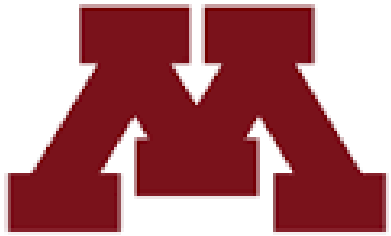


UNIVERSITY OF MINNESOTA

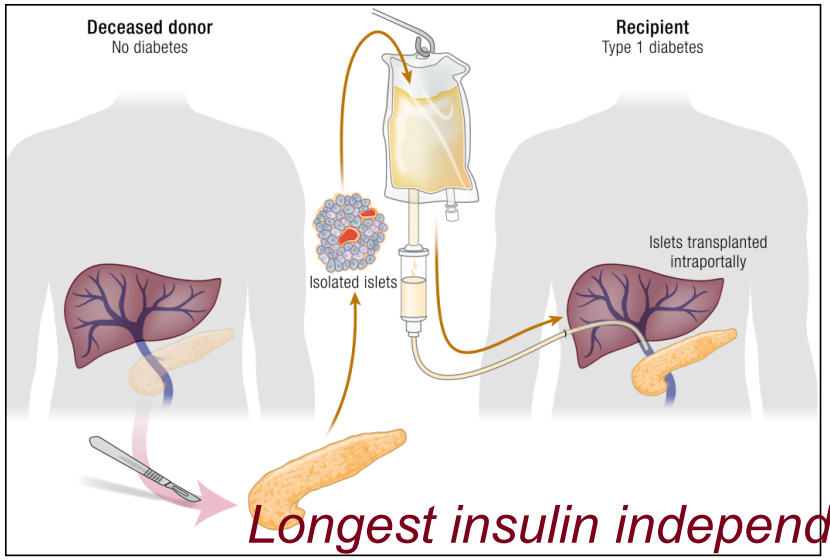
Driven to Discover®

University of Minnesota Site Updates CITR 2025 Meeting

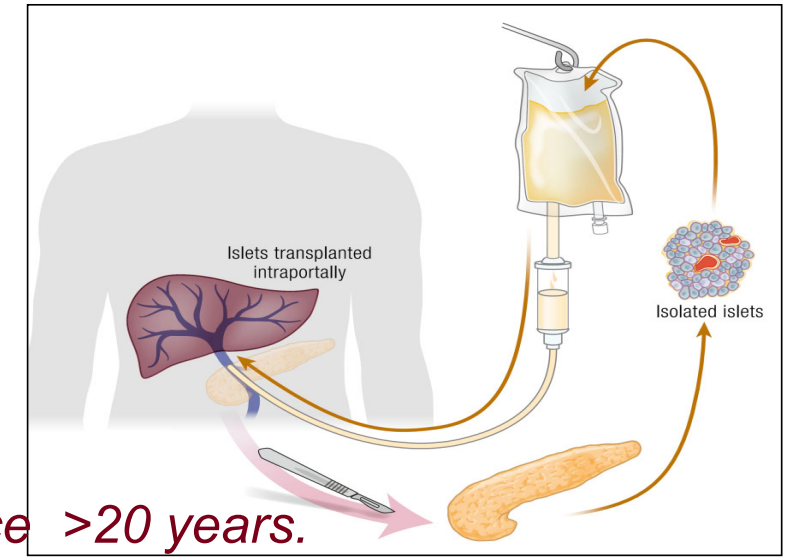
Melena D. Bellin MD
Professor, Pediatrics and Surgery
University of Minnesota Medical Center

UMN Program Activities

Alloislet transplantation for T1D (n=102)



