



ASX: LCT - OTCQX: LVCLY

Diabetes – Neurodegenerative Diseases – Cell Encapsulation

# Microencapsulated Neonatal Porcine Islet Implants without Immune Suppression Alleviate Unaware Hypoglycaemia

Professor R. B. Elliott on behalf of Living Cell Technologies



# Insulin Treatment

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The Golden Goals of insulin treatment of diabetes are:

- 1) Avoidance of episodes of hyper or hypoglycaemia  
(and as a corollary maximising time spent with normoglycaemia)
- 2) Reducing long term complications
- 3) Normalizing lifestyle

Allo-transplantation with immune suppression can sometimes attain goal 1) and perhaps 2) but never 3)



# Type 1 Diabetes Treatment

“Best Yet” non-transplant long term results

- Insulin pumps +
- Continuous blood glucose monitoring

Recent Data (averages after 6 months)

HbA1c	- 0.2%
Hours / day with hypoglycaemia	- 0.9hr
Hours / day with hyperglycaemia	- NS

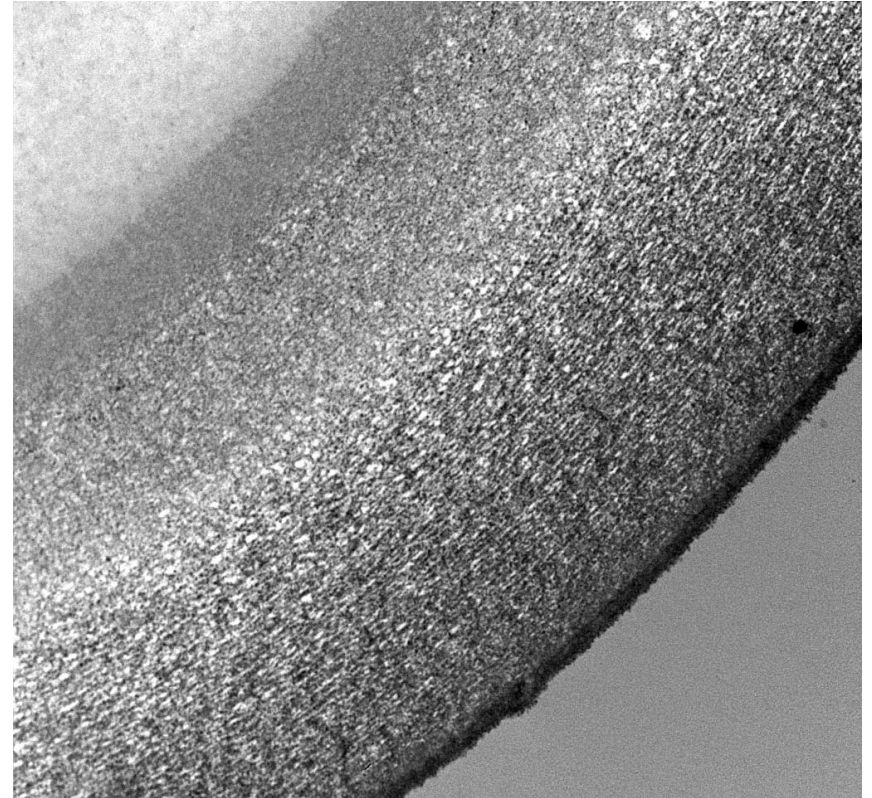
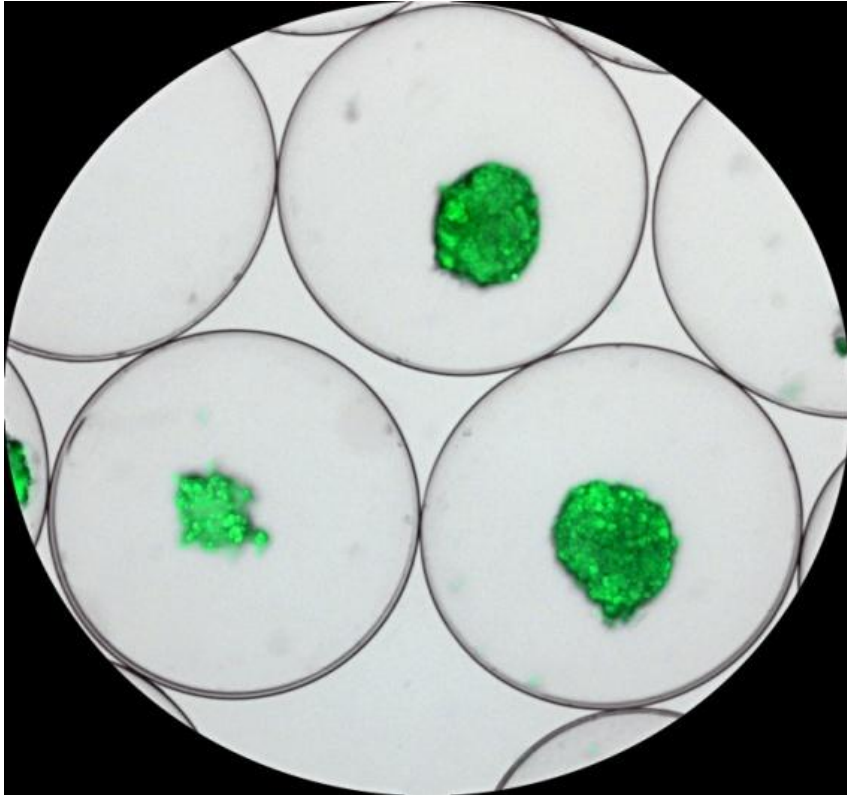


