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Selecting Patients for CAR T-cell Therapy

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. I will be talking to you about CAR T-cells, specifically focused on patient selection. Given that we have two CAR T-cell product, I think it's really important to consider patient eligibility for this CAR T-cell therapy.

So, as you can see out here, the majority of patients, in fact, who have the diagnosis of multiple myeloma are in fact eligible for CAR T-cells, and in fact, more patients are eligible for CAR T-cells, even when compared to stem cell transplant. There's certain factors which need to be taken into account. Patients need to meet sort of the trial guidelines, and the product labeling so that it gets approved by insurance. Most patients should have had at least three prior lines of treatment including a PI and a pro immunomodulatory drug, in general should have an adequate performance status, and should have reasonable comorbidities which should allow them to get CAR T-cell therapy.

So, because of the approval of these two drug products, including ide-cel and cilta-cel, the International Myeloma Society convened a consensus panel to try and figure out which patients should be referred for CAR T-cell therapy.

When it comes to patient eligibility, the patients should have had at least three prior lines of treatment, as mentioned. This should include a proteasome inhibitor, it should include an immunomodulatory drug, and more often than not, patients have also received a CD38 monoclonal antibody. They should have progressive disease, and in general should be refractory through their prior line of treatment. This is important because patients should not have rapidly progressive disease, because it takes about four to six weeks for that CAR T-cell product to become available through patients, and a rapidly progressive disease would not allow us to get those patients back to the CAR T-cells. There's really no age limit for CAR T-cells. And specifically in the older patient population, it's important that the treating physician and the CAR T-cell center physicians evaluate these patients and make sure that they're gonna be able to tolerate CAR T-cell therapy. Patients must obviously be willing to adhere to clinic and visit schedules and should be willing to stay close to the CAR T-cell center, at least for the first month following CAR T-cells.

There are certain factors which impact CAR T-cell therapy outcomes, as well as the risk of toxicities. And therefore, it is important for both the treating physician and the CAR T-cell center to appreciate and understand these. Patients with any disease burden can be taken on for CAR T-cells, even if they don't have a detectable monoclonal protein, but they have PET avid disease that would be adequate for patients to actually receive CAR T-cell therapy. There are certain important considerations for leukapheresis. One wants to try and get the best CAR T-cell product for our patients, and it is important to avoid certain lymphotoxic drugs such as melphalan and bendamustine prior to leukapheresis. Patient history is important, so that CAR T-cells should not be given immediately after stem cell transplant. You should have at least more than three months prior to getting a patient leukapheresis. The other things to note is that

plenty of other BCMA-directed strategies. And if you're thinking of CAR T-cell products with the BCMA-directed strategies, although we do not have data on the ideal sequencing of these, it is important to at least discuss whether or not they've had a prior BCMA-containing strategy.

There are certain comorbidities which should be considered. For example, cardiorespiratory function. A patient should have adequate cardiorespiratory function so that they should be able to tolerate some of the toxicities associated with CAR T-cells. One really important comorbidity is renal function, as it is important that patients have adequate renal function so that they can actually get fludarabine.

Certain other factors, like CNS disease, has traditionally been considered. And in eligibility criteria, we've opened that up, so that if you have somebody who had CNS disease, but it's well controlled, they could be considered, and one can have the discussion for CAR T-cells. As far as viral disease is concerned, obviously active viral infections are something wherein patients should not be taken for CAR T-cells. There are other important history considerations in the patient history. And this includes patients on chronic immunosuppressive therapy. They should be able to get off of that immunosuppressive therapy before going on to CAR T-cells. If they're on anticoagulation, they may need to have to be off of anticoagulation for the brief period when the platelet count is going to be low. And obviously, if patients have hypersensitivity to either cytoxin for therapy or tocilizumab, those are patients I would not consider taking to CAR T-cells.

There are certain other factors which impact CAR T-cell therapy, the outcomes and the risk of toxicities. One very important one being adequate bone marrow function. Otherwise, you are going to end up with prolonged cytopenias. Patients with amyloidosis can certainly be considered, but you have to make sure that their cardiac and their renal function is adequate in these cases.

Again, it is really important to plan early for CAR T-cell therapy. Patients should be considered for CAR T-cell therapy as early as eligible because there's more and more data to show that earlier on in the course of disease the T-cells and the lymphocytes are healthiest and the product is better. You get better expansion and you're gonna get better responses. And the durability of responses is going to be better if you end up with doing CAR T-cell as early as possible.

There are certain practical, real-world considerations which we need to think about. Most patients, when they relapse, have already had multiple agents and are refractory to both an IMiD, a PI, and almost always now a CD38 monoclonal antibody as well. It is important to recognize, that even at first and second relapse, most of our patients are triple plus refractory. Therefore, the ideal time for referral is early, after they first or second relapse, because both the treating physician, as well as the CAR T-cell center has to plan on salvage therapy in these patients. There are obviously supply constraints with CAR T-cells, and therefore early referral is key, so that patients can adequately get onto a list and can go on to receiving these CAR T-cell therapies. Other BCMA targeted approaches are available including antibody drug conjugates as well as bispecific antibodies. And it's critical to try and figure out what the best sequencing of these is.

So, what am I take home points for the ideal patient selection for CAR T-cells? Well, consider CAR T-cell in all patients with multiple myeloma. Discuss potential eligibility with your referral CAR T-cell center to make the experience as beneficial to the patient as well.

Announcer:
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