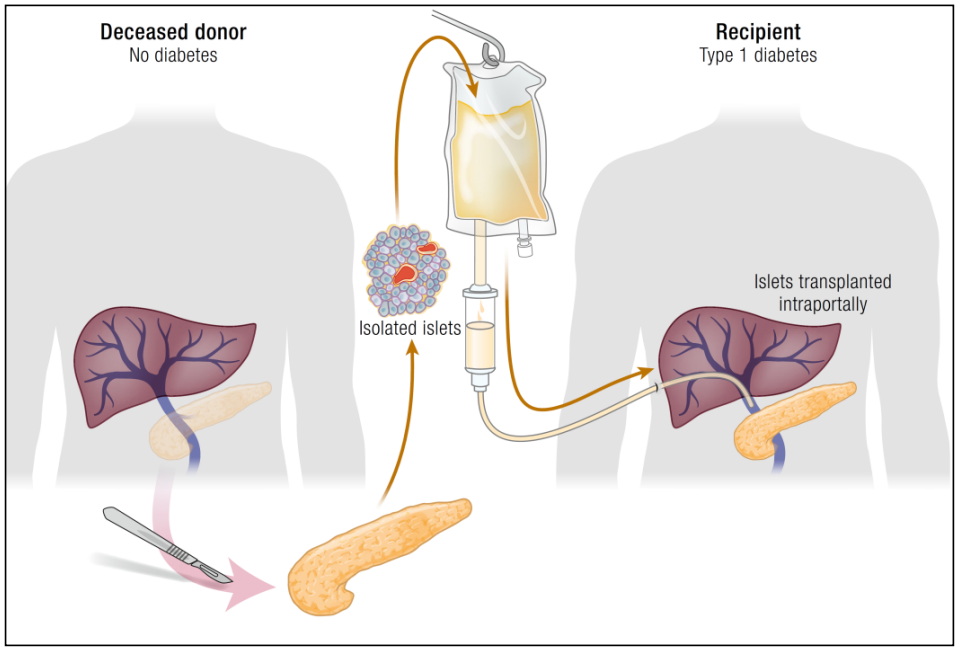
TPIAT (n=890)



Longest insulin independence >20 years.

Site for early Viacyte stem cell derived PP transplants
Active preclinical programs and immunology work

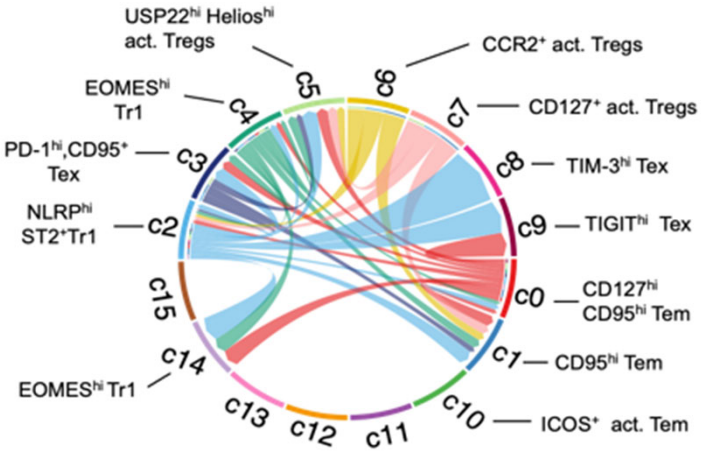
Allotransplant recipients in CITR



- 12 with partial islet fx or insulin independence continue to follow closely with our program
  - 16.5 years mean duration post-tx
- 4 remain off insulin at 10-16 years post-op (includes 2 single islet donor pts)

