Bringing CAR T Cell Therapy to the Bloodless Medicine Community-Transcript

Melanie Cole, MS (Host): Welcome to the podcast series from the specialists at Penn Medicine. I'm Melanie Cole and joining me today is Dr. Patricia Ford. She's the Director of the Cellular Therapy and Transplant Program at Pennsylvania Hospital at Penn Medicine, and she's here to highlight bloodless CAR-T therapy for us today.

Before we begin, I'd like to mention that the Bloodless Medicine Program at Penn Medicine can be reached directly by calling 215-829-6280 or via fax at 215-893-6799.

Dr. Ford, welcome back. And we've discussed bloodless medicine previously, you and I, but could you briefly review the field and its history just a little bit for us?

Patricia Ford, MD: Yes, and thank you for the opportunity to speak on this area in cellular therapeutics. So bloodless really is a terminology for individuals who decline blood transfusion support for whatever reason. So, it really is any opportunity where you can provide a surgery or strategies without the support of blood products, which usually includes packed red blood cells and platelets. And about 90 percent of our patients in our Transfusion Free Medicine or Bloodless Center are Jehovah's Witnesses who decline transfusions based on religious convictions, but about 10 percent of patients also want to have the same strategies available provided without transfusion support.

Host: Well, thank you for that. So today we're talking about bloodless CAR-T therapy, which involves the removal and reinfusion of lymphocytes that have been modified to produce chimeric antigen receptors. Give us a little brief overview of what bloodless CAR-T therapy is and how it differs from traditional CAR-T therapy.

Patricia Ford, MD: For our patients who qualify for this, and this is a new kind of immunotherapy where we take the patient's own T cells, a form of lymphocytes, and they're genetically engineered in a laboratory specific for whatever hematologic malignancy we're addressing.

And that can be leukemia, the lymphomas, multiple myeloma, and now there even are some studies looking at CAR-T in solid tumors. Once the cells are genetically engineered, they're then transfused back into the patient.

So, of course, the advantage is these genetically engineered cells will cause significant tumor response, but also they can cause some pretty significant toxicity, so patients do remain in the area. Now this is a therapy like autotransplant and allotransplant that is not routinely offered to patients without blood product support, so we are opening up our CAR-T here in hopes of being able to accommodate the same type of patients that we performed a bloodless autotransplant on that now require CAR-T.

Host: Fascinating, and before we discuss procedures involved in bloodless CAR-T, I'd like you to speak about the indications for CAR-T in the bloodless population. How do you assess and select patients for this advanced treatment approach?

Patricia Ford, MD: We use the same selection criteria for whatever indication that you would normally select CAR-T consideration, So, that would include things such as refractory non-Hodgkin lymphoma or relapsed non-Hodgkin lymphoma.

Those who have follicular or low-grade lymphoma, after they've failed two or three lines of therapy would be appropriate candidates to try to screen. And then it's also for patients who have either refractory multiple myeloma or have been through prior multiple lines of therapy and are still fit enough to undergo additional treatment.

Host: So, Dr. Ford, the Jehovah's Witnesses have a great issue with blood transfusions, as you've mentioned, but reports suggest that the decision to accept blood components and stem cells is left up to the individuals. And stem cells are not considered a blood product because they originate in the bone marrow. Has this been your experience or does bloodless CAR-T work in the absence of reinfusion?

Patricia Ford, MD: You're absolutely right with Jehovah Witnesses, the larger population that we offer this to and trying to be very respectful of their religious convictions and abide by that. In general, Jehovah's Witnesses will not allow blood; and they define the word blood a little differently than us medical providers do. So, they define the word blood as having four major components; packed red blood cells, platelets, plasma, and white blood cells.

Any other product that is a fraction of those components, the patient can make an individual decision to take, but it is allowed within their religion. So that also includes genetically engineered T cells. Just like it also included stem cells that we use in auto and allogeneic transplant.

We take our lead from the elders in the Jehovah Witness population who have looked at the new techniques. We actually have met with the Watchtower, which is where their leaders and elders interpret new strategies to see if it would be acceptable within their religious belief system to accept.

I went to the Watchtower about two years ago when CAR-T was coming to the forefront, reviewed all parts of the process, all the different cellular components, and they made a decision that this would be acceptable for a Jehovah Witness to undergo.

Host: So, Dr. Ford, CAR-T therapy is associated with a number of risks as we've discussed, including anemia and thrombocytopenia and cytokine release syndrome. What are some of the greatest risks to the bloodless population with regard to CAR-T therapy?

Patricia Ford, MD: Right. So, for CAR-T, there are two major risks that you look for. So the cytokine release syndrome, we know that we have to educate, identify, and treat patients appropriately and quickly with one of the agents such as tocilizumab, which can be very helpful.

There could be some significant neurologic effects, so another reason the patients have to be closely monitored for at least one month, so that there also can be interventions done there. So that doesn't differ in the patient who does or does not accept transfusion. But what does, is the cytopenias that may occur with CAR-T, and they could be fairly prolonged.

Host: When we last spoke, you mentioned the approaches and techniques undertaken in bloodless medicine that reinforce a patient's blood cell count and encourage hemostasis. Are similar procedures used in bloodless CAR-T?

