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Practical Considerations With Using CAR T-cell Therapies in Multiple Myeloma

Announcer:
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Dr. Raje:
My name is Noopur Raje. I am the Director for The Center For Multiple Myeloma at the MGH Cancer Center, and also Professor of Medicine at Harvard Medical School. We will go over the practical considerations of the use of CAR T cells. We're fortunate that we have two CAR T cell products available for our patients. We have both Ide-cel and Cilta-cel.

There are certain considerations to manage patients before and even after CAR T cell infusion.

So, before we go into that, I just want to give you an overview of the actual CAR T cell administration process. It is something which requires planning. It is something which requires coordination between the treating center, as well as the referring provider, and the patient, and their caregivers. It's pathed out by identifying the ideal patient who's eligible for CAR T cell. This patient then needs to be referred to the cell therapy center. That patient then needs to be evaluated and selected for the CAR T cell. One then needs to undergo leukapheresis or collection of those lymphocytes. These are then manufactured into CAR T cell and once they're manufactured, the patient is hospitalized for the lymphodepleting chemotherapy followed by giving back the CAR T cells.

So obviously with all of that history that I've told you, there are certain logistic considerations which need to be taken into account. One of them is how far is the closest treatment center and what CAR T cell products does that center actually offer? Can the patient travel or remain close to the center for extended periods of time, approximately four weeks after the infusion? Does the patient have the resources and insurance coverage to undergo CAR T cell therapy? And what is the optimal timing for the harvest of those lymphocytes, for the ideal outcome for our patients?

This is what the patient journey actually looks like. And it involves starting from the patient identification referral to the center for CAR T cell, assessment for eligibility, the patient then undergoes leukapheresis, undergoes lymphodepleting chemotherapy, and infusion. And in general, is in the hospital for approximately 10 days to two weeks. Discharged and is monitored close to the CAR T cell center for approximately a month or so.

The Apheresis procedure actually includes collecting those T cells. The minimum threshold for the lymphocyte count is not required for all products. Some of the products required it to be above point three. There's few considerations to think about prior to leukapheresis, patients should not be getting steroids so that they have the best lymphocyte function in the leukapheresis product. There is no real minimum washout antimyeloma therapy period, but in general, we like at least two weeks from standard regimens, such as the protosome inhibitors as well as CD38 monoclone antibodies. Sometimes a patient might require central venous catheter and the volume of blood required for actually collecting the leukapheresis product really depends on the proper blood mononuclear cell counts.

Oftentimes these are patients who are relapsing and there is a time between the leukapheresis product, and the actual manufacturing of

the CAR T cells. It takes anywhere between four to six weeks. And oftentimes when you have progressive disease you have to plan on bridging therapy. This planning of bridging therapy should be in coordination with the CAR T cell center, and you have to try and maintain adequate organ function prior to going to CAR T cells. The choice of bridging therapy is really patient-dependent. Depends on what the patient has had prior, up until recently when we were doing clinical trials, we were restricted but now that we do not have these in clinical trials one can be a little more innovative on choice of bridging therapy. Typically, the bridging therapy should be stopped two weeks prior to giving back the CAR T cell products.

For lymphodepleting, we are typically using both Cytoxan and Fludarabine. Studies have been done with both Fludarabine Cytoxan or Cytoxan alone. When you give both Flubaradine and Cytoxan we see the best CAR T cell expansion. So, in general, for all CAR T cell products we try and use both Flubaradine and Cytoxan. And for this reason specifically, for dosing the Flubaradine in our patients, it's important that the patients have adequate organ function.

The take-home points for me for practical considerations of CAR T cells is that CAR T cells is obviously a planned procedure, which requires a lot of care coordination between the referring physician, the coordinating treating center, as well as the patient, as well as their caregivers. Work closely with the referral center to have the best chance of success for your patient with CAR T cell products which have really been showing incredible responses with incredible duration of responses as well.

Announcer:
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