# DIABECELL Phase 2 NZ Clinical Trial

- Results of NZ Phase 2 clinical trial of microencapsulated neonatal porcine islets implanted into the peritoneal cavity via laparoscope
- Dose escalation (5,000-20,000 islets /Kg) as one dose
- Trial subjects:  
14 Type 1 diabetics with severe unaware hypoglycaemia



# DIABECELL Encapsulated Islets





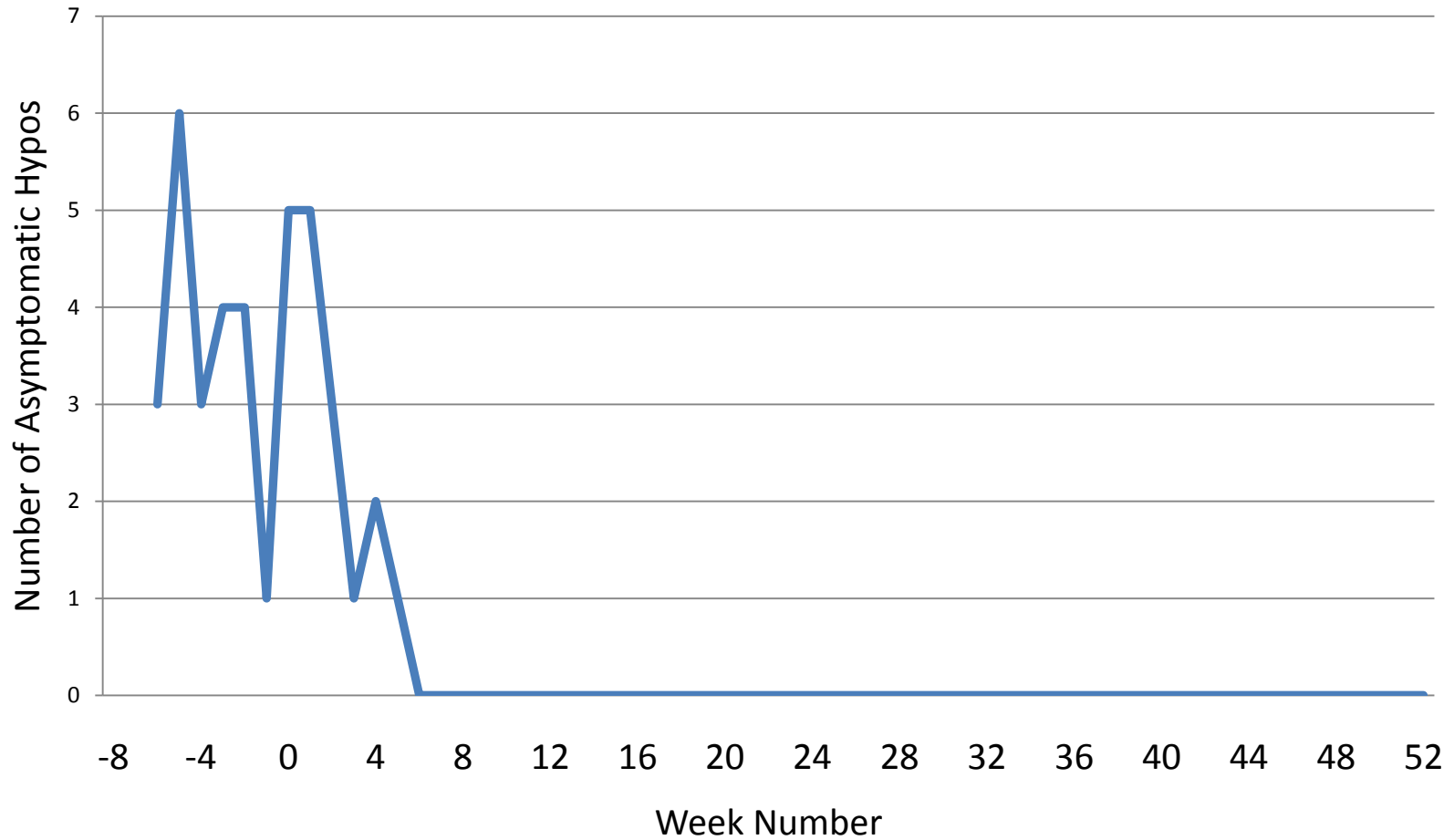
# Specifications of DIABECCELL

Product Specification	Acceptance Criteria
<b>DIABECCELL® (encapsulated islets)</b>	
% Viability	≥85%
Maximal Insulin Release	≥39μU/100 IEQ/h
Insulin Stimulation Index 1	≥3
Insulin Stimulation Index 2	≥3
Capsule Size	600-900 um diameter
