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Pancreas after islet and islet after pancreas transplantation offer a durable insulin independence to patients with type 1 diabetes mellitus and problematic hypoglycemia

Sarah Gondek[1], Mateusz Ogledzinski[1], William Lin[1], Kamila Milejczyk[1], Piotr Bachul[1], Braden Juengel[1], Lindsay Basto[1], Laurencia Perea[1], Lingjia Wang[1], Rolf Barth[1], John J Fung[1], Piotr Witkowski[1].
[1]Surgery, University of Chicago, Chicago, IL, United States.

Background: Islet, as well as pancreas transplantations, are alternative procedures providing diabetic patients with insulin independence and optimal blood glucose control. Here, we assessed the utility of islet transplantation after the failure of a pancreas graft and the utility of pancreas transplantation in patients with declining islet graft function.
Materials and Methods: Four patients with insulin-deficient diabetes and problematic hypoglycemia were transplanted with islets allografts after the failure of prior pancreas transplants (IAP). Another four patients who had previously received islet allotransplants were transplanted with a pancreas after their islet graft function declined (PAI patients). Tacrolimus and mycophenolate were used for immunosuppression supplemented with steroids for PAI patients.
Results: All four IAP patients became insulin independent after their first islet transplant. Two remained insulin independent 11 and 12 months later; the remaining two patients required a second ITx to extend insulin independence over 3 years and one of them a third ITx to extend freedom from insulin over 8 years.
All 4 patients receiving PAI had uncomplicated clinical courses and maintained optimal blood glucose control without insulin more than 4 years after the pancreas transplant. None of the patients developed de novo HLA antibodies after PAI or IAP transplantation.
Conclusions: Pancreas and islet transplantations are alternative beta cell replacement transplant procedures, allowing successful extension of insulin independence in case one type of those therapies had initially failed.
The study was supported by the Dompé Farmaceutici S.p.A. The authors would like to acknowledge the generosity and support of Dr. Martin Jendrisak and the entire team of the Gift of Hope Organ & Tissue Donor Network in Chicago, NJ Sharing Network, Lifebanc Ohio for providing the human pancreas tissues used in the present study. We also acknowledge support from the NIDDK P30 DK020595 and the Kovler Family Fund.

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Emerging data from a study of tegoprubart for the prevention of rejection in kidney transplant recipients: Implications for a similar study in islet cell transplantation

John Gill[3], Patrick Coates[6], Jean Tchervenkov[4], Jeffrey Bornstein[1], Paul Harden[5], Matthew Kadatz[3], Piotr Witkowski[2].
[1]Eledon Pharmaceuticals, Irvine, CA, United States; [2]Surgery, University of Chicago, Chicago, IL, United States; [3]Nephrology, University of British Columbia, Vancouver, BC, Canada; [4]Surgery, McGill University, Montreal, QC, Canada; [5]Nephrology, Oxford, Oxford, United Kingdom; [6]Nephrology, Royal Adelaide, Adelaide, Australia.

Introduction: Islet cell transplantation has the potential to be a functional cure for type 1 diabetes, but this option is infrequently used, in part because of the untoward effects of one of the anti-rejection medications, tacrolimus, which can be toxic to the implanted cells, necessitating multiple transplants. Tegoprubart is a monoclonal antibody directed against the CD40 ligand (CD40L), a key mediator of co-stimulation. Inhibition of CD40L should result in a decrease in both cell and antibody mediated immunity and create a more tolerogenic immune environment. Importantly, tegoprubart is not toxic to islet cells. Tegoprubart has been shown to be effective in animal models of both islet cell and kidney transplantation and is currently being studied in kidney transplant recipients.
Methods: In the ongoing kidney transplantation study, up to 12 adults receiving a kidney transplant from either a living or deceased donor will be enrolled. To be eligible, this must be their first transplant, they must be seropositive for EBV, free of donor specific antigens, have low panel reactive antibodies, and the organ cannot be from an extended criteria donor or have a prolonged cold ischemia time. All participants will receive rATG induction and a maintenance regimen consisting of tegoprubart 20 mg/kg IV administered every 3 weeks after an initial loading regimen, mycophenolate and corticosteroids. Enrollment of the first 4 participants is staggered such that the Data Monitoring Committee (DMC) needs to review the data from the first 28 days on study of the preceding participant before the next participant can be enrolled. Participants will remain on study for a year, after which time they will have the option of continuing tegoprubart in an extension study. The primary endpoint is safety. Secondary endpoints include characterizing the pharmacokinetic profile of tegoprubart, the incidence of biopsy proven rejection (BPAR), changes in estimated glomerular filtration rate (eGFR) and exploratory biomarkers including donor derived cell free DNA.
Results: The study is ongoing. As of the abstract submission deadline, May 2023, 5 participants have been transplanted, and 3 are ongoing. No participant has experienced rejection. One discontinued due to an SAE of BK viremia and another for mild alopecia and fatigue. BK viremia was the only SAE reported to date, and the drug appears safe and well tolerated. Participant information is summarized in Table 1, and mean eGFR is summarized in Figure 1.
Conclusions: Data to date from this calcineurin free study are encouraging, with no rejections, a good safety profile and excellent allograft function. These data support studying tegoprubart in a population of islet cell transplant recipients to assess whether this will improve outcomes in this setting. Such a study is planned by investigators at the University of Chicago.

Table 1. Summary of Ongoing Participants

Participant	Demographics	LD vs DD	Status	Last eGFR
1	60 yo white ♀, PCKD, pre-dialysis	LD	EDC Day 232	77mL/min/1.73 m² Day 217
2	77 yo white ♀, DKD, hemodialysis	DD	Ongoing	85mL/min/1.73 m² Day 217
3	62 yo white ♂, PCKD, pre-dialysis	LD	EDC Day 56	54mL/min/1.73 m² Day 49
4	68 yo white ♂, DKD, peritoneal D	LD	Ongoing	93mL/min/1.73 m² Day 49
5	23 yo white ♀, IgAN, peritoneal D	LD	Ongoing	44mL/min/1.73 m² Day 14

Figure 1. Mean eGFR in ML/min/1.73m²