



AT THE FOREFRONT

**UChicago
Medicine**

Piotr Witkowski Lab



Breakthrough T1D™

Formerly JDRF



Eledon
Pharmaceuticals



Safety and Efficacy Assessment of Islet Transplantation

with CD40L Monoclonal Antibody (Tegoprubart)

for Calcineurin Inhibitor-Free Immunosuppression in T1D: A Pilot Study

Preliminary results

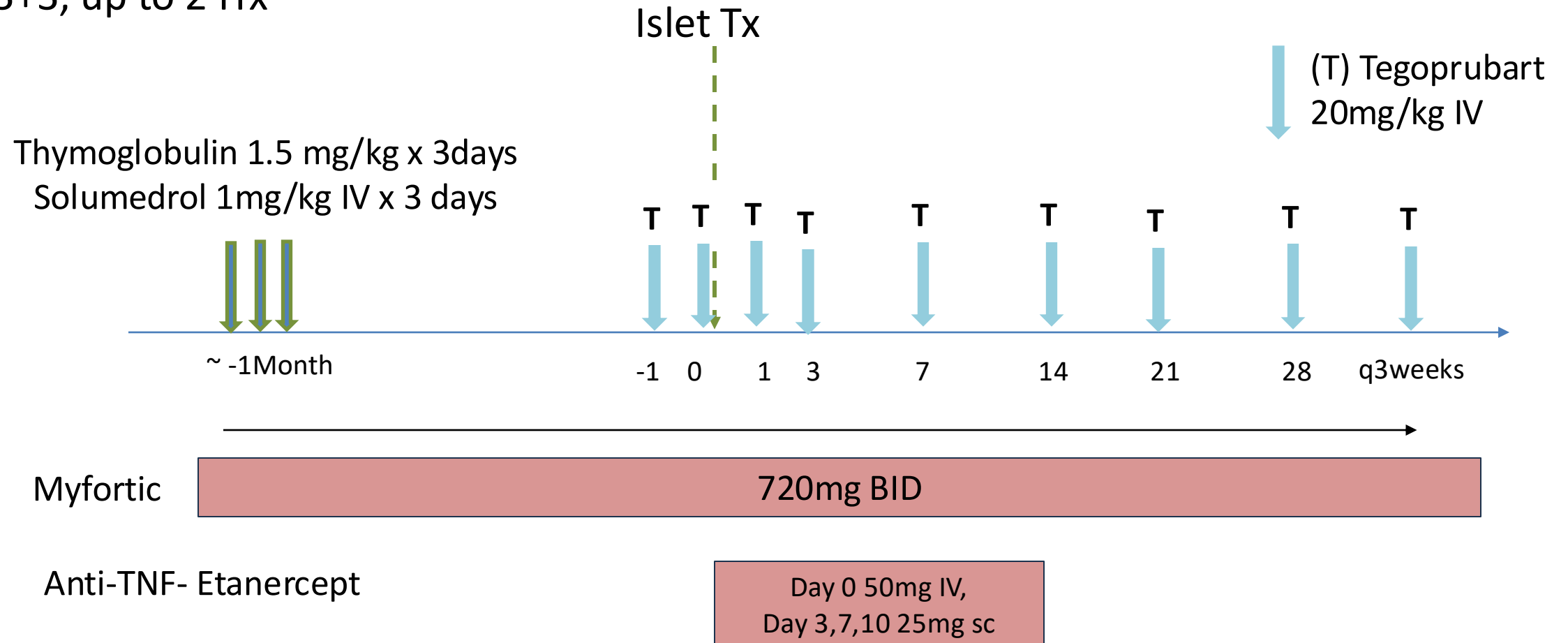
Nicole Wojcik, John J. Fung, Camillo Ricordi, Norma Kenyon, Piotr Witkowski

Background

- Anti-CD40L mAb has been shown to be safe and potent immunomodulatory agent in preclinical studies of kidney and islet transplantation
- Unfortunately, first clinical applications of anti CD40L mAb led to thrombo-embolic events, which halted its further clinical use.
- Now, over 20 years later, modified version of anti-CD40L mAb without thrombo-embolic activity became available for clinical testing under name of Tegoprubart by Eledon Pharmaceutical.
- Enrollment into phase 2B multicenter trial testing Tegoprubart vs tacrolimus has been recently accomplished (N=120) in kidney transplantation.
- Preliminary results indicate safety and efficacy of Tegoprubart therapy without nephrotoxicity and diabetogenic effect typical for tacrolimus.

