

THE BLOODLINE WITH LLS

A PODCAST FOR PATIENTS AND CAREGIVERS

Episode: 'Treating Acute Lymphoblastic Leukemia'

Description:

Join Alicia and Lizette as they speak with Dr. Mohammad Maher Abdul-Hay, a hematologist and bone marrow transplant physician in New York, New York who is affiliated with multiple hospitals including NYC Health and Hospitals, Bellevue, and NYU Langone Hospitals. On this episode, Dr. Abdul-Hay explains how ALL is treated and addresses pre-treatment considerations. He also shares the long-term effects of treatment and the importance of getting a second opinion and open communication between a patient and their healthcare team.

Transcript:

Alicia: Welcome to The Bloodline with LLS. I am Alicia.

Lizette: And I am Lizette. Thank you so much for joining us on this episode.

Alicia: Today, we will be speaking with Dr. Mohammad Maher Abdul-Hay, who is a hematologist and bone marrow transplant physician in New York, New York and is affiliated with multiple hospitals including NYC Health and Hospitals, Bellevue, and NYU Langone Hospitals. We encourage you to listen to our other episode with Dr. Abdul-Hay where we spoke about symptoms, risk factors and diagnosis of acute lymphoblastic leukemia, known as ALL. Thank you much for joining us again Dr. Abdul-Hay.

Dr. Abdul-Hay: Thank you very much for having me.

Alicia: On this episode, we are going to chat about the treatment of ALL and current and emerging therapies, but before we jump into that, what is ALL?

Dr. Abdul-Hay: So, ALL is acute lymphoblastic leukemia. It's a malignant transformation and proliferation of lymphoid progenitor cells in the bone marrow and the blood and sometimes it has extramedullary presentation, like it can go to CNS. So, lymphoid progenitor cells are a type of white blood cells. They misbehave. They start to increase production and they take over the rest of the white blood cells. It's usually a disease of the young, actually, 80% of ALL is in children. Unfortunately, when it presents in the elderly or older people than children, it can become a devastating disease because, the treatment becomes more challenging and, at times, less

effective. In the USA, there's about 6,500 cases a year of ALL diagnosed, 80% in children, but there's also, another peak, around the age of 50.

Alicia: What are some pre-treatment considerations?

Dr. Abdul-Hay: All this chemotherapy, most of the time, leads to infertility so what happens is, early on when someone is at the child-bearing age, we need to have a discussion, either for sperm donation or even for egg preservation if we do have the time to do that. Unfortunately, a lot of times, they present, they are in a very aggressive form; we do not have the luxury to wait, but if we do, yes. And that's actually the first discussion we have with the patient before we start treatment.

Alicia: That's so great to hear because, you know, last week Lizette and I we were actually filming a young adult video, and the young adults, they were diagnosed with and we were talking to them and many of them said that, you know, when they started treatment either the issue of fertility never came up with the doctor or the doctor just said, you know, from the beginning, you will never be able to have children. And, thank God, that ended up not being the case but how important is it for the patient to ask these questions.

Dr. Abdul-Hay: It is very important. They should do that in any type of cancer when they get in chemotherapy, they should ask about that. We bring it up the first visit; actually, the first time we diagnose them and we have ways. As I said, in men, it's easier because sperm donation, we can do that in the hospital. We can actually arrange for them in the clinic, all of that, but when it becomes to--for female, it becomes harder because then egg preservation, all of that, but however, there's a lot of times we try to, —not doing like egg preservation—like doing some treatment to try to decrease the toxicity on the ovaries, like giving them some growth factor inhibitors or trying to shut down their period, their cycles, all of this. And we do that routinely so, at the moment of their diagnosis, this is the discussion we have with them and we do tell them that, even with all this, modalities that we are going to do, there's still a chance, unfortunately, of them being infertile.

Lizette: I'm glad that you bring it up, though, because, a lot of times, you don't know what to ask. You don't know to ask about fertility. You can't ask what you don't know...

Dr. Abdul-Hay: It's true.

Lizette: ...so it's very important what you are doing which is bringing it up.

Dr. Abdul-Hay: A cancer patient should understand that life doesn't stop there. They should continue their life as they have planned to, and they should bring up the things they have in mind; their plans, their future, all of this so they should not just life

stop there and just start to get over, they should plan ahead. And I think when they do plan ahead, it gives them a peace of mind as well.

