Mayo Clinic Q&A - Dr. Yi LIn - Multiple myeloma

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SPEAKERS

Dr. Halena Gazelka, Dr. Yi Lin, Narrator

N **Narrator** 00:01

Coming up on Mayo Clinic Q&A: Multiple myeloma is a cancer of plasma cells. These plasma cells are found in the bone marrow and are an important part of the immune system making antibodies that recognize and attack germs. Having multiple myeloma affects the cells by producing abnormal proteins that can cause complications. Today we'll look at the treatment options of multiple myeloma and how the development of immunotherapy is helping control the disease.

D **Dr. Yi Lin** 00:30

We have some new agents that really help extend the amount of time that patients are able to live with multiple myeloma, and immunotherapy is really one of the major backbones, now our current treatment for multiple myeloma. The way immunotherapy works is we're trying to use the patient's own immune system, engage them or make them work stronger to fight off cancer.

D **Dr. Halena Gazelka** 01:03

Welcome everyone to Mayo Clinic Q&A. I'm Dr. Halena Gazelka. Multiple myeloma is a cancer that forms in blood cells called plasma cells. Healthy plasma cells help the body fight infections by making antibodies that recognize and attack germs. In multiple myeloma, cancerous plasma cells accumulate in the bone marrow and crowd out the healthy blood cells. Immunotherapy, which uses the body's immune system to fight cancer, is a standard treatment option for those with multiple myeloma. March is Myeloma Awareness Month. Here with us to discuss is Mayo Clinic hematologist, Dr. Yi Lin. Welcome to the program, Yi.

D **Dr. Yi Lin** 01:46

Thank you. Thank you so much for having me.

D Dr. Halena Gazelka 01:49

Well, it's delightful to have you here today. Thanks so much for being here. Let's start with the basics for our listeners. What is multiple myeloma?

D Dr. Yi Lin 01:57

I think you explained it really well. This is exactly how I would explain it to my patients. It is a cancer of a blood cell, a subgroup of white blood cells called plasma cells. They normally live in the bone marrow. We all have them, and each plasma cell amazingly for its whole life is only going to make one type of protein or immunoglobulin. And we have lots of them in the bone marrow. So, they make lots of different immunoglobulins to help us fight off things like infection. And for whatever reason, we think as part of the aging process, the wear and tear on the machineries, for some patients a group of these plasma cells that makes one type of protein, are no longer dying off when they should. And they're sticking around. They're growing in the bone marrow, sometimes outside the bone marrow as well. And they're making more of that type of protein that they're making. So, we call that a monoclonal or one clone, one type of immunoglobulin. A monoclonal process and the main treatment for it is to try to kill these plasma cells, or myeloma cells that are no longer dying off on their own.

D Dr. Halena Gazelka 03:22

So, then what is immunotherapy? So, immunotherapy is literally the new kid on the block, if you will. It has a huge role in the treatment of multiple myeloma. I am probably dating myself a little bit from when I was in medical school. At that time, the treatment for multiple myeloma was pretty much chemotherapy, what we think about as traditional chemotherapy and stem cell transplant. Those were the only options for a myeloma patient at that time. And so, since then we have some new agents that really help extend the amount of time that patients are able to live with multiple myeloma. And immunotherapy is really one of the major backbones, now our current treatment for multiple myeloma. And so, some of the recent ones, for example, includes the immunomodulatory drugs. And that was started out with the thalidomide, we now have a kind of a next generation called lenalidomide, pomalidomide. These are all pills you can take by mouth, and they are really used along the treatment journey for the patients from the time of initial diagnosis to subsequent progression or relapse. We also have since then monoclonal antibody treatments. So, these are again drugs that can be given IV that target certain markers that can show up on plasma cells, sometimes not exclusively on plasma cells but can be expressed on these plasma cells, including myeloma cells, and is trying to engage the patient's own other immune cells to help engage, and fight, and kill these plasma cells. So, there we have daratumumab, and isatuximab that targets CD38. That's just the name of the marker that's on these white blood cells. And we also have elotuzumab that targets a different marker called CS1, that can also be seen on plasma cells. And again, these drugs are often given in combination the antibodies, along with another class of drug called proteasome inhibitors. And these can be considered the main backbone of myeloma treatments. So Yi, how do you as a hematologist decide which of the immunotherapies to use for a certain patient?

