



# Emerging Immunotherapy Treatments for B-Cell Non-Hodgkins Lymphoma

## Bispecific Antibodies

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The field has evolved even a bit further now and is a very related type of immunotherapy, which is in now ways a bit simpler and possibly so far, it seems a bit safer as well. But it's the same idea. This other type of immunotherapy we call Bispecific Antibodies. Bispecific antibodies are not that different from common antibodies that folks have heard of if they've had lymphoma. A very common therapy for lymphoma is Rituximab. It's an antibody that binds to lymphoma cells, and it binds its little protein and lymphoma cells called CD-20. This is a very similar idea. These Bispecific antibodies you can hear, they bind to things. The Bispecific antibodies frequently bind CD-20 and lymphoma cells, but then they also bind something on the immune cells (the T-cells I was just talking about before). So, they bind both the lymphoma cell and the immune cell at the same time, kind of drags the immune cell over and activates the immune cell so it will kill the lymphoma cell. And this idea has even around for a while. Really, just over the past three or four years we've had some excellent versions of these Bispecific antibodies. There's about four or five of them that are in late-phase clinical trials now. And, these Bispecific antibodies in folks with diffuse large B-cell lymphomas, follicular lymphoma, mantle cell lymphoma, a few others are also inducing remissions in the majority of people; some of these 70/80% of patients going into remissions, and in some of these, more than half of patients going into complete remission, meaning that we cannot see any residual lymphoma on the fanciest tests have; PET, CT-scans, and blood tests. We cannot detect any lymphoma. It does not mean these patients are cured, it's possible, but at least a complete remission is the most important step to cure. We'll really only know if those patients are cured if we follow them one year, two years, and we don't ever see the lymphoma coming back. But we've had patients from these Bispecific antibodies with all those types of lymphomas, in complete remission for one year or two years already; so it's extremely promising. And, the side-effects are in some ways similar to the CAR T-cells, but overall just more mild. We've had patients get that cytokine release syndrome, the high fever and low blood pressure; but it's very rare that patients get a lot of that, one out of 20 patients or one out of 40 patients. And, overall, it's so rare that we don't usually have to observe folks in the hospital for very long. For some of these Bispecific antibodies, we observe patients in the hospital for just one day just to make sure they're not getting those high fevers; for some of them it's two or three days, but usually it'd one day. And you can hear that's a lot less that the 10 or 11 days that we have to keep people in the hospital for CAR T-cells. So, another benefit of these is that it doesn't take time to make this therapy for each patient. The CAR T-cell is a personalised therapy. It is made for each person using their own immune cells. For the Bispecific antibodies, we don't have to ship anything off to Santa Monica, we just infuse the Bispecific antibody into the person. It's what we say an "off-the-shelf therapy", and in that ways, more accessible. You don't have to wait three weeks to get your (as you do with CAR T-cells) you don't have to wait three weeks to get your Bispecific antibodies. And for some patients that need therapy quickly, that makes a big difference. So, similar ideas. Both of therapies are getting you immune cells, your T-cells, to kill you lymphoma cells. And patients and their families find that very gratifying that they're sort of part of the fight against the cancer. Their immune cells are the thing that is killing the cancer; not the chemotherapy, not radiation therapy,



but they're all immune cells. They're own immune cells may not be able to do it without some help, but with these types of help (CAR T-cells, Bispecific antibodies), their own immune system is getting rid of the cancer. And that idea has been around for a long time but these are easily the most striking examples of those ideas actually working. Really putting our patients into remission, and some of them complete remissions lasting for years, and as i say, as we make more advances, seems to be doable in a safer and safer, and more practicable way. So, very exciting time over the past few years for immunotherapies, for patients with many types of B-cell and Hodgkins lymphomas; and we think the progress is even going to continue to improve over the next couple years.