Tolerance to Transplanted Islets

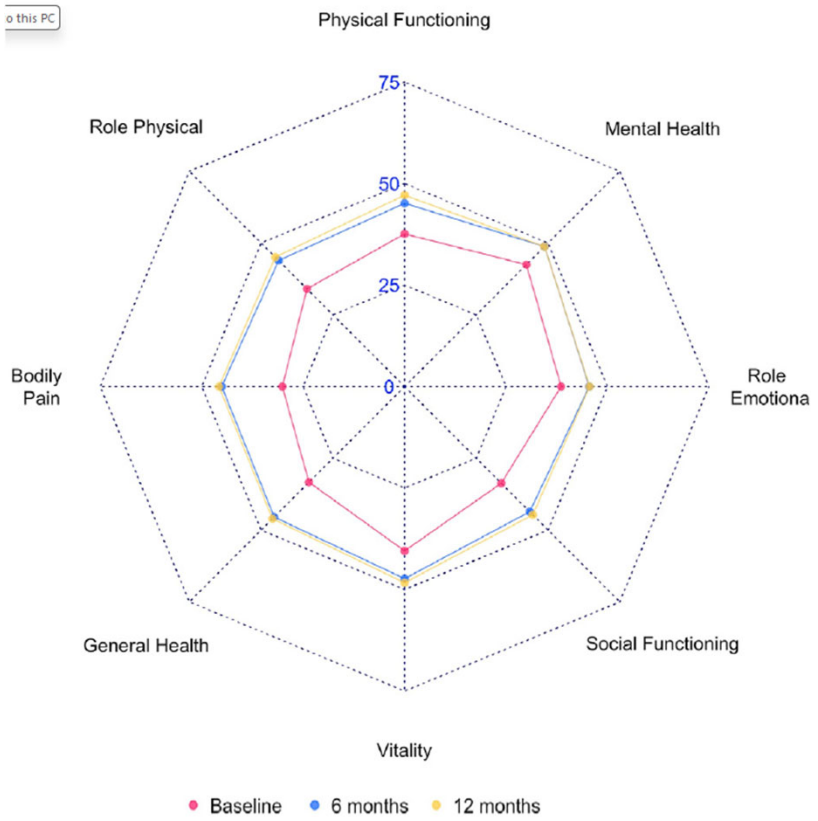
- Preparing for clinical trial to translate tolerance induction via peritransplant administration of apoptotic donor leukocytes
- Building on demonstration of long-term tolerance in NHPs (*Nat Comm* 2019)
- Building on deep profiling of long-term tolerance to islets in NHPs (*in final revision*)



TPIAT: Pain relief and improved QoL

POST

Advancing Treatment for Pancreatitis:
A Prospective Observational Study of TPIAT (POST)



- Multicenter outcomes (1 year):
  - Avg daily pain score 4.9 → 2.3
  - Seldom/no pain in 48%
  - Opioid use 24% (daily in 20%)
  - Pain interference, depression, and anxiety all decreased– largest decrease is in pain interference (10 points)
  - SF-12 scores increase
    - PCS by 13.7 points, MCS by 5 points
    - 70% with ≥5 points, 50% with ≥10 points change in PCS

R01 R01DK109124; Trikudanathan et al; Gastro 2025

POST Predictors of Diabetes Outcomes at 1 Year After Islet Autotransplantation: Data From a Multicenter Cohort Study

Background and Methods

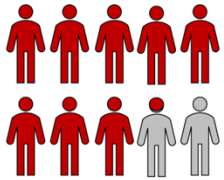
- **Total pancreatectomy with islet autotransplantation (TPIAT)** relieves pain in recurrent acute and chronic pancreatitis
- **We studied diabetes outcomes and predictors of outcomes in this multicenter prospective cohort (POST)**

Participants undergoing TPIAT enrolled at 12 centers in U.S.

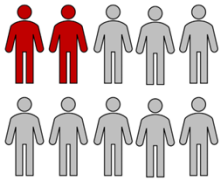
STUDY COHORT (n=384):

Age	Male	DM pre-TPIAT
29.6y	38%	16%

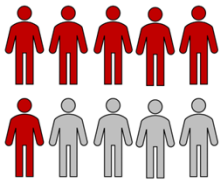
Diabetes Outcomes of TPIAT at 1 year



83% Islet function



20% Off Insulin



60% HbA_{1c} <7%

Predictors of Diabetes Outcomes

Predictors of Islet Function:

- **Fasting C-peptide***
  - **OR 2.2 (1.4, 3.4) per 1 ng/dL ↑**
- **HbA_{1c} Level***
  - **OR 1.9 (1.2, 3.0) per 1% ↓**

Predictors of Off Insulin:

- **Pediatric Age**
  - **OR 2.3 (1.3, 4.3)**
- **HbA_{1c} Level***
  - **OR 4.0 (1.7, 9.1) per 1% ↓**

Predictors of HbA_{1c} <7%:

- **White Race**
  - **OR 4.3 (1.7, 11)**
- **HbA_{1c} Level***
  - **OR 2.2 (1.1, 4.3) per 1% ↓**

DM, diabetes mellitus; POST, Prospective Observational Study of Total Pancreatectomy With Islet Autotransplantation.