Immunosuppression regimen

N=3+3, up to 2 ITx



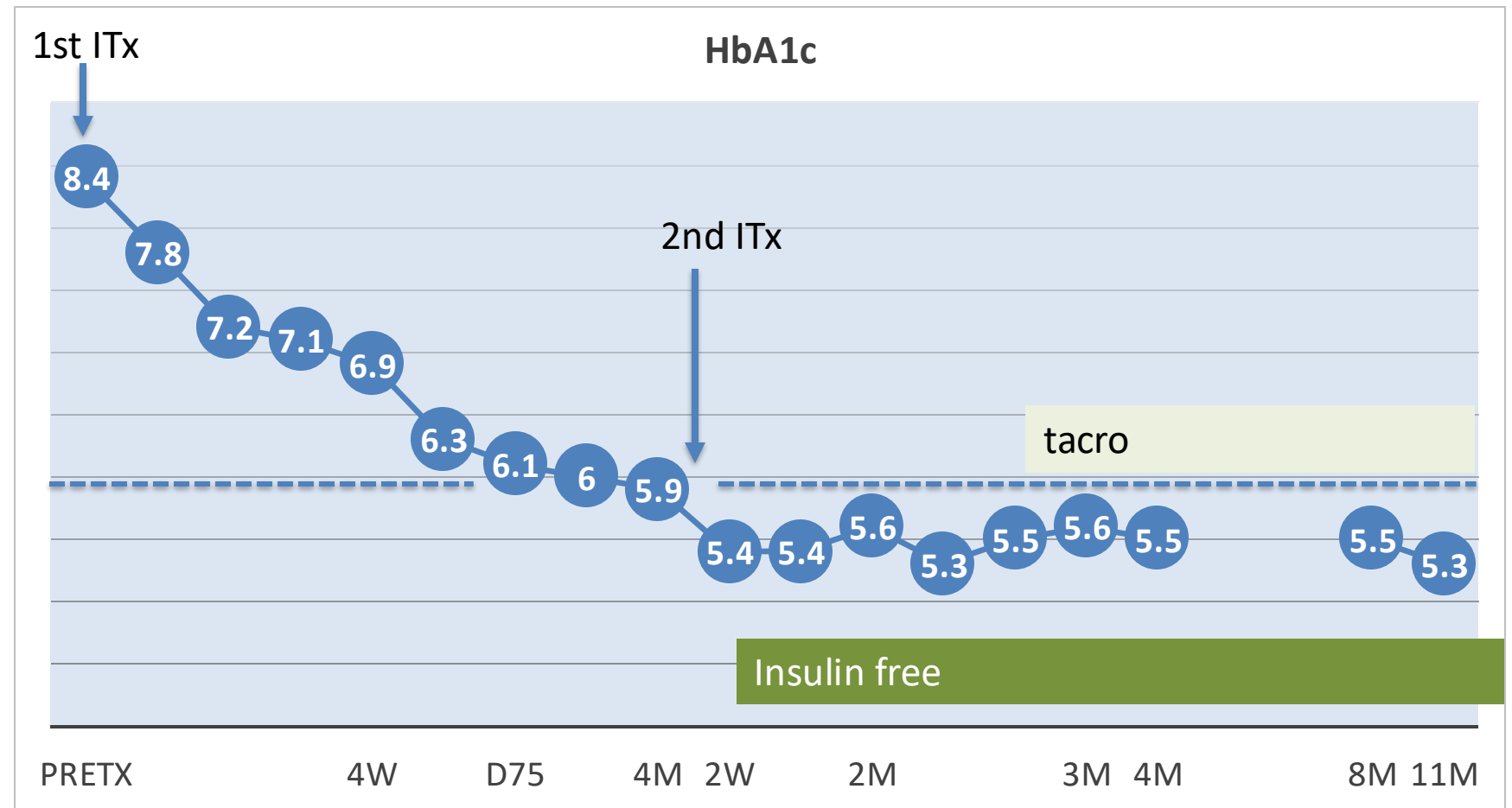
Patient 01 follow up now: 13 months

- 42 years old female
- Weight 88kg→93kg
- BMI 30 → 32

- **Tx nr 1** (4/25/24)
- Islet IEQ= 363,000
- Islet IEQ/kg= **4,092**
- pellet- 2.5ml

- **Tx nr 2** (8/23/24)
- Islet IEQ= 505,000
- Islet IEQ/kg= **5,500**
- pellet- 2ml

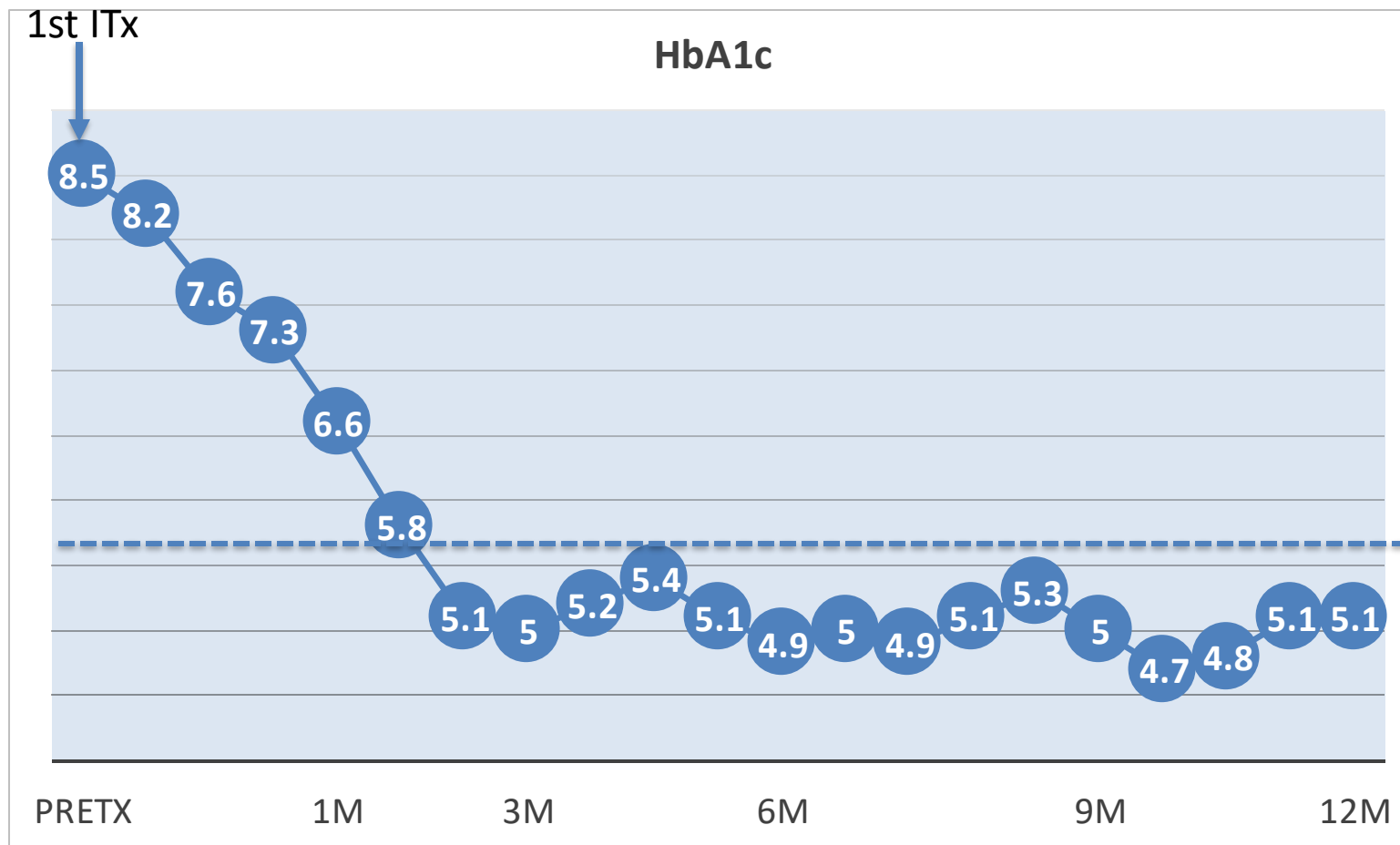
- no AEs,
- labs wnl (WBC 3-4)
- 10/22/24 started tacrolimus



