



Vanskeligregulerbar diabetes – pankreas-eller øycelletransplantasjon?

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Universitetet i Oslo

Interessekonflikter

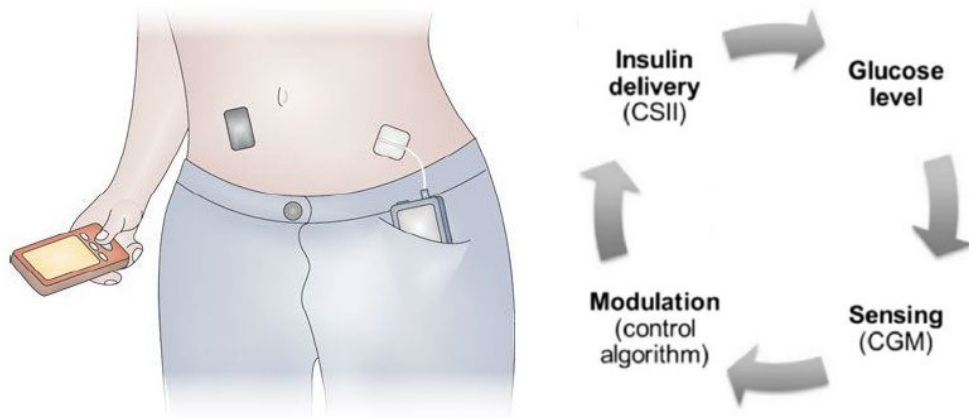
Ingen

Children and adult diabetes in Norway

'Cause-specific deaths'

- n=7.871, 132.143 person-years
- Mean follow-up 16.8 yrs
- Mean age at end of follow up: 25.6 yrs
- 241 deaths (3.1%)
 - 5% dead in bed
 - 26% acute diabetic complications (hypoglycaemia, ketoacidosis)
 - 28% CVD

Insulinpumpe-sensor system



Hybrid closed-loop system

Medtronic

CamAPS FX

Control IQ

Omnipod 5

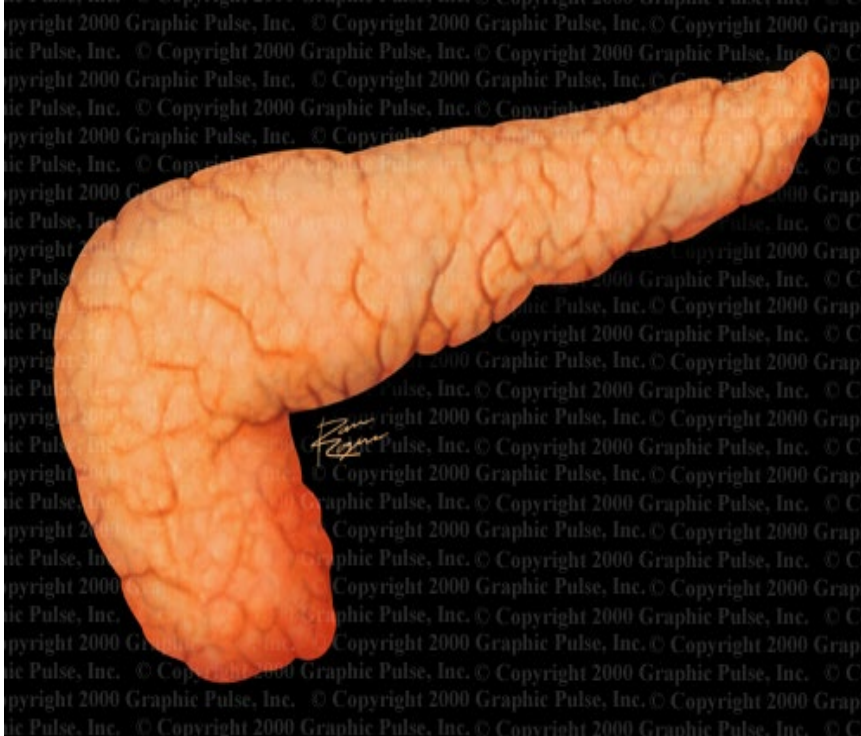


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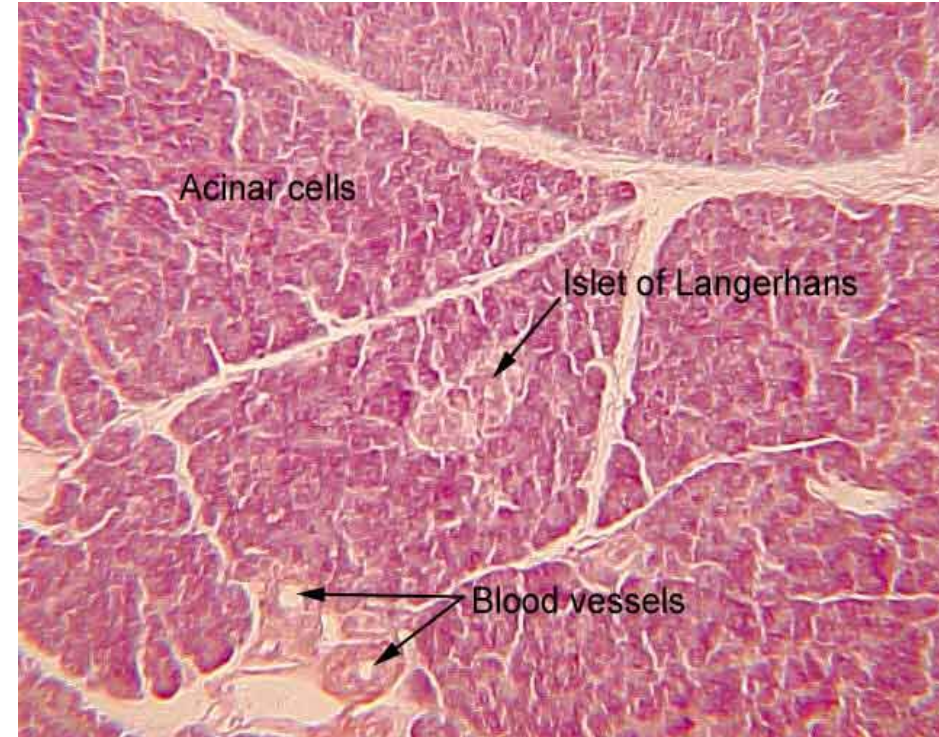
Norway

Pancreas



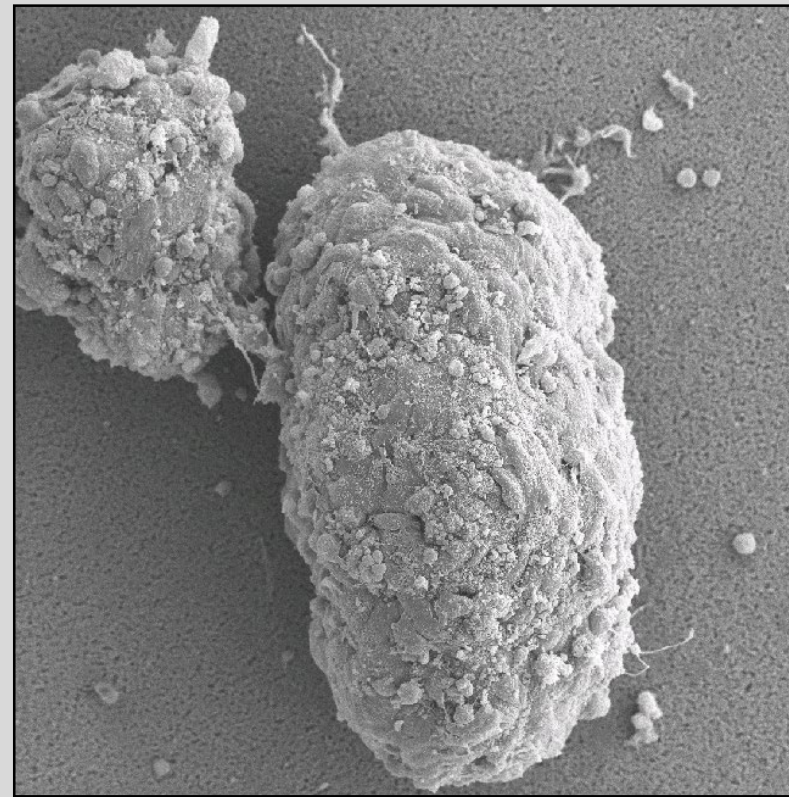
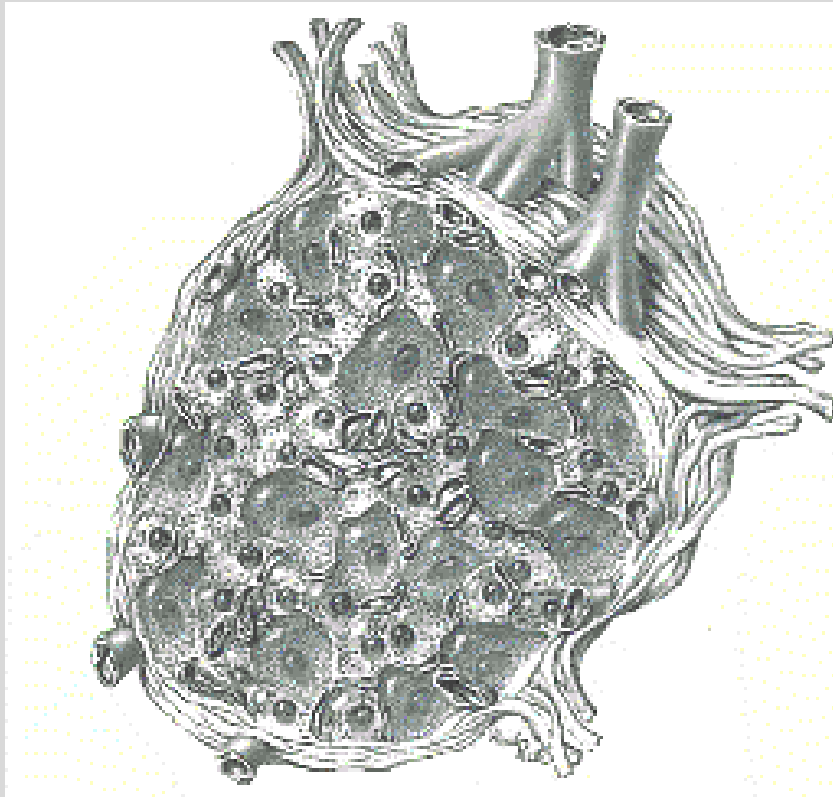
1983