Capsule Uniformity	≥90% are ± 100 mm of mean diameter
Capsule Integrity	≥90%
% Capsules with Islets	≥70%
In-process Sterility	No growth after 14 days
<b>Final DIABECCELL® Product Sterility</b>	No growth after 14 days
Bacteriology and Mycology	days
Mycoplasma	Negative
Endotoxin level	<1 EU/mL



# Current NZ Trial

## Patient #1: Asymptomatic Hypos



# Current NZ Trial

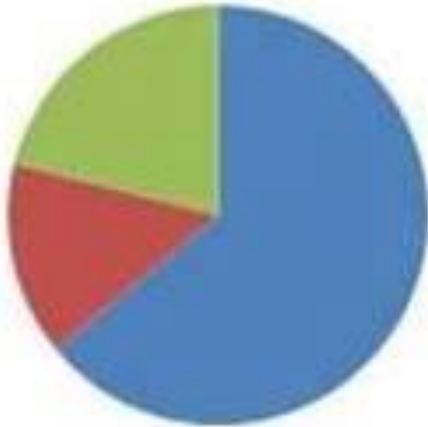
Parameter	Pre-Tx	Post-Tx	
		Up to Week 12	Up to Week 12-52
Insulin Dose (Weekly Average)	41	36	30
Hypo Score (Weekly Average - Severity Indicator)	20	12	8
Number of Unaware Hypos (Weekly Average)	3.2	1.5	0.8
HbA1c (%)	7.5	7.5	7.6



