



Keeping Hope Alive: Alternative Options for Bone Marrow Transplant

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Introduction

Andrew Schorr:

When someone needs a stem cell transplant, which could be lifesaving, finding a match can be a real challenge, and there are about 30 percent of the people who have difficulty finding a perfect match. Fortunately, researchers like Dr. Paul O'Donnell from the Fred Hutchinson Cancer Research Center and the Seattle Cancer Care Alliance are making it possible for more people to receive a transplant without an exact match. We'll talk about it all next on Patient Power.

Andrew Schorr:

Hello and welcome to Patient Power sponsored by the Seattle Cancer Care Alliance. I'm Andrew Schorr. Well, over the years I have done videos and audio discussions about bone marrow transplant and stem cell transplant, and actually right here in Seattle is where it got a great start at the Fred Hutchinson Cancer Research Center, and one of the leaders there actually was awarded the Nobel Prize for his ground-breaking work in that.

Well, of course, the effort has been how can transplant benefit more people and really give people the hope of a cure for so many conditions, and a lot of it has been about could you find a match. Was there your identical twin, or sibling or maybe a matched unrelated donor. And unfortunately about 30 percent of the time they can't find that perfect match. Well, what is so encouraging now is there are new leading-edge approaches to transplant that are allowing people who don't have that perfect match to have a transplant and hopefully the hope of a cure, and we're going to discuss that today.

Ronni's Story

First, I'd like you to meet someone who has benefitted from one of those approaches, and we'll meet someone who has benefitted from another leading edge approach, and you're also going to meet their doctor who is one of the leaders in the field. So let's go to Walnut Creek, California, Ronni Maestas. Ronni is in Walnut Creek, as I said. She's 44. But back when you were 27, Ronni, is when it all began with Hodgkin's lymphoma, am I right?

Ronni:

Yes, that's correct. At 27 I was diagnosed with Hodgkin's lymphoma, and I was very fortunate at that time in that it was stage I, early stage that you could find it. I went through the, you know, at the time was the recommended radiation, and that did give me a little over a three-year remission. Unfortunately, I had a recurrence, went through six months of chemo. That again gave me about a three-year remission. And then I travelled to Houston, to MD Anderson to have a transplant, an auto transplant using my own cells, and unfortunately that only gave me a six-month remission at that point.

So at that time I was kind of forced to look around and see what else was available, and I found a clinical trial up in Seattle at Fred Hutch that I participated in, and unfortunately I had progressive disease on that. So at that point we were kind of looking around and figured pretty much my only option was a full bone marrow transplant using a donor. Unfortunately my only sibling, my sister Vicky, was only a half match to me, so in the traditional allogeneic transplant I couldn't use her. We did a search through the nationwide registry and international registry and could not come up with even a close match to me at that point.

So I was kind of left looking for another option. I had minimal disease, but it was advancing. It had advanced to my bones at that point. And I was introduced to Dr. O'Donnell and this clinical trial, which was able to use my sister as a half match as my donor. And that was five years ago. I am now five years with no evidence of disease, and I'm doing well, I'm feeling good. And in fact I'm even doing a little bit of work. I have a website of my own. It's introtocancer.com, and it's pretty much just your basic introduction to when you're first diagnosed, what do you do. There's information on there for patients, caregivers, family and friends.

Andrew Schorr:

You're helping a lot of people just doing this, too. So as we're about to meet Dr. Paul O'Donnell would you say this is a physician who helped lead the team that saved your life?

Ronni:

Yes, absolutely. I believe wholeheartedly that if I had not met Dr. O'Donnell I would not be here today.

Andrew Schorr:

All right. Well, we're glad you are. Now let's meet this man--

Ronni:

Yes. As am I.

Haploidentical Transplant

Andrew Schorr:

Dr. Paul O'Donnell is the medical director for adult stem cell transplant service at the Fred Hutchinson Cancer Research Center, and of course the Seattle Cancer Care Alliance. Dr. O'Donnell, let me see if I've got this right. The type of transplant that Ronni had is called haploidentical transplant? Is that right?

Dr. O'Donnell:

That's correct. So "haplo" essentially means half, so if you're haploidentical you have half of your genes from your parents, from your mother and half from your father. So in Ronni's case, flip of the coin, the chances that she and her sister got both sets, the same two sets from her parents was not successful, but her sister got half of them.