** Laboratory results before TPIAT*

Diabetes Care. 2025;48(9):1493-1501. doi:10.2337/dc25-0620

American Diabetes Association®

Similar outcomes out to 4 years post-TPIAT

Supplementary Table 1: Long-term diabetes outcomes.

Outcomes	Pre-TPIAT	1 Year	2 Years	3 Years	4 Years
N	384	363	268	168	118
Insulin in past 14 days	39 (10.2%)	270 (80.1%)	177 (72.8%)	109 (69.9%)	71 (72.4%)
Insulin regimen*					
Insulin pump	5 (12.8%)	125 (46.3%)	93 (52.5%)	61 (56.0%)	36 (50.7%)
Multiple daily injections	22 (56.4%)	117 (43.3%)	67 (37.9%)	37 (33.9%)	28 (39.4%)
Once daily	12 (30.8%)	28 (10.4%)	17 (9.6%)	11 (10.1%)	7 (9.9%)
Insulin dose (units/day)*	5.41 (26.28)	22.54 (25.64)	23.88 (30.28)	29.95 (83.91)	22.51 (28.20)
Insulin dose (units/kg/day)*	0.06 (0.29)	0.34 (0.36)	0.34 (0.41)	0.57 (2.73)	0.31 (0.32)
Insulin dose <0.5 unit/kg/day**	367 (95.6%)	248 (74.0%)	181 (74.5%)	118 (76.1%)	76 (77.6%)
Non-insulin medication use	15 (3.9%)	11 (3.3%)	11 (4.5%)	7 (4.5%)	8 (8.2%)
HbA1c level (%)	5.61 (1.07)	7.02 (1.93)	7.07 (1.98)	7.17 (2.25)	7.34 (2.14)
HbA1c < 7%	341 (93.2%)	204 (60.4%)	132 (60.0%)	83 (58.5%)	53 (54.1%)
Fasting glucose (mg/dL)	99.6 (28.5)	130.4 (61.4)	131.4 (63.1)	127.7 (56.8)	136.3 (57.1)
Fasting C-peptide (ng/ml)	2.01 (1.47)	0.98 (0.79)	0.98 (0.76)	1.00 (0.72)	1.05 (0.71)
C-peptide >/= 0.3 ng/mL	361 (97.6%)	252 (82.9%)	144 (86.2%)	84 (84.0%)	55 (88.7%)
Any severe hypoglycemia episodes in past year	22 (5.8%)	46 (14.2%)	28 (11.6%)	21 (13.5%)	14 (14.4%)
Number of severe hypoglycemia episodes per year	0.23 (1.54)	0.79 (3.74)	1.18 (7.62)	0.50 (2.09)	1.08 (6.05)

Received: 6 June 2023 | Revised: 31 July 2023 | Accepted: 14 August 2023

DOI: 10.1111/ctr.15106

Clinical TRANSPLANTATION
The Journal of Clinical and Translational Research

WILEY

ORIGINAL ARTICLE

Islet graft function by mixed meal tolerance testing is sustained over 4 years in young children undergoing total

