FA Connect: Question & Answer Transcript

Session Title: Stanford Fanconi Anemia (FA) Program & Clinical Trials
Invited Speaker: Drs. Agnieska Czechowicz, Rajni Agarwal-Hashmi & Alice Bertaina
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Access a recording of Drs. Agnieska Czechowicz, Rajni Agarwal-Hashmi & Alice Bertaina's presentation by vising www.fanconi.org. The recording has been uploaded with Spanish subtitles.

Have additional questions for the speaker? Email our speakers directly.
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Q: Do they use this exact same protocol in hospitals in Rome?

A: Dr. Bertaina: Yes, in terms of the Alpha beta protocol. However, they don't have the same trial that we are presenting today, which combine the Alpha beta depletion with a monoclonal antibody.

Q: When do you think International patients might be able to participate?

A: Dr. Czechowicz: The trial covers all the research aspects and the investigational treatments, but it does not cover a standard of care transplant, which is part of the treatment. So, patients do have to have some insurance support to enable that, and so we work with whatever insurance patients have. It can be a little trickier for international patients and, although in theory still possible, and so the trial is open to international patients and to all patients, but we do have to navigate things on an individual basis, just to get all those pieces have figured out. It does take a little while to navigate that and so also encourage patients to reach out to our program as soon as possible, so we can start that process to understand what treatment options are available for patients.

Q: You've used this antibody-based conditioning on patients with combined immune deficiency. How are those patients different than FA patients and, therefore, do you expect a different response with FA patients, then in the with the patients in your initial trial with this anti body condition?

A: Dr. Agarwal: Yes, we initially used this protocol on patients with severe combined immune deficiencies, so they only needed the antibodies because their immune system was already low. We have proven at the point that the antibody is extremely safe to use in all age groups and the age group, that we have used it in the severe combined immune deficiency trial is from age three months to 38 years. So, we are confident in the use of antibody, and we have learned a lot. We also found using the dosage of 0.6 milligrams is a better dose. Now we have this new trial with Fanconi anemia patients where we optimize the antibodies, and we hope that we will be successful.

Q: Are there any toxic treatment used in the protocol?

A: Dr. Czechowicz: So, I can answer that so as Dr Agarwal was alluding to in the severe combined immune deficiency setting, we were able to use it antibody alone as a single agent. And that's because those patients have no immune system so have no way of immunologically rejecting the donor cells or if a patient's do have an immune system, it may not be a completely perfect one, but they do have one. It is important to eliminate that immune system, so we

don't get rejection of that graft. We've kept the same immune suppression backbone that has been used in the prior FA transplant protocols. To not change too many agents, our protocol still includes ATG which is also an antibody and then it includes a low dose of cyclophosphamide. Both are chemo therapeutics but very, very low doses. This eliminates the use of that total body radiation that is used in other protocols.

Q: The criteria to be eligible for the study seem a bit more liberal than I've seen elsewhere, can you discuss why that is?

A: Dr. Czechowicz: I think the decision to go to transplant is a very personal decision between the patient, the family and all of the physicians on the care team and for different patients that live in different places. There are clearly risks and benefits to transport protocols and it's important to think about when is the right time and we believe that this Protocol should be a safer protocol than the traditional ones, and so it could be offered in an earlier time point and we didn't want to have extremely strict cut off criteria. So, that's why they're written and the way they are. Also, we wanted to make sure that patients didn't have extra blood transfusions.

Q: Do you recommend we make an appointment to meet the team at Stanford before my child needs a transplant?

A: Dr. Agarwal: I think that would be very wonderful to see them. The other thing I could suggest is we have a Tele health call. This way we can get to know the children and then from there we can talk one on one more about the trial. Then, make the in-person appointments after more discussion.

A: Dr. Czechowicz: We offer that for all of our patients the opportunity to do telehealth visits and have consultations with us to expand our program and different treatment options for right.

Q: Do you recommend bone marrow biopsy after everything is stable for over 10 years?