Andrew Schorr:

So we were talking and for years we talked about find a match, find a match, find a perfect match, and here you had half match, and here's a woman who is doing well five years later. How did we get to that point?

Dr. O'Donnell:

Haploidentical transplants had been studied for probably a decade before I got involved, and one of the drawbacks of haploidentical transplants is the complication called graft-versus-host disease, where the donor's immune system attacks the patient. And that was the big hurdle for haploidentical transplants for a long time. About 10 years ago I was working at Johns Hopkins University in Baltimore, and one of my colleagues came up with a brilliant idea of using a very low tech approach, extremely low tech, and that is to give the patient the stem cells or bone marrow in this case from the half-matched donor and let them settle in and start revving up, and if the immune system revs up too much, like I said, it will--potentially kill the patient from the autoimmune disease.

But at three days after transplant we give a single dose of chemotherapy, fairly common chemotherapy, it costs about \$300, and that's sufficient to destroy most of the bad-acting immune cells from the donor leaving behind immune cells that can potentially work for the patient's benefit. And it's not to say it couldn't cause some graft-versus-host disease, but it's manageable. And the trick, the entire trick was to get rid of the bad actors.

Andrew Schorr:

Wow. Wow. So now, this was part of a trial that Ronni was in, and since then, the last five years, you've continued to perfect that approach.

Dr. O'Donnell:

So when I left Johns Hopkins about 2001 I came out here and continued the work that we'd started there. They continued it as well, and people started to take notice, and we've just finished a national, multicenter trial. There are about 16

centers, transplant centers. We just finished that, so I think the method is starting to be more accepted because initially it sounds somewhat outlandish --the idea that you're going to give chemotherapy right after you've just given a bone marrow transplant, but it's safe, and it works.

Andrew Schorr:

Wow. And of course the bottom line as we'll continue to discuss on this program is there are now approaches to transplant that make it a very viable option for more people, people who for whatever reason could not find a perfect match.

Jessie's Story

Let's meet Jessie Quinn, who is in Sacramento, California. She has a young child, Luna, who is just two, and she is very well educated, has a Ph.D. herself. And unfortunately there was an interruption in her career as she got really sick a little less than a year ago with AML. And found yourself hospitalized and really in the hospital for quite a long time, isn't that true, Jessie?

Jessie:

Yes. I went to the ER actually, with symptoms that I didn't know what they are were. I had been feeling some slight symptoms before that that hadn't been recognized as leukemia, but after an hour or so in the ER they were able to identify the leukemic cells after a blood test and basically told me that with the acute leukemia I would be staying there that night and starting chemo the next day. And so I stayed for my induction round which involved about five days of chemotherapy, high-dose chemotherapy, and another three weeks while my blood counts dropped and came back up to normal levels.

So I was in the hospital for 30 days right off the bat. And once they had identified the particular cytogenetics of my leukemia they knew pretty quickly that I was going to need a stem cell transplant because my particular leukemia was one that was known not to respond well to chemotherapy alone.

Andrew Schorr:

Right. Now, let's talk about the fly in the ointment, if you will, is you have a mixed heritage, correct?

Jessie:

Right.

Andrew Schorr:

So I think you told me it's Irish...

Jessie:

Right.

Andrew Schorr:

...Black, or African-American, and Native American?

Jessie:

Yes.

Andrew Schorr:

And also that years before you had participated in a drive to have--have people be typed for transplant, and you were typed--

Jessie:

Right.

Andrew Schorr:

...and when a search now years later goes on to look for somebody with that mixed-race background, you were the one who popped up.

Jessie:

That's right. I was the only perfect match in the database.

Andrew Schorr:

Right. Okay. So, Jessie, let me see if I understand this right. You were a perfect match for yourself, but that wasn't going to work because now you were sick with AML. So you heard about at Fred Hutchinson and the Seattle Cancer Care Alliance that there might be the hope of doing a new kind of transplant?

Jessie:

Right. They went through a search for several months, as long as I could continue with consolidation chemotherapy, and when I came to the last possible treatment at that point we started discussing alternative types of transplant, and it seemed that I would be a good candidate for an umbilical cord transplant because they don't have to be as well matched as an adult stem cell transplant and so there tends to be more available. They had already identified two cords that would be good enough matches for me that would work and suggested I go to a facility that was experienced in doing adult cord blood transplants. So I chose Seattle.

Andrew Schorr:

Okay. And we should mention that you had the transplant, when, in the fall of 2010?