Patient 02

follow up now: 11 months

- 30 years old female
- Weight 50kg
- BMI 21
- 2 weeks after Thymo- serum sickness, fully recovered
- **Islet Tx** (7/17/24)
- Islet IEQ= 326,000
- Islet IEQ/kg= **6,775**
- AEs, labs wnl (WBC 3-5)



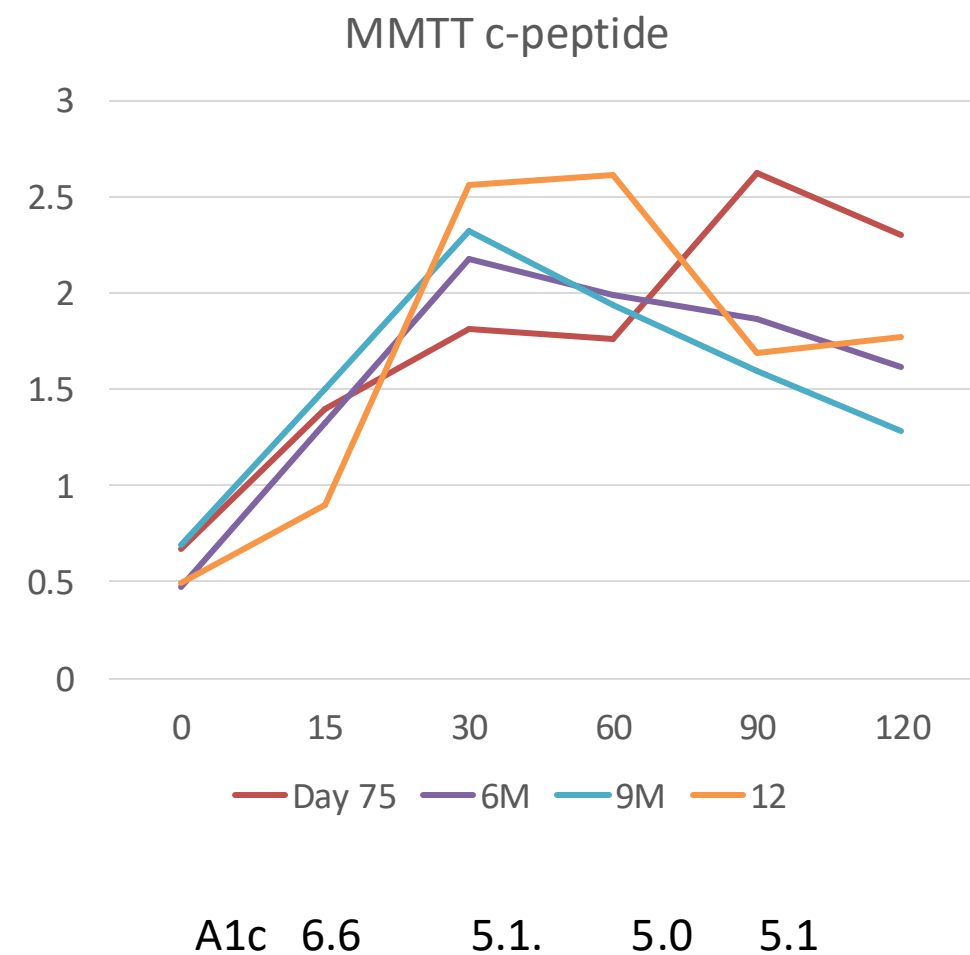
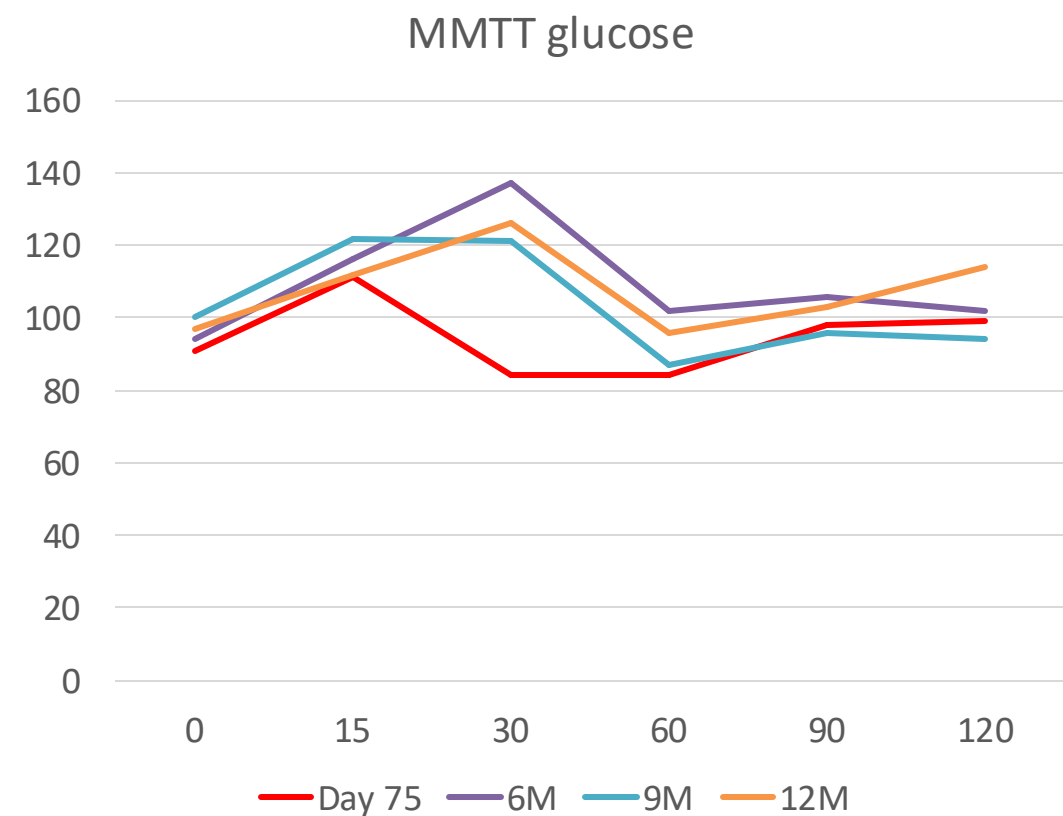
Insulin free