D Dr. Yi Lin 06:05

So, for these types of drugs we really are using them from initial diagnosis and to subsequent relapse. We think there is value in using three, even four drug combinations to try to induce response. Now, of course, these are conducting clinical trials. So, there is some sequencing to it in terms of the likelihood of response. There is a little bit as well in terms of potential side-effects and what patients are able to tolerate. And so, there is a somewhat, if you will, a rational sequencing of these drugs. Now, in general the way that clinical trials are being done to investigate a new treatment modality is that we want to make sure patients have gone through known treatment that we know how well it would work before we consider something more investigational. So, usually a new treatment will be first approved by FDA in later lines of treatment, and then be allowed to study in earlier and earlier lines of therapy including upfront. One of the arguments for immunotherapy is because the way immunotherapy works is we're trying to use the patient's own immune system, engage them, or make them work stronger to fight off cancer from a biologic standpoint these drugs may potentially work better earlier before the immune system may get too beat up by chemotherapies and other types of drugs. And so, there's a lot of research about, you know, how we can try to make sure we're most efficiently testing the use of drugs in the most rational settings. So, in that context we also have just in the last few years some very exciting new advances as well for treatment for multiple myeloma. We have really, completely new modalities of treatment that is FDA approved. So, just last year we had the first CAR-T that's FDA approved to treat multiple myeloma.

D Dr. Halena Gazelka 08:31

What in the world is that Yi?

D Dr. Yi Lin 08:34

So, CAR-T is a chimeric antigen receptor. T cell therapy in the current FDA approved form, is taking the patient's own T cells. So, there is a different type of white blood cells. Often, they will be circulating in the blood streams already, so we can take them from the patient's blood. And we'll be taking them to a lab and genetically changing those T cells so they express a combination called chimeric, an artificial receptor that they would normally not express that really empowers that T cell to be able to recognize better a marker that's on these plasma cells or myeloma cells and becomes more automatically activated to kill these myeloma cells when it recognizes those receptors. So, that's conceptually how CAR-T cells work.

D Dr. Halena Gazelka 09:39

That's fascinating. It's totally like science fiction. Sometimes I try to explain it like, and I have a son so to put that in context I explain to patient it's like Robo cops, you know your T cell, their normal job is to try to help things like infection, like cancer cells, but by the time we find myeloma cells in the body, it means that the myeloma cells have figured out ways to try to outsmart the T cells, have figured out ways to live despite having T cells around, their own T cells aren't able to kill the myeloma cells as well. And so, we're trying to in the lab genetically modifying these T cells to be stronger and be able to recognize them better and fight them

better. So, it's a little bit like, you know, super cop, super Robocop. Now, I'm gonna date myself, because what it makes me think about is Pac-Man games from my childhood. Yi, are there some patients for whom immunotherapy is not an option?

D Dr. Yi Lin 10:42

So, generally, we do think, for example, the monoclonal antibodies that I have talked about, we do try to use them in most settings for our patients. You know, I think as long as they are well enough, strong enough to get some type of treatment, there will be some role to use these drugs. It's a matter of, you know, what combination, what dosing, what frequency to balance the treatment for myeloma and the side-effects. CAR-T is a little different from a patient experience, patient journey perspective it's more complex. In some ways, it mirrors stem cell transplant even though the technology, you know, treatment, there are aspects that are different. But it mirrors that in the sense that CAR-T is not available at all oncology/hematology practices right now, because of the logistics and the specialized expertise that is needed to give the treatment, to monitor and manage the side-effects, particularly the immediate sid-effects in the first month of the cells being very active and trying to kill the myeloma cells. Those are only available at specialized treatment centers. So, there is somewhere a little over 100 treatment centers in the U.S. that are accredited and certified to give these treatments. So, the patient has to be able to travel to those centers in order to get the treatment. The patient does need to be healthier in some aspect to be able to withstand some of the side-effects, if you will, off the CAR-T treatment. So, there's a lot of evaluation and assessment involved to find which patient could benefit from the treatment. So, there are some limitations in, you know, who might be able to get CAR-T therapy.