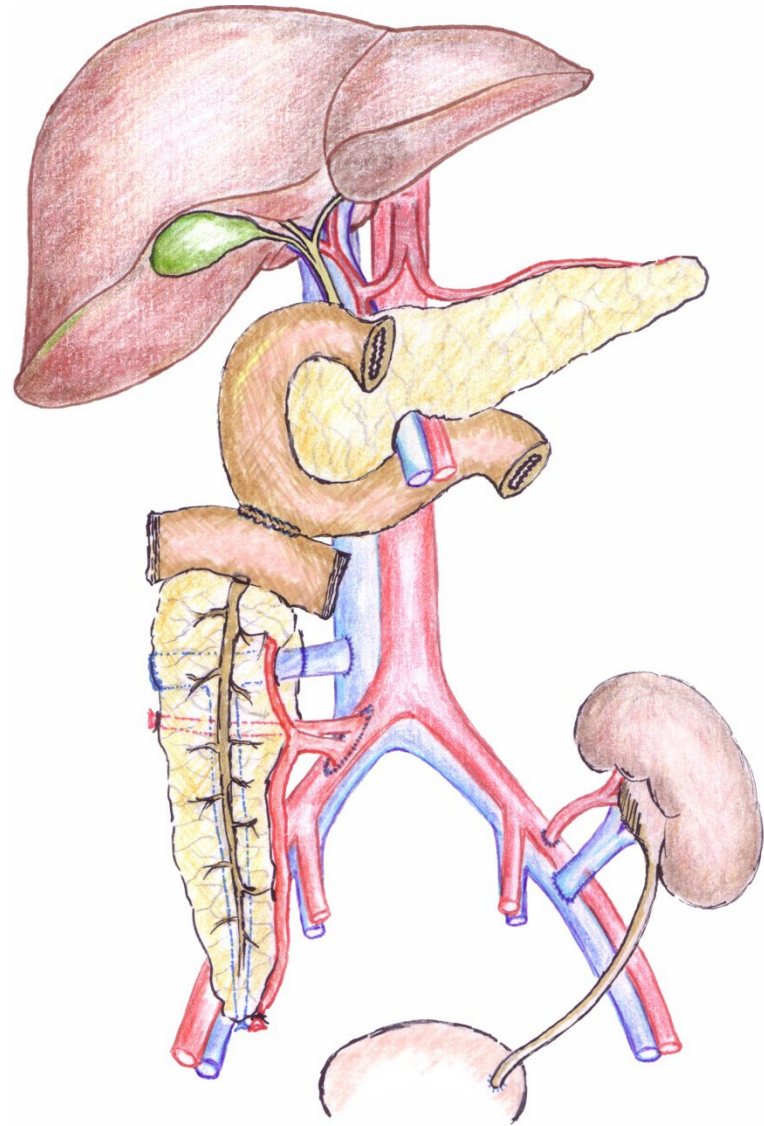
Islets of Langerhans



2001

Islet of Langerhans - a microorgan

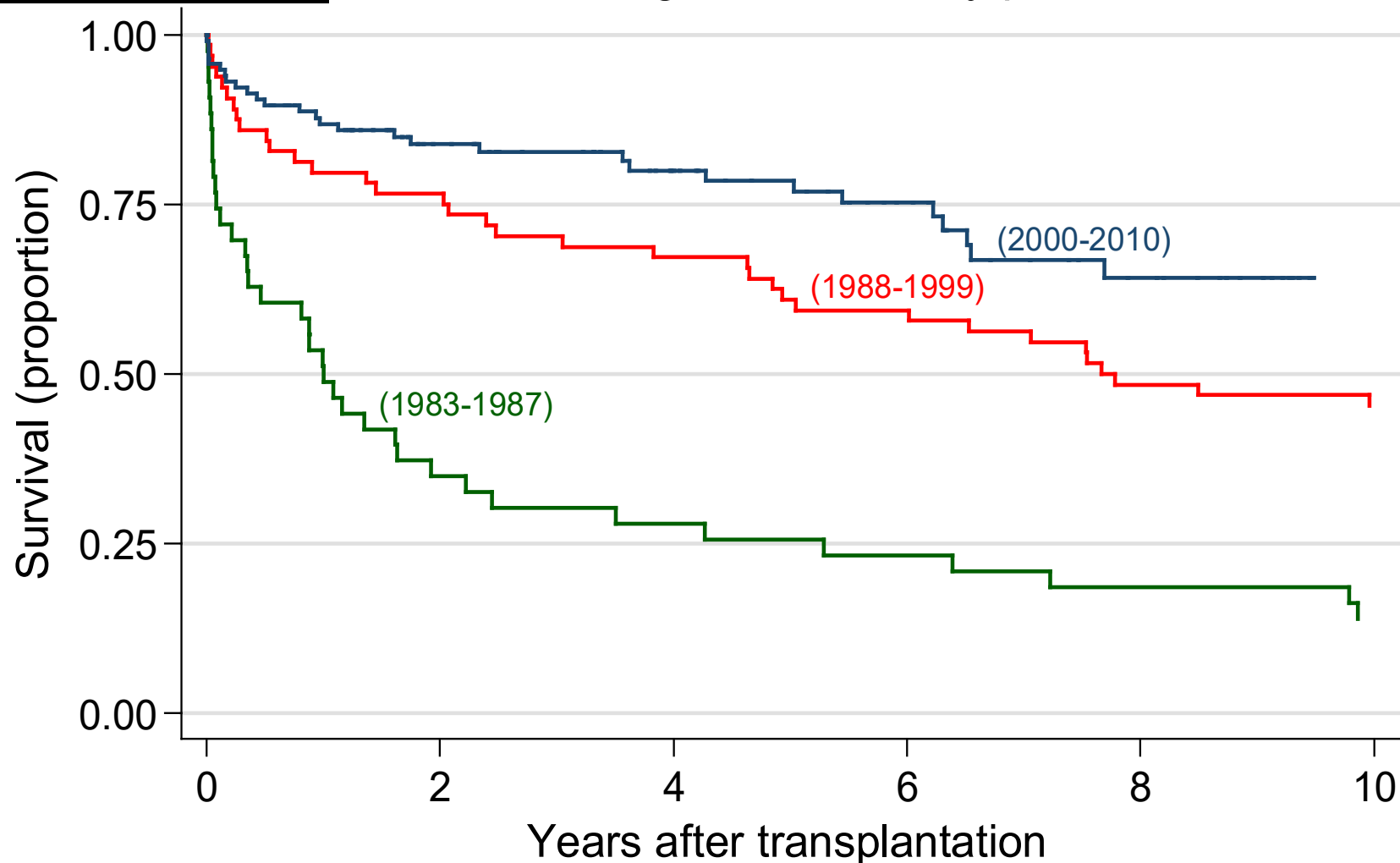




Rune Horneland
2014

Nyre-pankreas tx

Pancreas graft survival by period



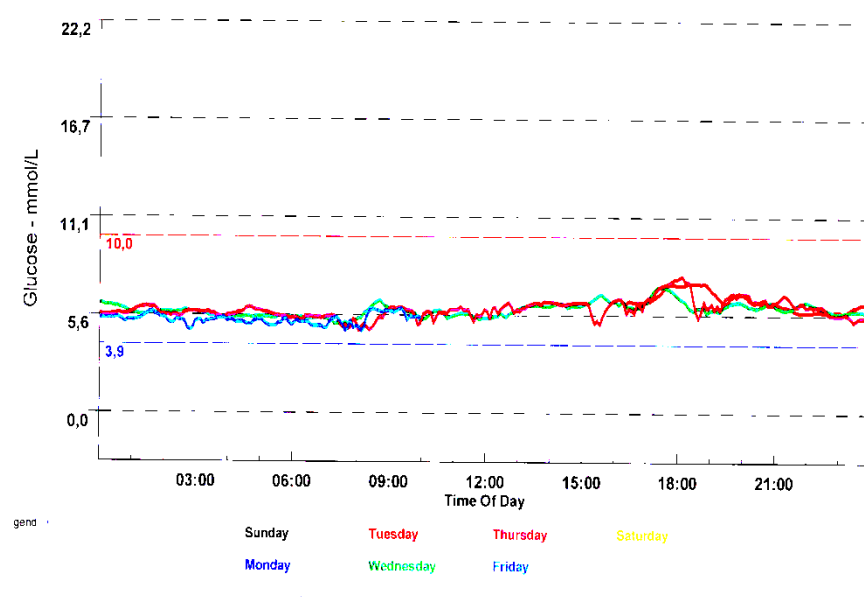
Patients at risk

(1983-1987)	43	15	12	10	8	6
(1988-1999)	64	49	43	38	31	29
(2000-2010)	115	76	56	39	23	9