Lizette: Sure; it gives you, you know, some of that control that you lose when you hear that you have a cancer diagnosis. Like you said, you feel like, you know, there is no more and it is so refreshing for you to tell everyone, as a specialist, that there is life after diagnosis. That's very important.

Dr. Abdul-Hay: That's true. When we do get a consent for them to get chemotherapy, in the consent of the chemotherapy, we do actually mention every side effect including infertility. So, they are notified from the beginning and it's very important they know what to expect from side effects, not just for their own health benefit, but also to plan the next step in their life and, also, because there is a trust. If I tell the patient, "oh, you're going to get chemo, nothing can happen to you" and then something happened and this trust is gone. And once the trust is gone, it is never restored.

Alicia: It's so true. You mentioned chemotherapy, of course, as treatment. What are other treatments for ALL?

Dr. Abdul-Hay: So, the key is really the age. So, if someone is young, meaning they are like, say, adult young adolescents up to the age of 38/39, they are going to get a pediatric-inspired regimen; and usually this pediatric-inspired regimen, it consists of induction, followed by consolidation, intensification maintenance, and then if they need to go for transplant. That induction, usually, and consolidation involve a drug called Peg-Asparaginase. That drug, the elderly cannot tolerate so, someone over the age of 60, I never really use it.

So, then another combination comes in if someone is above the age of 40 and not in great shape, or above the age of 60, then they get another induction regimen. However, in this era, we have more what we call targeted therapy. So, two of the targeted therapies that been approved for ALL, they are not approved for, really, first line. They are for more refractory relapse or second line or if people have, what we call, minimal residual disease. So, the most important aspect in treating ALL is to make sure they do not have minimal residual disease. What does minimal residual disease mean? It's that when they have induction, after induction, they get a bone marrow aspirate. If they have down (10 to the power minus 4) left over, that means they have minimal residual disease. If this minimal residual disease is left on, it is going to come back because this is what is resistance for your treatment so you know you left, like, some troops. They are going to gather themselves and they are going to grow, and grow, and grow and then they are going to come back; and they usually come back with vengeance because this their resistance for chemotherapy. So, if someone has minimal residual disease or they have disease after chemotherapy

because the first line of treatment, in most cases, is chemotherapy and then they got targeted therapy.

And targeted therapy that have been approved for ALL, there are two and they are actually very cool. The way they work is this. One of them is called blinatumomab. It actually gathers your own immunity to go and fight the leukemic cells. So, what it does, it's a bispecific molecule. It takes your T-cells, which is CD3+ and attach them to B-cells, which are CD19+ and, basically, your own T-cells go after your B-cells and destroy them. So, this is a very cool way to destroy your own leukemia because think about it? Your immunity system should have seen that these cells are not normal and they should have gone after them to destroy them, but somehow these cancer cells are clever. They find a way to protect themselves so that the immunity system cannot see them. So, when you introduce BiTE-- bispecific therapy, CD3 attached to CD19, they go and your T-cells destroy your B-cells. This is used as a second line, or refractory relapse, or people that have not gone into remission after chemotherapy and still have some minimal residual disease; and it is very effective. And it's even superior to second line chemotherapy.

And then another drug is called inotuzumab which is a monoclonal antibody that targets CD22. So, because these B-cells in ALL, they express CD22 so there's a monoclonal antibody now that goes after it and destroys it and the toxicity is limited because, you know, it is an antibody. It's not like a chemotherapy that destroys everything including good and bad cells. This is a targeted therapy. They have a down side, each one of them. They have some other complications than chemotherapy or side effects, but they are resounding as the future.

Lizette: Being a targeted therapy, would it have less side effects than a chemotherapy regimen?

Dr. Abdul-Hay: Definitely. However, because, you know, when you lose that immunity, that immunity can get hyper and what happened with blinatumomab, that one that takes a CD3 to fight a CD19, you can end up having what we call cytokine release syndrome, meaning that there's so much hyper-immunity, you can get fevers with it. You can get low blood pressure. All of this. It's fixable with steroids and it doesn't happen always.

The other medication, the targeted therapy, the inotuzumab it has one side effect on long term; not on initially. So, if people get inotuzumab, , and then they end up going for tests then, they have about a 11% chance of developing a disease called veno-occlusive disease, which is really a complication of post-transplant because they got this targeted therapy; and veno-occlusive disease can be, , deadly so, unfortunately, they don't come without a price. The cytokine release syndrome in one of them is usually very, very, very well managed. The veno-occlusive disease is 11% risk, but again, in some cases, it is also manageable. So, the toxicity profile is completely

different than your nausea, vomiting, hair loss, decreased white blood cell count, neutropenia that you see with your chemotherapy. There are some chemo that can affect the heart. This is completely different. The toxicity, the side effects are completely different. They are usually well-managed.

