Transcript Details
This is a transcript of a continuing medical education (CME) activity. Additional media formats for the activity and full activity details (including sponsor and supporter, disclosures, and instructions for claiming credit) are available by visiting:
https://reachmd.com/programs/cme/state-of-the-union-car-t-cell-therapy/13658/

Released: 03/31/2022
Valid until: 03/31/2023
Time needed to complete: 15 minutes

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

State of the Union: CAR T Cell Therapy

Announcer:
Welcome to CME on ReachMD. This activity, entitled “State of the Union – CAR T Cell Therapy” is provided by Prova Education.

Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

Dr. Martin:
CAR T cell therapy is providing patients with multiple myelomas the possibility of deep and durable responses.

There are currently 2 available CAR T cell therapies. One is called idecabtagene vicleucel, or ide-cel. And the second is ciltacabtagene autoleucel, or cilta-cel. Today we're going to discuss how these therapies fit into the current myeloma treatment paradigm.

This is CME on ReachMD, and I'm Dr. Thomas Martin. And I'd like to welcome my co-host, Dr. Larry Anderson. Welcome, Larry.

Dr. Anderson:
Hello.

Dr. Martin:
Ide-cel was the first CAR T cell therapy to be FDA-approved based on the KarMMa study. Dr. Anderson, can you give us some highlights of the results from the original KarMMa study?

Dr. Anderson:
Yes, the KarMMa study was a pivotal phase 2 study of ide-cel CAR T cell therapy in relapsed refractory multiple myeloma patients who had received at least 3 prior lines of therapy, including an IMiD [immunomodulatory drug], a proteasome inhibitor, and a CD38 antibody. The patients enrolled on the study actually had received a median of 6 prior lines of therapy. Expected outcomes in this triple-class exposed myeloma population with other previously approved therapies has been historically dismal with overall response rates in the 25% to 31% range, progression-free survival [PFS] of 3 to 4 months, and an overall survival expectation of less than 9 months. However, in the KarMMa study, 128 patients were treated with ide-cel across the target dose range of 150 to 450 million CAR T cells. At a median follow-up of 24.8 months. The overall response rate was 73% across all target doses and 81% response rate at the 450-million target dose. Complete responses were seen in 33% overall and 39% at the 450-million dose. The median progression-free survival was 8.6 months across all target doses, and 12.2 months for the 450-million dose. Most important, the median overall survival was 24.8 months, and this did hold up to over 20 months of overall survival in most high-risk subgroups analyzed, including those 65 years and older, those with extramedullary disease, those with triple-class refractory myeloma. The median time to first response was 1 month, and the median time to complete response was 2.8 months, and the duration of response to ide-cel increased with depth of response and was 21.5 months for those achieving a complete response.

Dr. Martin, cilta-cel is now approved by the FDA based on the CARTITUDE-1 study, which you were part of. Can you discuss the results with us?

Dr. Martin:

The CARTITUDE-1 study was a phase 1b/2 open-labeled multicenter study. And the primary objective was to characterize the safety of cilta-cel and confirm the recommended phase 2 dose. Just like ide-cel, eligibility included patients who had received 3 or more prior lines of therapy or were double refractory, and they had to have exposure to a prior PI, IMiD, and anti-CD38 antibody.

Now they had a standard, CAR T cell therapy, meaning they underwent apheresis, then bridging chemotherapy as needed. And then lympho-depleting chemotherapy with cyclophosphamide and fludarabine, followed by a single infusion of cilta-cel. And the median administered dose was right around 50 million cells.

Now, this was a heavily pretreated population. They had received 6 prior lines of therapy, 88% of them are triple-class refractory, 42% were penta-drug refractory, 99% were refractory to their last line of therapy. Just under a quarter had high-risk cytogenetics. So a really refractory population.