24-timers glukosemåling i 3 døgn før og etter transplantasjon av single pankreas



Report Printed: 02.02.2010 08:26



Dr. Jenssen

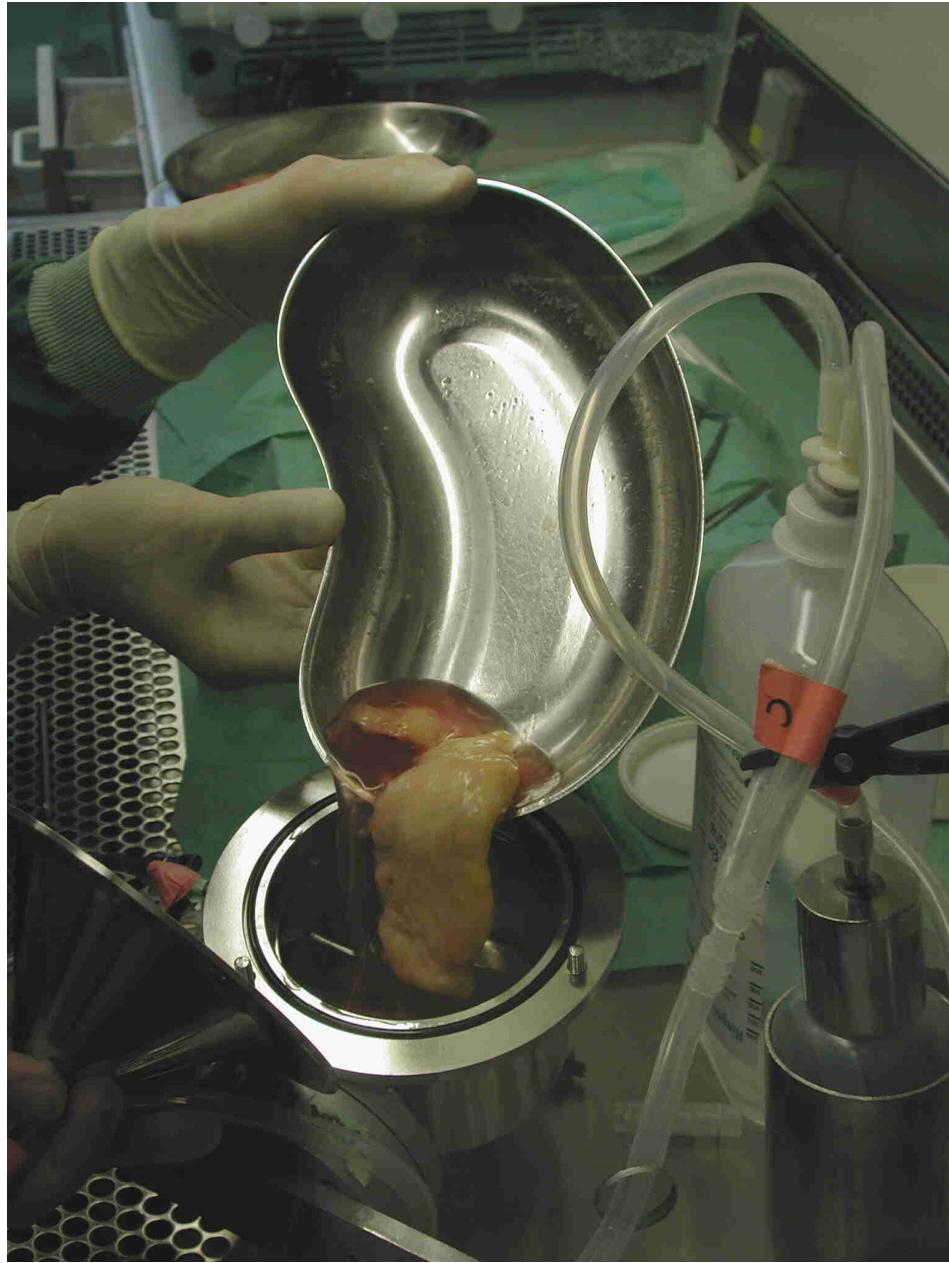
Report Printed: 31.08.2012 10:20

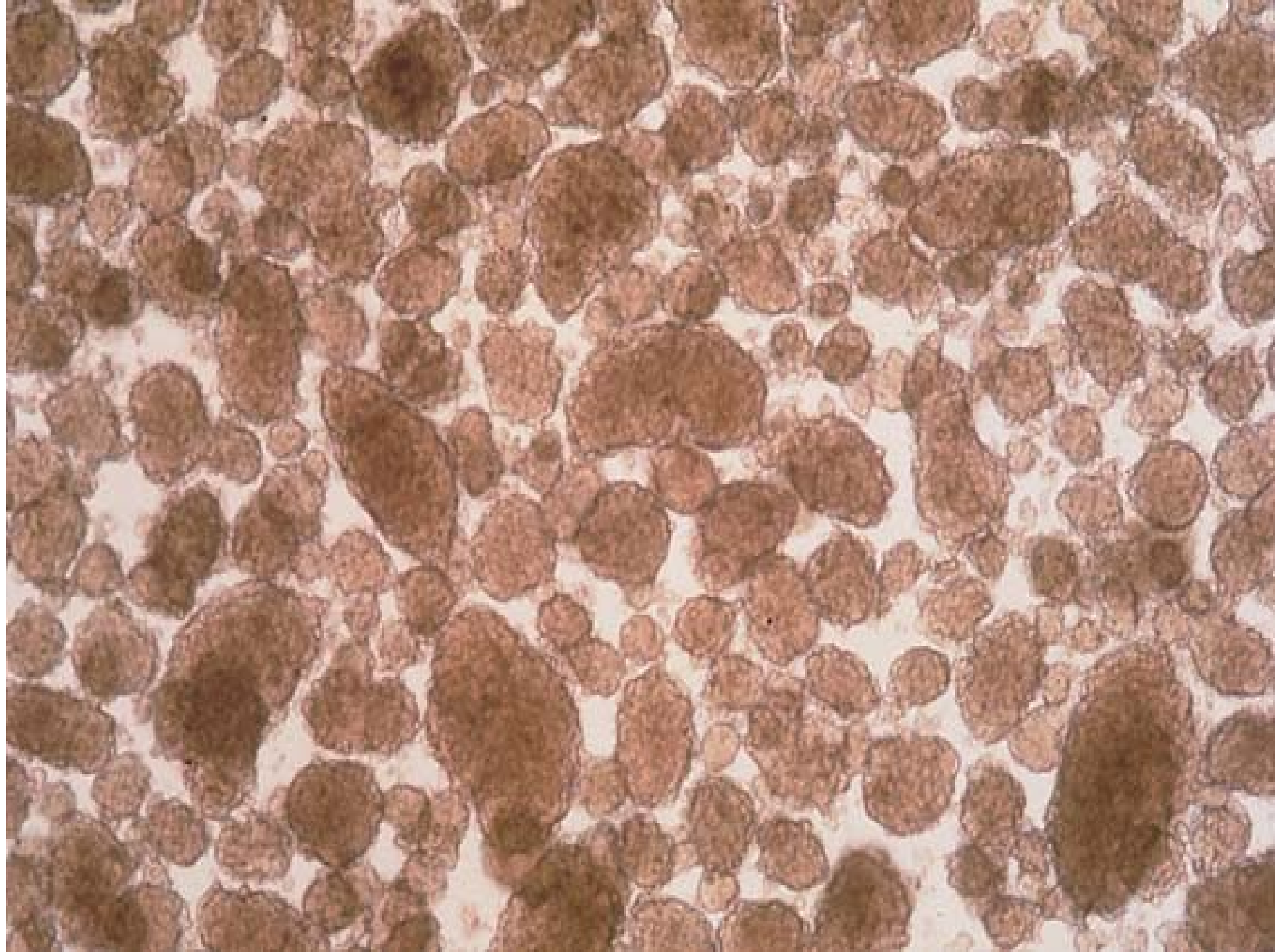


Øycelleisoleringslaboratoriet ved OUS

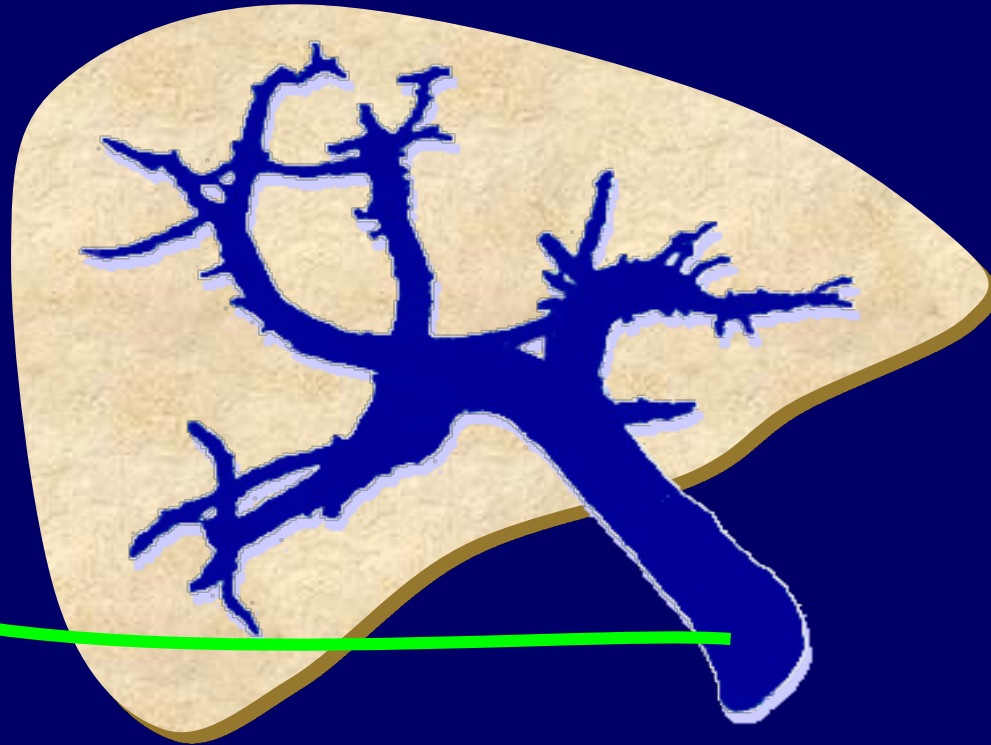
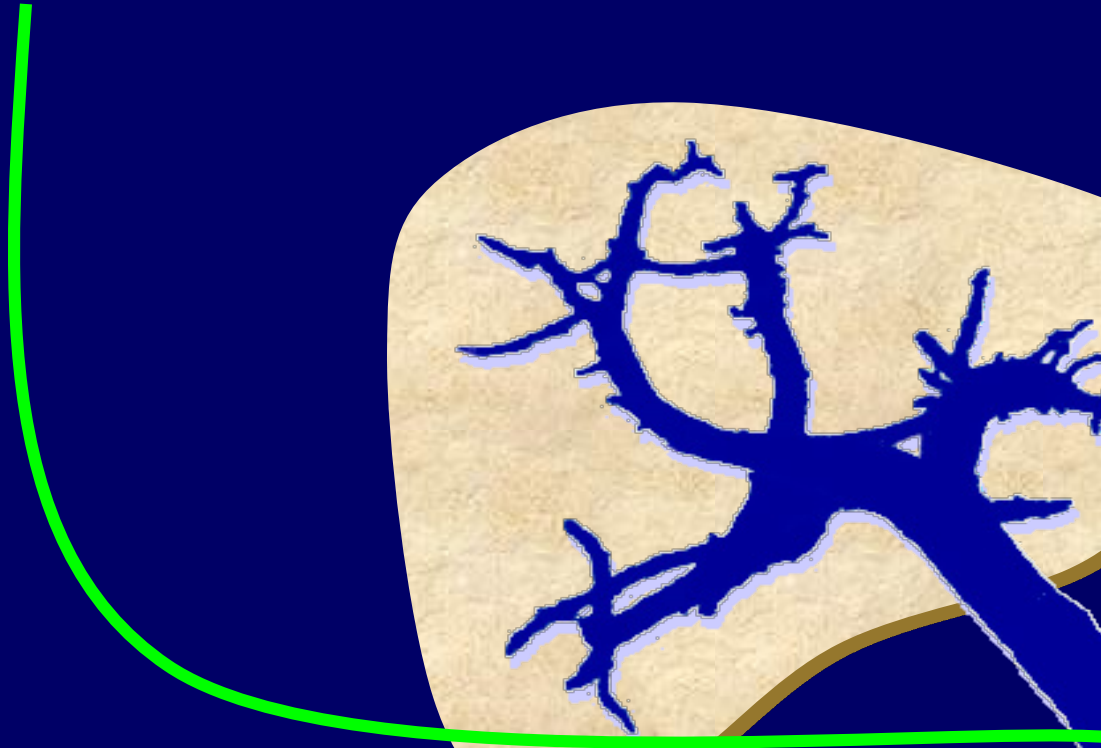
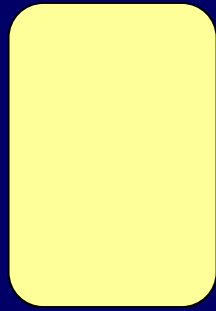


