Managing Myeloma

JCARH125, Anti-BCMA CAR T-cell Therapy for Relapsed/Refractory Multiple Myeloma: Initial Proof of Concept Results from a Phase 1/2 Multicenter Study (EVOLVE)

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My name is Philip McCarthy. I am here at the ASH meeting in San Diego 2018. A lot of exciting things are going on and I am very excited to be able to talk about an abstract that was presented that discussed a CAR T-cell therapy, a chimeric antigen receptor therapy, directed against BCMA (B-cell maturation antigen) for patients with heavily pretreated multiple myeloma.

This study presented in the abstract the first eight patients and discussed that these were all daratumumab exposed, multiple lines of therapy, I believed there were seven lines of therapy in our median, and so they are heavily, heavily pretreated. These are patients who do not have a lot of options left, and so this involved taking the patients' own T cells. They are sent to Juno's manufacturing site where a chimeric antigen receptor is placed in the T cell. What this is is an anti-BCMA that has been engineered to be expressed on the surface of the T cell and it kind of hijacks the T cell, which normally would be doing other things but now it is being directed to recognize BCMA, which is expressed on plasma cells, bind to it and kill the plasma cell. The thing that is very exciting about this is these patients who often come in with a lot of disease respond very quickly. They respond within days and they do get the cytokine-release syndrome, so that is something that we are going to have to be watchful for. It does not seem to be too severe. There have been some patients who have had both CNS toxicity as well as cytokine-release syndrome. They do get elevations in ferritin. They do get inflammation. They do require tocilizumab and steroids very similar to the anti-CD19 CARs which were initially protocol and which are now commercial. These are not unexpected toxicities. They do have dramatic responses as I mentioned. They will often clear out their marrow fairly quickly. Their day 15 marrows are pretty much wiped out. I mean there may still be disease there, but there is a much reduced amount of plasma cells. Then serum-free light chains, in particular, plummet if that was the biomarker for the patient. The issue is long term. We do not see a lot of long-term data because there is none, these are all new studies, it is same thing with Bluebird. Bluebird is a little bit further ahead, but again median follow-ups just over a year, so we are looking at something that is very new and we want to see durability, so what we are going to need to see is two, three, four, five-year follow-up just as the same thing that was needed to be seen with both the commercial products, the eschar and chimera, directed against CD19.

So again, wonderful information, great news for our patients. This is a great opportunity. This is open around the country at several sites. I know that Janssen will be opening up a BCMA CAR T-cell, so we will have Bluebird, Janssen, Juno, all having this therapy in many sites available, so we expect a lot of patients to be taking advantage of this because this is something that for many patients, they do not have a lot of options left. We do have a lot of drugs, we are trying to figure out how to use them properly, where to place them, but this is yet another great option for our patients which hopefully will lead to someday a cure of multiple myeloma.

Reference

Mailankody S, Htut M, Lee K, et al. JCARH125, Anti-BCMA CAR T-cell Therapy for Relapsed/Refractory Multiple Myeloma: Initial Proof of Concept Results from a Phase 1/2 Multicenter Study (EVOLVE). ASH 2018. Abstract 957.