Alicia: Right; and you spoke about the cancer cells being clever and it is interesting that you said that because, I was talking to another doctor who compared, you know, finding out the right treatment to a Rubik's cube. And he was saying, you know, how the treatment is there and there is a lot of advancement, but these cancer cells are so clever that it has gotten to a point where patients are saying, "you know what, what is taking so long basically and why didn't you guys catch this earlier?" They have all these questions, but it's the understanding that these cancer cells are so clever and go under the radar.

Dr. Abdul-Hay: That's true; because if you take a look at, say, adult ALL, unfortunately, with chemotherapy, induction chemotherapy, you have a response rate sometimes, I don't know, 50% so why the other 50% not responding. And this is because you are attacking these cancer cells and destroying them with chemotherapy, but there are some of them, they have found a mechanism, a way, to make this treatment ineffective so they are still there; they are not dying. And what happened is they start grouping themselves and they will start growing and then—they take over. And this is why multimodality treatment is sometimes the key when you start adding—mixing a, say, monoclonal antibody, a targeted therapy with chemotherapy, you are like attacking the disease from multiple aspects and that is why you have a better success. So, in this era, we are actually—there are a lot of clinical trials testing the monoclonal antibodies. They are testing the BITE as a first line, especially in the elderly as a combination between each other or, actually, as a combination with chemotherapy. And the data we have so far and the results are actually very, very promising. It is even better what we have, as of now, just by chemotherapy. So, you just need to attack from multiple places.

Alicia: Right; and I am happy you mentioned clinical trials because that is also something that LLS, you know, we strive to educate our patients and our caregivers on is that, a lot of people hear that word and I think the ideology behind it, may be shifting. I am not sure entirely, but I know that when I first started here at LLS, there was always a conversation of, patients hearing that word and thinking "guinea pig", or "sugar pill", and clinical trials, they advance science and they're what are able to present the next standard treatment because of those who participated in that. So, for those listening, what's new in acute lymphoblastic leukemia research?

Dr. Abdul-Hay: So, there's a lot actually going on in ALL. Unfortunately, most of what's going on in ALL is in B-ALL more than T-ALL. The majority of the ALL is B-ALL. So, I mentioned in the first episode that there's, what we call, Philadelphia-like and Philadelphia-like is completely different than a Philadelphia chromosome-positive

patient with ALL. So, in an ALL patient Philadelphia chromosome, they get a second-generation pro kinase inhibitor, like dasatinib, and they have a very good outcome. So, what are the Philadelphia-like? And this is what is going on in clinical trials and we are seeing, actually, a response, but that's not the standard of care, but this is because people are not good about staying in clinical trials; and we find that people that have Philadelphia-like, the CRLF2, if you add the drug, which is actually up there, approved, which is a JAK inhibitor, called tofacitinib. If you add it, you can target that pathway, that is Philadelphia-like and you have a better outcome. And then then the other Philadelphia-like, which is a CDKL2A and, if you add dasatinib, which is the TKI inhibitor we used in CML, another type of leukemia, chronic leukemia, you can actually attack it and you have a better outcome. So, this is what is going on in clinical trial in Philadelphia-like.

What's also going on is other drugs that have been approved for other types of cancers like Bortezomib, which has been approved in multiple myeloma. It's being tested in ALL. and then there's another drug that we know actually has a lot of efficacy from before in T-ALL. It's called nelarabine. It's a purine analogue that we are noticing now if you put it up front with chemotherapy, you can have a better outcome. But what's most exciting in ALL is CAR T-cell.