Seksjon for Celleterapi, Radiumhospitalet



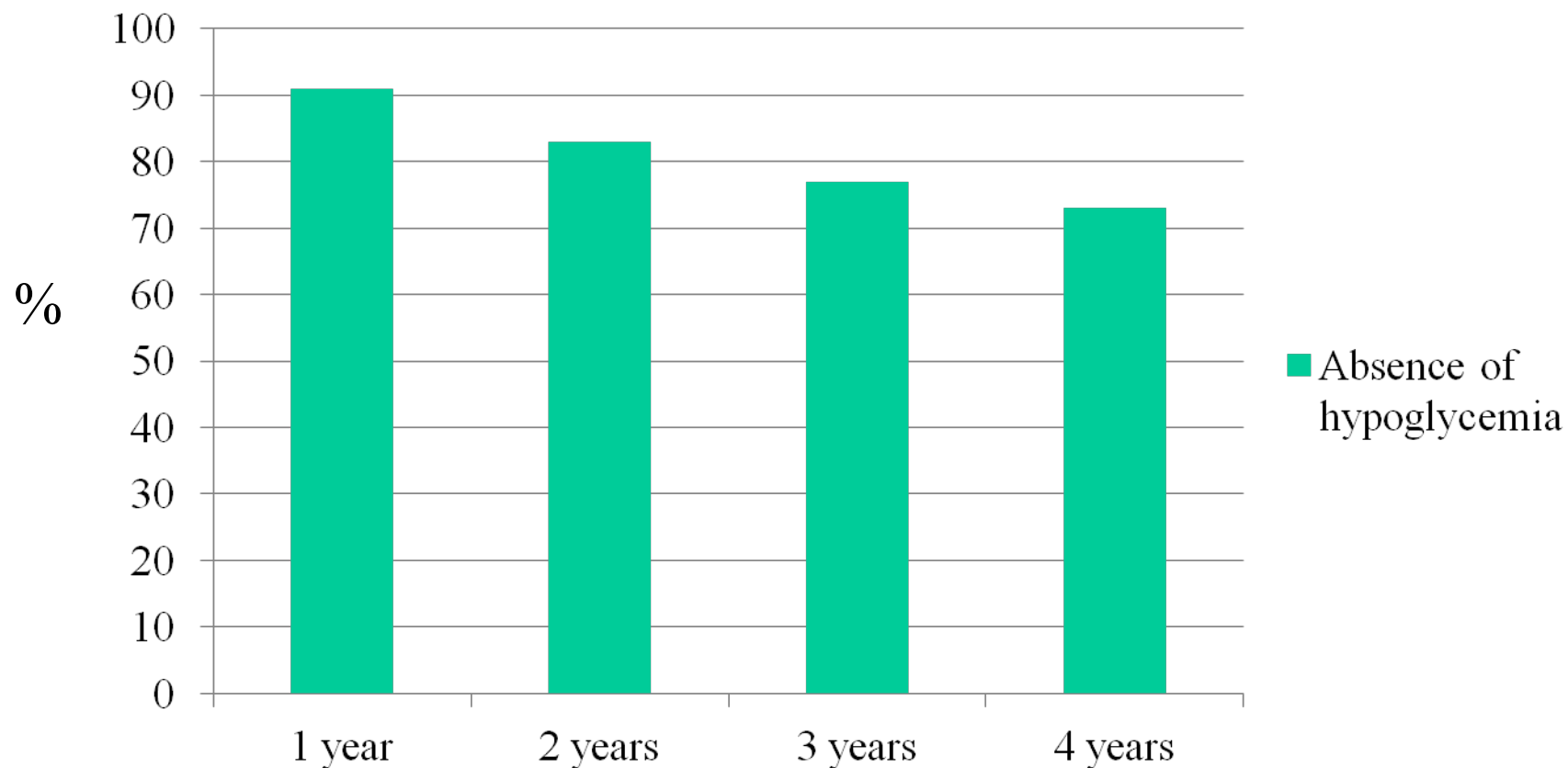


Islet infusion



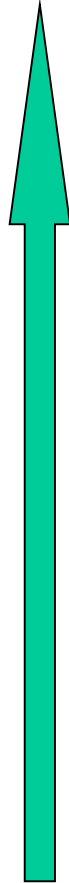
Clinical Islet Transplantation Registry

(n=347 allogeneic islet transplant recipients)



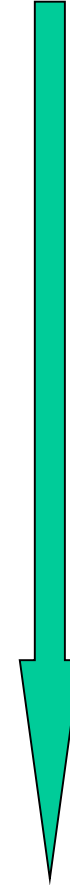
Hvem er kandidatene?

Pancreas tx



- Kronisk hyperglykemi (HbA1c > 10% «når alt annet har vært prøvd eller vurdert»)
- Glukosesensor løser ikke problemet tilfredsstillende
- Betydelig nedsatt livskvalitet på grunn av ustabile blodsukker
- Unawareness
- Clarke score ≥ 4