Daily insulin use

60u 17u 15u stopped

Patient 02

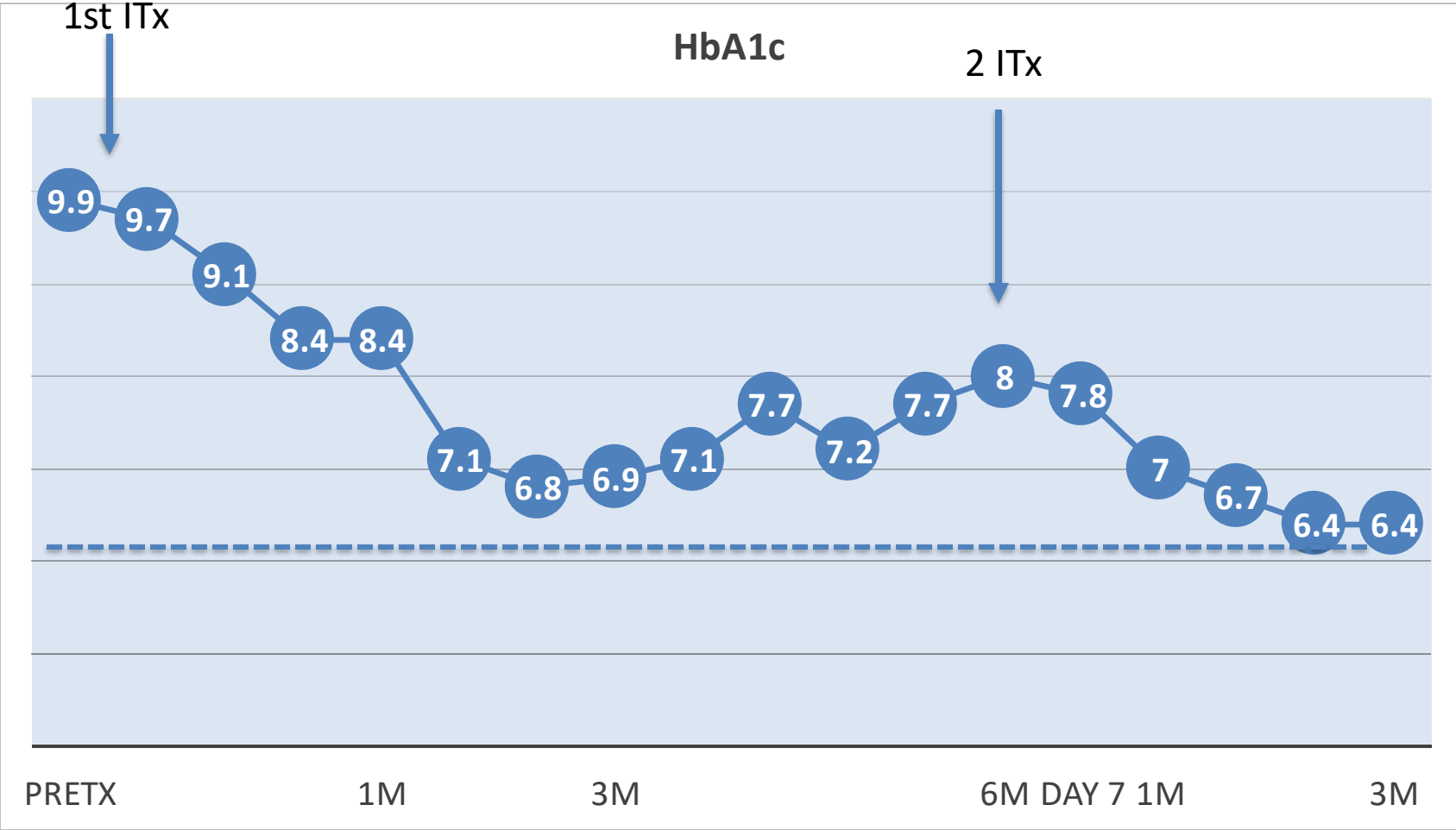
follow up now: 12 months, stable islet graft function



