THE UNIVERSITY OF CHICAGO MEDICINE

Sernova Corp Cell Pouch™ Clinical Trial

Title: A Safety, Tolerability and Efficacy Study of Sernova's Cell Pouch™ for Clinical Islet Transplantation

ID: PROSVA201701

Principal Investigator: Dr. Piotr Witkowski, M.D. Ph.D.

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Dear Patient,

I am writing to let you know about an opportunity to participate in a research study designed for patients with Type 1 Diabetes.

This study is being conducted by myself, Dr. Piotr Witkowski at the University of Chicago. This research study will assess the safety, tolerability and efficacy of the Sernova Cell Pouch™ that will be implanted under the skin, and transplanted with islets.

You may be eligible for this study if you are between the ages of 18-65, have been diagnosed with Type 1 Diabetes for longer than 5 years, and suffer from sudden and unpredictable drops of blood glucose leading to confusion or passing out despite the best medical treatment of insulin under the guidance of an experienced diabetologist.

If you are interested in learning more about this study, please review the patient information sheet and contact Lindsay Schenck, RN, BSN, 773-702-2504 for more information.

It is important to know that this letter is not to tell you to join the study. It is your decision, and your participation is voluntary. Whether you show interest, and participate in the study or not, will have no effect on your treatment with your doctors.

Thank you for your interest and considerations,

Piotr Witkowski M.D. Ph.D.

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Patient Information Sheet

This is a research study. This study is designed for patients with type 1 diabetes who suffer from sudden and unpredictable drops of blood glucose leading to confusion or passing out despite the best medical treatment with insulin under the guidance of an experienced diabetologist. The current treatment options for such patients are continuing with insulin therapy, pursuing solid organ pancreas transplantation or experimental islet cell transplantation through a medical center.

To date, in research studies using islet cell transplantation with donor islets isolated from the pancreas, the cells have been infused into a blood vessel (vein) which enters the liver. The vein is accessed through a puncture in the skin conducted by an interventional radiologist under ultrasound and radiologic guidance. Antirejection medications are used to protect the islets from immune system attack, and they are the same medication, which are used to protect pancreas , kidney or heart transplant.

The cells are not retrievable, this approach has been partially successful, and the infused islets may produce insulin in the patients. The current transplantation of islets isolated from the pancreas is still an experimental procedure in the United States.

In this new study, we are trying to improve the outcome and function of the isolated islets by placing the islets into the Sernova Cell Pouch™, a specially designed medical device, which is implanted under your skin and then transplanted with islets. This study still involves the procedure where we isolate insulin producing cells called islets, from a decease donor pancreas and transplant them into the patient with diabetes. Antirejection medications are used to protect the islets from immune system attack.

The Sernova Cell Pouch™ is an experimental device, and is thought to be a more natural environment for islets to functionally remain long term. Thus, the purpose of the study is evaluation of the Sernova Cell Pouch™, implanted under the skin for islet transplantation.

To improve the results of the islet transplantation, the Cell Pouch™ was developed so the islets can be transplanted in a more accessible and retrievable site, just under the skin into small chambers within the device, providing a lower risk of bleeding or clogging of the vein. Here the islets may have improved conditions for survival and potentially improved outcome. However, we need to carry out a safety study, with transplanted islets in the Cell Pouch™ to determine improved glucose control in patients with diabetes.

The Sernova Cell Pouch™ is a scalable device about the size of a business card designed to form tissue lined chambers with blood vessels for transplantation of islet cells. Once the device is inserted under your skin, tissue incorporated with small vessels develops through pores in the device around removable plugs, which when removed, form chambers into which islet cells are transplanted.

In this study, participants with Type-1 diabetes will have the Sernova Cell Pouch™ implanted in under the skin over the muscles of your abdomen and allowed to develop the tissue chambers prior to transplantation of islets into the Cell Pouch chambers. You will also have a small 'sentinel' Cell Pouch™ removed at a specified timepoint to examine the islets and their survival.

We anticipate that you may require either one or two islet transplants into the Cell Pouch™ for improved glucose control.

During the study, you will be asked to closely monitor your blood glucose levels and visit the clinic for follow up visits. Depending how you respond to therapy, you would need to participate in the study from 24 months to 36 months.