134 kids (n=52 young, n=82 adolescents)
645 MMTTs over 4 years

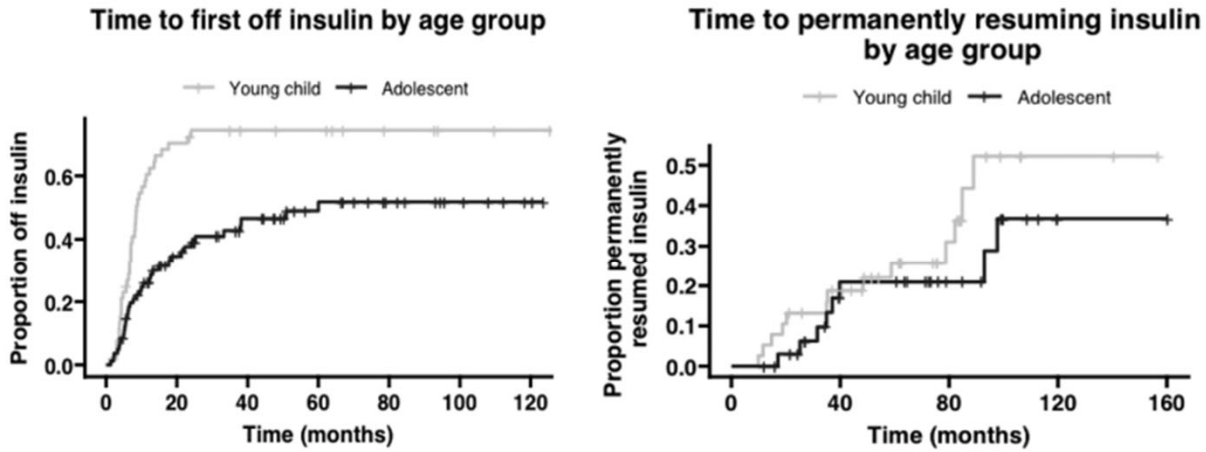


FIGURE 2 (A) Time until first off insulin in TPIAT, showing young children (age 3–11 years) and adolescents (age 12–18 years). Young children were more likely to achieve insulin independence compared to adolescents ($p < .001$), and this difference remained significant after adjusting for IEQ/kg. (B) Time to resuming insulin among those coming off insulin therapy, with non-significant differences between age groups. Gray indicates

Received: 6 June 2023 | Revised: 31 July 2023 | Accepted: 14 August 2023

DOI: 10.1111/ctr.15106

Clinical TRANSPLANTATION
The Journal of Clinical and Translational Research
WILEY

ORIGINAL ARTICLE

Islet graft function by mixed meal tolerance testing is sustained over 4 years in young children undergoing total pancreatectomy with islet autotransplantation

134 kids (n=52 young, n=82 adolescents)
645 MMTTs over 4 years

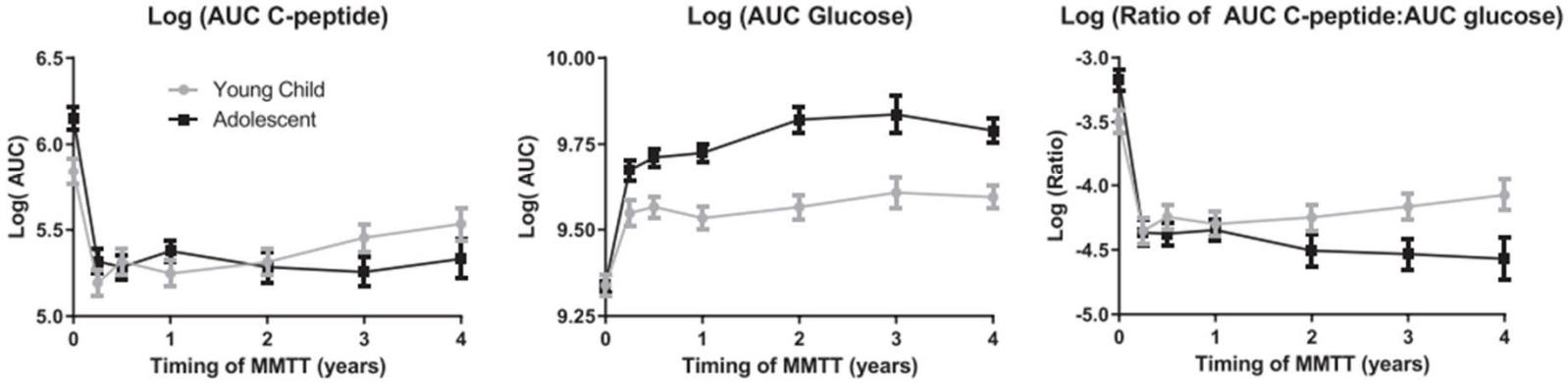


FIGURE 1 Mixed meal tolerance data for young children and adolescents by time point of assessment relative to TPIAT, showing (A) log transformed AUC C-peptide; (B) log-transformed AUC glucose, and (C) log-transformed ratio of AUC C-peptide to AUC glucose. Gray indicates

