CAR-T Interview with David Maloney MD

Dr. Brian Koffman – Hi. I'm Dr. Brian Koffman. I'm a family doctor and a CLL patient myself, and I'm here up at Seattle at the Seattle Cancer Care Alliance, associated with the Fred Hutch for CAR-T therapy.

Dr. David Maloney – And I'm Dr. David Maloney. I'm the Medical Director of the immunotherapy program at the Fred Hutchinson Cancer Research Center and the Seattle Cancer Care Alliance.

BK – CAR-T therapy is in its infancy, but it's been very exciting and there's been some amazing cases. Can you tell us a little bit, from a CLL patient's point of view, what they should know about CAR-T therapy at this point?

DM – Yeah. So, CAR-T cells are obviously one of the new darlings in terms of new cancer therapies. And basically, the whole treatment is where we take out your normal T-cells and we genetically engineer them in the laboratory so that they can actually go and attack the underlying CLL cells. The target that most people have been using is CD19, and this has led to the commercial approval of two CAR-T cells, in leukemia and lymphoma… none yet for CLL… but there's a lot of excitement about that, as well. So, the idea is, we take your T-cells out, kind of like you would for an autologous transplant. You get… patients that are hooked up to a machine, called an apheresis machine. The cells are collected. It takes a few hours. You're just kind of bored sitting there getting your blood…

BK – Been there, done that, yeah.

DM – It's pretty easy. The cells are then taken to a lab and CAR-T cells are produced, and that takes about three weeks or so… two to three weeks. And then patients receive a round of chemotherapy that is actually making space for the T-cells to grow. And right after that round of chemotherapy, the cells are injected back. But unlike any therapy most patients have ever seen before, this is a living therapy. So, the T-cells actually go into the body, and they reproduce, and grow, and they look for the targeted cells that, in this case, CLL cells, and when they bind to them, that gives the T-cell a signal to grow and divide and to kill the target that it bound to. And so, these cells really become, I guess the best word is “serial killers” going after the tumor. And we've seen really exciting results in leukemia, lymphoma and in now in CLL. And so, many of the first parts of the studies were figuring out the correct dose, and how to do this safely, because there can be very serious toxicities. And so, you need to do this at a time when you've run out of other options where, for example, ibrutinib, or some of the other common drugs used to treat CLL, are starting to potentially fail. So that's kind of the key thing. The two treatment toxicities that we generally see, one is this new term called “Cytokine Release Syndrome”, and that's feeling like the worst case of the flu you've had, where people have high fevers and can have low blood pressure. And this can be very serious. We can usually treat it with medications, including steroids or drugs that block some of the cytokines that the T-cells make. The second one is a little more obscure and harder, and actually scarier for both the physicians and patients, and that's a neurologic toxicity, where people get confused and we think that this is a problem

with the blood-brain barrier getting disrupted by these high levels of cytokines. And so again, that is largely treatable and patients recover from this over a few... in a short period of time, usually days to a week or so. So, this is an intensive therapy. It's really not for the faint-hearted yet, because we're still learning. But we've seen tremendous results with 80 to 90% of people clearing their blood and bone marrow of their CLL. We have a little harder time getting rid of very large lymph nodes, so the timing is probably important in the course of when we would have the most success. So that's why people are so excited about this treatment. I think it offers a chance of getting the disease into remission, as opposed to our current strategies of keeping people on medications for years and years.

BK – It seems like the response rates are pretty high, and you're getting better at controlling the side effects. I know it's very early on, but can you tell us anything about the durability of those responses?

DM – Yeah. We don't yet know. It largely depends on the depth of the remission. So, we're now doing molecular testing and if we can get people into deep remissions, it looks like those remissions last many years. Now, everyone wants to know is this curative therapy? We don't know yet. We're very excited about having some people in remission for many years. But, obviously, “cured” takes time. Unfortunately, there are ways that your tumor can still escape. We have seen very rare cases where the tumor loses the target, and then the T-cells obviously can't kill it if it doesn't have the target. So, learning and understanding how these escape mechanisms occur is also important for going forward.

BK – Any final words for patients on CAR-T therapy?

DM – No. I think it's just an exciting new treatment option that'll likely be able… be an improved type of therapy. But, that's going to take another two to three years, probably, before those trials are mature. So, right now, the only way to get CAR-T cells are on clinical trials. They're not yet approved for this indication. They are approved for the other leukemias and lymphoma, and so inquiring at centers that are doing CAR-T cell trials is really the only access at this point.

BK – And let me echo that. You know that I'm alive today because I entered a Phase I clinical trial, and I think clinical trials are not only good for advancing the science but can be very good for the patients who do them because you get access to cutting edge therapies and you get access to the best medical care. Dr. Maloney, thanks so much for what you do.

DM – Thanks very much. Good to see you.

BK – Thanks.