Patient 03

Follow up now: 9 months

- 37 years old male
- Weight 92kg
- BMI 29.9
- HbA1c 9.9%
- 90u of insulin per day
(34u Tresiba +56u short acting)
- 9/6/2024 Thymoglobulin induction
- No SAEs
- **Islet Tx** 10/4/24
- IEQ= 376,000, **IEQ/kg 4,086**
- **Islet Tx** 4/18/24
- IEQ= 396,000, **IEQ/kg 4,211**



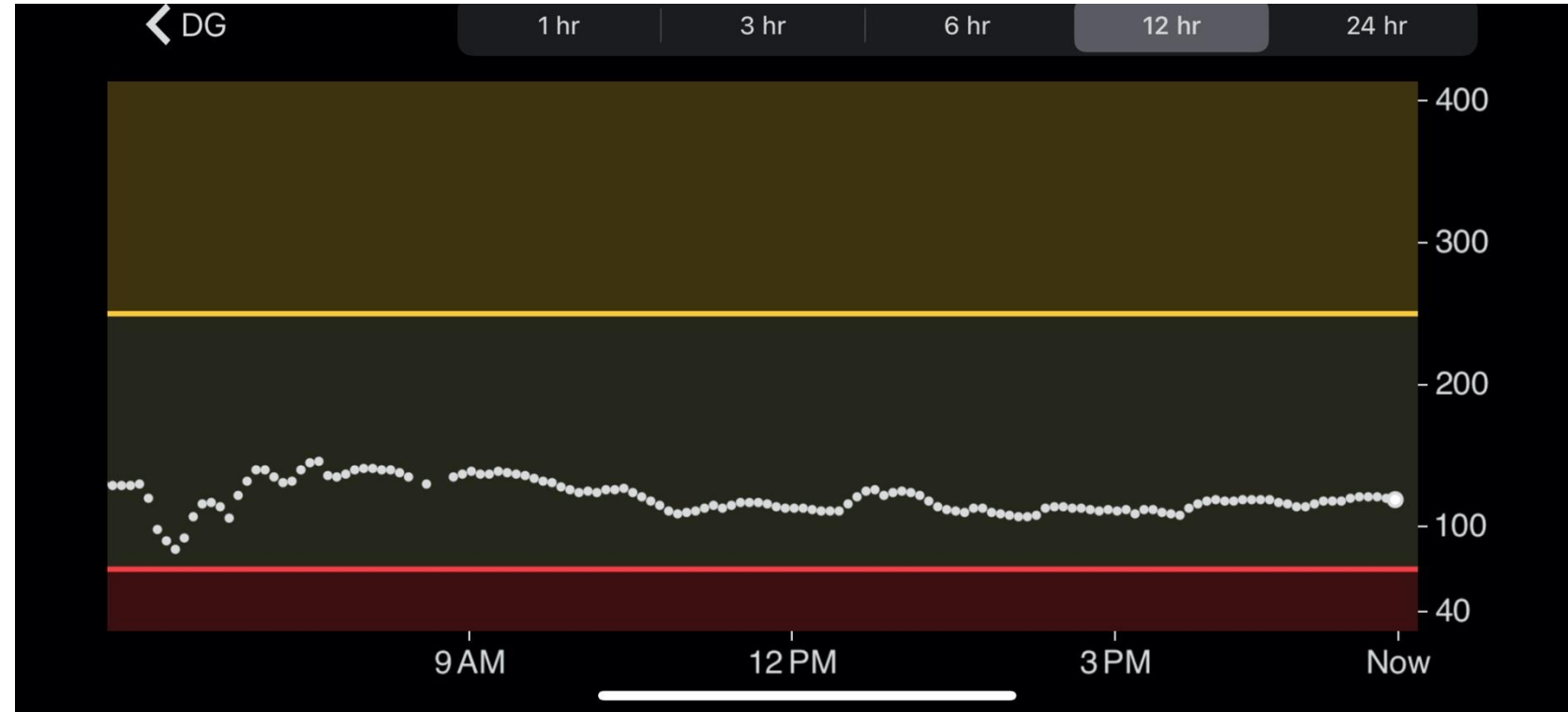
Daily insulin use

Time Point	Daily insulin use (u)
PRETX	90u
1M	26u
2M	20u
3M	14u
4M	20u
5M	12u
6M	16u
7M	16u
8M	25u
9M	45u
10M	28u
11M	14u
12M	0
13M	0

