U of Chicago Docs Perform First Human Islet Transplant Successfully Using Antibody To Replace Toxic Anti-Rejection Drug

A critical step to cure millions with diabetes: Chicago woman is first to have successful human islet transplant using novel antibody to prevent rejection.

The Cure Alliance and Juvenile Diabetes Research Foundation fund Historic islet cell transplant with a new antibody to prevent rejection without toxicity of current standard of care drug.

MIAMI, FLORIDA, USA, May 8, 2024 /EINPresswire.com/ -- The Cure Alliance, a 501(c)(3) nonprofit, is announcing a patient with type 1 diabetes has successfully received the first ever pancreatic islet transplantation utilizing a novel monoclonal antibody, Tegoprubart, in place of the toxic Tacrolimus, the standard anti-rejection therapy. Based on studies in non-human primates, Tegoprubart (Eledon Pharmaceuticals, Irvine, CA) has a great potential to be more effective and much less toxic than Tacrolimus.

The historic transplant was performed on April 25, 2024 by Dr. Piotr Witkowski and Dr. John Fung at the University of Chicago Transplantation Institute, in collaboration with the University of Miami Diabetes Research Institute. The pilot study was funded by The Cure Alliance (TCA) and the Juvenile Diabetes Research Foundation (JDRF).

The patient, who has asked for anonymity, is a female in her 40s, who had spent over 30 years unable to control her blood sugar despite using modern technology for insulin delivery and blood glucose monitoring. She lived in constant danger of debilitating, potentially lethal episodes of low blood sugar (hypoglycemia).

Donor pancreatic islets (the mini-organs containing the insulin-producing cells) were infused into the liver as a minimally invasive procedure through a catheter placed by interventional radiologist under local anesthesia. The entire procedure took less than 40 minutes. Tacrolimus

anti-rejection drug was replaced with the novel antibody, Tegoprubart.

The patient was monitored for four days and released from the hospital without any adverse reaction. At this point patient has already benefited from 50% reduction in daily insulin requirements and much more stable blood glucose control. Over next 2 months, patient will be observed for the progression of islet engraftment and function allowing for the complete elimination of insulin injections.

T1 diabetes is caused by a patient's own immune system attack that selectively destroys the insulin-producing cells of the patient's pancreas, damaging it's ability to produce insulin which controls blood sugar. Uncontrolled blood sugar can lead to organ failures, blindness, amputations and early death. In addition to the approximately 10 million patients with type 1 diabetes worldwide, over 500 million are estimated to live with type 2 diabetes and between 150 to 200 millions of them also rely on insulin injections to try to maintain health.

There is clinical evidence from our studies and others conducted by the NIH's Clinical Islet Transplantation Consortium that demonstrate islet transplantation may reverse diabetes. This new anti-CD40 antibody has a great potential for success.

Novel Treatment: 30 Years in the Making

The first successful islet transplants were performed in the early 1990s by Dr. Camillo Ricordi and collaborators at the University of Pittsburgh, using the Ricordi Chamber and a method he developed for isolating and purifying hundreds of thousands insulin-producing islets from the human pancreas. The islets were obtained from organ donor pancreases and infused through the portal vein into the liver where they produced life-sustaining insulin. This initial success was made possible by treatment of the recipients with the powerful anti-rejection drug, Tacrolimus. However, harsh side effects are associated with this drug, including toxicity against the patient's kidneys, nervous system as well as the transplanted islets, leading to recurrence of after an initially successful treatment.

At the University of Miami Diabetes Research Institute (UM-DRI), Dr. Norma Kenyon and Dr. Camillo Ricordi developed a novel strategy to prevent rejection of transplanted islets using "anti-CD40L" antibodies, to replace Tacrolimus and its feared side effects. Compared to Tacrolimus, this antibody allows transplanted islets for improved insulin secretion. Now, after years of collaboration with Drs. Kenyon and Ricordi, Eledon has developed an improved, safer version of the antibody.

"It has been a long journey to help people with type 1 diabetes become free from dependence

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> *Piotr Witkowski, M.D., Ph.D.*
> *University of Chicago Medicine*

on insulin. This strategy holds great promise," said Dr. Ricordi.

A second T1 diabetes patient has already been enrolled at the University of Chicago and is awaiting her first islet transplant with Tegoprubart. Proof of concept will be evaluated and released as soon as possible.

"There is clinical evidence from our studies and others conducted by the NIH's Clinical Islet Transplantation Consortium that demonstrate islet transplantation may reverse diabetes by eliminating need for exogenous insulin and reinstating metabolic control in patients with difficult to control type 1 diabetes. However, the use of current standard of care anti-rejection medications, specifically: Calcinerin inhibitors like Tacrolimus have limited the benefit of these procedures due to well-known associated toxicity to the islets, nephrotoxicity, neurotoxicity and risk of hypertension. We hope that Tegoprubart will effectively protect islets from rejection without side effects related to current standard therapy" said Piotr Witkowski, M.D., Ph.D., Director, Pancreatic and Islet Transplant Program, University of Chicago Medicine who together with Dr. John Fung as a principal investigator conducts the trial.

Additional fundraising, necessary to expand this important proof-of-concept clinical trial, continues at www.thecurealliance.org/donate/ where 100% of secure tax-deductible donations go directly to this pilot study.

The Cure Alliance is a 501(c)(3) boutique non-profit dedicated to ending human suffering by helping scientists working to prevent and cure chronic, debilitating and fatal diseases. We support those struggling to move their successes in the lab to the patient's bedside, Shelley Ross is President.

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