And CAR doesn't mean that's the car you drive, it's actually different. It's chimeric antigen receptor T-cells. And these are, genetically modified T-cells that we obtain from patients. So, we obtain your own T-cells, which are your own immunity, and we modify them, genetically, in the lab and then we give them back to the patient to expand in the patient and they go after their leukemia and destroy it. So, how do we do that? So, we collect the T-cells, by apheresis machine. They sit on the machine. They collect the T-cells and then we take their T-cells to the lab. And what we do in the lab with a retrovirus, we infect these T-cells to express on their surface a modality that can identify the leukemic cells and go after them and destroy them. In the case of ALL, they express CD19 receptors. So now, when we put back these T-cells in the human, in the patient with ALL, they are going to go and see every cell that expresses CD19. They are going to go after it and destroy it. And to make sure that only these T-cells are present in the patient, we do, what we call, lymphodepletion for the patient before we do that. So, what we do is we give them chemotherapy made of two drugs, fludarabine and Cytoxan that destroy all your T-cells. So, basically, you have no more T-cells. And then, in the lab, we have generated these T-cells from you that are going to go after your leukemia. And then we re-introduce them to the patient and now these T-cells expand, and they take over, and now all your T-cells are armed to go after CD19, to go after your leukemia.

Alicia: And what are some side effects of CAR T-cell therapy?

Dr. Abdul-Hay: So, two things that we worry about in CAR T-cell: Cytokine release syndrome, which is much more real than the BITE that I mentioned and much more

higher grade. There's about 5 grades in CAR—in cytokine release syndrome--grade 4, which is sometimes get up to 20% of these cases.

People can end up being on a respirator because it's the cytokine release syndrome is so severe and they can have hypotension. They can have continuous fevers. There's medication that blocks the cytokine release syndrome. It's called tocilizumab. It's an interleukin 6 inhibitor that we try to give then to patients when they start having fevers and low blood pressure. And, a lot of times, we can also use steroids that can actually get rid of the cytokine release syndrome. So, that's one of the aspects that we worry about in CAR T cells, the cytokine release syndrome.

The other is CRES, which is basically cytokine release encephalopathy. It can cause encephalopathy. It can cause neural toxicity. Again, steroids usually are very effective in that aspect, but we need to monitor the patient. Actually, they get to be asked a set of questions called CARTOX. This is CARTOX and stands for CAR T-cells toxicity and the question is made of 10 points. Every day, we ask them to see if they are having any toxicity. One of the questions actually would be to write a sentence for us; what's the date today; what's the name of the President and, a lot of times, that question, what's the name of the President, some of the patients will not answer for us.

We don't know if it is the toxicity or is it because of some political statement that they are trying to make it. But, actually, I think we are going to change this question instead of what's the name of the President, maybe, what's the name of someone more famous, other than the President so...

Alicia: Right.

Dr. Abdul-Hay: ...so that's really...

Lizette: Well, it's good that people have a sense of humor.

Dr. Abdul-Hay: Yes; actually, I have a patient every day, he kept not answering this question and I, like, okay, "I'm worried." And, he refused to answer the question and so I changed it for him. I start asking him what's my name instead of the name of the President.

Alicia: There you go. Something less controversial.

Dr. Abdul-Hay: Correct. So, these are the two main things that we worry about. The cytokine release syndrome and the then encephalopathy and neural toxicity.

Alicia: And how easy is it, I guess, for an ALL patient to obtain CAR T-cell therapy? Do they have to be on a clinical trial to access this?

Dr. Abdul-Hay: So, unfortunately, as of now, the CAR T-cell that is approved for ALL—it's limited to the age of 25. So, if you are above the age of 25, you cannot get that commercial CAR T-cell. So, about the age of 25, they go on a clinical trial.

Alicia: Okay; that's good to know.

Dr. Abdul-Hay: Yes; it's very expensive and, so far, the FDA hasn't approved it above the age of 25. I have no doubt in my mind it has a role in the future and is going to be for people above the age of 25.

Alicia: Ahh; that was going to be my next question. I was going to say, where do you see CAR T-cell therapy going in the future?

Dr. Abdul-Hay: I think it's going to have a big role for patients in the refractory relapse setting. It could be a cure and the problem with CAR T-cell, you can lose the construct. With time, you can get back your other T-cells, you know, the T-cells that you have that doesn't have the armor and, basically, the leukemia can come back. So, in my mind, CAR T-cell—has a very big role and the big role is going to be in the future; possibly is that it is going to be used in the cases where you have refractory relapse. The chemotherapy is not going to work, you know, and this month-long antibody and this BITE is not going to work. So, this is where CAR T-cells are going to come in; going to put the patient into remission. It has a very high chance of putting them into remission and then they can go for transplant to make sure the disease stays there and they don't relapse afterwards.

Lizette: Yeah; that is what I was going to ask you if—because you do have the expertise in transplant because some people are looking to CAR T for cure and some people are really looking for CAR T as a bridge to transplant.

