

***Being a Person Who Is Also a Survivor: Meryl Selig on Cancer Jargon and CAR T Therapy***

Jennifer Cohen

Welcome to the Voices in Bioethics podcast. I'm Jennifer Cohen and it's my great pleasure to welcome Meryl Selig to the podcast today. Meryl, thank you for joining us.

Meryl Selig

My pleasure, Jennifer, thank you.

Jennifer Cohen

You are finishing up your master's in bioethics at Columbia University. You're a West Coast bioethicist located in the Bay Area in California. And you bring your own personal experience as a consumer of some of the latest most cutting-edge medical technology. Before we get to that discussion, can you tell the audience a little bit about yourself, your education, your professional life, and your decision to pursue a bioethics master's?

Meryl Selig

Sure. So, I feel like if you live long enough, you start collecting degrees. But I got my undergraduate and my masters at the University of Pennsylvania. And I basically was a social scientist. And I still think of myself that way. At the time, after I got my master's, I thought I'd gone for a PhD, but there weren't many jobs then. And so, I went off to business school, actually in international business. And after that, I finally got a job, and worked in international consumer products and marketing for a pharmaceutical company. And so that's how I first became interested in healthcare and how people were dealt with by big industry and so on. Let's see. So that's that fast forward, I actually moved to Chicago from the East Coast and worked for advertising agencies and kind of moved away from healthcare. So, I did that for a while, had a family, etc. And then I wound my way out here to the Bay Area. I live just about, oh gosh, not even 10 miles from Stanford University, just to put that on the map where I am. When I moved out here, I had to kind of restart my life and was remarried. That may be TMI, but I had always wanted to work in a hospice. And so, I became a hospice volunteer at the Palo Alto VA, hospice at their medical center. It's spectacular. And I've been doing that for 14 years. And then I expanded and started doing patient facing volunteer work at the Stanford Cancer Center. So, I'm tacking this onto my education. But it really has been much of what's kind of led me to where I am today.

Jennifer Cohen

Wonderful. And how did you decide to go back and get another degree in bioethics?

Meryl Selig

I've always been actually interested in bioethics and much more so, just kind of in the back of my mind, because of all those years of hospice, and certainly watching how cancer patients move through the process, diagnosis, multiple treatments, you know, all the chemo and radiation and surgery. And because I was at Stanford up until COVID started and I could really track patients over the years. So, I became interested in how people traveled through that system through the healthcare system - you name it. The funny part, Jennifer, really is that I was carrying a stack of newspapers out to be recycled. And on the very top was an ad on the New York Times for the master's program at Columbia. And that's how I found out about it. It just happened to be on the top of my stack of recycling. So, I applied. It was pretty cool.

Jennifer Cohen

That's a wonderful story. Okay, let's turn to your experience with a novel and incredibly exciting new treatment known by its acronym CAR-T therapy, that stands for chimeric antigen receptor T-cell therapy, a treatment that's been available for only about five years. What was this treatment for? And what were the circumstances that led you to be one of the small group of people who have received this treatment?

Meryl Selig

Okay, well, I was diagnosed out of the blue with a form of non-Hodgkin's lymphoma. I was asymptomatic. That was way back in 2009. Five years past when I became somewhat symptomatic and went through six cycles of chemo. We thought everything was peachy. It wasn't. And again, out of the blue, I felt fine, but just blood tests turned this up. Not only did the lymphoma come back, but it came back in an aggressive form. That was back in...so, the second round of chemo was in 2016 to 17. And although it was non-Hodgkin's lymphoma, of which there are dozens of varieties, this was a different thing. The first one had actually transformed and presented itself as a new one, an aggressive form. So, I went to chemo again, we thought we won. Another, oh gosh, another year or so went by and once again, no warning, just went back for a checkup and I found out you can come back again. And so, this counted as several failures of treatment, and there wasn't much else that could be done. So, we were going to do a bone marrow transplant, a stem cell transplant. That was kind of the last-ditch effort. And there are several rounds of different kinds of chemo that happened before that the called lympho-depletion that get basically all the cancer possible out of your body before they harvest your stem cells and clean you out and put them back in. Okay. So, things are going along, and I was having a lympho-depletion chemo, and then I failed the last bag of chemical on the very last day after two and a half days in the hospital. So that avenue closed - and I hope I'm not being too complex about this. It's all seems straightforward to me. But when I recount it, please Jennifer told me if it's too convoluted. So, I basically failed the prep for the stem cell transplant. And then we just said, now we can't do that. And so, they rolled out the possibility of my doing a CAR-T. And that's how I ended up there. I was not happy, actually. Because it's so new and it definitely has some impossible, unpleasant outcomes, like death. So yeah, it was a little scary when I realized that this was my last straw.