Patricia Ford, MD: So, we do use similar strategies that we also incorporate for the transplant population. For instance, if the patient's experiencing significant anemia, of course, we'd want to do a basic workup to see if anything there is treatable.

For the anemia, it is growth factor support and minimizing any kind of iatrogenic blood losses from repeated phlebotomies, certainly performing phlebotomies when they're needed, but trying to minimize. If the blood cell line is the platelets and you're dealing with a very prolonged thrombocytopenia, we know the biggest risk occurs for spontaneous hemorrhage when patients have platelet counts under 10,000, so we're very aggressive with using alternatives to enhance hemostasis, and the alternatives we use that have been very effective have really incorporated antifibrinolytics, so drugs that enhance clotting and prevent the breakdown of any clots that are forming.

We use a lot of aminocaproic acid and tranexamic acid in this population. And when we looked at our 200 transplant patients where we've used this, we have not seen any significant increase in thrombotic complication. Most of what we saw were catheter related clots that were easily managed.

And then, of course, we also are very liberal with vitamin K, which is the important vitamin there to help with the coagulation cascade and clotting. So, to prevent bleeding, when we cannot transfuse; platelets, very aggressive with platelet counts under 10,000, with aminocaproic acid and vitamin K. And certainly, even if it's a 20 or a 30,000, we may have a decreased dose of those agents.

Once the platelet count's above 30,000, there is minimal risk of a spontaneous bleeding event. And it's at that time where we feel very comfortable allowing the patients to be, to travel back to their local oncologist and continue monitoring there.

Host: Dr. Ford, based on these many considerations you just mentioned, how important is collaboration between different medical specialty, specialties in the implementation of bloodless CAR-T? Can you elaborate on the role of that multidisciplinary team in optimizing patient outcomes?

Patricia Ford, MD: Yes, so I'm glad you mentioned this because it could not be more important to really have all of your consultants in the hospital very aware of this patient population, and I know this includes all the way from the emergency room where the emergency room is going to be taking care of a lot of our patients as the front line there.

We go through a large education and training process with them. With our intensive care unit providers, both physicians and nurses are educated and trained in all the alternatives that we use, and any consultants. We frequently will need the help of cardiologists when patients have low blood counts, hypotension, arrhythmias, a change in their chronic blood pressure and cardiac medications.

Certainly, for interventional radiology, they're putting in catheters and for any bleeding that may happen, we rely on them very heavily for identifying and embolization and also our gastroenterology consultants. All the providers here at our hospital, all of our physicians are very aware and respectful of Jehovah Witnesses belief system.

And having done this for 20 years with about a thousand patients a year, not in CAR-T, but in other scenarios where they've had to address bleeding, anemia, thrombocytopenia, similar situations, they've also developed an expertise.

Host: Dr. Ford, bloodless CAR-T is only the latest advance from the Bloodless Medicine Program at Penn Medicine, a program that began under your leadership more than 20 years ago with bloodless surgery. What are some of the other innovations that have been introduced in the years since by the Bloodless Medicine Program at Penn? Tell us about any ongoing research efforts, things that are really exciting you.

Patricia Ford, MD: I agree, there's a lot more that's being done just in treating anemia in general that I'm real excited about in terms of research. Right now our basic tools that we use are growth factors to stimulate red cell production and intravenous iron. But we're learning so much more about anemia as it relates to malignancy and chemotherapy.

The identification of hepcidin released from the liver is an important iron regulator. So I know that we also are looking at new agents to actually help anemia, looking at that pathway with it. The hepcidin in the HIF pathway. So very exciting treatments, I think, upcoming in the treatment of anemia in general, that will be helpful.

Also, just in terms of other groups within our entire health system, I've been working recently with the kidney transplant team here who are now willing to evaluate and offer kidney transplants to Jehovah's Witnesses and others declining transfusion. So that is very exciting to have that new collaboration also and open up this area here within our health system for those patients with chronic kidney disease or dialysis who may need a transplant.

Host: What an informative episode this is, and Dr. Ford, as we wrap up here, should someone have an interest in bloodless CAR-T, how might they contact the Bloodless Program at Penn Medicine and summarize anything you'd like as key takeaways from this episode today.

Patricia Ford, MD: Yep, so I think the way to contact us would be through the Transfusion Free Medicine program. They are coordinators who work within my team. There's also a direct number that can be utilized to my office. My office is at 215-829-6088 number, and these can be easily found also on the Penn Medicine website through Transfusion Free Medicine.

And I think to wrap up, one thing I do just want to highlight is with all the new advances in oncology and all the new exciting treatment and opportunities we have, I want to highlight the fact we try to treat Jehovah's Witnesses with the standard of therapy, the new and promising agents, just like we would anybody else, and with good alternatives, the majority of the time that is quite successful in offering them standard and new treatments.

Host: Thank you so much, Dr. Ford, for joining us today and sharing your incredible expertise on this topic. To refer your patient to Dr. Ford at Penn Medicine, please call our 24-7 provider only line at 877-937-PENN, or you can submit your referral via our secure online referral form by visiting our website at pennmedicine.org/refer-your-patient. That concludes this episode from the specialists at Penn Medicine. I'm Melanie Cole. Thanks so much for joining us today.