is a continuous down-sloping trend. Meaning that over time, we expect that patients treated with the currently available CAR T-cell therapies for mantle cell lymphoma will be expected to relapse.

In terms of duration of response, we understand that complete responses will maintain their response longer than those patients who only achieve a partial response, but even among those who achieve a complete response, durability is still not ideal. We're still following this data as they mature to see if there's going to be any subset of patients that do achieve long-term disease control with CAR T-cell therapy. Remember, this hasn't been around all that long. Our median follow-ups are continuing to move to the right on the curve, and as they do so, we'll learn more about if there is a fraction of patients that achieve longer-lasting disease control.

Dr. Caudle:
And for those of you who are just tuning in, you're listening to *Project Oncology* on ReachMD. I'm your host, Dr. Jennifer Caudle, and I'm speaking with Dr. Matthew Matasar about the real-world evidence and long-term follow-up data on CAR T-cell therapy for relapsed/refractory mantle cell lymphoma.

So, Dr. Matasar, if we take a step back from the data and look at the big picture here, can you tell us about some of the challenges associated with the long-term follow-up of patients treated with CAR T-cell therapy?

Dr. Matasar:
This is a real challenge for many of us in the lymphoma community. And this is partially because CAR T-cell therapy is largely restricted at present to so-called centers of excellence, right? Places that have access to these treatments and have the infrastructure to use them safely and effectively.

The vast majority of patients in America are not routinely getting their care at such centers. They're getting treated by their community oncologist, who may lack experience or expertise—certainly in the administration of CAR T-cell therapy, which is out of their bailiwick at present—but even in best understanding how to take care of survivors of CAR T. We don't have a great system in place nationally for how academic oncologists—those who are administering the CAR—communicate and collaborate effectively and seamlessly with the community oncologists, who are really the primary oncologists for the majority of patients.

However, mantle cell lymphoma is largely a disease of older patients—it certainly can affect the young and old equally—but the median age of diagnosis is already in the 70s. By the time we're treating relapsed/refractory disease, 70s and 80s is quite common. These are patients that not only are being treated by community oncologists but may have limitations on their ability to travel great distances, may place a greater demand on their psychosocial support, and they may be facing comorbidities that further complicate their follow-up care, so very complex treatment patterns.

So I think that one of our greatest challenges at present is how do we support community oncologists with understanding the optimal follow-up and management of survivors of CAR T-cell therapy, and that can include when and how to follow blood counts. When and how to use growth factors if there are cytopenias that emerge. The management of hypogammaglobulinemia, which following treatment with CD19-directed CAR T-cell therapy for mantle cell lymphoma is very common. When and how should you be giving supplementary IVIG? How do you follow patients in terms of scans and blood tests for monitoring for relapse? And if you see signs of early relapse, how to intervene most effectively at those points in time? All of these are challenges that we need to do better as a community while aligning academic expertise with the community oncologists, who are really the most important treating doctors in this scenario.

Dr. Caudle:
With that being said, why is it so important that we overcome those challenges and continuously monitor our patients?

Dr. Matasar:
It's very clear to me that we need to do a better job as a community for taking care of our patients across their journey, right? We're very good at attending to the delivery of treatment, referral for intensive therapies, giving these treatments with the appropriate pre-medications, and supportive care throughout that treatment, and yet we need to do a better job for our delivery of survivorship care. And this is true across a number of different contexts, both after giving curative therapy for diffuse large B-cell lymphoma or Hodgkin lymphoma but equally true for taking care of our survivors after they've received CAR T-cell therapy.

We understand that there's a range of toxicities that these patients may experience and adverse outcomes that can be ameliorated or mitigated with appropriate monitoring and intervention. The key is in getting that done. And I think that we can do this best by partnering between academic expertise and community oncologists, who are the most important treating doctors for these patients and their journeys, and bringing together all of those different parties to really get our patients the best possible outcomes.

Dr. Caudle:
And just to bring this all together before we close, Dr. Matasar, what impact can CAR T-cell therapy have on patients with relapsed/refractory mantle cell lymphoma based on the data we discussed today?

Dr. Matasar:
There's no doubt to me that the availability of CAR T-cell therapy for patients with relapsed or refractory mantle cell lymphoma is a game changer. Its activity in that context is really unparalleled. Even though we recognize that it's not a home run in some ways—it may lack durability and it doesn't hold curative potential as currently developed—but the ability to really alter the course of illness and get patients disease control, where otherwise we would have had great difficulty, is truly paradigm-changing for this disease state.

My hope is that we'll continue to develop CAR T-cell therapy and find ways to supplement or offer adjunctive therapies to continue to improve upon these meaningful changes and these meaningful outcomes as we try for better outcomes for our patients.

Dr. Caudle:
Well, with those final comments in mind, I'd like to thank my guest, Dr. Matthew Matasar, for joining me to share what we've learned about CAR T-cell therapy for relapsed/refractory mantle cell lymphoma from real-world evidence and long-term follow-up data. Dr. Matasar, it was great having you on the program today.

Dr. Matasar:
Thank you so much, Dr. Caudle.

Announcer:
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