Jennifer Cohen

Yeah. So, as you described through your work in hospice and VA that there are traditional cancer treatments - surgery, radiation, chemo - then there were these advances in what's called targeted therapies. We just had a podcast interview of Dr. David Solit at Memorial Sloan Kettering, who went through this new way, this new paradigm of drugs based on the genetic or molecular makeup of the cancer cell. And the next step seems to be immunotherapy. Using the patient's own immune system to fight off the cancer. It's really been sort of a mystery for so long as to why our immune system was not able to kill off cancer cells. What was your understanding of how CAR-T therapy worked? What did your team tell you? How much of your understanding came from your own research? What did you know going in?

Meryl Selig

Well, I learned a lot from my team. And I have to say that it was quite unusual. But my lymphomas specialist has a joint appointment in cancer cell therapy and stem cell transplant. And so, I was fortunate enough to have my same doctor throughout, and he knew my whole history been treating me for years. And so, it just rolled over into cancer cell treatment into the CAR-T. And he was very explicit, very detailed. He knows I'm kind of an info nerd. I like all the details. And so yes, I learned a great deal from him. My daughter is also very heavily involved in biotech and also cancer treatments. She's a venture capital partner in a firm out here. And so, she went to work, calling in all of her contacts and finding out more information. But I felt incredibly well informed about CAR-T. I did not think I had to go to Dr. Google or look up things anywhere, because I had really good, real life, human beings who knew what they were talking about.

Jennifer Cohen

That's wonderful. Can you explain how CAR-T works? What the processes of extracting these T-cells, and as I understand it, genetically re-engineering them. How does that work?

Meryl Selig

Yeah. So, you know, I may be getting some of the sequence out of order, but they hook you up to an apheresis machine, which just basically it looks like a little washing machine, and your blood goes out one tube in this particular setting, they take out your T cells, which is a very important part of your immune system, there are T cells and B cells basically. And they pack them up and they send them to a lab. And when your blood goes back into your body, it's really kind of a cool thing. It doesn't - it just takes a couple of hours. And off they went - there was a cooler sitting there next to this little apheresis machine and off went my T-cells. They came back a few weeks later having been engineered and what happens is - I like to think of it as a Trojan horse in a way. The engineering has them sensitized to pick up proteins on the surface of cancer cells. And so, when you go into the hospital after lympho-depletion and after they kind of make you all clean and wonderful. And in about 10 minutes, they re-infuse your new T-cells back into your body. And again, I hate this picture of these little almost Trojan horses running around eating up - connecting to and eating up my cancer cells, and actually that's what happened. It's so cool. And they take your cells who are anyway even for non-cancer people, your T-cells go after things that shouldn't be in your body, you know, invaders. And so, they primed them, they engineer them to go specifically in my case, it was CD-19 was the protein on the surface of the cancer cells. And now some

CAR-T cells are primed to go after CD-22. I mean, it gets kind of arcane, I suppose. But mine was a CD-19. And so, it happened, and in they went, and it worked.

Jennifer Cohen

That's such a brilliant image of a Trojan horse, because as I understand it, that's one of the incredible aspects of cancer, that it can fool your immune system into thinking it is not a danger. And it's sort of waking up these T cells and re-arming them to go after them. So, it's really a living drug. And it's completely unique to each person. Once these cells are re-engineered, they can't be used in other people. Is that right?

Meryl Selig

Oh gosh, no, not that I know- at least not at this point. I mean, they're natural killer cells. They're doing all kinds of work now and other kinds of CARs – these chimeric antigen receptors - so the antigen receptors, what I said that like the CD-19, in my case. So, I think they will be trying to use other components in the CAR manner. In fact, I just read this past week, I think they've come up with a CAR-T for multiple myeloma, which would be spectacular. And that's really been a rough disease to treat. And maybe not too far out in the future to be able to engineer T-cells to go after solid tumors. That would be just spectacular.

Jennifer Cohen

So exciting.

Meryl Selig

Mhmm, it is.

Jennifer Cohen

Okay, let's circle back to some of the issues you raised specifically around consent. So, as you describe this had been a number of years up to this point. How did you approach the issue of giving informed consent to the CAR-T? How did that compare to other times you had consented to other sorts of cancer treatment?

