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

Can I Expect Better Outcomes With Idecabtagene Vicleucal Therapy Compared to Other Treatment Options in the Triple-Class Refractory Myeloma Patient?

Announcer:
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Dr. Cohen:
Hello, my name is Adam Cohen from University of Pennsylvania. And today I'll be discussing the topic; Can I expect better outcomes with Idecabtagene Vicleucal Therapy compared to other treatment options in the Triple-Class Refractory Myeloma Patient?

We know that once patients become refractory to a proteasome inhibitor, IMiD, and CD38 antibody. The so-called triple class refractory patient. That outcomes unfortunately can be very poor. On the left, you can see data from the retrospective multicenter MAMMOTH study, in which 80% of patients were triple-class refractory. Regardless of what treatment option was chosen, the overall response rate was somewhere between 30 and 35%, with median PFS roughly between three to four months. For patients who were triple and quad refractory, the median survival was 9.2 months. And for those that were penta refractory median survival was, unfortunately, less than six months. On the right, you can see data from the more recent prospective locomotion study in which 248 patients, 74% of whom were triple-class refractory, were observed following the receipt of any number of standard-of-care treatment options based on their physician's preference. Again, regardless of the treatment chosen the overall response rate was around 30%. With a median PFS of 4.6 month, and a median survival of about 12 months.

We're fortunate to have two new drugs recently approved from multiple myeloma in the past two years. Both of them for this tough to treat triple class refractory population. On the left you can see data from the DREAMM-2 study. Which tested the antibody-drug conjugate Belantamab. At the 2.5 milligrams per kilogram dose given IV once every three weeks. The overall response rate in this study was 31%. With a median PFS of 2.8 months, and a median duration of response of 11 months. Median survival was 13.7 months in this study. On the right you can see data from the Selinex or Dexamethasone study. Selinexor is a novel oral XPO1 inhibitor. In this study, which enrolled 122 patients, the overall response rate was 26%. With median PFS of 3.7 months, and median survival of roughly eight to nine months. Thus, while these are nice additions to our armamentarium, you can see that the overall efficacy outcomes are not that different from what we've had historically. And we clearly need additional treatment options for this difficult to treat population.

Idecabtagene Vicleucal, or ide-cel, is aBCMA-targetedd autologous CAR-T cell product. The structure of the CAR is shown on the left. It has a mirroring derived SCFE targeting BCMA a CD8 hinge trans membrane domain, a 4-1BB costimulatory domain, and a CD3ζ activation domain. Ide-cel was approved based on this pivotal phase two single arm KarMMa study. The scheme of which is shown here. Patients underwent Leukapheresis, and then ide-cel was transduced into their T cells using a lentiviral vector. After a four to five-week manufacturing process. The CAR T-cells were given back as a single infusion following standard fludarabine and cyclophosphamide conditioning. Eligible patients had to have at least three prior lines of therapy and had to be previously exposed to an IMiD proteasome inhibitor and CD38 antibody, and also be refractory to their most recent line of therapy. On the far right you can see

that 148 patients underwent apheresis and 128 were ultimately dosed with one of three different doses of ide-cel. The primary endpoint was overall response rate.

Here you can see the primary efficacy outcomes. Patients had a median of six prior lines of therapy and 84% were triple-class refractory. The overall response rate in the whole population was 73%, including 33% achieving a CR or better. At the highest dose level of 450 million cells, which is the FDA-recommended dose. The overall response rate was 81%, with CR better than 39%. On the upper right, you can see progression-free survival. Median PFS was 8.8 months for the entire population, but again was highest in the patients receiving the highest dose level of 450 million cells. Where median PFS was 12.1 months. Median overall survival for the entire study was 19.4 months. And if you recall, this is significantly greater than what had been seen with the historical controls in the MAMMOTH or LocoMMotion studies. Suggesting a significant improvement over our prior therapeutic options.

In terms of toxicities the most common toxicities were hematologic. As expected from patients receiving lymphodepleting conditioning and CAR T-cells. Almost 90% of patients developed grade three or higher neutropenia. And roughly 50 to 60% developed grade three to four thrombocytopenia and anemia. The majority of these cytopenias had recovered to grade two or less by two to three months after CAR T-cells, though a subset of patients did have prolonged cytopenias. That could last for several months. 84% of patients developed cytokine release syndrome after ide-cel. With I median onset of around one day. Fortunately, most of these were low grade and only five to 6% of patients developed high-grade CRS. 18 to 20% developed neurotoxicity. And again, most of these were low grade with three to 6% developing grade three or higher neurotoxicity. 52% of patients did get Tocilizumab.

So, to conclude ide-cel has significant activity and highly refractory myeloma, and has now been FDA-approved for relapse refractory myeloma after four or more prior lines, including a PI, IMID, and CB38 antibody. I do think it represents a new standard of care option for patients with triple-class refractory myeloma. There are a number of ongoing studies looking at ide-cel in less heavily pretreated patients as shown here. Including the randomized phase three KarMMA three study, in which ide-cel is compared to doctor's choice of standard of care regimens in patients with two to four prior lines of therapy. And hopefully, by moving this up into less refractory patients we may see even more durable remissions. Thank you very much for your attention.

Announcer:
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