Jessie:

Yes, it was in September of 2010.

Andrew Schorr:

And now as we record this we're at the very end of January, and you're doing pretty well?

Jessie:

Yes. So far so good. I'm still a hundred percent donor, and I have some mild graft-versus-host disease, but, knock on wood, it hasn't flared up too badly yet.

Andrew Schorr:

And you're back with Luna, you're little kid.

Jessie:

Yes, I'm back home taking care of my daughter.

Double Cord Transplant

Andrew Schorr:

Okay. Well, Dr. O'Donnell has been your doctor, too. Dr. O'Donnell, just briefly, the cord blood, my understanding as it developed was there would be sort of naive stem cells in the cord blood that could be used certainly for transplant for a child, but you didn't have enough maybe for an adult, so Jessie mentioned this double cord blood, so that I imagine would create more available stem cells. But we took it even further in a clinical trial with Jessie being patient number one. What was that next step? Not just combining two sort of matched cords but what else?

Dr. O'Donnell:

That's correct. Because it's a quantitative effect. For adults who weigh more, two cords are better than one, but still there's a lag for the cells to take and get growing, or called engraftment. And so Dr. Colleen Delaney, whose trial Jessie was on, has been involved in some very exciting research in the last few years, and one of these is to take cord blood cells and grow them up in the laboratory in a special clinical laboratory that's good manufacturing and freeze them in a freezer. And the idea is to take out these third-party or off-the-shelf cords and infuse them with the other cord blood units as an attempt to add even more cells to the mix to help engraftment occur earlier. And that's in a nutshell what the trial was that Jessie was the pioneer.

Andrew Schorr:

And so far so good. All right. Well, we're going to learn a lot more about these approaches, both the approach of haploidentical and also cord blood or the latest in cord blood transplantation, recognizing that it's experimental and Jessie was patient number one here in Seattle. We're going to learn a lot more about it as we continue our Patient Power discussion on transplantation right after this.

Welcome back to Patient Power as we're visiting with one of the leaders in transplant at Fred Hutchinson Cancer Research Center and the Seattle Cancer Care Alliance. That is Dr. Paul O'Donnell, medical director for adult stem cell transplant. And we also have two patients that he's helped, and I think they both are of course very grateful. You heard from Ronni Maestas who is in Walnut Creek, California, who a little over five years ago had a transplant, haploidentical transplant where

her sister, Vicky, participated with her and played a key role and she's doing well now as she looks like for an extended time she's beaten back, no evidence of disease of Hodgkin's lymphoma.

And then we have Jessie Quinn who just a few months ago had a double-cord transplant, but she was patient number one where there was yet a new variation in this. And I want to understand more about that, Dr. O'Donnell. So cord blood transplant for adults is pretty new and has been evolving. So you've had this double transplant idea to have more cells that could work for an adult, but the idea of having yet cells from a third cord, what's the idea there? Is it to try to lower the risk of infection, or where does it come in?

Dr. O'Donnell:

Well, I think the remarkable thing about cords is that because, as you said, they're naive, the immune system from the cord is also naive and is not apt to cause as significant a graft-versus-host disease as one would expect from mismatching. But unfortunately because the size of the cords is much smaller than the size of the bone marrow transplant that Ronni received, there is often a delay in the time to--to growth of cells that fight off infections. And so what Dr. Delaney has been working on is a way of boosting that engraftment rate by adding other cells, another set of cells, that remarkably don't cause graft-versus-host disease and provide sort of a boost initially but don't survive--the two cords that are partially matched do--one of them usually survives, and so it's basically just a way of sort of boosting the system.

Andrew Schorr:

And it's sort of a safety bridge while things fall into place.

Dr. O'Donnell:

Right. It's a bridge. It's to try to reduce the time to engraftment because it's that time after transplant when the patient's own cells are destroyed and there's no cells available to fight off infections that people are most vulnerable.

Andrew Schorr:

Now, let's talk about the potentially curative nature of transplant. So these therapies have developed over the years, and there was a mortality and morbidity that went with it, and fortunately that's been changing much more to the positive over time, but nobody goes into any kind of transplant lightly. But the hope is that if it works you could be cured, am I right, with an allogeneic transplant, with a donor someone other than yourself?

Dr. O'Donnell:

Cure is always a big, a big word in cancer treatment, but, yes, a long-term survival is equivalent to cure, so that's true.