D Dr. Halena Gazelka 12:50

If I could ask, do you do virtual consultations for patients? Or do they typically come here for a consultation to be considered for therapy?

D Dr. Yi Lin 13:00

Yeah, so to know for sure if a patient can definitively go on to get the treatment that will require an onsite face-to-face visit and not only with one of the myeloma specialists who are trained to give CAR-T therapy, but with a number of other specialists including neurologists, cardiologists, sometimes infectious disease doctors to really evaluate the patient, right as a whole person to make sure we are comprehensively assessing all potential risks. However, during the COVID pandemic era, given that we have to balance the risk of, you know, travel and potential exposures, I really think, you know, that became an opportunity for us to see how we can advance telemedicine virtual visits to be able to help more patients, right. And so, we do offer right now the initial virtual visit for patients where we're not 100% sure if that is the right fit, or there's a little bit more complexity to the patient's prior medical history, treatment history. And so, that virtual visit is helpful. It's a two way-street, right for the patients to think already ahead of time before they come to Mayo Clinic or one of the treatment centers to understand what's involved and think through how they can coordinate some of those aspects of their care, and for the providers to already have some a better grasp of the patient's situation and be able to pre-schedule certain things so that when they do arrive at the

treatment center, it's a more streamlined visit. So, we are finding that having a virtual visit in some situations can be very helpful to facilitate that. And occasionally, it may be at the virtual visit we may identify the patient may not be the best candidate for the treatment, save them a visit, and offer some recommendations for treatment that, you know, they can get at home.

D Dr. Halena Gazelka 15:14

Thinking about immunotherapies Yi, what is Mayo Clinic's approach to the use of these therapies in treating multiple myeloma?

D Dr. Yi Lin 15:23

So, this is a very fast-moving field, right? And what we're always trying to strive toward is, can we find a cure, you know. Can we confidently say a cure, and in myeloma it's been challenging. I think we have treatments that are demonstrating longer and longer periods of remission, where we can't find multiple myeloma by the available clinical test in their bone marrow, in the blood, in the body, you know, which is great. But we're still a little bit like, wow, you know, this may still come back. And we need to watch, we need to see you know, what additional treatment we may have. And what we always want to strive towards is the treatment that we think can offer the longest period of remission, but balancing that with side-effects that, you know, can be reversible, can be manageable, because we want to keep the patient's not only living as long as they can with multiple myeloma, hopefully with, you know, a lot of this the myeloma free period. But also, it's important, it's quality of life, right. If right now we don't have a treatment where we can guarantee that the myeloma will never come back, we want to make sure that the time they have are the time that they can do what they want with their life, you know, the activities that are important to them. And so, it's recognizing a potential side-effect, it's very, very achieved through part of that. Now, we are also a CAR-T Treatment Center. We are a transplant center. And so, you know, I personally do believe in the powers of these technologies. And I think we're just beginning to see, you know, what CAR-T can do. There's a lot of clinical trials, innovations in research, and to try to advance this technology. And so, whenever a patient that we think is fit enough to potentially get CAR-T, it is something that we would preferentially consider, because this is the only treatment right now that we have in multiple myeloma. That is, the way that is approved by FDA is a one-time treatment. We give them the cells as a one-time infusion, and if they are in response, we give no other treatment. We just monitor. There is no maintenance therapy. There's no other drug that's given as long as they are in response from CAR-T. Everything else that I just talked about, whether it's chemotherapy, the antibodies, those are given continuously in some fashion until the patient's progress. And so, I have personally heard from patients, you know, who did respond to CAR-T treatment tell me this is the best they have felt. They're now remembering what it's like before they were diagnosed with myeloma. And so, that quality of life, right, it's not trivial. Sometimes the patients get nervous because, you know, CAR-T right now is offered as in the relapse setting after they've already had at least four lines of treatment. So, up until then they we're used to, okay, you know, every week I may need to come into a chemotherapy unit. Every month I need to see my doctor. And once we tell them, You're good, we'll see you in three months just for testing, there's no treatment we're giving you, there a little bit like, oh, my gosh, what would I do with my time? I can go to my lake cabin, and that's a great thing to see. And that's, you know, not trivial, I think, in terms of the benefit that this treatment could offer.