A: Dr. Czechowicz: Our recommendations right now follow the recommendations set by the FARF FA Clinical Care Guidelines which are annual bone marrows both before transplant, and after transplant just to ensure that bone marrow stability. We do extremely detailed bone marrow testing here both the clinical basis and a research basis to look very carefully for that stability.

Q: Who do I contact to make appointment?

A: Agnieszka Czechowicz, MD, PhD, aneeshka@stanford.edu
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Q: Your trial flyer mentions close follow up for two years and then one to two times a year for the next eight years. Does that mean that families would need to travel to Stanford for those appointments or some of those appointments are you guys able to work with their local physicians in their communities?

A: Dr. Agarwal: I think that some visits could be done locally, but there will be some major visits that would need to be done at Stanford. There are a lot of visits in the first three months and after that they could be intermittent blood count checking. The six-month, nine-month and twelve-month visits are important and would need to be done at Stanford.

Q: If child is on Quercetin will he need to stop or not?

A: Dr. Agarwal: I think it is fair to stop it about 30 days prior to coming in.

Q: How would you compare a Minnesota transplant to your transplant?

A: Dr. Agarwal: There are two parts to this. One we can do a standard of care alpha beta depletion transplant and I'm not sure what type of a graft they use they use at other centers. We've already shown you the excellent outcomes we've seen with very low levels of graft versus host disease so that's point number one. The second point is that have the same backbone minus the total body radiation, but the antibody which we think would be safer now I wish I could tell you if I had done 10 patients on that.

A: Dr. Czechowicz: We are an FA center and have a comprehensive program here. We take care of patients from all different aspects and have different subspecialty care provides that are involved in their care, including ENT, dermatology, and gynecology.

Q: Back in 2004 Stanford used 10/10 or 9/10 match, has that changed?

A: Dr. Czechowicz: We think about what's best for the patient, we run a full donor search to see what the options are and then make recommendations, but I'll let Dr Bertaina and Dr Agarwal comment on that more.

A: Dr. Agarwal: Traditionally we did use the sibling donors or unrelated match donors, or maybe a single mismatch 9 of 10 donors, but like we said the field has really moved forward, we did some cord blood transplants later in the 2008/2009 and then we did five transplants with CD34 engraftment. Then Dr. Bertaina joined our team here at Stanford.

Q: Is an individual receiving Eltrombopag (bone marrow stimulant) able to join this study?

A: Dr. Czechowicz: Patients are eligible to join the study once they are off of experimental treatments for 14 days prior to initiation of the study, but for the actual study we just asked that patient stop for a couple weeks to clear out of the system, prior to starting a new experimental therapy.

Q: When will close the trial? If it looks like my child will not need transplant in next 12 months but may need one in the next 1 to 5 years.

A: Dr. Czechowicz: We anticipate closing this trial when we reach the enrollment capacity. Right now, the trial is written for three plus nine patients so 12 in total, and we have funding for three patients and then hope to receive more funding to support the following nine patients. That's where we are and we don't know how long it will take us to accrue those patients and so don't know exactly how long the trial will be open, but we hope to see.

Q: What is the main difference between this study and the last study Stanford FA program was enrolling for?

A: Dr. Czechowicz: As I mentioned, we add take every patient as an individual and think about what best treatments are available for them, and we have many different treatments that are available, depending upon the type of FA and we're in the disease process patients are. The study that was more widely publicized from Stanford was the gene therapy study that Dr Bertaina actually mentioned which was really a preventative study for patients only with subtype A.

Q: How can I follow this trial oner the next year or two? Or when will Phase1 Results be available?

A: Dr. Agarwal: We will be giving periodic updates as the trial progresses and will provide updates to FARF to share out with the community

Q: Why aren't other FA centers using this protocol?

A: Dr. Agarwal: The alpha beta depletion technique is starting to get more and more used by other FA. I think the major centers are still doing CD34 engraftment but now looking at the numbers, they are moving into doing the Alpha beta depletion now. I am not so sure there is a center like us, who has the experience of doing 500 alpha beta depletions with all the graft manipulation and engineering. And all the experience that goes with it, so I think that puts us in a very good position to be able to analyze the graft. Additionally, our antibody conditioning is something very unique to Stanford and it is not commercially available.