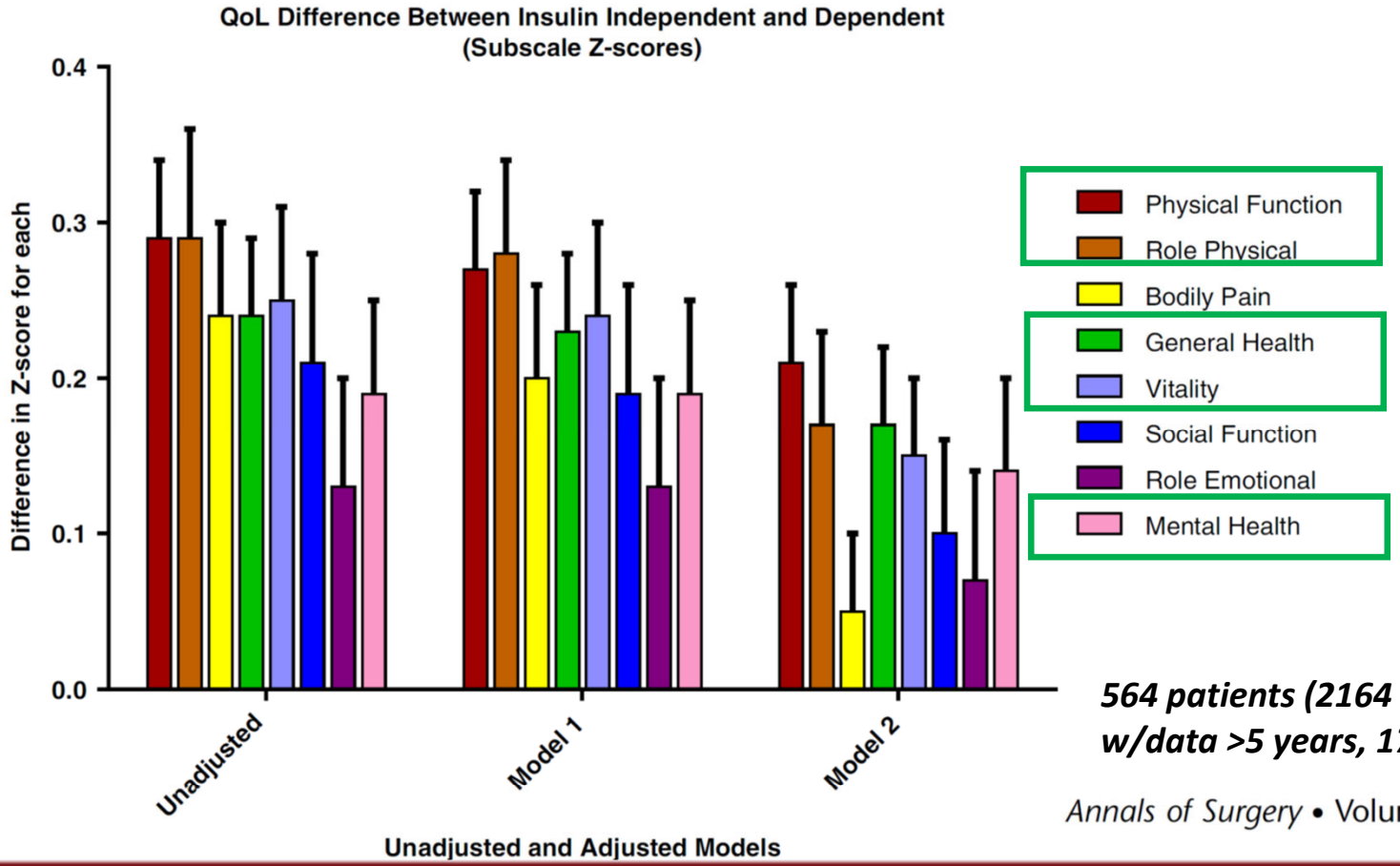
More Recent Data from the "LIFT" Study = Most Retain Islet Function Long-Term