Dr. Abdul-Hay: True. I still at this moment, I still believe that it's going to be more of a bridge for transplant than a cure because, unless we have a better construct. I mean, we are in the fourth generation of CAR T-cell. We have many of them. They have done even better constructs. As of now, I don't believe that it's going to be a cure for most patients. It's going to be as a bridge for transplant.

And the good part is that you can monitor it. So, you know, you can monitor the construct so, when you start losing the construct, that doesn't mean you are already relapsed, that means you are going to relapse. So, this is a time, you know, you can get ready to go for a transplant. You are still in remission, but you just, you know, you are starting to lose a construct. You're starting to see some B-cells that you should not, then this is the time you start working on your transplant before you relapse.

Lizette: And we've mentioned cure and I just want to be clear to our listeners that there are several types of leukemia and there's chronic types and there's acute types. And usually, Doctor, for the acute types of leukemia, isn't the goal cure?

Dr. Abdul-Hay: Of course.

Lizette: Whereas the chronic types, is more to manage the disease?

Dr. Abdul-Hay: Correct. So, in acute, as in acute myeloid leukemia or acute lymphoid leukemia, the ALL or AML, you are not going to accept anything less than a cure. There's no here, what do you call, a partial response. You are either going to aim for a cure or the patients, you know, the disease can take over. It is different than your chronic, and when you are treating someone with ALL, you really should tell the patient and the patient aware of this and the physician aware of this that we are not going to accept anything less than a cure because, really, if you have minimal residual disease, even 0.0, 0.8%, this means that this 0.0, 8%(0.8%) is going to come back. This is not a cure. So, you know you want a cure. You want zero. You want complete remission. You want to make sure the disease doesn't come back.

Alicia: Thank you for clarifying that.

Dr. Abdul-Hay: Sure. My pleasure.

Lizette: And you mentioned that, for adults, it is a harder disease to treat whereas we do know that, for children with ALL, there is a pretty good prognosis at this point. Why is that?

Dr. Abdul-Hay: That's true. And that's why I mentioned that if we have someone what we call "adult young adolescents" up to the age of 39, we try to treat them with a pediatric-inspired regimen. The reason is that a pediatric-inspired regimen are really strong regimens. They have a drug called pegaspargase. They have other drugs that have even higher doses and that's because pediatric patients can tolerate these with low toxicity. Unfortunately, when you become an adult, when you get these drugs and you can end up having a lot of toxicities. A lot of these patients, an adult, cannot get the same treatment that they get in pediatric. They get a less—I don't want to say the word inferior—they get lower intensity chemotherapy and because of that reason, the outcome is worse.

And the second reason why the outcome is worse is because pediatric ALL is associated less frequent with genetic abnormalities compared to the adult ALL. The adult ALL, most of the time, I would say there are genetic abnormalities, and the poor one, and the bad risk and the bad players like Philadelphia are positive, Philadelphia-like, high 11q23 deletions and some other translocations that are, actually, poor risk

and these genetic abnormalities and translocations make your leukemia more resistant for treatment and chemotherapy.

Alicia: So, Doctor, what are some long-term effects of treatment?

Dr. Abdul-Hay: So, some long-term effects of treatment, depends about age. So, the younger you are, you know, you have been exposed to chemotherapy. It can increase your risk in the long-term to develop actually some changes in the marrow, which you call MDS, myelodysplastic syndrome. It can also lead for second malignancies, unfortunately, because, you know, you can live 40 years afterwards and you have already been attacked. Your cells have been attacked with some chemotherapy toxic so it can increase your risk of secondary malignancies.

Short term: The thing that we worry about is infertility. That is actually common with this toxic chemotherapy medications. And then some long-term effects, you know, if people get transplant, then we worry about—the most thing we worry about long-term is graft versus host disease, which is chronic GVHD that actually can develop at any time post allogeneic stem cell transplant. Usually, the chronic form presents after the hundred days and can sit there for years. It can be of a mild nature to a severe nature. It can produce a skin rash or something more serious. So, there is short-term and there is long-term. The short term is usually that the toxicities are very well manageable and they don't leave any long-term effect. The long-terms are, as I said, secondary malignancies, other hematologic malignancies and if you get transplant, the GVHD.

Lizette: Doctor, here we usually encourage patients, if they can, to get a second opinion. How do you feel about second opinions?