Mini Transplant

Andrew Schorr:

Dr. O'Donnell, let's talk about one other type of transplant, and that's one for older patients, and sometimes it's called mini transplant or reduced intensity nonmyeloablative transplant. Tell us about that.

Dr. O'Donnell:

Right. So I think it's important for people to understand what--I always tell patients, well, what's really treating your disease here in the transplant, and there are really two things in the conventional allogeneic transplant that treats people's diseases. One is administration of very high-dose chemotherapy or chemotherapy and radiation which will hopefully destroy the disease but an innocent bystander is the patient's own bone marrow so they're unable to produce any more blood, blood elements. So that's where the stem cells come in. So the stem cells are really the rescue, rescue from the chemotherapy.

And then the second element of treatment comes from the donor's immune system that travels in with the stem cells. In a conventional allogeneic transplant, the treatment is from the high-dose therapy plus the immune response of the donor's cells hopefully against any disease that remained after the high-dose therapy. However, most older individuals can't tolerate the high-dose therapy, so in the mid 90s Dr. Rainer Storb at this center introduced, after a lot of studies in dogs, what he called a mini transplant which basically leaves out the high-dose therapy or conditioning therapy beforehand. So in the case of the mini transplant, the benefit to the patient in terms of treatment of their disease is entirely due to the donor's immune system, the second component of the conventional type of transplant I first described. So the immune system that comes in from the donor is the treatment.

The stem cells from the donor do eventually take over, but-- in the first case you have chemotherapy or chemoradiation and the donor's immune response, and in the second case for older or less physically well individuals, with heart disease,--for example, then the treatment is just from the donor's immune response.

The haploidentical transplant that Ronni got was the mini type of transplant, whereas the cord blood transplant that Jessie got was the full conventional high-dose therapy plus the cord blood.

Andrew Schorr:

Lots of variations here. What is the bottom line? Is it that four people where physicians recommend that transplant may be the best option whether or not there's a match or whether or not they're a young, physically fit person there may be a reasonable option for them?

Dr. O'Donnell:

I think today, as I said I think earlier, if transplant is recommended as a treatment option, it is almost certainly available to virtually every patient that's able to withstand a transplant.

Andrew Schorr:

Now, let's talk about matches for a minute. We said about 30 percent of the time there's not a perfect match, but if there could be one found would that be better?

Clinical Trials and the Evolution of Transplant

Dr. O'Donnell:

Now you're getting into questions involving current-day research. So, you know, the transplant field is continually evolving. Ronni got a haploidentical transplant, Jessie got double-cord transplant. We have ventured into those areas because we wanted to provide the option to people who didn't have a match. The expectation is that maybe the outcomes wouldn't be as good, but I think both in terms of survival and graft-versus-host disease it may turn out that they are just as good.

Andrew Schorr:

Wow. Wow. This is a field that continues to evolve. So what would you say to someone as far as seeking an opinion of someone like yourselves? People come from all over the world, and so it sounds like you have a lot to discuss with them, evaluating their situation and trying to see maybe, sure, is there a perfect match or if not what are these other options, and it may be there's a clinical trial they can participate in that may be good for them hopefully as it has been for our ladies here, but also help answer these questions.

Dr. O'Donnell:

That's correct. At this center of course we're always trying to improve on what we do, so we're always trying to ask patients to enroll in clinical trials. And I have to say how grateful we are at a research center that's continually trying to improve on our transplant methods that patients like Ronni and Jessie are really willing to be the pioneers, very courageously be pioneers to help us develop these new methods that, when they're successful, we can then bring to larger numbers of patients.

Andrew Schorr:

Let's talk to the ladies about that for a second. Ronni, people may be listening, and they hear the word clinical trial and they just, you know, they're overwrought about the seriousness of their illness, maybe going to a city far away and they hear about these approaches of the clinical trials. You were in one and then you were in another. What would you say to people about participating in a clinical trial? For you, it's turned out to be lifesaving.

Ronni:

Well, you know, I actually was one of those people who was deathly afraid of clinical trials because the first thing you think of is I don't want to be a guinea pig.

But once I looked into it a little further and understood what was going on then I wanted to be part of the--part of a clinical trial because it really is the most up-to-date--I mean, this is what--this is what can help me today, not things that were developed years ago which for many, many people are perfectly curative for them, but in my case it just wasn't working out. So I say absolutely consider clinical trials, absolutely consider traveling away from home.