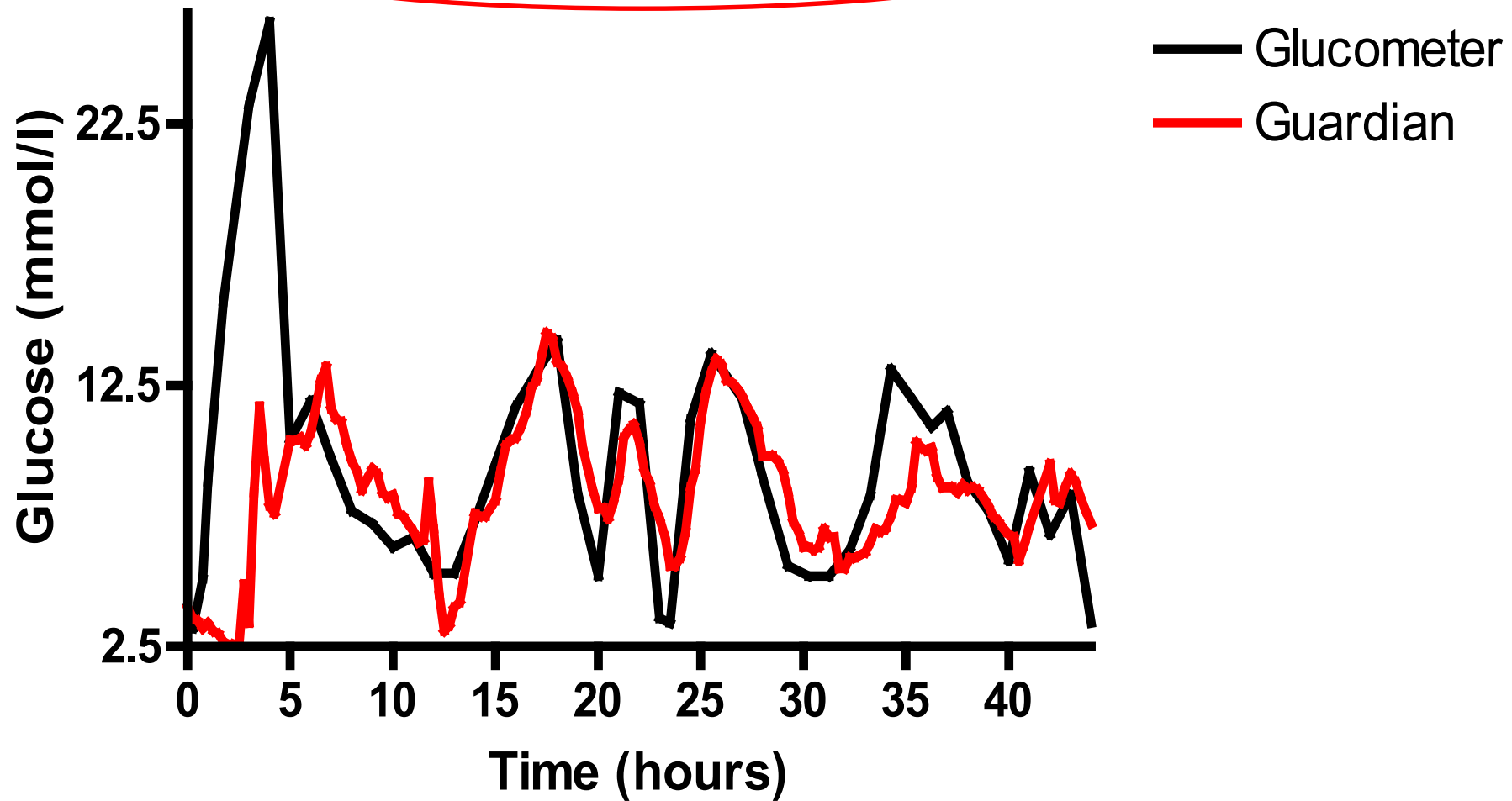
Øycelle tx



Insulinbehov ≥ 40 enh/ dag

Insulinbehov < 40 enh/ dag

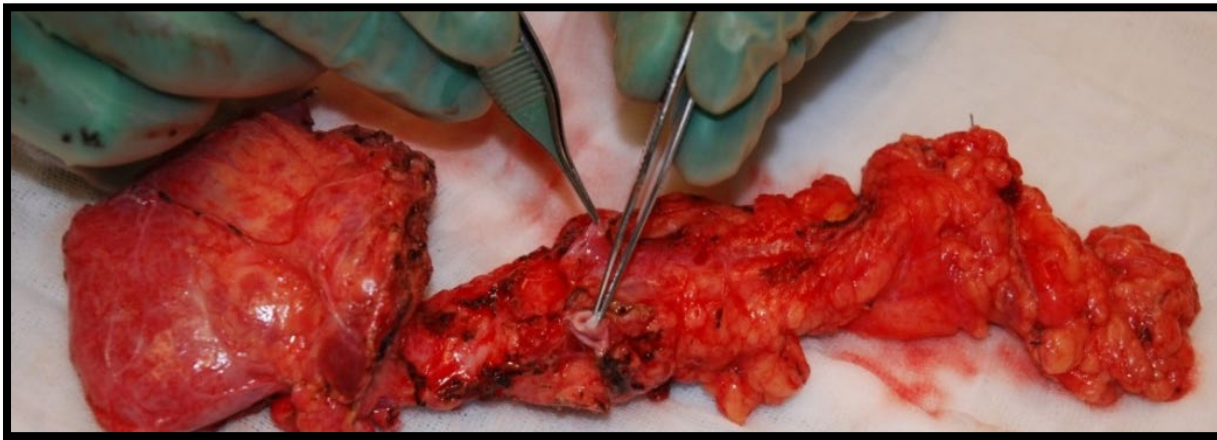
HbA1c: 52 mmol/L / 7 %



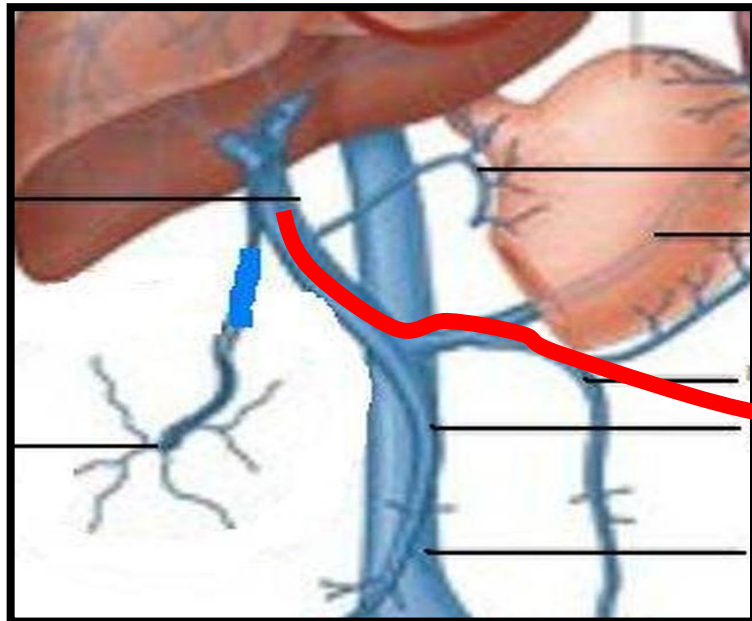
Kontraindikasjoner

	Vaskulær pancreas	Øyceller
GFR < 30 ml/min/1.73 m ²	X	X
Uttalt arteriosklerose, og/ eller EF<30%	X	
Alder >60 år	X	
Aktivt stoffmisbruk Ukontrollert psyk. sykdom	X	X
Malignitet som ikke er i remisjon	X	X

Total pankreatektomi med øycelletransplantasjon (TPIAT)

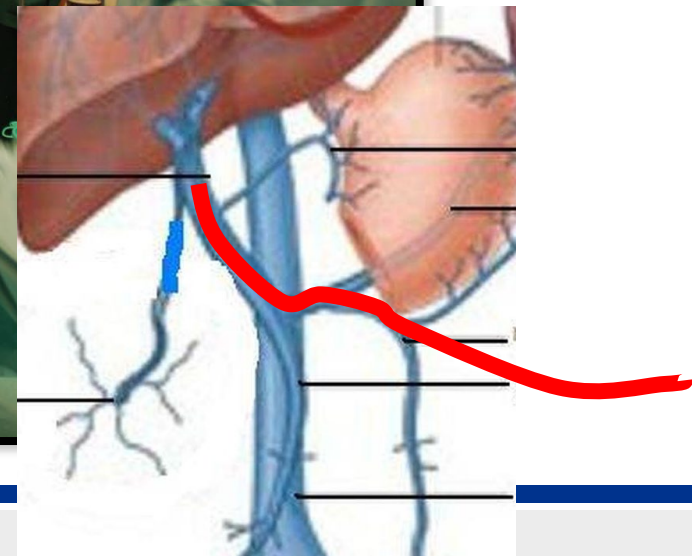
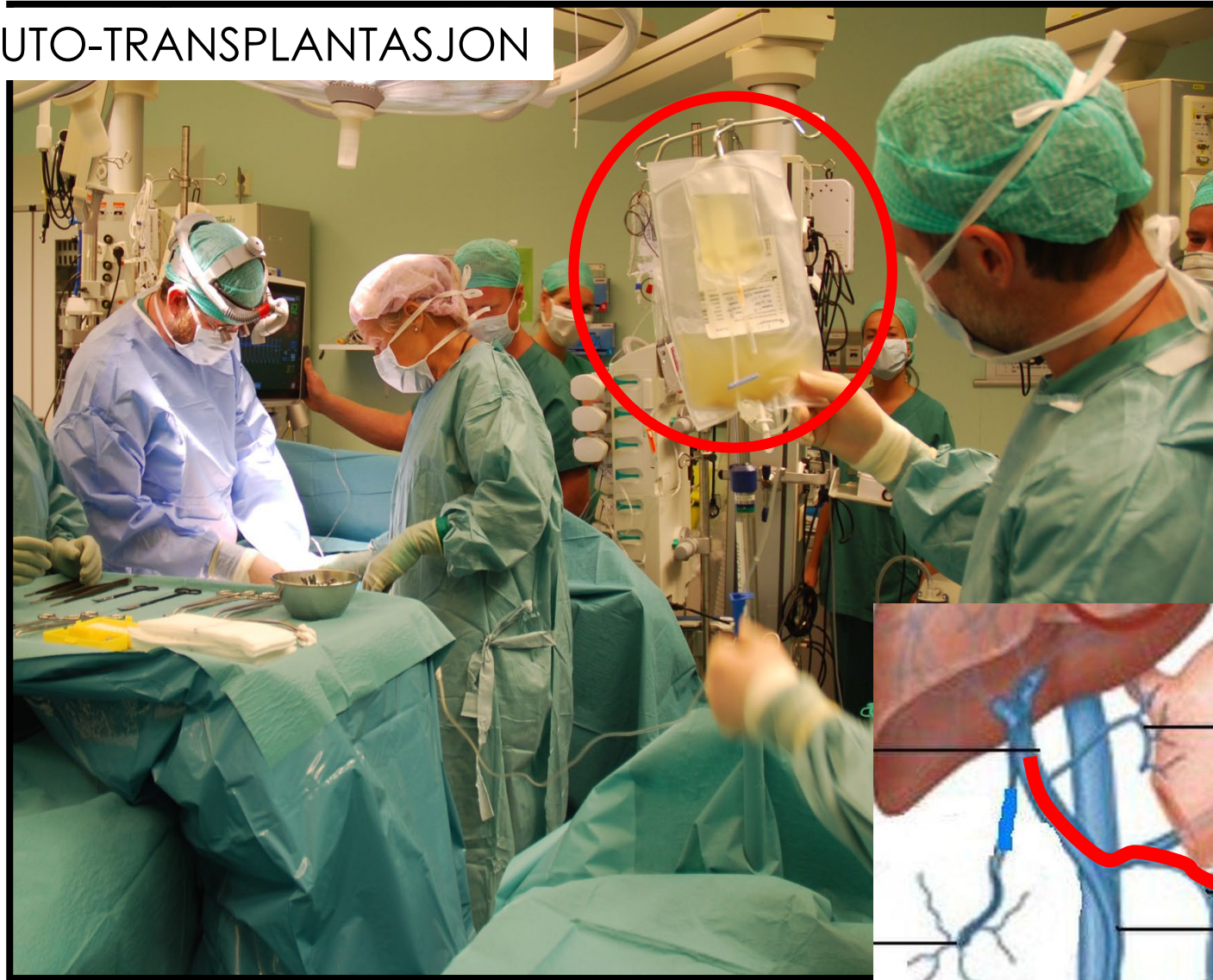


Øycelleisolasjon



To-lumen kateter fra
Vena mesenterica inferior til vena porta

AUTO-TRANSPLANTASJON



Immunsuppresjon

Øyceller

- Thymoglobulin eller basiliximab
- Calcineurin-hemmer
- MMF eller mTor hemmer

Hel pancreas

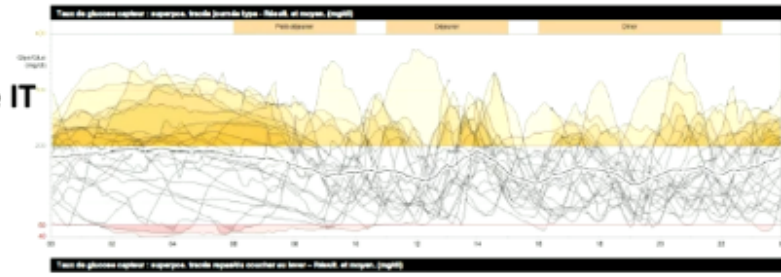
- Thymoglobulin
- Prednisolon
- Calcineurin-hemmer
- MMF

IAK

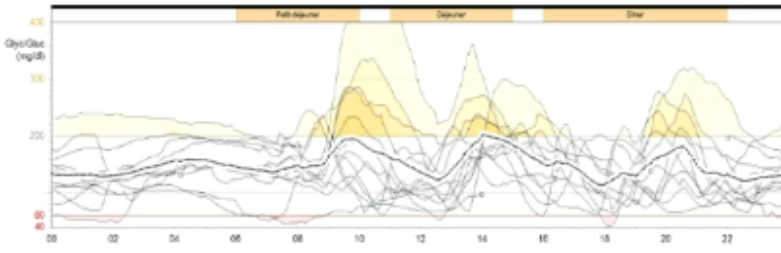
(Islet After Kidney transplantation)