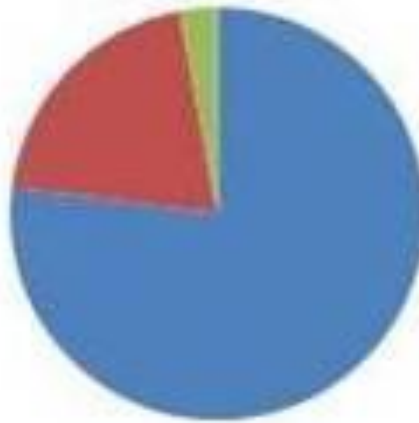


# CGMS

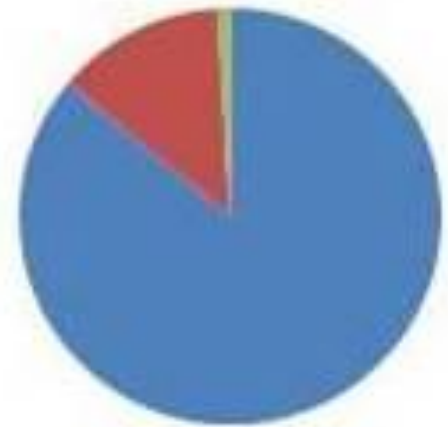
Week 1






Week 8



Week 16



-  % Time  $\leq 10.0$  and  $\geq 4.0$
-  % Time  $> 10.0$
-  % Time  $< 4.0$



# Lack of dose effect on amelioration of hypoglycaemic events

Parameter		10,000/kg	15,000/kg	20,000/kg
Hypo Score: Weekly Average – Severity Indicator (Percentage Change from Baseline)	Pre-Tx	20	14	30
	Week 0-12	12 (40%)	11 (21%)	19 (37%)
	Week 13-52	7 (65%)		
Number of Unaware Hypos : Weekly Average (Percentage Change from Baseline)	Pre-Tx	3.7	2.3	5
	Week 0-12	1.6 (57%)	1.5 (35%)	3 (40%)
	Week 13-52	0.8 (78%)		



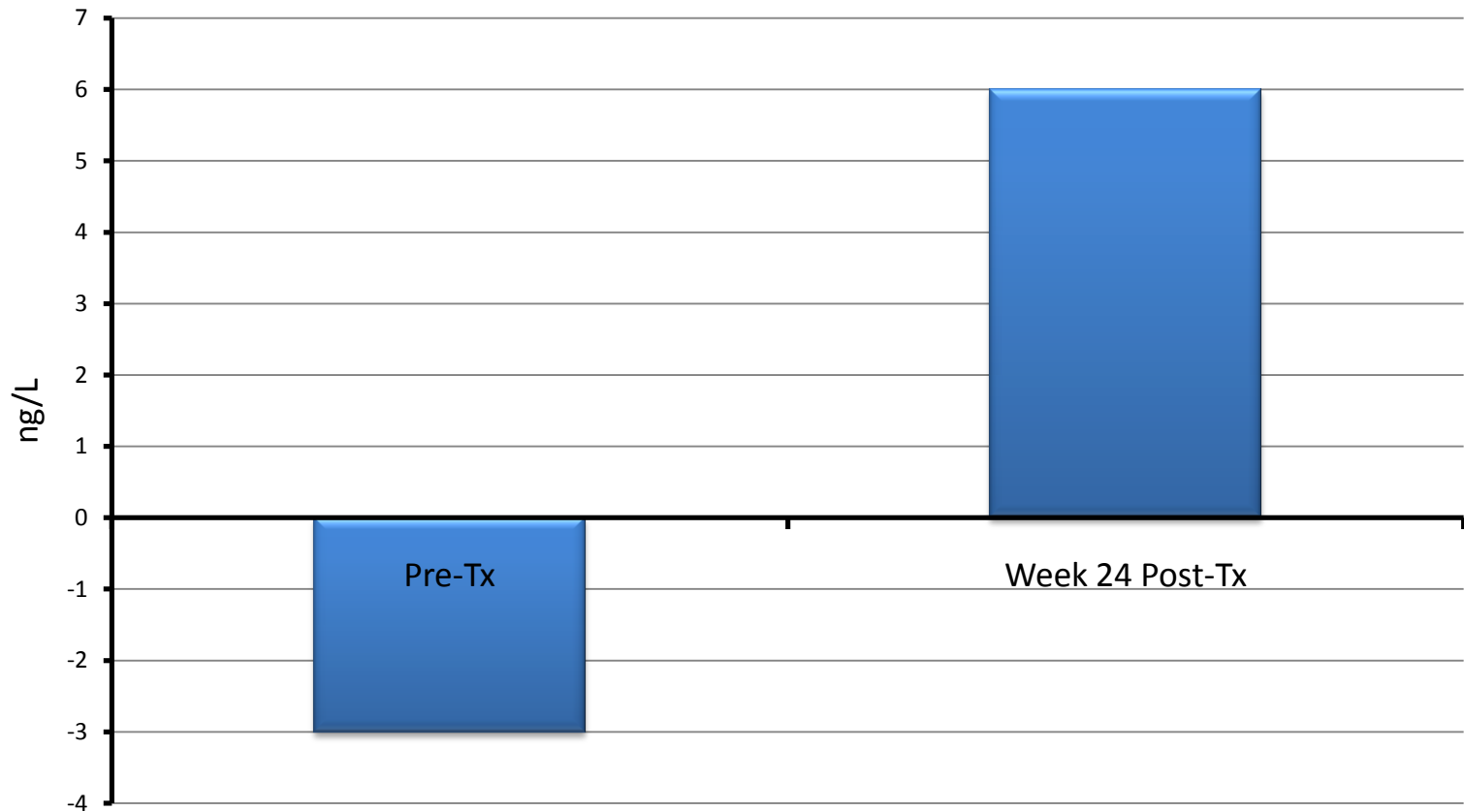
# Effects of dose escalation of encapsulated islets on diabetic status