LiFT
Long-Term Islet Function and Impact after TPIAT

		32%	60%	8%	
Characteristic	**Overall**, N = 122	**Off insulin**, N = 39	**Partial Function**, N = 73	**Islet Graft Failure**, N = 10	**p-value**
Duration Post-TPIAT (y)	9.5 (6.9, 12.0)	8.7 (6.6, 11.3)	9.4 (6.9, 11.8)	11.8 (10.5, 13.8)	0.066
IEQ/kg transplanted	4,022 (2,849, 5,475)	5,480 (3,959, 6,735)	3,374 (2,730, 4,599)	2,844 (1,532, 4,554)	<0.001
HbA1c (%)	6.60 (5.80, 7.60)	5.80 (5.60, 6.00)	7.00 (6.30, 7.83)	7.90 (7.20, 8.45)	<0.001
HbA1c < 7%	72 (60%)	36 (92%)	34 (47%)	2 (20%)	<0.001
Insulin dose (units/kg/day)	0.19 (0.00, 0.39)	0.00 (0.00, 0.00)	0.28 (0.15, 0.46)	0.44 (0.34, 0.54)	<0.001
Ever off insulin	56 (46%)	39 (100%)	17 (23%)	0 (0%)	<0.001
% TIR 70-180 mg/dL	75 (58, 94)	95 (89, 97)	67 (52, 82)	45 (38, 63)	<0.001
% TIR 70-140 mg/dL	51 (27, 76)	78 (61, 83)	38 (24, 59)	25 (17, 31)	<0.001
% time < 70 mg/dL	0 (0, 1)	0 (0, 1)	0 (0, 1)	1 (0, 2.5)	0.4

R01-DK126728 (LIFT)

Long-term insulin independence => ↑ QoL



- **PCS score 3 points higher if off insulin**
- All except bodily pain, social function, role emotional significant *after adjustments for opioids, pain scores, and age*

564 patients (2164 surveys), time-adjusted, 46% w/data >5 years, 17% w/day >10 years after TPIAT

Annals of Surgery • Volume 276, Number 3, September 2022

Peri-Transplant Inflammation and Long Term Diabetes Ourcomes Were Not Impacted by Either Etanercept or Alpha-1-Antitrypsin Treatment in Islet Autotransplantation Recipients

Randomized Pre-TPIAT

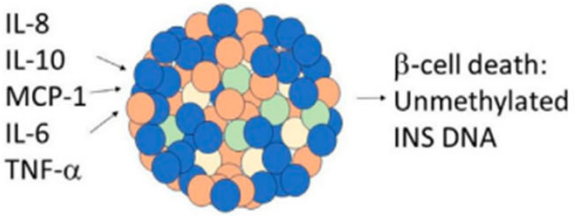
A1AT
n = 13

Etanercept
n = 14

Standard
care
n = 16

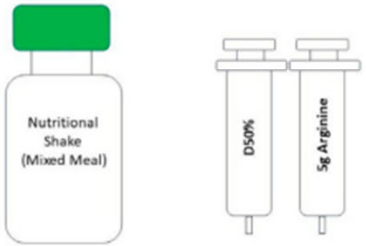
Peri-Transplant Measures:

- Cytokines
- Beta-Cell Death Biomarker
- Serum A1AT level (drug monitoring)



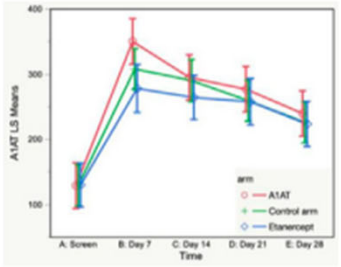
Long-Term Islet Function (2 years):

- Insulin secretion by Mixed Meal, IVGTT, GPAIS



Results:

- Serum A1AT elevated above normal, even in etanercept and standard of care groups



-No differences overall in cytokines, unmethylated INS DNA, or islet function between groups post-TPIAT

Conclusion: There was not a clear benefit derived from either etanercept nor A1AT. Circulating A1AT levels rose in all groups, representing endogenous secretion in etanercept and control arms, which may explain the lack of therapeutic benefit from treatment with A1AT.

Abdel-Karim, et al. *Transpl. Int.* 2024doi: 10.3389/ti.2024.12320

ESOT Leading the way in transplantation

Transplant International

GRAPHICAL ABSTRACT

Acknowledgements

Grant Funding:

R01-DK126728 (LIFT)
R01-DK109124 (POST)
R01-DK138809 (POST biomarker)
R01-DK109914 (anti-inflammatory)
U01-DK127367 (T1DAPC)
U01-DK126300 (CPDPC)
DoD- HT9425-23-1-0307

Pancreatitis Clinical Team

POSTLiFT

Long-Term Islet Function and Impact after TPIAT

Clinical research group