And in terms of the efficacy, the overall response rate was 98%, and 82.5% of patients achieved a stringent complete response. Just like with ide-cel, their responses occurred quickly. The median time to first response was 1 month, and the median time to best response was about 2.6 months. Now, if we look at progression-free survival, the 2-year progression-free survival, just updated at ASH, was 60.5%, and the 2-year overall survival was 74%. Pretty amazing, actually. In those patients who achieved MRD [minimal residual disease] negativity sustained for 6 months or sustained for 12 months, the PFS at 2 years was 91% and 100%, respectively.

What do you think the impact of this is, Larry, in terms of for our relapsed or refractory myeloma patients? You know, how should we try to get them this therapy?

Dr. Anderson:
Yeah, I mean, the results of both of these studies are definitely unprecedented in the history of refractory myeloma clinical trials. And it is exciting to have potentially 2 different options for our patients now.

Dr. Martin:
I agree with you that having 2 on the market is really important and maybe can enhance our access. So how has it been for access in your area to get these CAR T cell therapies to patients?

Dr. Anderson:
So far, ide-cel has been approved for about a year now. And we have had production capability limitations. For example, each cancer center has been granted 1 or 2 slots per month for T cell collection while we have dozens of patients waiting, so it's really timely that we have this second approval of cilta-cel, which will hopefully expand the access for our patients.

Even though both of these studies only required 3 prior lines of therapy, both the FDA labels require 4 prior lines of therapy. When they're starting a fourth line is definitely a good time to refer because these patients may quickly progress and need to move on to CAR T cell therapy.

Dr. Martin:
I completely agree. I think the one thing that everybody has to remember is to keep track of the lines of therapy for patients, and they're so potent that we want to get patients to these therapies as their fifth line. When a patient goes on to a fourth line, or even when they're progressing on a third line, I think that's an appropriate time to send a patient, even stable patients on the third line, just to get them in to CAR T cell therapy and to get them lined up.

What do you think in terms of eligibility for CAR T cell versus eligibility for transplant?

Dr. Anderson:
We use a lot of the same organ function criteria, so these patients often have a workup that looks similar to a transplant workup. These patients have to be fairly fit; they have to be able to travel to the CAR T center.

Dr. Martin:
That's really important. This therapy has to be given at one of our CAR T cell centers, one of the 70-plus centers across the US. So it is going to require a support system from the patient and their caregiver to actually come to the treatment center and literally stay here. We have patients stay for 30 days after their CAR T. And we keep a close contact with them for at least the first 90 days after. We want to see them quite regularly during that period of time. So they have to be here with a caregiver that can help support them.

You know, in terms of fitness, totally agree the patients have to be fit. But the difference in my mind between autologous transplant and CAR Ts is there's not really an age limitation for CAR Ts. We've done them in patients that are 80 years old or higher. And I routinely ask my patients what was harder? And hands down, patients have told me that the autologous transplant has been more difficult than the CAR T cell therapy.

For those of you just tuning in, you're listening to CME on ReachMD. I'm Dr. Thomas Martin, and I'm here with Dr. Larry Anderson, and we're discussing the State of the Union for CAR T cell therapy in relapsed and refractory multiple myeloma.

During the therapy, patients certainly get significant toxicity. There's a difference between these 2 products in terms of the timing of the toxicity and including the timing of the CRS [cytokine release syndrome]. So as you know, ide-cel, the CRS happens about day 1. For cilta-cel, the CRS happens about day 8. How do you deal with that at your center, Larry?

Dr. Anderson:
All of our patients going through CAR T for myeloma are admitted to the hospital before their infusion. So they're there waiting to see if they're getting fevers or neurotoxicity. We have tocilizumab for the cytokine release syndrome ready and waiting for them. Most of these cytokine release syndrome and neurotoxicity typically occur within the first couple of weeks, whereas after they get out of the hospital, we typically have some other possibilities of longer-term toxicities like cytopenias, as well as increased risk of infections, hypogammaglobulinemia from the plasma cell aplasia. With ide-cel, the median time to recovery from grade 3 or worse neutropenia and thrombocytopenia was 2 months. But we can, in the minority of patients, see more prolonged cytopenias. And these sometimes require growth factor support, transfusions, and then intravenous immunoglobulin replacements.