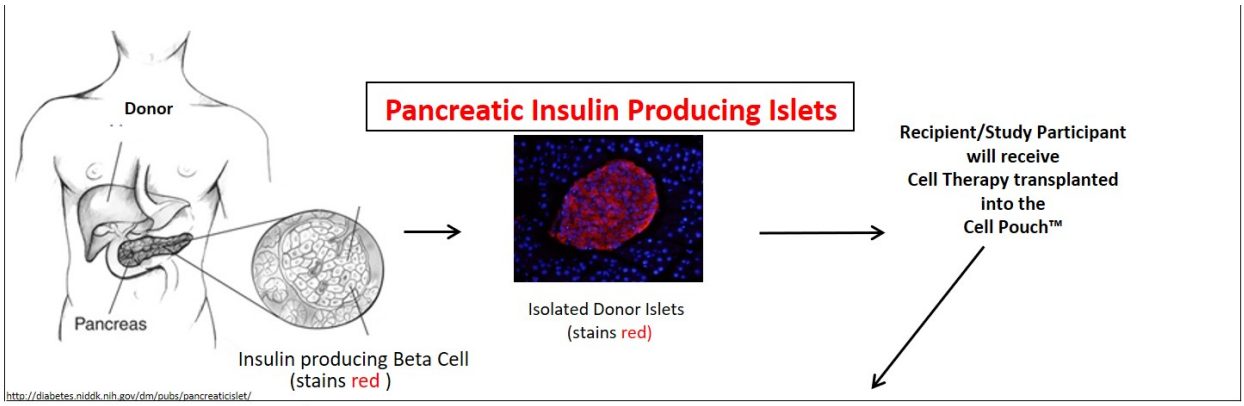
Your responsibility would be to follow the study protocol under the guidance of Dr. Witkowski and his research team, follow all their recommendations and inform them about any side effects or any medical problems you are experiencing, related or not related to the study.

You may or may not receive direct medical benefit from participating in this study. Your diabetes may be controlled by the transplant(s) without the need for additional insulin shots. This may also offer better protection against long-term complications of diabetes, but this is still unknown. It is still possible that islet will not survive to provide any beneficial effect to you, therefore at the end of the study, you will be offered another islet transplant, this time into the liver which was shown to have some positive in most of the patients, improving their glucose control and allowing to stop insulin completely in minority. After islet transplantation or at any point of the study, you may choose to stop participating and proceed with the whole pancreas transplant, which is standard of care procedure for your condition, if you qualify.

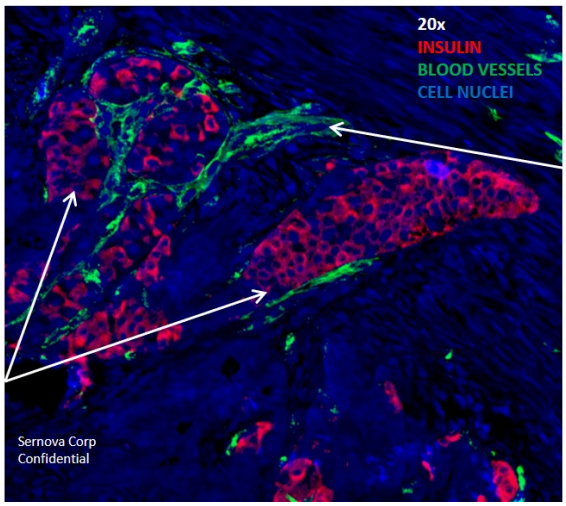
Nevertheless, the participation in the proposed study could bring you the following benefits:

- You will get access to the novel, minimally invasive intervention with a potential for improved blood glucose control and prevention of sudden blood glucose drops
- Participating in the study, you will also benefit from being very closely watched by the study team coordinators and Dr. Witkowski, who can answer all your concerns related to your participation in the study at any time point. Members of the study team will be advising you what to do in case of any medical condition related or not related to the study. They will be happy to answer all your questions and address any needs you may have.

Evidence of Surviving Cell Therapy Containing Donor Human Islets within the Sernova Cell Pouch™



An image of surviving Transplanted Pancreatic Islets surrounded by new blood vessels and healthy tissue in a representative area of the Sernova Cell Pouch ™ that has been removed



Insulin producing Islets
(Beta Cells stain red)