Patient 03

Follow up now: 8 months

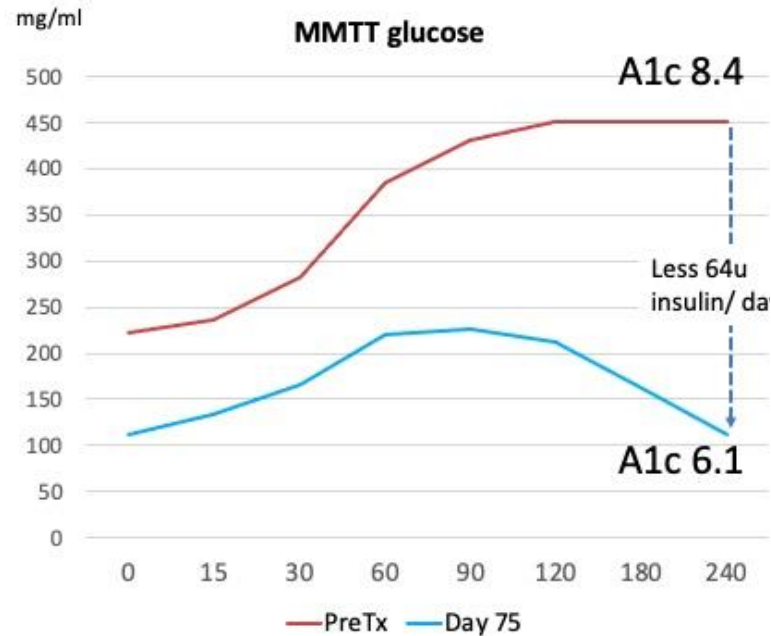
- 37 years old male
- Weight 92kg
- BMI 29.9
- HbA1c 9.9%
- 90u of insulin per day
(34u Tresiba +56u short acting)
- 9/6/2024 Thymoglobulin induction
- No SAEs
- **Islet Tx** 10/4/24
- IEQ= 376,000, IEQ/kg 4,086
- **Islet Tx** 4/18/24
- IEQ= 396,000, IEQ/kg 4,211