It's scary. It's overwhelming, but don't just stay, you know, in your neighborhood and think that there's nothing else available to you. There are things out there. You just have to be willing to look, and quite frankly you have to take control of your own health. I found the trials at Fred Hutch and brought them back to my doctor. My doctor didn't give me the options. I found them and brought them to him. So nobody cares as much about you getting better as you do, so you have to be proactive and be perfectly willing to consider clinical trials.

Andrew Schorr:

Well, we call this program Patient Power. That's what it's all about. Jessie, how about you? You're a scientist yourself, so--and you were very sick, and so it was a big deal to, you know, with a young, young child to make this move and also be patient number one. Did you go into that with some confidence that in thinking about the science behind it just seemed like it could be exactly what you needed?

Jessie:

Yes, I did actually. I read a lot of the journal articles, the journal literature before I went to transplant and before I even made the decision to go to Seattle, and that really helped my confidence in the methods. Another part of me just as a scientist could look at the science and say, wow, this is a really interesting idea, not even thinking of myself in the mix. But thinking from a more personal standpoint I also realized that we had gotten where we are in cancer therapy through clinical trials and it was more of an opportunity to have something available to you that wasn't available to anybody else yet.

So I was--I was pretty excited actually to be--to be part of a trial, and it was a big part of the reason that I ended up going to Seattle. Not to say that there wasn't some element of fear involved, but I think that would be happened even if I would have stayed at home and had a conventional transplant, so, yes, I would just have to echo what Ronni said and just, you know, to really do your own research and take control of your own treatment.

Andrew Schorr:

Well, I know, you count your blessings every day and to be there with Luna, and you're still certainly very much in the recovery mode, so, you know, hopefully things will continue to go well. And I know how scary it must have been to go to the emergency room for one thing and then out of the blue be told it's an acute leukemia. So hopefully the storm clouds are all behind you now, and we wish you all the best, Jessie. Anything you want to say to Dr. O'Donnell publicly here?

Jessie:

I just want to express my gratitude, and thank you so much for the treatment in the hospital. And I don't feel as though I was always the easiest patient, so I wasn't a patient patient, so I just really appreciate his help and he had a very calming presence, and it really is very helpful for me. And the work he's doing is just--it's fantastic, so thank you.

Andrew Schorr:

Well, I'm glad we got you all together. Ronni, I want to wish you all the best and your dedication as being a patient advocate. You, and your sister does it with you, right?

Ronni:

Yes, she does.

Andrew Schorr:

What a team. She donates to you, and you two work together to help others. That's really a cool story.

Ronni:

Actually I'm a very fortunate girl, and I know that.

Andrew Schorr:

Okay. Well, all the best. I want to give the last word to Dr. O'Donnell. So, Dr. O'Donnell, you talked about this being an evolving field, and you talked about certainly the partnership between people like Ronni and Jessie as they work with you and other scientists. You mentioned Dr. Delaney. But it sounds like where we are now is a good place as far as transplant goes. Not that we can't do better, not that we can't limit side effects and lower all the concerns that can go with it, but it sound like it's accelerating.

Dr. O'Donnell:

Yes, I think that, you know, now that we're at a point where we can literally offer a transplant to any patient, now the issues are how can we make them safer, more effective, so that we don't even have the problems with chronic--or acute or chronic graft-versus-host disease, infections. So there's a lot to be done, but I think we're making a lot of strides. I think that this is really a time in stem cell transplantation that it's a pretty mature field, and a lot of progress is still to be made but a lot of progress, incredible progress has been made, and it's all--it's really by virtue of wonderful patients like Ronni and Jessie, and we're--just to know that they're doing well is all the--we're very grateful for that.

Andrew Schorr:

Well, I know that I speak for many, many people locally, around the country and around the world who thank you and your colleagues at Fred Hutchinson and the Seattle Cancer Care Alliance for the work you do and the work you will do to make



this even better. Dr. Paul O'Donnell, medical director for the adult transplant service at Fred Hutchinson Cancer Research Center and Seattle Cancer Care Alliance thank you, very much, for being with us today.

Dr. O'Donnell:

Thank you all.

Andrew Schorr:

All right. Well, this is what we do on Patient Power is connect you with leading experts like Dr. Paul O'Donnell and also leading-edge science as we've talked about transplant and where we are now and the people it benefits like Ronni and Jessie. Thanks again for being with us. I'm Andrew Schorr. Remember, knowledge can be the best medicine of all.

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