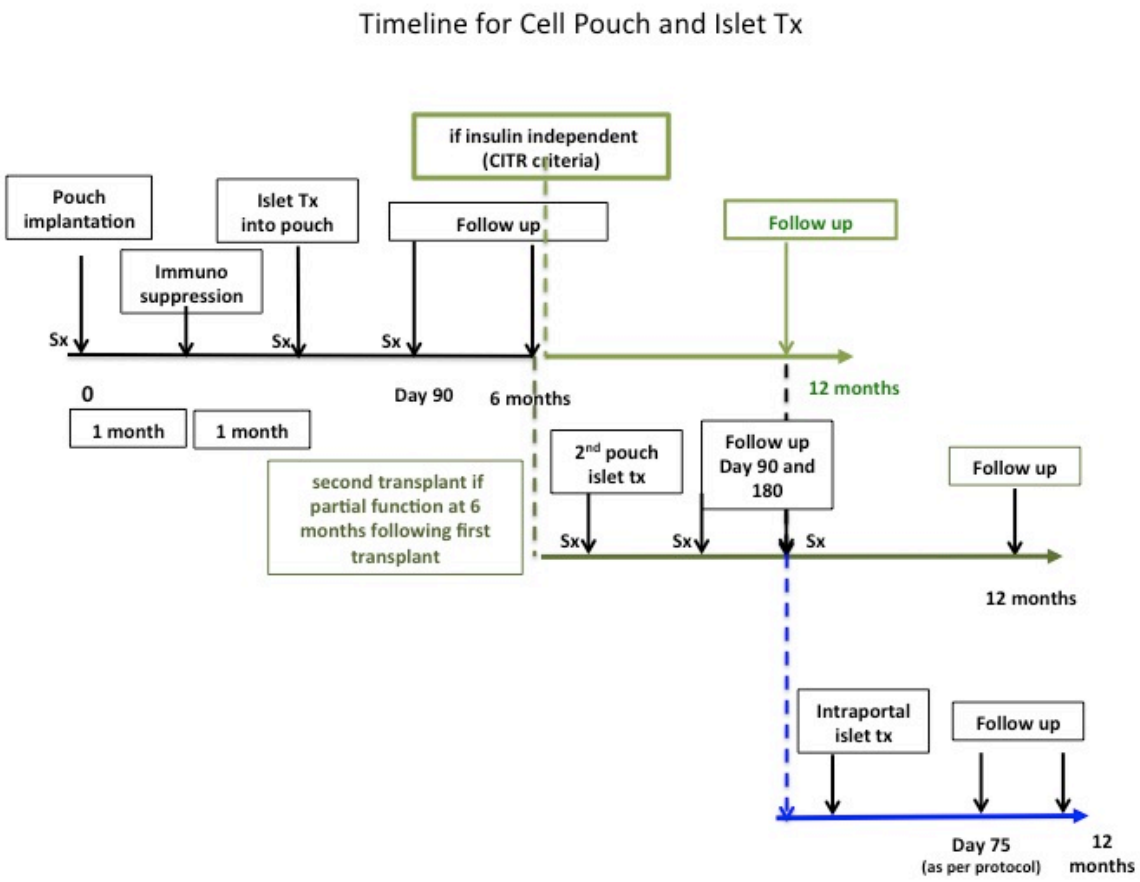
New Blood Vessels
(stained green)
Blood vessels surrounding and communicating with the islets

Healthy Tissue
(stained blue)
Newly developed healthy tissue supporting the islets and blood vessels

REFERENCES

1. Pepper AR , Pawlick LR , Gala-Lopez BL, , MacGillivary A, Mazzuca DA, White DA, Toleikis PM, Shapiro AMJ.Diabetes Is Reversed in a Murine Model by Marginal Mass Syngeneic Islet Transplantation. Using a Subcutaneous Cell Pouch Device. Transplantation 2105; 99, 11, 2294-2300.
2. Gala-Lopez BL, Pepper AR, Dinyari P, Malcolm AJ, 1, Kin T, L.R. Pawlick LR, 1, P.A. Senior PA, 1, Shapiro AMJ. Subcutaneous clinical islet transplantation in a prevascularized subcutaneous pouch – preliminary experience. CELLR4, 2016; 4 (5): e2132.

STUDY SCHEMA



Sx- surgery

LIST OF SURGICAL PROCEDURES

List of Surgical Procedures for the Sernova Cell Pouch™		
Number of Surgeries	**Description**	**Further Details**
1	Implantation (General Anaesthetic)	Implant 4 (or up to 6) Cell Pouches™ subcutaneously into the study participant (plus 2 sentinel Cell Pouches™] [This procedure can range from 30 mins-90 mins]
2	Transplantation (General Anaesthetic)	Transplant 2 (or up t o 3) Cell Pouches™ + 1 Sentinel Cell Pouch™ (Total # of transplanted pouches will depend on total volume of purified islet prep); Monitor for safety/efficacy until decision for a second transplant is made [This procedure can range from 30 – 60 mins]
3	Explantation of Sentinel Cell Pouch™ (General Anaesthetic)	Explantation of 1 islet transplanted Sentinel Cell Pouch™ approx. 90 days post-transplant [This is a short procedure , ~20 mins for explant]
4	Transplantation (General Anaesthetic)	Transplant 2 (or up t o 3) Cell Pouches™ + 1 Sentinel Cell Pouch™ (Total # of transplanted pouches will depend on total volume of purified islet prep); [This procedure can range from 30 – 60 mins]
5	Explantation of Sentinel (General Anaesthetic)	Explantation of 1 islet transplanted Sentinel Cell Pouch™ approx. 90 days post-second transplant [This is a short procedure , ~20 mins for explant]
**6	**Only if required Explantation of Cell Pouches™ (General Anaesthetic)	**Explantation of Cell Pouches™ [Depending on number of Cell Pouches™, This procedure could take 1-2 hours]