Islet transplantation

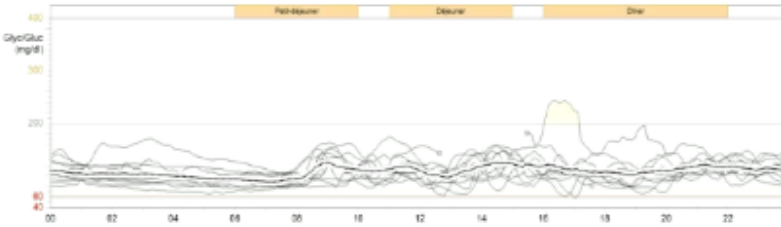
Glycaemia before IT



After 1st IT



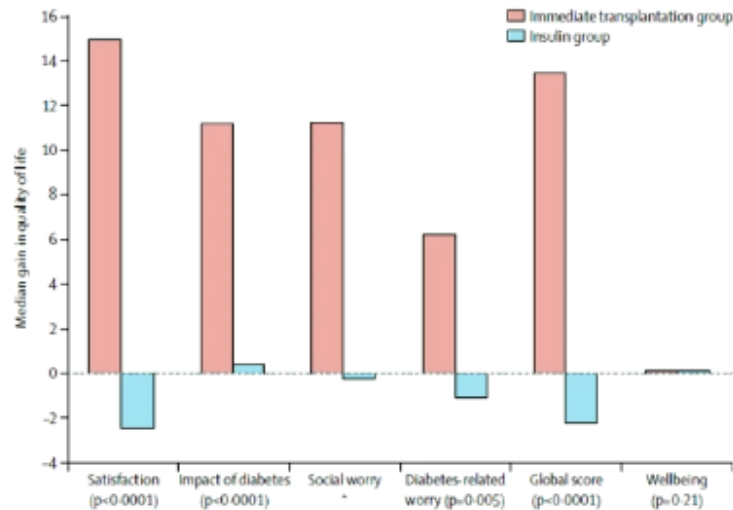
After 2d IT



Laurence Kessler, Université de Strasbourg, SFD 2023

73,9% of patients
→ No severe hypoglycaemia after 10 years

50% of patients
→ HbA1c < 7% after 8 years



Lablanche S, et al. Am J Transplant. 2021

Rickels MR, et al. Diabetes Care. 2022

Lablanche S, et al. Lancet Diabetes Endocrinol. 2018

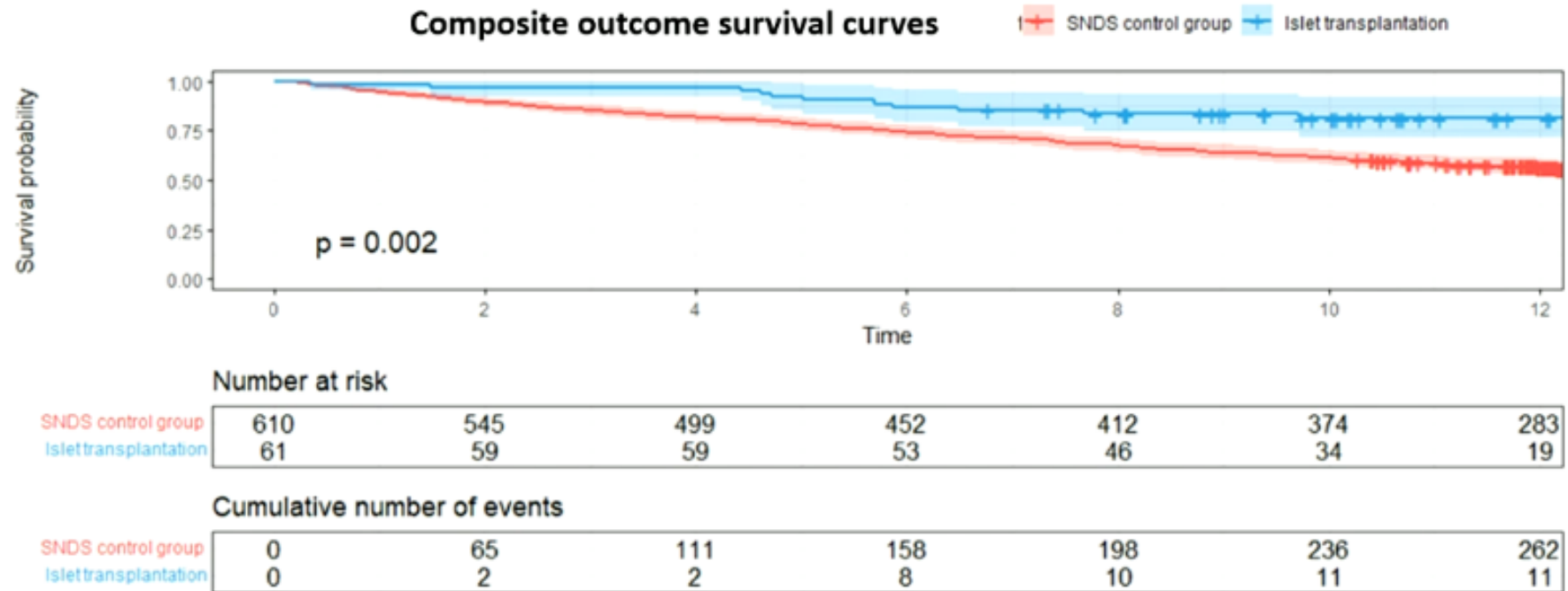


Quentin Perrier

Effect of islet transplantation on the incidence of diabetic complications and mortality in patients with unstable type 1 diabetes



Primary endpoint → Composite



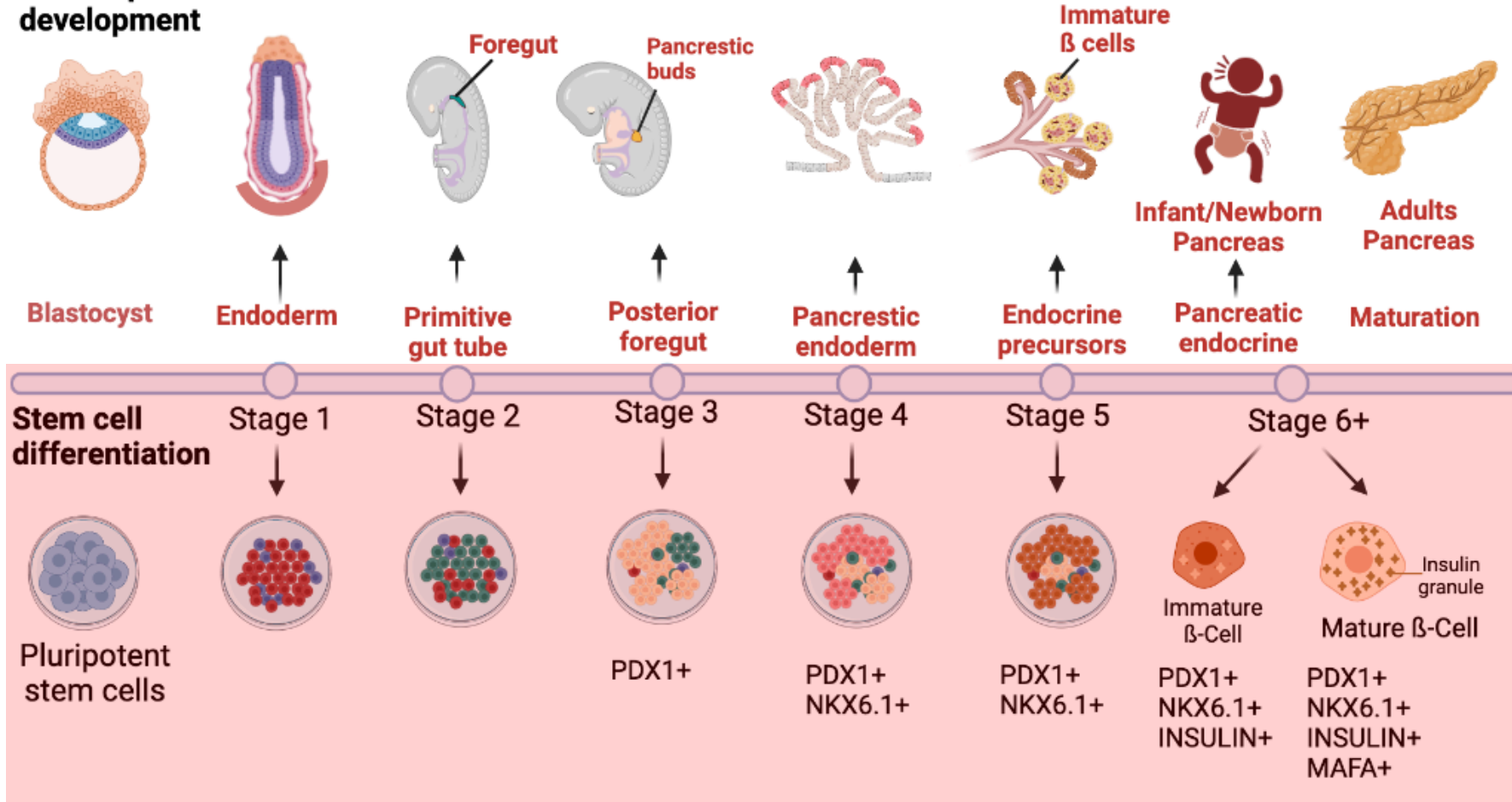
Composite endpoint = Graft and patient survival (death, re-transplantation or return to dialysis)



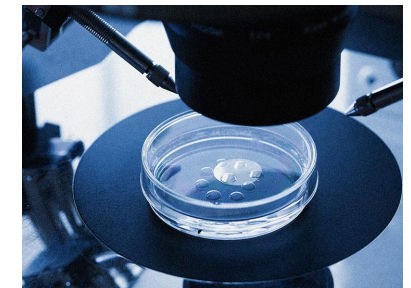
Hvordan lages nye betaceller (øyceller) fra stamceller?

