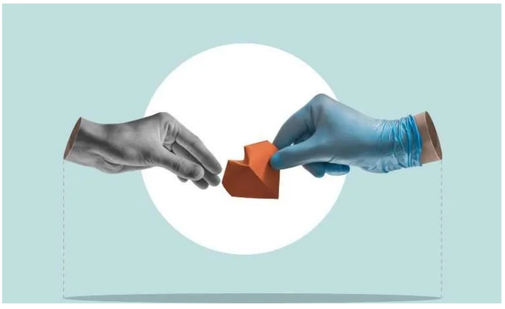
Turning Science into Business: Can regenerative medicine treat heart attacks?



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DDW's ***Reece Armstrong*** *speaks to* ***Hendrik Streefkerk****, Chief Medical Officer and Drug Safety Officer of CellProthera about the company's cell therapy for acute myocardial infarction (AMI) and why regenerative medicine could be key to treating cardiac diseases.*

Based in France, CellProthera is a small, regenerative cell therapy developer that specialises in cardiovascular diseases. The company's lead therapy is an autologous cell therapy named ProtheraCytes(R), that aims to regenerate various damaged tissues throughout the body and heart. In particular, the company is focused on repairing tissue damage after events such as AMI, i.e. a heart attack, ischaemic stroke and refractory angina.

Ischaemia, in which blood flow and oxygen are restricted from certain parts of the body, occurs during heart attacks and strokes, causing a lot of damage due to cells not getting the sufficient oxygen they need to survive.

"The normal reaction in the body to help repair damage is to send signals to the stem cells in your bone marrow to create new cells," Dr Streefkerk explains. This enables the cells that need to receive vessels to supply blood to the damaged area.

"The stem cells that do this are typically living in the bone marrow, and they're activated upon this signal of damage and then they travel to the side of the damage and help repair the heart. Unfortunately, this is not enough," Dr Streefkerk states.

The stem cells Dr Streefkerk mentions are CD34+ stem cells. After something like AMI, these stem cells move from the bone marrow into the peripheral blood, migrating to the damaged heart to help repair any damaged tissue. But the number of stem cells that migrate isn't high enough to compensate for the damage. As such, increasing this number consistently is key.

Despite a range of treatments for heart failure, Dr Streefkerk argues that there are still a lot of patients dying or ending up in hospital due to the condition. Cardiovascular diseases actually represent the leading cause of death worldwide, killing around 17.9 million people every year.[1]

According to Dr Streefkerk, "this means that we need better treatments."

CellProthera is aiming to do this by getting more stem cells out of a patient's own bone marrow, expanding them according to GMP manufacturing, and then delivering them back to patients into the heart. The company has a GMP-compliant cell expansion process alongside its own automation technology for in vitro production of large quantity of purified CD34+ stem cells.

ProtheraCytes' underlying repair mechanism works by combining cell differentiation – the process in which a stem cell is changed to a more specialised type and a paracrine effect, a mechanism where those specialised cells then help stimulate the patient's cells to repair damaged tissue.

Having the right supply chain methods at hand is key in an area of drug development that relies on patients' own cells. In terms of manufacturing ProtheraCytes, this is an area that Dr Streefkerk says the company has struggled with. To develop its therapy, CellProthera must first take blood from a patient and bring that through to manufacture.

One of the drawbacks of this kind of personalised medicine is just how scalable it is. Logistically, the company must get patients' blood from hospital sites, liaise with transport companies to receive the blood and following that, manufacture it into a viable therapy that can be delivered back to the patient. Limitations for the company currently include a machine that is only GMP certified for the cell expansion of one patient at a time.

Dr Streefkerk states how CellProthera is working on a next version of the machine that is able to do five patient expansions at once. Other strategies to improve scalability could include placing these machines at hospitals to reduce the burden of logistics.

CellProthera's regenerative medicine approach to heart failure isn't a new idea. Scientists for years have been trying to understand how research involving endothelial cells, the womb conditions of heart muscle cells, and stem cell patches can be used to repair heart damage and regrow blood vessels.

But despite high levels of research, treatments are still limited and surgical interventions are commonplace for many heart conditions. As such, the burden on the healthcare system is huge and new treatments could drastically improve the outcomes for patients and remove strain on hospitals. In fact, recent studies indicate that invasive procedures such as stents do not reduce the risk of heart attack in patients with stable ischaemic heart disease compared to medication and lifestyle changes[2]. These limited forms of treatment coupled with high healthcare costs (in the US for instance, heart failure costs could rise to at least $70 billion by 2030)[3]

More so, a severe heart attack can lead to chronic heart failure, where the heart's function is weakened and life expectancy is reduced. Worse still is that treatments largely focus on reducing symptoms of this condition and are coupled with lifestyle changes to decrease pressure on the heart. As such, regenerative medicine could play a major role in curing the disease, as it's capable of repairing the structure of the damaged cardiac area, thus improving the heart's function.

This is the market CellProthera wants to enter. At the end of last year, the company extended its EXCELLENT clinical trial with the addition of another investigational site in the form of St Bartholomew's Hospital in London UK. The company's EXCELLENT clinical trial is a Phase I/IIb study evaluating ProtheraCytes as a minimally invasive ATMP cell therapy targeting the regeneration of heart tissue following severe Acute Myocardial Infarction (AMI) to prevent heart failure. The primary endpoint for the trial is no treatment emergent major adverse cardiac events, with secondary endpoints assessing efficacy trends, quality of life and the safety of the delivery method,

Importantly, the trial is combining factors which the company believes will make it more likely to have a successful cell therapy for treating AMI. Factors including the appropriate cell type – in this case CD34+ stem cells – the number of cells injected, the administration route, and the timing of injection are four key considerations that CellProthera states make for a successful cell therapy and which reduce the likelihood of secondary heart failure.

With a final read-out expected in 2023, CellProthera is now looking towards initiating a Phase III trial and is even aiming for potential marketing authorisation in 2025.

Dr Streefkerk states that whilst the current study is taking up a lot of CellProthera's resources, the company is looking into other applications for its lead therapy.

"We have also looked for applications in refractory angina, meaning patients who don't have an occlusion of the coronary arteries, but they still have a lot of pain. And it has been shown in the past in clinical trials with stem cells that those patients can be treated," Dr Streefkerk says.

The company has also looked into using ProtheraCytes as a treatment for ischaemic stroke and osteoarthritis, since CD34+ stem cells could also improve regeneration in the cartilage after being damaged.

For now, the results of the EXCELLENT trial will dictate the future steps of the company. If successful, CellProthera could be a major player in the cardiology market and bring a new treatment into a disease area which is desperate for new approaches.

In terms of impact, Dr Streefkerk puts it simply: "To me it would be a game changer. If we can reduce hospitalisation, or if we can improve quality of life for patients who suffered a heart infarction, that would be great. So, hugely impactful."

References

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