Dr. Joshua Brody: Hi, my name is Josh Brody. I am the director of the Lymphoma Immunotherapy Program at the Icahn School of Medicine at Mount Sinai here in New York, New York. At this recent meeting, ASH 2019, for the American Society of Hematology annual meeting. We had a lot of exciting updates on new types of therapies for our patients with lymphomas and leukemia's. One particular type of lymphoma that has been very difficult to develop new therapies for is called mantle cell lymphoma. Mantle cell lymphoma in some ways has been one of the worst types of lymphomas historically, especially 10, 15 years ago. What we saw was that standard chemotherapies put most of these patients into remission for a few years, but generally those patients eventually relapsed and when they relapsed we didn't have very good therapies to get them back into remission and it didn't seem like we were able to cure certainly the vast majority of these patients.

So over the past 10 and 15 years, we have had some advances. We have new therapies for mantle cell lymphoma that are FDA approved, a class of medicines called BTK inhibitors like ibrutinib and acalibrutinib. Some other targeted therapies, one called revlimid lenalidomide and another called bortezomib velcade. All of these medicines have been pretty good, but generally they put patients into remission temporarily. And those patients again relapse within a year or two on average. We also have a newer medicine called Venetoclax which has been very promising for mantle cell lymphoma, but not yet FDA approved for that disease. Although Venetoclax is FDA approved for some other types of lymphoma and leukemia. So the update at this year's ASH was a type of immune therapy that has been extraordinarily promising in other aggressive lymphomas. And this is an immune therapy called CAR T cells. CAR T cells are so unbelievably cool that when I describe them to my patients and their families, they think that I'm describing an episode of Star Trek.

It seems unbelievable. But the concept of CAR T cells is that we actually take some of the patient's immune cells out of their body with a procedure called apheresis, which is basically like a long blood draw. We take some of their immune cells, we send them off to a special lab where the immune cells have a new gene inserted into the immune cell. And that gene allows that immune cell to target lymphoma cells specifically. So we take the patient's immune cells, we do this gene therapy to their immune cells, put the new gene that allows them to lymphoma cells. And then we reinsert, reinfuse those immune cells. And now we call them CAR T cells. They were T-cells, that's the type of immune cell that they were. And we've inserted this gene called the CAR, C A R, into them. So CAR T cells reinfused back into the patient, and CAR T cells have an unprecedented ability to induce remissions in patients with some very aggressive lymphomas and leukemia's. And CAR T cells are currently FDA approved for an aggressive type of lymphoma called DLBCL diffuse large B cell lymphoma.

For patients with mantle cell lymphoma, there've been previously only some small trials of CAR T cells or other immune therapies like them for patients with mantle cell lymphoma. So at this year's ASH 2019 meeting, we've got an update

of the largest trial ever performed for CAR T cells for patients with mantle cell lymphoma. And the exciting result was that the vast majority of patients went into remission and a good proportion of those patients seem to stay in either partial or complete remission four months or even in some cases, well more than a year that they have been followed for so far. And we don't know for sure how long these remissions will last. But for this other type of lymphoma I mentioned diffuse large B cell lymphoma, we see that if those patients stay in remission for six or 12 months, it seems like that most of them stay in remission forever. So in DLBCL, that other lymphoma it seems like many of those patients are cured. So whether that will be the case here in mantle cell lymphoma, we still have to see, but we have a very promising precedent from other lymphoma types that we've treated with CAR T cells. So to get these results of the high response rate for CAR T cells in patients with mantle cell lymphoma, very exciting for us and hopefully will lead to eventually an FDA approval so that we can routinely use these CAR T cells for our patients with mantle cell lymphoma.