Dose	Group Size	% non-diabetic 100 days post tx
<b>Alloxan diabetic rabbits</b>		
10,000 IEQ/kg	N=17	53%
50,000 IEQ kg	N=17	6%
0	N=8	0%
<b>Diabetic NOD mice</b>		
10,000 IEQ/kg	N=36	28%
50,000 IEQ kg	N=12	0%
0	N=5	0%



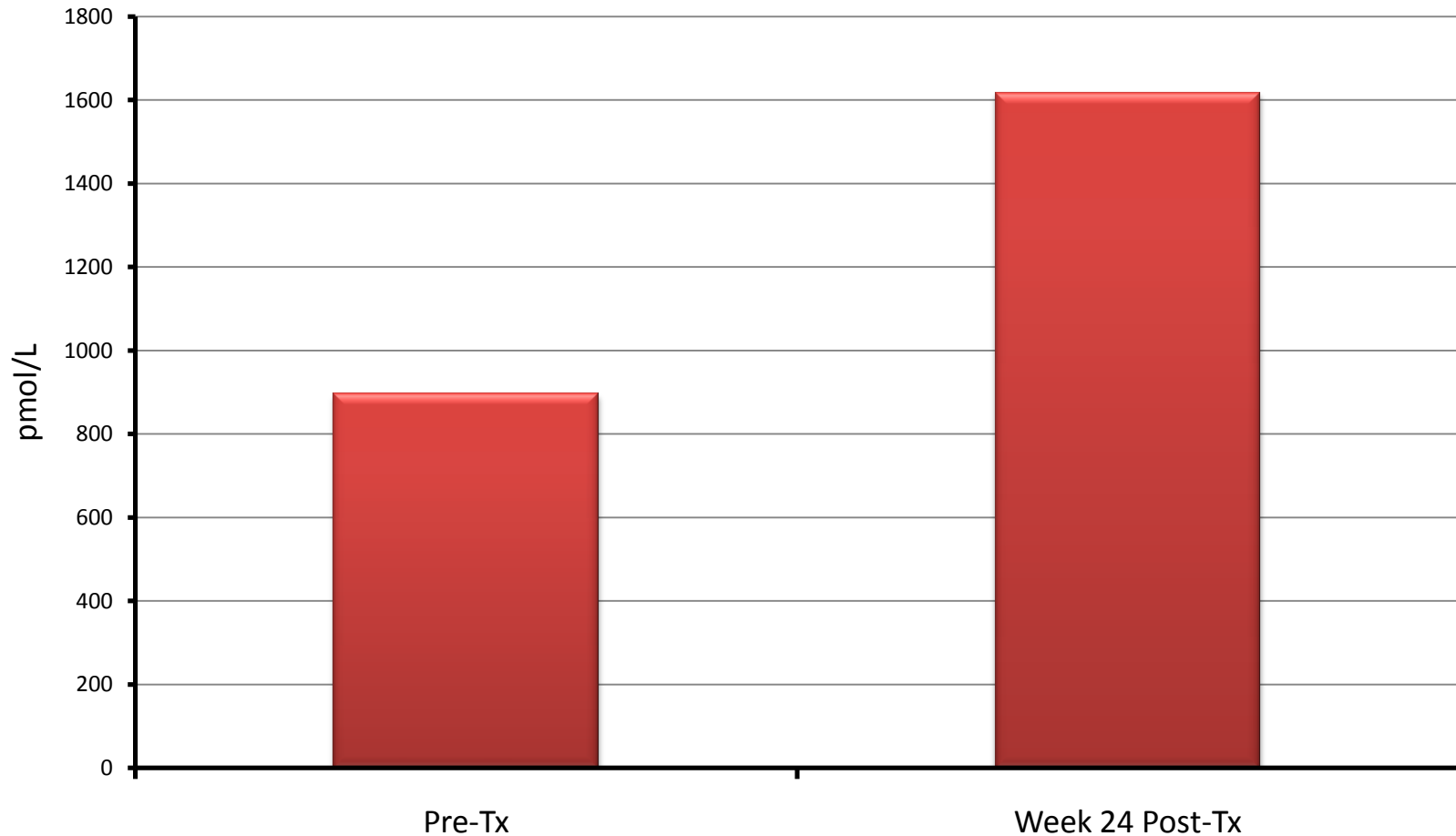
# Responses to hypoglycaemia of adrenalin and glucagon compared to pre-transplantation

