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Updates from ASH 2019 - New Treatment for Diffuse Large B-Cell Lymphoma and Follicular Lymphoma: Bispecific Antibody Therapy

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Dr. Joshua Brody: Hi, my name is Josh Brody. I am the director of the Lymphoma Immunotherapy Program at the Icahn School of Medicine in Mount Sinai, New York. We've had a large amount of progress in therapies that we're developing for patients with lymphoma and also CLL. And some of that progress was manifest at a large meeting we just had called the Annual Society of Hematology meeting the ASH meeting 2019 in Florida just last week in early December. One of the best examples of progress is especially important for our patients with some of the worst clinical situations. These are patients with relapsed and refractory, diffuse large B cell lymphoma or Follicular lymphoma. Both of these are very common types of B-Cell Non Hodgkin's lymphoma. And for both of these diseases, DLBCL and Follicular lymphoma, we have a number of good therapies, both chemotherapy, rituximab therapy, some targeted therapies as well. But for a large group of patients, those therapies are not sufficiently effective. And so this new class of medicines that we're learning about is a new type of immunotherapy called Bispecific Antibody Therapy.

And immunotherapies generally are different than chemotherapy. They are different than radiation therapy, different than small molecule inhibitor pills that are approved for some types of lymphoma. These are therapies, immunotherapies, which actually

mobilize their patient's own immune system to go out and kill lymphoma cells throughout the body. So this class of therapies is very exciting to us. And by specific antibodies or one particular type of immunotherapy. Very specifically just to explain how they work a bit Bispecific Antibodies are different than other antibodies who may have heard of like rituximab. Rituximab binds to one thing, it binds to lymphoma cells, it binds to the CD-20 molecule on the surface of lymphoma cells. By contrast here, these Bispecific Antibodies bind to two things. They bind to, for example, CD-20 on the surface of an lymphoma cell. And then they separately bind to our T-Cells the immune killer cells, which can be recruited to kill those lymphoma cells if they are brought next to the lymphoma cell. So the bi-specific antibody actually grabs these immune soldiers, these

immune killer cells called T-Cells and brings them over to the lymphoma cell and concurrently activate them.

So they will start to kill that lymphoma cell. And this idea of Bispecific Antibodies has been around for awhile. There's actually a Bispecific therapy that was FDA approved for a type of acute leukemia and that medicine is called blinatumomab. But we have generally not been able to use that medicine for patients with lymphoma partly cause it's just very difficult to use. It requires continuous IV infusions over weeks and weeks. So these new Bispecific Antibodies are in some ways much easier to use. They can be intravenous infusions that patients could get once every two or three weeks. And hopefully they would be given in the clinic, not in the hospital because they should be a little bit safer and simpler to use. So the big update at ASH 2019, is that we saw that for these two types of lymphoma for patients with relapsed and refractory DLBCL aggressive lymphoma and also Follicular low grade lymphoma, we saw patients having high proportions of both partial and complete remissions after these Bispecific Antibody Therapies. And there's a few of these being developed. We had presentations from a couple of different companies.

One company is called Regeneron, the other company is called Roche Genentech. And they both have anti CB-20, anti CB-3 Bispecific Antibodies where they were showing some of the data updates at ASH 2019. So we saw that both of these therapies can induce remissions in patients who have had many prior therapies, even if those prior therapies were not working, even patients that have had a very aggressive type of new therapy called CAR T-Cells, which was one of the newest and most recently FDA approved therapies for aggressive lymphomas, even patients for whom CAR T-Cells were not working sufficiently well, these Bispecific Antibodies could be effective. So we've seen patients go into complete and partial remissions, some of those remissions lasting for months, and certainly even some of them more than a year. We've only had these trials open for a couple of years. So hard to say if maybe those remissions could last for many years, possibly. We're still trying to find that out now. This has been very

exciting to us. The Bispecific Antibodies are in some ways more elegant than things like chemotherapy, but we should be clear that they do still have some risks. Some patients when we push their immune system to kill the lymphoma cells, we push the immune system too hard and the immune system reacts aggressively and the patients develop a syndrome that's almost as though they had an infection.

They don't have an infection, but their immune system is going crazy and they develop a syndrome called cytokine release syndrome. And this can be very serious. Patients get hospitalized for this. They can get transferred to the intensive care unit. Usually this cytokine release syndrome, this like infection without an infection syndrome lasts for a few days and just requires patients to get careful hospitalized standard care, meaning IV

fluids, sometimes medicines to help their blood pressure. But it can be a very important and potentially serious side effects. So that's probably the thing that we're most carefully trying to watch for in these clinical trials. We've actually developed some new ways to try to improve upon that side effect called cytokine release syndrome. So hopefully if we can improve the safety of those by specific antibodies over the next months in the year I can see where these therapies could be fairly safe and highly effective, even for patients that don't have a lot of options left, and even for patients for whom chemotherapy and other therapies haven't been good enough. So the whole field of Bispecific Antibodies, very exciting. And this specific data from the Regeneron and Roche clinical trials, extremely exciting. Hopefully these could become FDA approved medicines within a year and things that we could bring to our patients very quickly.