Meryl Selig

Gosh, okay, I'm sighing here, Jennifer. Well, two things happened. One is just, well, I guess funny, when all this came down, which was in the spring of 2019. That's when it all first happened. Just about this time in 2019. I was enrolled in class at Columbia, and one of my courses was Clinical End of Life Ethics. And so, you know, the whole semester, we were discussing end of life, and its various forms and legal aspects and all. Fantastic course, by the way. And just about the time when I was still able to take the classes, we started covering informed consent and advanced directives and proxies, and all this, just at the same time that I was going through all of it.

So, when the doctor took me through the process, and I refused to use consent as a verb, but I know medical people do like the doctor consented me. But anyway, that's what they say. It took a while because there were so many possible bad effects and really adverse, as in death. I listened to every word - I was sort of stunned. I paid attention to it much more carefully. There were many, many points he covered. It did not feel perfunctory as it did certainly when I had chemo. I knew there'd be side effects and all of that, but I didn't...I was getting standard of care every time I had chemo, so I wasn't that worried. This one was a different animal and just going through the process...while taking courses on how people approach death, with the end-of-life issues, was something that is really hard, really difficult to adequately express, but made me very sensitive to it.

Jennifer Cohen

Had there ever been a point where you were considering not going through with the CAR-T?

Meryl Selig

Yeah, briefly, and this has to do with COVID actually, but the CAR product, and I guess Yescarta, was fairly new, and it was the only FDA-approved product for aggressive B-cell lymphoma. Stanford had some good experience with it, not huge, the numbers were pretty small. And I thought, you know, if this were not COVID time, I would look into other options just to satisfy myself that we were doing the best possible thing. And so, my daughter again who I described, kicked in and started contacting people at MD Anderson and City of Hope and different places to see what kind of treatment they would do. And I came close to considering either one or the other of those - City of Hope and MD Anderson. But COVID started blooming and both required two weeks quarantine before even getting ready for treatment there. I would have had to rent apartments and you know, fly there. And, you know, the world started caving in safety-wise. And here I was basically with no immune system with lympho-depletion and all that. So, my options were removed for me, in a sense, because of what happened with COVID. I wasn't about to travel, I wasn't about to find an apartment, have my husband moved down there with me to get me to and from treatment and stay there, actually. So, it became a logistical impossibility. I mean, it all turned out well, as we know, but yeah, I did not have any other options, actually, at the time.

Jennifer Cohen

Okay. And how did the hospital set you up? Once you were through with the treatments, as you said, you went through lympho-depletion, and that left you with a very little immune system, if any. So, what kind of situation where you went in the hospital? And then how did you replicate that once you were discharged?

Meryl Selig

Okay, well, again, now, I went in May 12 or 13th of last year, and everything was on lockdown. Just you know, the normal units in the hospital were shot, there were no voluntary surgeries and all that. And so, there was no visiting. I was on an immune ward anyhow, an immune unit. And they have CAR-T and BMT people or stem cell people all together in two units, all kind of mixed together. But no family members, no visiting, no one could

bring me a cup of coffee, and I really wanted good coffee. I was inpatient for two weeks. And they just had to wait to make sure I was out of the woods, so to speak, that my body was stabilized that I was strong enough to go home. So, after two weeks, I was able to go. While I was there, as anticipated, I had a what they call a "cytokine release reaction." And yeah, it's pretty bad. You spike a fever, you get chills, it's bad, like a high fever. And they can go south fairly quickly. I was prepared, I knew about them. Because my doctor did such a good job. The staff was remarkable. They were on it. Like before, it really sunk in that this was what was happening. They were on it and administering an infused antidote to kind of turn around the reaction. It was bad - that went on for I don't know, I don't even know if I was totally conscious, because I was so fevered. But it left me pretty weak. And so, I guess I was in the hospital for five days after that, to get my strength back. But they knew what they were doing. I mean, these people...I can't say enough things about the nursing staff especially. They're so dedicated and so specialized, and just can practically read anything on your body and respond to it. So even though I couldn't have any family, the staff was just remarkable. And COVID was going on. So, I think they were scared to these people went home. And I don't know what they went through every day in order to get back on an immune unit. It was really a rough time. If we think about a year ago for how, in a way, terrified everybody was of COVID. And what kind of precautions to take, you know, things have gotten so much better.

Jennifer Cohen

And the spectacular news that you've alluded to, but that you can confirm is that your CAR-T therapy was successful.