~9 måneder versus 5 uker

Human pancreas development



I fosteret

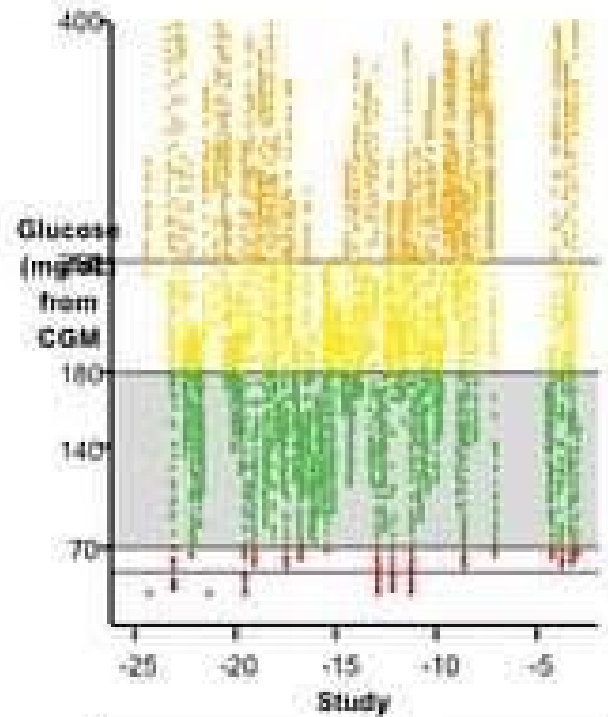


I laboratoriet



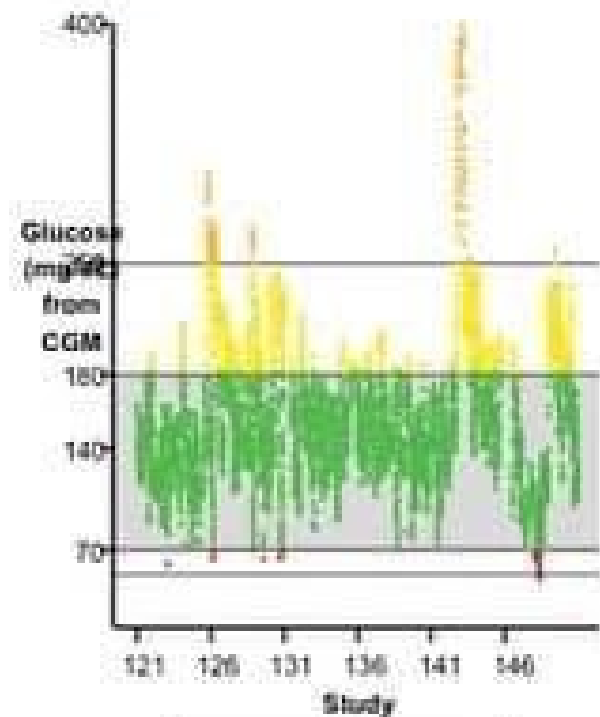
Patient 1 Achieved Insulin Independence with 99.9% Time in Range^a

Baseline



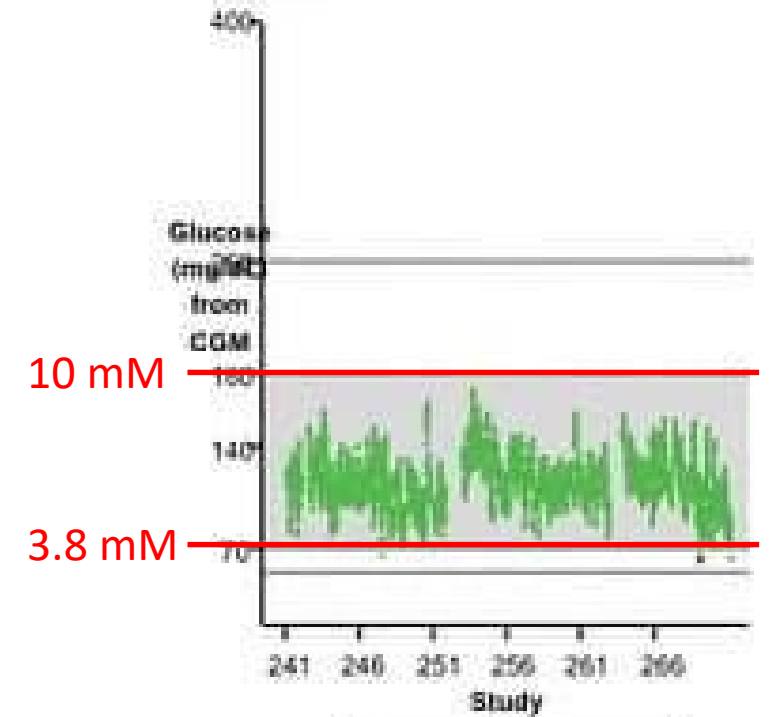
Daily Insulin	34 units
HbA1c	8.6%

Day 121-150



Daily Insulin	2.6 units
HbA1c	6.7%

Day 241-270



Insulin U/ dag
HbA1c (33 mmol/mol)

Daily Insulin	0 units
HbA1c	5.2%

Glucose values conversion: 1 mmol/L = 18 mg/dL

^aTime in range 70-180 mg/dL. Data from latest data cut evaluated (Day 241-Day 270)

CGM, continuous glucose monitoring



IMPROVEMENT IN GLYCEMIC CONTROL AND ELIMINATION OF EXOGENOUS INSULIN USE IN PATIENTS WITH TYPE 1 DIABETES INFUSED WITH FULLY DIFFERENTIATED ISLET CELLS (VX-880):

UPDATED DATA FROM THE FORWARD VX-880 CLINICAL STUDY

Trevor Reichman¹, Piotr Witkowski², James Markmann³, John Fung², Jon Odorico⁴, Martin Wijkstrom⁵, Fouad Kandeel⁶, Leslie Kean⁷, Chantal Mathieu⁸, Anne Peters⁹, Bote Bruinsma¹⁰, Chenkun Wang¹⁰, Janet Hong¹⁰, Bastiano Sanna¹⁰, Gautham Marigowda¹⁰, Felicia Pagliuca¹⁰, Doug Melton¹⁰, Camillo Ricordi¹¹, Michael Rickels¹² on behalf of the FORWARD VX-880 Study Team

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Trevor Reichman

Improvement in glycaemic control and elimination of exogenous insulin use in patients with type 1 diabetes infused with fully differentiated islet cells (VX-880)





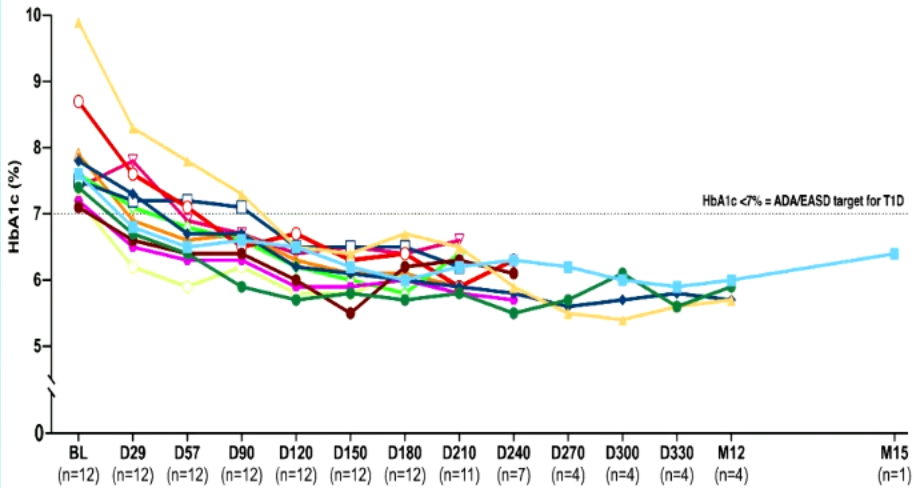
Trevor Reichman

Improvement in glycaemic control and elimination of exogenous insulin use in patients with type 1 diabetes infused with fully differentiated islet cells (VX-880)

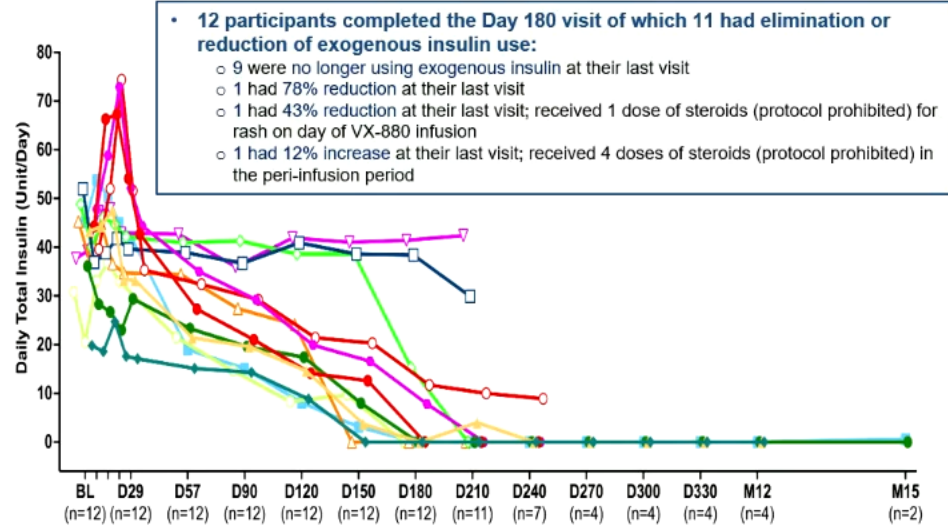
Participants Receiving the Full Dose of VX-880 in a Single Infusion had Improved Glycemic Control, & Reduction or Elimination of Exogenous Insulin Use

- All 12 participants achieved a **reduction in HbA1c** to <7%
- All 12 participants had **elimination of severe hypoglycemic events (SHEs)** during the evaluation period (day 90 onward)
- 11 of 12 participants had **reduction or elimination of exogenous insulin use at most recent visit**