patient 01

Weight **89kg**, BMI **30**

IEQ 363,000 IEQ. **4,091 IEQ/kg**



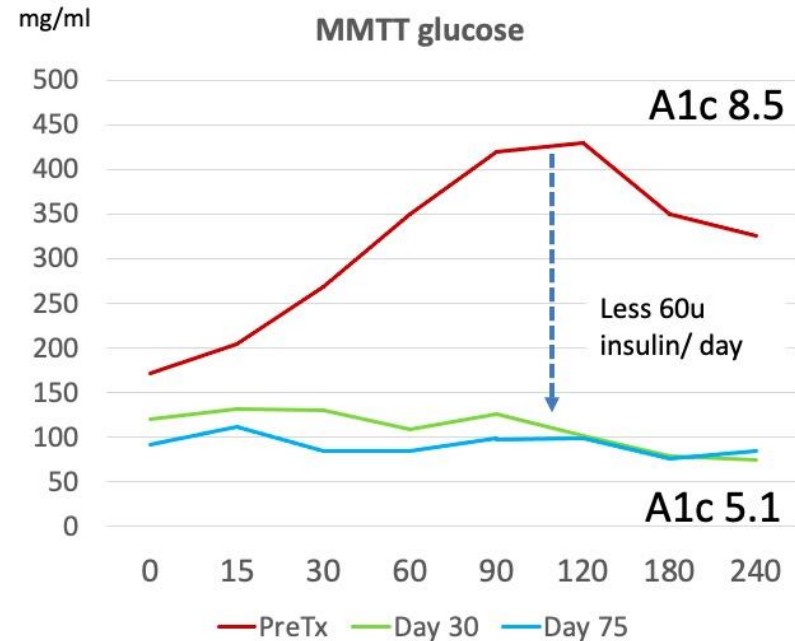
Day 75

Insulin requirements **down 64 u/day**
from 80→16u/day

patient 02

Weight **50kg**, BMI **21**

IEQ 326,000 **6,775 IEQ/kg**



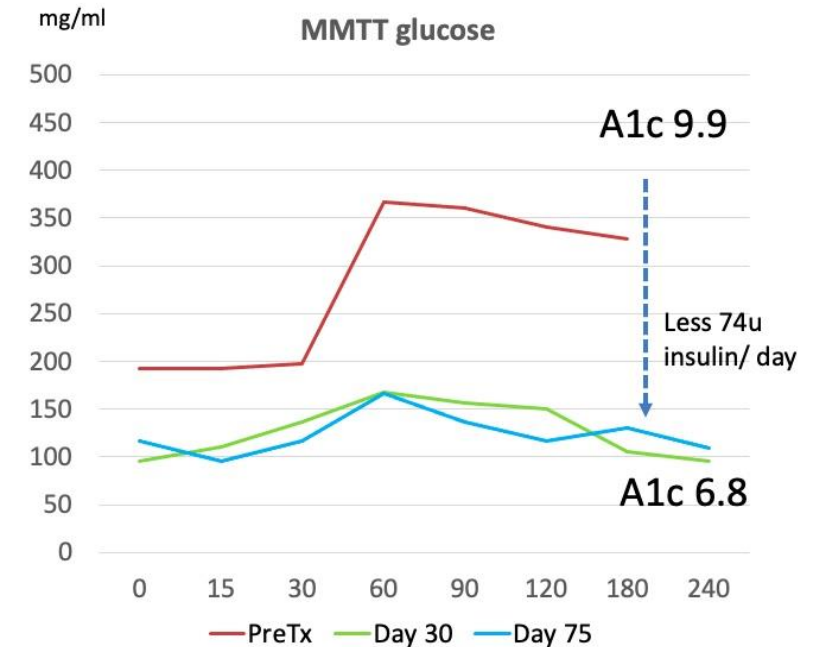
Day 75

Insulin requirements **down 60 u/day**
from 60→0u/day

patient 03

Weight **92kg**, BMI **30**

IEQ 376,000 **4,086 IEQ/kg**



Day 75

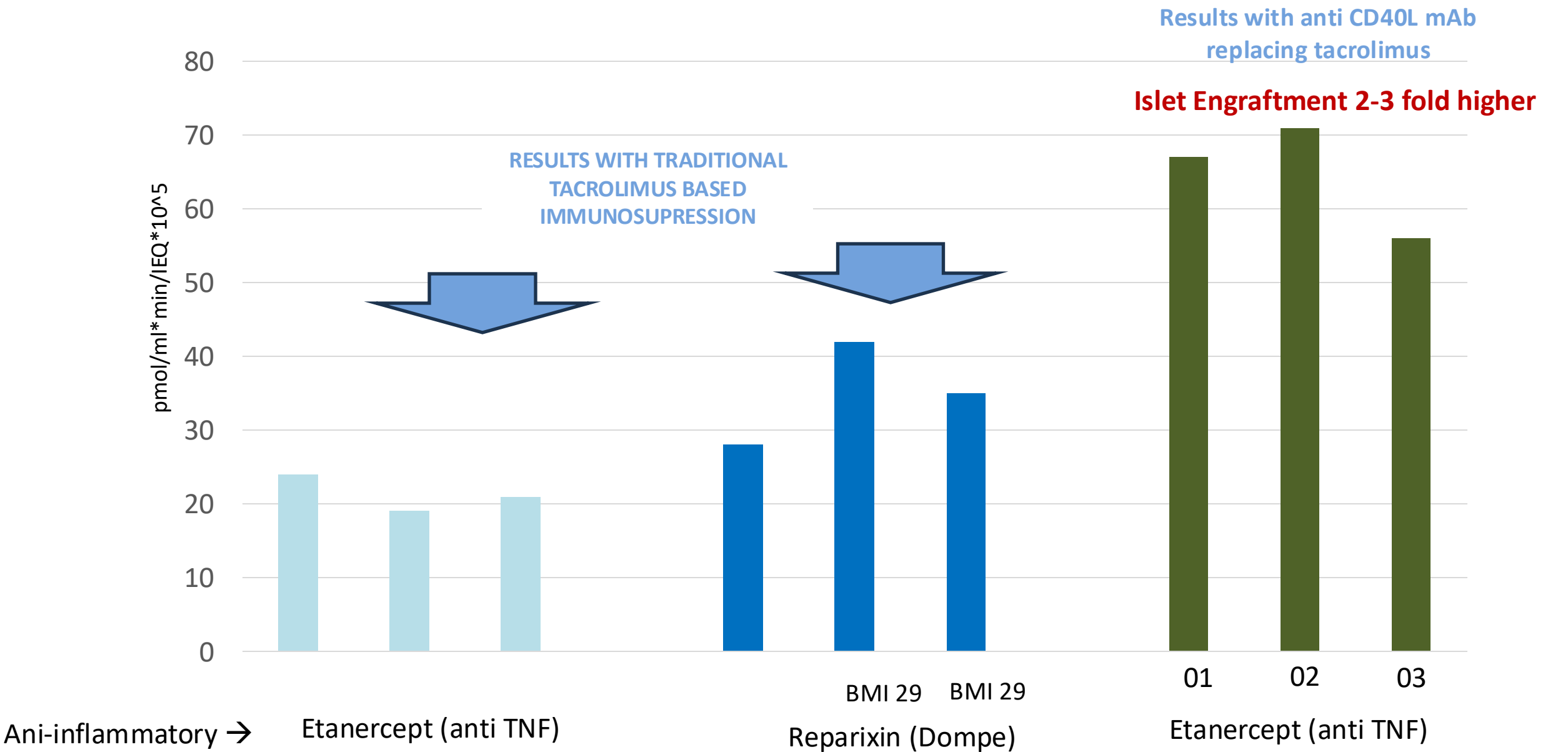
Insulin requirements **down 74 u/day**
from 90→16u/day

A single donor islet transplant in dose < 380,000 IEQ allowed to lower insulin requirements by over 60u of insulin per day

Summary

- All 3 subjects:
- experienced improved BG control with **no need for insulin support**
- present **stable islet graft function allowing for insulin independence**
- there were **no unexpected Adverse Events**, no severe hypoglycemic episodes
- no infections
- no thromboembolic events
- no signs of rejection, no *de novo* Donor Specific HLA antibodies
- All labs remained within normal limits or not clinically significant, consistent with myfortic (WBC 3-4) , no GI symptoms
- **No signs of kidney and neurotoxicity observed in historic controls on tacrolimus**