Meryl Selig

Yep. I have. In about a month I go for my 12-month checkup. We'll get another PET-CT and all the blood work, and I probably will get an antibody test just to see if the COVID vaccine works. But we think it didn't actually. Again, this is an aftermath of CAR-T that it basically disables all vaccines I've had so we're going back to measles, polio, shingles, certainly vaccines I've gotten for travel - everything's gone. So hopefully starting May I'll get re-vaccinated and I may need to get vaccinated again for COVID. If I didn't get a good response, it's a small price to pay after this. I feel great.

Jennifer Cohen

Great. Oh, that's wonderful. Okay, let's turn to the way cancer is talked about outside through beyond the clinical setting and that sort of language framing cancer. It seems to me that every person is going to respond differently to the physical process of recovery. And the same can be said about the emotional aspects of recovery. I think no two people go through that return to emotional equilibrium the same way. For some people, enormous strength is found in support groups, and the identity of being a cancer survivor. For others, there might be a different way to go. What was the path that worked for you as you return to health?

Meryl Selig

Well, you raised some good points there. Everybody brings their individual self to, I guess anything you do. And

certainly, when you're dealing with adversity, you know, how we respond, how resilient we are and all that. I've always even before I became really good in the sense, I hate to say the sick, but needing this much treatment, I didn't like the idea, the imagery, the metaphors around cancer survivors. And that's just me. As you noted, people have to seek out what's comfortable for them, and how they see themselves with the experience with the process. I never, never wanted to have cancer as part of my identity, my self-image. And that goes way back to when I was first diagnosed, after the first six cycles of chemo, the second six cycles of chemo. It just confirmed to me that, maybe because I did well, basically, and I never felt horribly sick, that I just didn't want to be a cancer person. And that meant not looking at myself as a survivor. I mean, we're all survivors of something or other right? I feel it just isn't me. I don't like to identify with that. I feel pretty strongly about. And it's, sometimes it's hard to maintain that because people with the best possible intentions come up with how are you and we're so concerned, it's lovely, it's so sweet. But they'll use terminology like well, you beat it, or you really, you know, you're a soldier or a fighter, and I am not a soldier or a fighter. I am a resilient person. But I don't like to use warfare metaphors. I think they're negative. And I think keeping the sense of humor and being as positive as possible when going through any of these things is just going to serve at least served me well in the long run. And I assume it will serve most people well. But if you put on that cloak of being a warrior for yourself - I guess again, it works for some people. And I understand if you were dealing with heaven forbid, a child's illness, but for myself now, I'm just thought, "Okay, this happened. I'm going to cope with it." I'll just put, as they say one foot in front of the other and it's still me. I just kind of walked into this buzzsaw. That's all and I'm going to walk out of it. That's just how I see it.

Jennifer Cohen

That's such a helpful attitude. I think a lot of people feel that way. And I love the way you've articulated what helped you. How are people most supportive to you when you were going through treatment? What did you want to hear - If anything - from friends and family?

Meryl Selig

I wanted to laugh. And in the past the previous treatments, oh, when I lost my hair, and I was sick for a few days after infusions, but then I got back on the hiking trail with my posse - with my buddies. I wanted life to just continue as normal as possible. After the CAR-T I was completely isolated at home for a month after the two weeks in the hospital. I was locked in. In fact, my husband had everything kind of hermetically sealed. I couldn't see my dogs because I couldn't pick up any fungal or bacterial infections from our backyard. Normal, healthy people never get anything from that. But I was really hermetically sealed in a bubble almost. I couldn't see my friends. But they would come to the window and talk to me through the window. I mean, it's like a bad commercial. I wanted to laugh. And people who know me just knew they had to keep it light. And tell me how skinny I looked and how bad I looked. You know, I mean, they made me laugh. That's all. That's what I liked from people. I didn't like it when people came up all sorts of hangdog. People are uncomfortable, they just don't know how to address other people's situations, whether it's cancer or anything else. I think when people are having hard times, it's often difficult for people to know how to discuss it, have conversations around it.

Jennifer Cohen

I agree. Have you processed the experience enough to think about positive aspects? You've already talked so beautifully about your resiliency and your approach to this and your positive aspect towards it. Are there other aspects of this that you feel that have helped you in some way?