HbA1c



Total Daily Insulin



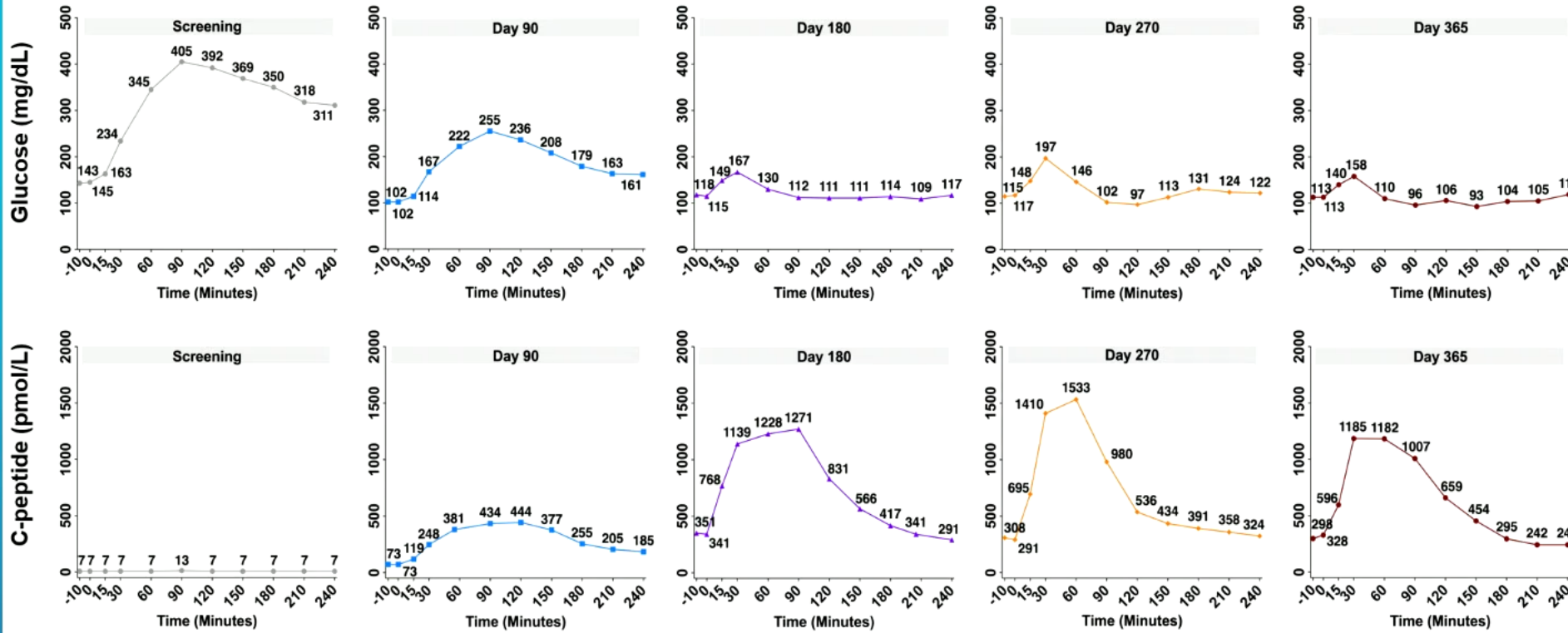
- **12 participants completed the Day 180 visit of which 11 had elimination or reduction of exogenous insulin use:**
 - 9 were no longer using exogenous insulin at their last visit
 - 1 had 78% reduction at their last visit
 - 1 had 43% reduction at their last visit; received 1 dose of steroids (protocol prohibited) for rash on day of VX-880 infusion
 - 1 had 12% increase at their last visit; received 4 doses of steroids (protocol prohibited) in the peri-infusion period

ADA, American Diabetes Association; BL, baseline; D, day; EASD, European Association for the Study of Diabetes; HbA1c, hemoglobin A1c; M, month; SHEs, severe hypoglycemic events; T1D, Type 1 diabetes



All Participants Demonstrated Islet Cell Engraftment with Clinically Meaningful Endogenous Insulin Production and Improved Glucose Levels by Day 90

MMTT results from a representative participant demonstrating significant endogenous C-peptide production and improvement in glucose levels over time



MMTT, mixed meal tolerance test



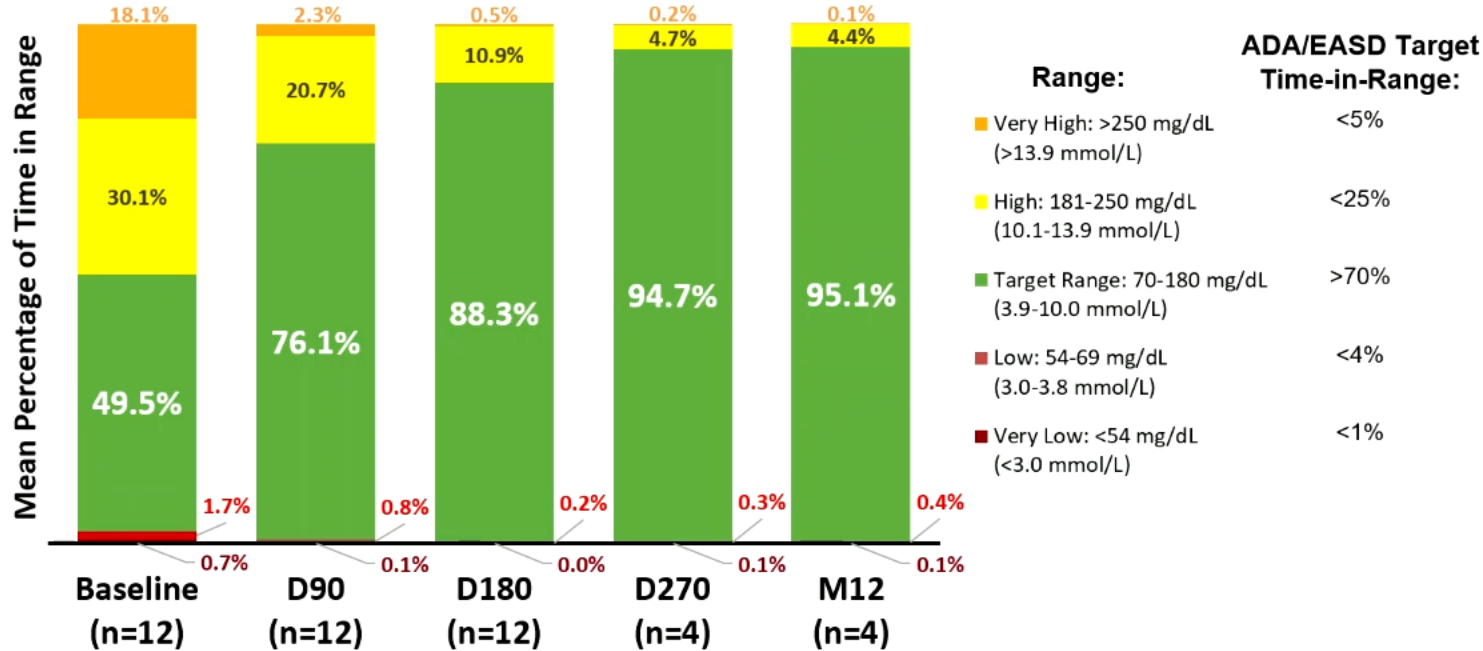
Trevor Reichman

Improvement in glycaemic control and elimination of exogenous insulin use in patients with type 1 diabetes infused with fully differentiated islet cells (VX-880)



All Participants Receiving the Full Dose of VX-880 in a Single Infusion Demonstrated Improvements in CGM Metrics and Achieved >70% Time in Range

Mean time in range for all participants over time



ADA, American Diabetes Association; CGM, continuous glucose monitoring; D, day; EASD, European Association for the Study of Diabetes; M, month



Trevor Reichman

Improvement in glycaemic control and elimination of exogenous insulin use in patients with type 1 diabetes infused with fully differentiated islet cells (VX-880)



Successful use of stem cell-derived islets to treat T1D at the
Toronto General Hospital: February 14, 2023

The Washington Post



UHN Ajmera
Transplant Centre

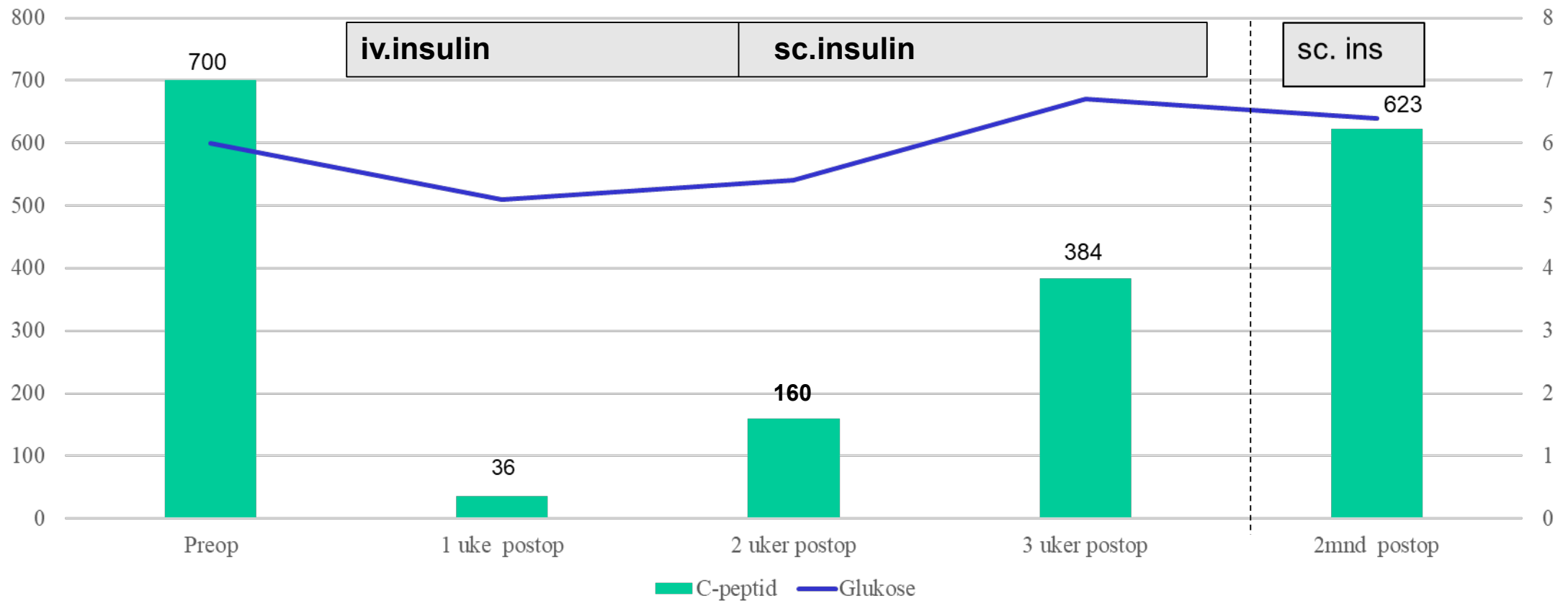


Trevor Reichman, EASD 2024

Takk for oppmerksomheten



Forløp autolog øycelle-tx



HbA1c 38 mmol/mol
6 enheter Lantus x 1
2 enheter Humalog/måltid