Stem Cell Transplant As a Treatment for Myelofibrosis: When Is the Right Time?

David Snyder, MD
Associate Chair, Hematology & Hematopoietic Cell Transplantation
City of Hope

Andrew Schorr:
Hello. Welcome to Patient Power. I'm Andrew Schorr. I'm sitting with someone we've met before, Dr. David Snyder from City of Hope, a noted MPN specialist and a really very famous hematologist. People come from all over to see him. Dr. Snyder, thank you for being with us.

Dr. Snyder:
Good morning. Glad to be here.

Andrew Schorr:
Dr. Snyder, some of us with myelofibrosis progress to a point where we need transplant, and I know sometimes you have to sit down with people—we met one of your patients, Jod, who has had that. Transplant has been an aggressive therapy. Where are we now with refining transplant so that the complications of it can be less?

Dr. Snyder:
That's a good question. There's a lot of work that's been done, a lot of progress over the last few years. First is in the front end of it, the conditioning regimen that people have to go through to prepare them for the transplant. It's a pretty intense kind of a process, or it has been traditionally. Now we use something called reduced intensity conditioning, or RIC, which is still effective at suppressing the patient's immune system, which is necessary for them to accept the graft that's coming, but it's less toxic in terms of injury to other tissues.

So it means that it opens the door to a lot more patients potentially than we could offer transplant to before. So, for example, we used to go up to about age 50, 55 as an upper age, now we're talking about 70, 75, in that range. And also if people have other health issues, maybe their kidneys, their heart function, their lungs aren't quite perfect, they still could be a candidate because of the use of this reduced intensity conditioning.

On the other end of transplant, and still the biggest obstacle to success is the problem of graft-versus-host disease, which is where the graft or the bone marrow cells, the stem cells, try to reject the patient instead of the patient rejecting the stem cells. And we've made some progress in trying to come up with newer ways of reducing the risk of that happening and newer treatments to treat it if it does develop, but there's still a lot of work to be done there.

Andrew Schorr:
Okay. Now, when you are doing a transplant, you're really giving someone else's immune system to the patient who is sick.

Dr. Snyder:
Right.

Andrew Schorr:
You have to do matching. Sometimes finding a match particularly for certain ethnic groups is difficult. Are we making progress in matching or ways of having kind of a better tolerance so that if it's not a perfect match maybe it still works?

Dr. Snyder:
Right. So the idea was to find a donor who was a perfect match, and we talk about a 10 out of 10, that's how many of the HLA antigens are matched, or maybe 8 out of 8. So we start with looking at brothers and sisters, because there's a one in four chance each sibling could be a match. But, you know, as the tendency is for families to be smaller, there's less of a chance that patients who need a transplant are going to find a matched—matched sibling.

So, fortunately, there is the National Marrow Donor Program registry, the worldwide registry that links into registries all over the world, and that has I think it's over 20 million volunteers worldwide who have signed up, so that opens the door to many more patients. There's something like 30 percent of people who will have a matched sibling, and so 70 percent don't, and so that group—it does depend on your ethnic background, because you're more likely to be successful in finding a match if there's a large representation of volunteers with a similar background.

So for people who don't have a 10 out of 10 sibling or 10 out of 10 unrelated donor, we can use a 9 out of 10 match unrelated donor. And now the newer approaches are possibly use cord blood or what's called haploidentical transplants, that's the latest innovation. That means half-matched donor. Now, almost everybody will have a half-matched donor, because that could be a child who is automatically by definition half-matched, possibly a sibling or even a parent if they're young enough. So it does open the door to even more patients potentially going through transplant.

I will say, however, that for myelofibrosis the approach of haploidentical transplant is still considered investigational or experimental, so we are actually in the process of writing a new protocol with some of our sister institutions in the country to be able to offer that type of transplant. Hopefully, though, that will make the option available to even more patients.

Andrew Schorr:
Dr. Snyder, we have people living longer with myelofibrosis with ruxolitinib (Jakafi), other drugs you have had in trials, JAK inhibitors, etc., other classes of drugs in trials. Will transplant as people live longer be needed then more, because still even with the drugs the disease may progress?

Dr. Snyder:
I think that's a fair statement. The drugs that we have right now—we will talk about more what their benefits are—but they're not cures, and for those patients who are young enough and otherwise healthy enough, transplant still remains their only curative option. And so we're seeing more and more with drugs like ruxolitinib that it can prolong survival. It certainly can improve patients' quality of life, and by things like shrinking the spleen and improving the symptoms it makes people even a better candidate for transplant ultimately.

Andrew Schorr:
But that brings up the question between doctor and patient when does that enter the discussion, right? So if somebody is doing well they say, well, I'm taking a pill, I'm leading a pretty good life. Transplant is an aggressive therapy no matter what, with even the changes.

Dr. Snyder:
Right.

Andrew Schorr:
I don't want to go there, you know.

Dr. Snyder:
Yeah. Right. And we talk about, I talk about the transplant option very early on with my patients just so they are aware of that option and where it may fit it. But I also talk about the idea of not moving too soon or too late to transplant. That's where it gets tricky. We don't want to compromise good quality of life. If patients are doing well on whatever treatment they have, they're doing the things that they want to do or they need to do, we wouldn't move to transplant at that point.

So it's—there are nuances, and it takes a lot of judgment, and, of course, it's a dialogue between the patient and the physician, when is the right time to move. So for me if a patient is—starts to have problems, that they can't get through their day because they're so fatigued or they have other symptoms, or they start requiring frequent red cell transfusions, for example, those are some of the triggers that would tell you maybe this is the time to move ahead.

Andrew Schorr:
Okay. That's very important what you just said. We patients know enough to be dangerous, some of us know a lot more, and we learn about these genetic mutations, calreticulin and JAK and etc., is there anything about our particular myelofibrosis situation that makes it more likely we'll need a transplant than not?

Dr. Snyder:
And so that's really been the amazing discoveries over the last few years that have increased our knowledge of these diseases. So we know the major driver mutations, and then there are many other sort of secondary mutations, and we're learning more and more about how—how this all impacts patients' prognosis. And right now the prognostic scoring systems that we have are mainly based on clinical features, but there are systems that incorporate some of these genetic or molecular markers.

And so we know that certain molecular markers may predict a better course than others. A CALR mutation, a deletion mutation, might predict a gentler, slower, rate of progression. Whereas someone who has none of those markers, the so-called triple negative, or has some of the other secondary markers, may have a more aggressive course, and therefore you might want to think about transplant sooner for that type of patient.

And I suspect over this next couple of years we're going to get more data about how that particular molecular signature for a given patient helps predict what their rate—the rate of their progression might be and therefore when it might be the appropriate time to go to transplant.

Andrew Schorr:
Okay. Dr. David Snyder is not just a clinician who sees people in the clinic, but he's really involved in the science, as you hear, particularly about transplant as we talk about where does that come in, how it can be improved and who is it right for, when. Key questions, and we'll continue our discussion on this with Dr. Snyder and other experts from around the world.

I think, listening to this as a patient, what's so important for you is if your situation is progressing you want somebody like this, Dr. Snyder, and other really renowned MPN specialists to be on your team to help you make these decisions together.

Dr. Snyder, thank you for all you do, and for being with us once again on Patient Power. I'm Andrew Schorr. Remember, knowledge can be the best medicine of all.