Glucagon Response (following ITT)



# Responses to hypoglycaemia of adrenalin and glucagon compared to pre-transplantation

Adrenaline Response (following ITT)



# Summary

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Transplantation of encapsulated porcine islets markedly improves adrenalin (and glucagon) response to hypoglycaemia, which may account for the improvement in both hypoglycaemia severity and unaware hypoglycaemia.

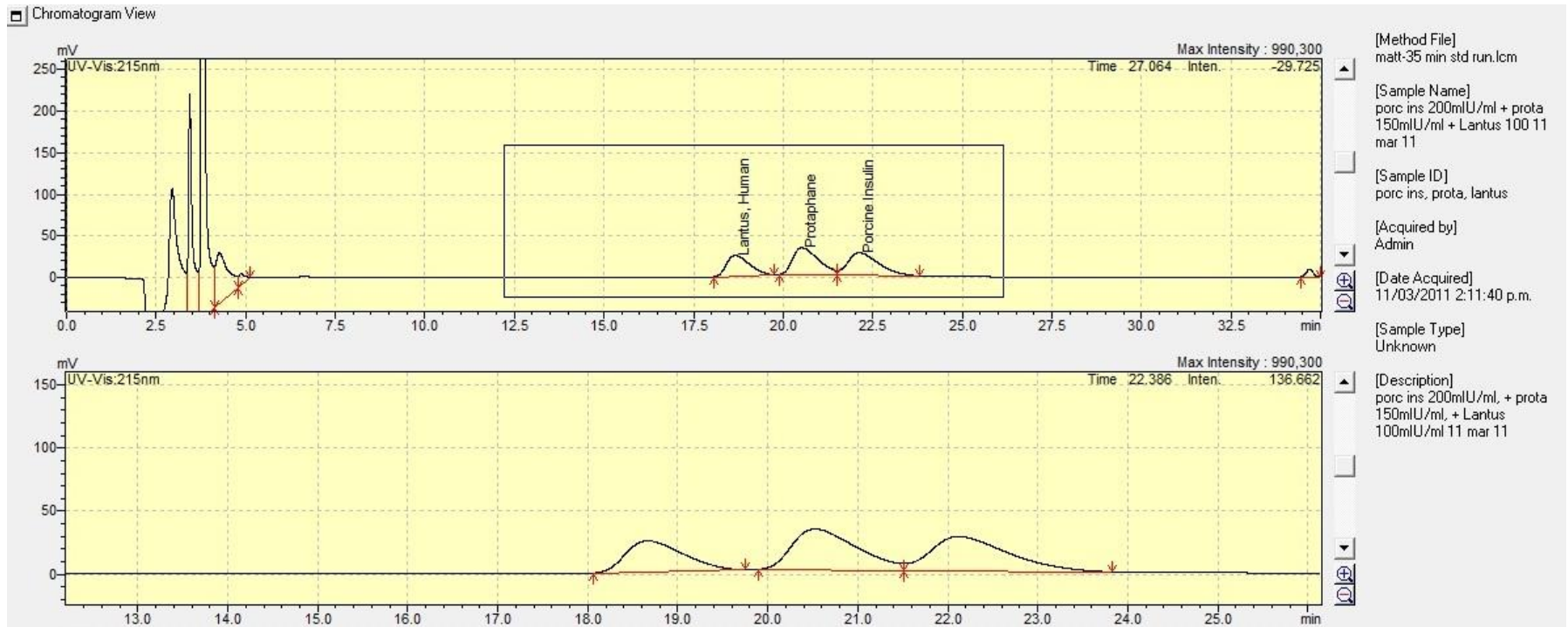
Speculation...