What about other, complications like second malignancies? Have you had any issues with that?

Dr. Martin:
You bring up a bunch of really good points. When patients leave the treatment center after 30 days, there is a lot of follow-up that has to happen together with their local docs and with their CAR T cell therapy doc. The cytopenias, they often don't resolve by the 30 days after the CAR T.

We do also recommend cytokine therapy as needed for count recovery. We also sometimes, if a patient has really severe cytopenias, would consider taking some stem cells out of the stem cell bank and giving them a hefty dose of stem cells to have count recovery. That's also something that we can do. But the local docs really have to be available, in my mind, to check their counts and also potentially to give them transfusions as needed.

We have seen some secondary malignancies after the CAR T cell therapy. And it's been a variety of things. But probably the most common thing is skin cancers. And what we've seen specifically in the CARTITUDE study, is we've seen some myeloid malignancies, too. We've seen some myelodysplasia cases, and we've also seen some cases of acute myelogenous leukemia, or AML.

I think part of it is, you know, in this patient population with 6 prior lines of therapy, when they get on relapse refractory myeloma therapy, you know, the PFS is typically around 2 to 3 months, and the average survival is about 9 months. And so here we have more than half of the patients living 2 years down the road. So longer survival and more opportunity for them to have a secondary malignancy. I don't think the secondary malignancy is from the CAR T cell therapy. It's from all the other alkylator-based therapies I think they've had in their past.

And so, again, following their counts and having heightened suspicion if they have more progressive cytopenias in 6 months, a year, year 2 – that person probably needs a bone marrow evaluation.

The other thing, the neurologic toxicity. There can be some delayed neurologic toxicity. And we did see that in the CARTITUDE-1 study. And some of it is cranial neuropathies, and some of it is Parkinsonian-like, symptoms. And some of those actually respond to Parkinson's disease medications. But certainly, if people were having delayed neurotoxicity, we start giving dexamethasone or steroids. The minute they had any late-onset neurologic toxicity, we want to see them back right away.

Dr. Anderson:
I think some of the newer trials are now using some mitigation strategies to help prevent some of those atypical neurotoxicities like more heavy bridging therapy for deeper cytoreduction and early and aggressive therapy of cytokine release syndrome and neurotoxicity before it leads to a lot of different complications.

Dr. Martin:
We have learned beneficial ways of treating these patients during their CAR T cell therapy like better bridging chemotherapy and like early treatment of CRS.

Larry, this has been great conversation. What's your take-home message for people who are listening to this discussion?

Dr. Anderson:
I would say overall, this is an exciting era of many new therapeutic options for our relapsed or refractory myeloma patients, most notably including 2 different CAR T cell therapies that are FDA-approved, as well as several other promising therapies under investigation. And

hopefully access to these therapies will soon catch up with the demands of the patient population.

Dr. Martin:
I completely agree. My take-home message is that in the era now of immunotherapy, these therapeutics are the most potent therapeutics we've ever had in the relapsed and refractory multiple myeloma space. And so we want to try to get patients who are eligible and who can tolerate this therapy to CAR T cell therapy as soon as they're appropriate candidates. In general, I think these therapies are safe, they have manageable toxicity, and I do think it's going to prolong quite a few patients' lives. And expanding the access is going to be so critical.

Unfortunately, that's all the time we have today. I want to thank our audience for listening in and thank you, Larry, for joining me.

Dr. Anderson:
It was my pleasure.

Announcer:
You have been listening to CME on ReachMD. This activity is provided by Prova Education.

To receive your free CME credit, or to download this activity, go to ReachMD.com/Prova. Thank you for listening.