



## **CAR T-Cell Therapy for Patients with Relapsed B-Cell Lymphoma**

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To explain CAR T-Cells, I'm first going to talk about some immune cells, the T-Cells, okay? So, your immune system has a type of cell called a lymphocyte, and there are two types of lymphocytes; one is a B-Lymphocyte, and the other is T-Lymphocyte. The B-Lymphocyte is what makes antibodies. And actually, patients with diffused large B-Cell Lymphomas have a cancer of the B-Lymphocyte, so that's what diffused large B-Cell Lymphoma is; it's a Lymphoma of B-Lymphocytes. But the T-Cells are usually healthy. The problem is the T-Cells they're like the conductors of the immune system. They basically secrete chemicals into the bloodstream (we call them chemokine for chemicals) that tell the immune system what to do. So when you're infected with a virus, like COVID or bacteria, the T-Cells have kind of organized the immune response to the infectious agent. Not only do they help kill the infectious agent, they then help the B-Cells form a memory to the infectious agent, so when you're re-exposed to this infection, you have a quick, swift removal of the infection and you don't feel so bad. It's kind of how vaccines work, and that's usually why when you're exposed to the infection for the second time, it's not as severe because your immune system's learned how to deal with it, and that's all done by the T-Cells.

So, we know that T-Cells in the body can actually recognize cancer cells and kill them because the cancer cells are a little bit different than the normal cells. The problem is you have a diffused large B-Cell Lymphoma that's growing, clearly, your T-Cells have not done the job. And that's usually the case for the majority of the patients. If the T-Cells were effective on their own on controlling cancer, then we would not develop cancer, but we clearly do develop many cancers. So what we do is we take a patient who is a candidate, and again, these are patients where the front-line therapy didn't work and where the stem cell transplant also did not work, okay? They also have to be, you know (and we'll talk about it when we talk about some of the side effects) they also have to be, you know, in reasonable, what we call, performance status. It is an aggressive therapy, so for patients that can't get out of their house or are confined to their bed, it is not an appropriate therapy; it would not be safe. What we do is we collect the cells, kind of like we did for the stem cells, but this time round, we filter out the T-Cells. So, now we have a collection of T-Cells from the patients (so these are the patients' own cells). We then take the cells, and we send them to the lab. And, the lab can be either our own clinical trial or for the FDA-approved products, for which there are now three CAR-Ts approved for diffused large B-Cell Lymphoma, we send them to the company. The company will then genetically modify the T-Cells. What they do is they engineer the T-Cells so now that the receptor on the surface of the T-Cell recognizes the Lymphoma. And on diffused large B-Cell Lymphoma, there is a target called CD-19 (you don't need to remember that, just think of it as a little spot on the surface of a diffused large B-Cell Lymphoma). It is expressed by all diffused large B-Cell Lymphomas. And what we do is we engineer the T-Cells from the patient to be specific for CD-19.



So that takes about two to three weeks from collecting the cells to the manufacturing of the product, and then they ship the product back to the hospital, or in our case, the cancer centre, where we administer it there. And what we do is, we usually admit the patients to the hospital, although there are now programs where they're doing this outpatient, but for the sake of this talk, we'll talk about all-patient administration, we admit the patient to the hospital, and they get three days of chemotherapy. Not a lot of chemotherapy, just a little bit of chemotherapy, and it's not meant to cure the Lymphoma; its meant to get rid of some of the patient's immune cells to make them more receptive to the modified T-Cells, okay? And then we get three days of chemotherapy, and then there's a day of rest, and then there's the day of cell day infusion, where we administer the CAR T-Cell. And now, remember, these have been modified to be specific towards the cancer cell. The administration is just like a bunch of parents, we're using it to brag of these T-Cells, okay, and then the T-Cells infuse into the patient. And this is where the side effects can happen.

