FibroBiologics Analyst Day – February 2025

Q&A Edited Transcript

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Question: Can you talk a little bit about the DFU study and its endpoints? Historically, I know regulators wanted to see 100% granulation on it. I wanted to know if that standard is true.

Hamid Khoja, Ph.D.: Granulation is certainly a biomarker the physicians look at as they are monitoring the patient. In terms of the endpoints for the clinical trials, the primary endpoints for all the clinical trials have been percent wound closure within 12 weeks for clinical trials.

Question follow-up: But regulators have been looking for 100% wound closure which is a pretty difficult hurdle.

Hamid Khoja, Ph.D.: It is, but you statistically design your clinical trial as compared to, let's say, a placebo, or in this case for diabetic foot ulcers, the standard of care. If you have a certain percentage higher than the standard of care, and the results are statistically significant, then you achieve the desired outcome. So typically, let's just say for Grafix®, they achieved about 20% in their clinical trial, and for their treatment arm, it was about 60%. So, with the number of patients they had enrolled, it had sufficient power to say that the result was statistically significant in terms of efficacy.

Question: You mentioned for wound closure that the cells in vivo seem to last around four days in spheroid? Does that vary depending on the environment that you're implanting them in, like with the hypoxic lower back environment, and how does that impact the frequency of dosing?

Hamid Khoja, Ph.D.: Yes, a very good question. What we have tested in all of our animal models is the use of chronic wounds. We generate a chemically induced chronic wound on the back of these mice for our animal model studies and based on the engraftment data that I showed you, it typically takes about four days for these cells to disappear, which is exactly what you want. You don't want the cells to graft on the surface of a wound, because that could potentially lead to scarring. What we've seen in our animal model studies is about four days, but that doesn't mean the impact goes away after four days. The impact is still there because you have recruited and initiated proliferation, so that continues. In our clinical trial, we will do weekly administration, which is done with Grafix® as well. We have designed our clinical trial to match very closely other clinical trials that have been completed in diabetic foot ulcers, so we could compare our results with theirs, with a statistically significant comparison at the end of the trial.

Question: When you talk about fibroblasts being created inside the wound and then the continuing effect, do they carry out a similar effect to actual implanted fibroblasts?

Hamid Khoja, Ph.D.: Yes, so once the senescent fibroblasts in chronic wounds are activated and they are proliferating, they secrete all the necessary factors that are important in the wound healing process. They begin secreting the same cytokines and growth factors such as VEGF, EGF, very similar to the cells that we are administering. We're initiating and jump-starting the wound healing process and continuing that weekly.

Now, with our clinical trial, some might heal very quickly, some might not. It's a 12-week clinical trial and we'll see the percentage of wounds that heal within that time. we will have some interim results after 6 weeks.

Question: With the inclusion of the psoriasis indication, can you speak to the translatability from wound healing and diabetic foot ulcers through psoriasis and any main mechanistic considerations?

Hamid Khoja, Ph.D.: The fibroblast spheroids for diabetic foot ulcers are topically administered. As you saw in that data, the impact on the tissue level is much higher than systemic administration. With psoriasis, an autoimmune disorder, intravenous administration has more of a systemic impact. A systemic modulation of the immune system back to homeostasis allows the cells to recover and go through the process of healing and reduce the skin immune cell infiltration that causes quite a bit of the issues with psoriasis.

Question follow-up: It would still be topical?

Hamid Khoja, Ph.D.: No, for psoriasis it's not topical, it's a systemic therapeutic approach. It'll be intravenously injected, because you want it to be systemic. As an autoimmune disorder, psoriasis can lead to multiple sites of impact, including damage to organs or joints. We want to tame down and bring back to homeostasis the inflamed immune system.

Question follow-up: So how does that work? The systemic administration, how do you avoid a first pass effect, and what homing mechanism is going on? It's not really an SDF1 hypoxic homing mechanism, so what is it?

Hamid Khoja, Ph.D.: The first pass is through the lungs, but the spheroids do stay in circulation for a while. Based on some of the data that we have, it stays in the system for about three to four days, systemically. The first pass being is in the lung, the second pass is in the liver, and we do see it in kidneys, but it goes away fairly quickly. We use spheroids, so unlike single cells which are removed from the system and have been shown to induce IBMIR, spheroids stay intact and they secrete the necessary factors to modulate the immune system.

Question follow-up: Based on reading the local environment from wherever they're flying around systemically?

Hamid Khoja, Ph.D.: Absolutely. Systemic, yes. And we're seeing that impact very quickly after administration. We're seeing modulation of the immune system.

Question: What might the dosing look like for these animal models?

Hamid Khoja, Ph.D.: For the animal model studies we have been dosing about 300 spheroids. Now the dosing goal in adults will be in terms of hundreds of spheroids per kilogram weight.

Question follow-up: How's the scalability work?

Hamid Khoja, Ph.D.: Very easily. And that's the good thing about our cells. They don't go through senescence even at higher passages. We've cultured up to 16 passages without noticing any senescence marker increase. It's very easily cultureable, very scalable, and very easy to manufacture. These cells do not go through senescence, they do not differentiate, and they're very stable. Just to give you an idea, our drug product will be at passage 9. So very early passage.

Question: Can you tell us the chemical composition of the spheroids? How those are manufactured, what are the steps involved?

Hamid Khoja, Ph.D.: We collaborate with Charles River, they're the manufacturer for our DFU clinical trial drug product. They have never manufactured spheroids for clinical use, so we are the first to use spheroids in a clinical setting. Fibroblasts are adherent cells, and they love being in close proximity to each other. What we do is to place a certain number of cells in these hydrophobic plates. The cells come together and just grow as a perfect sphere. That's how we manufacture and we have the capability of manufacturing millions of doses effectively.

Question follow-up: And are they coated in any way?

Hamid Khoja, Ph.D.: No, not at all. We have obtained tissue for commercial use, and we have isolated quite a few of the subtypes of fibroblasts that are available in dermal skin. Publications have indicated about 16 different subtypes. Some are inflammatory fibroblasts, some are not. We have identified one specific one that we use for the diabetic foot ulcer wound healing treatment that secretes a very high amount of the factors that are necessary in initiating the wound healing process. For multiple sclerosis and psoriasis, we have identified other subtypes of fibroblasts that are very good at immune modulation, and they secrete all the necessary factors that bring back the immune system to homeostasis. They seem to work really well in animal models. Our goal is to take those subtypes that we have identified and categorized on which clinical indication they fit best to produce for our clinical trials.

Question follow-up: And just to follow up on the manufacturing, is there anything you have to do to control for the size of the spheroid?

Hamid Khoja, Ph.D.: In terms of manufacturing, the number of cells you input into these hydrophobic containers or plates determines how big the spheroid become. For example, the spheroids for the diabetic foot ulcers are about 200 to 250 microns in size, and they contain about 3,000 cells. The spheroids that we utilize for multiple sclerosis and psoriasis are significantly smaller, about 100 microns. You don't want it to cause cloggage of any arteries or capillaries. They're significantly smaller, and they contain about 800 to 1,000 cells per spheroid. We can easily control the size, and as part of our manufacturing process, we have assays and instrumentation

that determine the size of the manufactured cells so that they're not too big or they're not too small for our clinical indication use.