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EP Vantage interview – Humacyte's lab-grown veins could reach the US in 2017

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The blood vessels Humacyte has created out of lab-grown human tissue have shown great promise as a way to aid dialysis in early clinical trials. Now the North Carolina company is on the verge of proving that the products can become incorporated into the patient's body in such a way as to become almost indistinguishable from native tissue.

More excitingly from a commercial viewpoint, the product is close – surprisingly close considering that pilot human trials have only just started reporting – to hitting the US market. "We could potentially reach commercialisation of the human dialysis graft as early as 2017," Shannon Dahl, vice-president of technology and pipeline development at Humacyte, tells *EP Vantage*.

Large-scale production

Patients with end-stage renal disease must undergo haemodialysis three times a week, necessitating a graft onto a blood vessel to enable the rapid extraction, filtration and reinfusion of blood. Current grafts are either made of polytetrafluoroethylene, better known as Teflon, in which case they are prone to infections or blockages, or of a vessel harvested from the same patient, which involves a separate surgery.

"There is a real need to replace the blood vessels. When we take peoples' veins from around the body in the name of replacing arteries we generate significant wound complications because it's a second surgery," says Jeffrey Lawson, professor of surgery at Duke University's division of vascular surgery, in a telephone interview. "Historically, synthetic dialysis grafts have an incredibly high failure rate – a recent study found that 70% of these grafts fail in a year. It's an incredibly morbid procedure for a high failure rate."

Humacyte makes its grafts, which Prof Lawson says look a little like calamari, using cultured cells, meaning that the technology is scalable. "We take cadaveric human aorta cells and grow the tissues from that cell bank," Ms Dahl says. "We seed the cells into a bioreactor onto a tube-shaped biodegradable scaffold. The cells multiply and produce an extracellular matrix and at the same time the scaffold degrades away, so at the end were left with tissue. Then we decellularise it, washing away the immunogenic cells, and we have the potential for a graft that's non-immunogenic."

The process takes around two months, Ms Dahl says. With trials of the grafts expanding and launch a potential three years away, the company is looking into ways to up production. "We've developed a manufacturing partnership with a company in Colorado called AlloSource which enables us to scale up," she says.

This ought to make the grafts cheaper to produce, and will help the company fix the price at which they will sell. "The next couple of years will help us determine the cost."

The company reported initial clinical data last autumn, and the results were promising (*AHA – Early success for Humacyte's off-the-shelf blood vessels, November 21, 2013*). This month, though, preclinical results emerged that further underline the technology's potential.

Studies in baboons have resulted in no evidence of graft deterioration or immune rejection at six months, Prof Lawson says, despite no immunosuppression having been used. More interestingly, though, the grafts are so compatible with the recipients that they are starting to become part of them.

The preclinical studies have demonstrated infiltration of baboon vascular smooth muscle cells and endothelial cells into the grafts. "What started as our structure became the baboons blood vessel," Prof Lawson says. "It's the most remarkable thing. We've seen it in every explant we've taken – a blood vessel made of the animal's own cells in the animal's own body."

Wildly fascinated

The phenomenon has not yet been shown in humans, Prof Lawson says, because none of the vessels has yet been removed.

“We have implanted over 40 grafts in humans in just over a year,” he says. “To date, we have not received any tissue we can analyse to look at how the blood vessels remodel in humans. Because these people need the blood vessels, the only way we could explant them is if they became infected or rejected, and to date that has not happened.

“It’s an area we’re wildly fascinated by, and we’re still studying and trying to understand it. But we can’t put patients through another operation just because we’re curious,” Prof Lawson says.

Consequently it is hard to know when Humacyte will be able to release data on remodelling in humans. But this may not be necessary for approval anyway.

“Regenerative medicine and tissue engineering are innovative spaces,” Ms Dahl says. “The process of growing tissue and using it in patients is still a relatively young field, and unlike in the medical device arena where there is an established history of prior product approvals, tissue engineering and regenerative medicine companies must work closely with regulators to ensure agreement on clinical development plans that could support an eventual approval.”

Humacyte knows that the grafts will be regulated in the US as a biologic therapy, under a BLA, but no more detail is yet available. “We’re still working out our future development plan. The process is that we complete this study and then we work with the FDA to design the next one,” Ms Dahl says.

Other applications

Humacyte’s closest rival is California-based Cytograft Tissue Engineering. Its artificial blood vessel technology, also intended for dialysis patients, is in phase III trials. LifeLine, as it is called, is made of cultured cells and extracellular matrix proteins that are cultured and then cut to form threads, which are then woven together to form grafts.

The process appears to be more complex than Humacyte’s and perhaps less scalable, but Cytograft’s technology is further advanced. It will be interesting to see whether it can gain first approval, as this will give insight into the regulatory path for Humacyte and the ballpark for pricing.

In the meantime Humacyte is diversifying into other areas, having recently initiated a clinical trial in peripheral arterial disease. Its vessels are implanted above the knee to bypass blocked arteries. “We have started in arteriovenous access, now we’re moving into PAD and in the long term we’ll consider other vascular applications,” Ms Dahl says.

For now, the company must feel its way forward, albeit with undeniably promising clinical data and a patient population that is likely to be highly receptive. Humacyte is extremely secretive about its financial situation; Ms Dahl declined to speak about its funding and even to discuss the firm’s reasons for keeping its details hush-hush. If its technology fulfils its potential, the company will have to get used to a greater level of scrutiny from many more interested parties.

Photo credit: Shawn Rocco/Duke Medicine

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