Meryl Selig

Yeah, I don't want to run the risk of saying one cliché after another but I...I guess some clichés are based in truth. But I certainly learned especially after having to what looked like complete responses to previous treatment, right. That hey - nothing I do, I can control nothing. I can control my attitude, I can control my exercising and keeping a light spirit. And I can control how I react to things. So, but all the other stuff, you know things befall us, right. So yeah, I feel like I live that out - without sounding again, you know I don't want to sound sappy, but I really feel that it was a gift. I got a chance to start my life again in a way with a lot of self-awareness and more compassion and a lot more medical knowledge than I ever thought I'd ever have to require. So, here there were there were all kinds of things. And I became so involved with the medical team of every type at Stanford, whether it was the people who put, you know, lines in and Hickman catheters and different lines and the nursing staff, the imaging staff, nuclear medicine, all these people, plus the doctors, and physicians' assistants, and you know, NPS, nurses, you name it. I just have such an appreciation for what they do. So much respect for them. I can't even articulate that adequately. So, it's been great. I've got to meet all kinds of people I never would have met before. I got to have platinum blonde hair, which I after it fell out. I had it all bleached, which was super fun. Yeah. Yeah. I mean, yeah, there. If you look at it, that way, you get to start over, you get to write your slate, you know, clean your slate a little bit and redo yourself, get rid of the icky parts if you can.

Jennifer Cohen

That's terrific. So let me ask you now to put on your academics or policy, bioethics, hat on and talk about access.

CAR-T is new, it's incredibly expensive. The cost is estimated anywhere from \$300-400,000 to over a million dollars. If you add in all the hospital stays, it's been incredibly lucrative for Pharma. Yescarta was developed by Kite pharmaceuticals that was sold to Gilead for nearly \$12 billion. Have you thought about how CAR-T can be made more accessible? How it can be paid for? I don't believe all insurance companies covered it at this point.

But how can more people have access to these types of cutting-edge treatments?

Meryl Selig

Okay, so one thing I would say is that, as more CAR-Ts attain or receive FDA approval, and there are more options on the market - I think that having competition and having a wider, you know, more tools in the CAR-T or CAR-NK or whichever CAR in that toolkit will force competition. I guess I'm a free market person. Now that I just said this. And I mean, when I did Yescarta, there was no other choice. I would have had to go into a trial. I already described how that panel got shut down because the COVID. And so yeah, I really, really advocate for more and more immunotherapy and cancer cell therapy research. Just because of that, as it becomes more widespread, the price has to go down. I would hope. I'm on Medicare. So, although it's not free, I did not get the full impact of what - I'm sure it's in the millions. I seriously Jennifer, when I see other statements for just chemo that I've had and for, you know, having lines placed or scans, I'm sure it's in the millions, and it's not a good thing. I have hope that as CAR therapy becomes more widespread, that obviously there'll be more access now. I



can't envision it going out to community hospitals because of the level of specialty involved. Maybe someday that will happen. I hope so. But you know, the next 10 years, I can't see it going much beyond teaching hospitals, university, academic hospitals, and maybe some if there are well, places like MD Anderson, you know, cancer special Dana Farber, City of Hope those kinds of places, right. MSK in New York. They're all big cancer centers. And I know at Stanford when I was inpatient, there were some patients from the VA. And there were quite a few patients from Kaiser from an HMO. And so, it wasn't just Medicare people, and it wasn't just I can't even imagine paying out of pocket. I mean, it's some people could, but it would be millions of dollars.

Jennifer Cohen

And my last question, Meryl, where do you think your master's in bioethics will take you?

Meryl Selig

I'm really interested in helping people understand and kind of demystifying and getting better access, wider access to advanced directives. People need to understand what a proxy is, what a directive is. I think what we've gone through in the past year with COVID, where people for the most part did not have any plans preparatory, you know, being taken suddenly and being hospitalized and, indeed passing away. And I think it shouldn't be relegated to making those decisions when you're actually facing possible death. So, I had a very perfunctory advanced directive that I'd done with our estate lawyer and I redid it the day before I was admitted to Stanford last May, because I really thought through it. You know, thanks to the program, by the way, I became much more informed about what I would want and wouldn't want and how to actually execute an effective proxy and a directive. I'd like to take that possibly back to Stanford because it's nearby and I pretty integrated there. And demystify it, as I said, work with patients, not just in cancer, not just palliative care patients, but patients all over, you know, counseling them, saying, "Hey, you know, you could be sending your child off to college, you really ought to think about it." it's not pleasant to think about, but it really should be thought about and people shouldn't be left to the devices of having things done to them that they wouldn't want. I feel super strongly about this.

Jennifer Cohen

Meryl Seelig, thank you so much for sharing your incredible story, your insights, your experience, and for all the people you are helping as well in your career, warmest wishes and best of luck to you in the future.

Meryl Selig

Thanks, Jennifer, for this was so much fun. Thank you very much.

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