D Dr. Halena Gazelka 19:24

That is very exciting. I'm wondering is Mayo Clinic conducting clinical trials of immunotherapies and multiple myeloma and other research?

D Dr. Yi Lin 19:36

Absolutely. You know, we really do believe clinical trial is what is needed to advance right, the treatment options we have for our patients. So, in addition to the FDA approved treatment that needs to be given at specialized centers that we offer, we do have clinical trials in CAR-T, bispecific antibody, which I'll touch on next as the next new treatment modality that we are very excited, awaiting FDA review later this year. But also, you know, now there's kind of new generations of antibody therapies, novel combination therapies, targeted therapies. We do think, and oftentimes, you know, once the patients have gone through these approved treatments, it's the clinical trials are, you know, what may potentially offer them additional response, right, additional time that they may have with their family and loved ones. So, we are definitely very excited to be able to offer a lot of these novel clinical trials to our patients. And so, what I was alluding to next was, there is another new class of treatment that we've been offering clinical trials to our patients. And we are anticipating the first drug of this kind will be reviewed by FDA for potentially as an approved treatment later this year. And that's called bispecific antibody. So, what I mentioned earlier, we have the monoclonal antibody, the daratumumab, isatuximab, elotuzumab, those are an antibody that just target one marker. In the bispecific, bi, two, is exactly as the name implies, is targeting two markers. So, one of the markers, it targets would be a marker that's on a myeloma cell. And then the other target is on a T cell. That's the most common one that's being studied. There trispecifics, three targets in clinical trial testing that try and engage T cells, sometimes T cells and NK cells. So, these are all white blood cells that can potentially kill, right, myeloma cells. And so, CAR-T is we try to take the patient's own T cells out of their body, do the genetic engineering to make the T cells work stronger, and then put it back in the patient. You can imagine that manufacturing time, that genetic modification time, that on average takes about a month. And so, not all patients can wait a month to get their own genetically engineered T cells back, right. And so, the bispecific antibody is again, it's an off-the-shelf drug. So, it's trying to say, hey, you know, maybe in some patients, their T cells are gonna work well enough without having to do the genetic engineering, can we simply use this drug to bring a T cell, the patient's own T cells that's already in their body, we're not doing any fancy genetic engineering, we're just trying to bring the T cell closer to the myeloma cells with this bispecific antibody. So, it is still more like all the other drugs we have on myeloma, it can be given IV, or as an injection under the skin. There's been a lot of technology advances to enable us to give it once a week, or once every two weeks, once every three weeks, depending on, you know, which drug that's in testing. It does need to be given kind of continuously until it stops working. But the advantage to that is, you know, there's no wait time for your patients. There's also no need to give chemotherapy to prepare the patients to receive the cells. And so, for some patients, that may be a very good choice, and we are seeing some very exciting clinical responses in clinical trials. So, you know, I think this may be an approved treatment in the very close future for our patients as well.

D Dr. Halena Gazelka 23:51

What fascinating information. Thank you for being here to share this, Yi.

D Dr. Yi Lin 23:56

Absolutely. I'm very excited to just even in my time, right, and I don't have as many gray hairs as many of my colleagues, you know, grew but just to see even in, you know, my time on staff at Mayo that we have so many new options for our patients and very, very honored to be part of the myeloma group to continue to do these clinical trials and hopefully offer even more treatments for our patients in the future.

D Dr. Halena Gazelka 24:28

We are so grateful for the work that you're doing.

D Dr. Yi Lin 24:31

Thank you so much.

D Dr. Halena Gazelka 24:33

Our thanks to Dr. Yi Lin, hematologist at Mayo Clinic for being here with us to discuss therapies for multiple myeloma. March is Myeloma Awareness Month. And I hope that you learned something today. I know that I did. We wish you each a wonderful day.

N Narrator 24:51

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