Islet Engraftment on day 75
(AUC c-pep)/IEQ



Patient 004

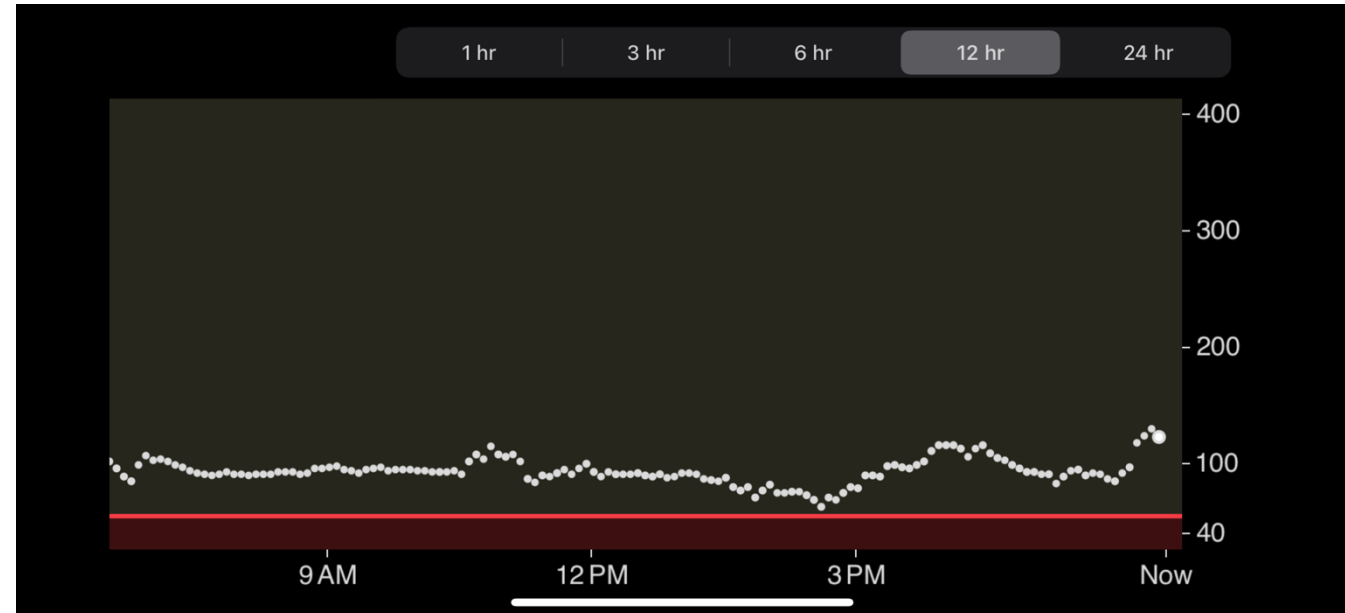
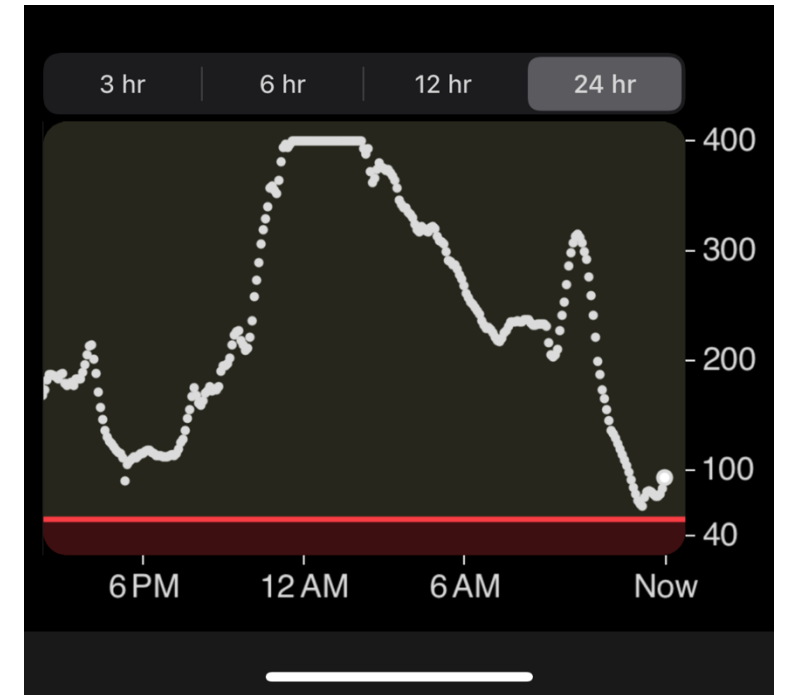
- 19yo male
- Weight 87kg
- BMI 30
- **Tx nr 1** (8/1/25)
- Islet IEQ= 473,000
- Islet IEQ/kg= **5,490**
- pellet- 6.5ml
- no AEs,

Patient 005

- 49yo female
- Weight 68kg
- BMI 25
- **Tx nr 1** (7/24/25)
- Islet IEQ= 352,000
- Islet IEQ/kg= **5,158**
- pellet- 1.7ml
- no AEs,

Patient 006

- 51yo female
- Weight 52kg
- BMI 19
- **Tx nr 1** (7/15/25)
- Islet IEQ= 298,000
- Islet IEQ/kg= **5,569**
- pellet- 1.5ml
- no AEs,



Conclusions

- Preliminary results of our pilot study indicate safety and effectiveness of Tegoprubart in islet graft protection after transplantation in patients with T1D

Next steps: Breakthrough T1D already funded extension of the study for six additional patients, 3 of them recently transplanted, subsequent 3 will follow.



Thank you