Dr. Abdul-Hay: I always tell my patients if you have any doubt, or if you want a peace of mind and you feel better talking to someone else, you should go after it. I highly encourage them to do that. So ALL, the treatment, say if a patient is just getting chemotherapy, the maintenance phase is two and two and a half years so you are going to develop a treatment relationship with a patient for three years. So, you want them to be really, truly believe that this is it. This is the person they trust. This is the one person they want to be with. This is a treatment. They are going to commit themselves for three years. They are committing themselves for three years so I do encourage them if they have, like, doubts or that they have concerns to go for a second opinion. I mean, this is a three-year relationship all in treatment, not to mention afterward for follow-up. And after they go home from transplant, they can see you very frequently post-transplant and they are even going to have a longer relationship with you. So, this is a big commitment and they actually have to make that commitment from their part, not just from your part. So, they have to be fully into their heart, their mind, everything to really sink into that commitment. So, I always encourage them if they have any doubt, they should go for a second opinion.

And a lot of the time, what happens, they go for a second opinion, they hear the same thing, it gives them reassurances and then they come back. They are feeling more reassured and you—you, basically, the same treatment. Very rarely, there's a—you hear different opinion from one physician or another. Most of the time, they are very consistent when they are seeing the same expert, leukemia expert. They are very consistent.

Lizette: And they are not hurting your feelings, because a lot of patients the more elderly, they seem to say that, you know, they don't want to get a second opinion because they don't want to hurt your feelings.

Dr. Abdul-Hay: So, I had a patient, actually, and she wanted a second opinion. And she went for a second opinion without telling me which was completely fine with me, but I think she felt guilty afterwards. And so, she wrote me a letter saying that, you know, she went for a second opinion and she put it in my desk in the office and that this was not because she did not trust me. She saw that I was young and she wanted someone elderly just to be sure to get their opinion. I keep telling patient(s), you should go where you feel is right for you. This a big decision. This is a big commitment. You should not really care about what I think or what I don't. You should—this is your life and you should make that decision in peace and you should be happy, also, making that decision. So, you should not really feel like, okay, you are hurting my feelings or making me—no, no—I'm fine and I believe most of the physicians are and they understand that part.

Alicia: Be mindful, though, that after this episode, you may very well become a second opinion for many of our listeners today.

Dr. Abdul-Hay: I don't mind about that.

Lizette: Doctor, you mentioned that it's a pretty long trajectory for treatment, two, three years. Is it different for males and females, how long the treatment lasts?

Dr. Abdul-Hay: No; it doesn't. It just differs if you are going to a constant or not. So, if you are not going for constant after all this induction, consultation and intensification, you are going to be on maintenance for most of the maintenance will be pills. One you take a day; one you take once a week and then injections, which is most of the time. Vincristine, you come every 2 to 3 months. But it doesn't differ between male and female. What differs is you going for transplant or not because if you do go for transplant, you know, there is no role for maintenance once you are into remission. After a few consolidations and you have a donor, you proceed with the transplant.

Lizzette: Doctor, I know you have an expertise in transplanting. What's the best type of transplant since there's different types of transplants for patients especially if possibly they don't have a donor for an allogeneic transplant?

Dr. Abdul-Hay: So, the only benefit in ALL is an allogeneic stem cell transplant. In this era, we very rarely not find a donor so the best is to find a match-related donor—full match like a sibling. That's really the best thing. The next best is to find a match unrelated and there's—there's NMDP, National Marrow Donor Program registry so a lot of times we do find a donor. But, like, I live in New York and in New York, there are so many different ethnicities so it is always a challenge, believe me, to find a donor. So, then we go for what we call the haploid match, meaning half a match. So, from a sibling, the chance of you having—if one of your siblings is half a match, it's 50%, full match 25% so the more you have sibling, the more you have a chance of half a match. And children, so if people have children, then their children it's going to be definitely 100% going to be a haploid because they are going to inherit half of the HLA type from their parents. So, if you have children, there you go. You find a donor. So, then that comes after the match unrelated to haploid. And there are still a lot of people who are single, or they don't have children, and you cannot find for them a sibling or a match unrelated or a haploid; and then we go for what we call the last resort which is umbilical cord. And most of the umbilical cord, you can end up finding someone. So, very rarely, a case that you cannot find a donor.

Alicia: Well, thank you so much for joining us on this episode Dr. Abdul-Hay and for all that you do for your patients. This is clearly your passion and it's great to speak with doctors like yourself.

Dr. Abdul-Hay: Thank you very much Alicia and Lizette for having me. I really enjoyed and thank you for having me.

Lizette: Our pleasure. Thank you.