*This may in part be due to islet neutrophin secretion.*

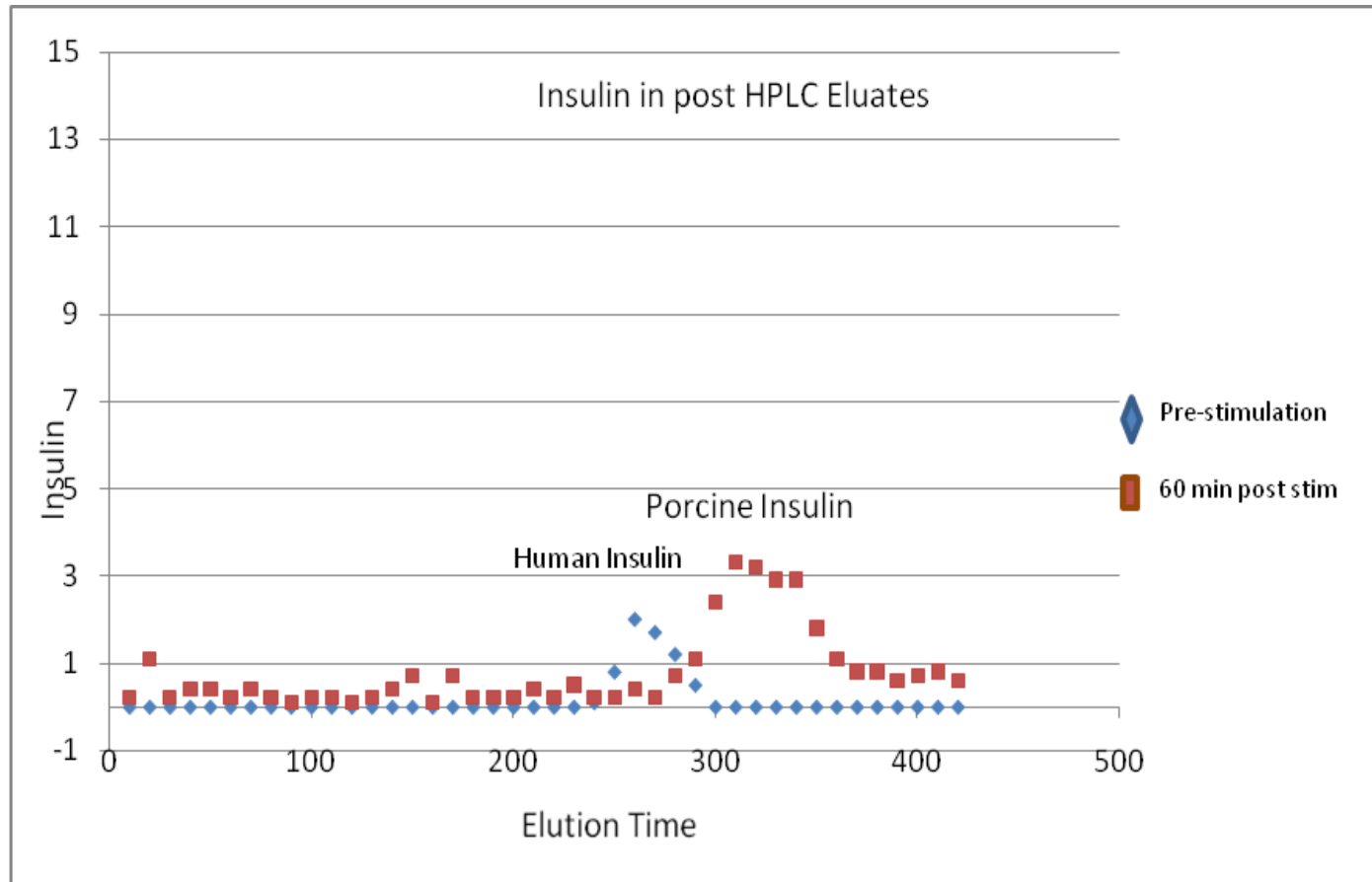




# HPLC Elution of Insulin Standards



# Insulin in post HPLC Eluates



# Conclusion

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Despite minimal insulin dose reduction and improvement in HbA1c, severe and unaware hypoglycaemia was much reduced by a single dose of encapsulated islets with no dose response seen.



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