

**Supplementary Table 1: Treatment-emergent adverse events (TEAE) across all treatment groups.**

Of note skin reactions were over-reported in the 10µg group due to an inconsistency in adverse event collection, these events were treated as expected adverse events in subsequent cohorts. Table shows TEAE reported by 2 or more patients. Excludes 2 uncoded TEAE. N=number of subjects; [E]=number of events; TSH=thyroid stimulating hormone.

Note: For subject counts (N) within each preferred term, subjects were counted only once, even if they experienced multiple events. For event counts [E], every event was included for the category.

	Placebo N=6 n (%) [E]	Study drug 10µg N=8 n (%) [E]	Study drug 100µg N=6 n (%) [E]	Study drug 500µg N=6 n (%) [E]	All Study drug Doses N=20 n (%) [E]
Any TEAE	6 (100)[107]	8 (100) [206]	6 (100) [80]	6 (100) [70]	20 (100) [356]
Hypoglycaemia	6 (100) [84]	8 (100) [156]	6 (100) [61]	6 (100) [53]	20 (100) [270]
Viral upper respiratory tract infection	4 (67) [7]	4 (50) [5]	3 (50) [4]	2 (33) [2]	9 (45) [11]
Vomiting	0	5 (63) [7]	1 (17) [1]	0	6 (30) [8]
Rhinitis	1 (17) [1]	3 (38) [3]	1 (17) [1]	2 (33) [2]	6 (30) [6]
Injection site erythema	1 (17) [1]	5 (63) [8]	0	0	5 (25) [8]
Headache	2 (33) [2]	0	1 (17) [1]	3 (50) [3]	4 (20) [4]
TSH increased	0	2 (25) [2]	1 (17) [1]	0	3 (15) [3]
Cough	0	0	2 (33) [2]	1 (17) [1]	3 (15) [3]
Productive cough	0	3 (38) [3]	0	0	3 (15) [3]
Dizziness	1 (17) [1]	0	2 (33) [3]	0	2 (10) [3]
Diarrhoea	0	2 (25) [2]	0	0	2 (10) [2]
Influenza	0	1 (13) [1]	0	1 (17) [1]	2 (10) [2]
Oropharyngeal pain	1 (17) [1]	1 (13) [1]	1 (17) [1]	0	2 (10.0) [2]

**Supplementary Table 2. Details of antibodies used for staining cryopreserved PBMCs to assess T cell immunophenotypes.**

Marker	Fluorochrome	Company	Clone
Live/Dead	Yellow	Life Technologies	NA
ICOS/CD278	BV650	BD	DX29
CD73	BV605	BioLegend	AD2
CD3	BUV805	BD	UCHT1
CD4	BUV395	BD	Sk3
CD8	BUV563	BD	RPA-T8
CD14	BV570	BioLegend	M5E2
CD19	BV570	BioLegend	HIB19
CD16	BUV496	BD	3G8
CD56	PE-Cy5	BD	B159
CD25	PE	BD	2A3
CD25	PE	BD	M-A251
CD127	BV786	BD	HIL-7R-M21
CD45RA	APC-Cy7	BioLegend	HI100
CD15s	BV510	BD	CSLEX1
CD49d	BUV737	BD	9F10
CD31	BV421	BioLegend	WM59
CD103	PE-Dazzle 594	BioLegend	Ber-ACT8
HLA-DR	BUV661	BD	G46-6
CD39	BV711	BioLegend	A1
CD27	APC-R700	BD	M-T271
PD-1	PE-Cy7	BD	EH12.1
FOXP3	AF647	BD	259D/C7
FOXP3	AF647	BioLegend	206D
Helios	PerCP-Cy5.5	BioLegend	22F6
Ki67	FITC	BD	35

**Supplementary Table 3. Details of individuals selected for transcriptional profiling of Tregs before/after treatment.**

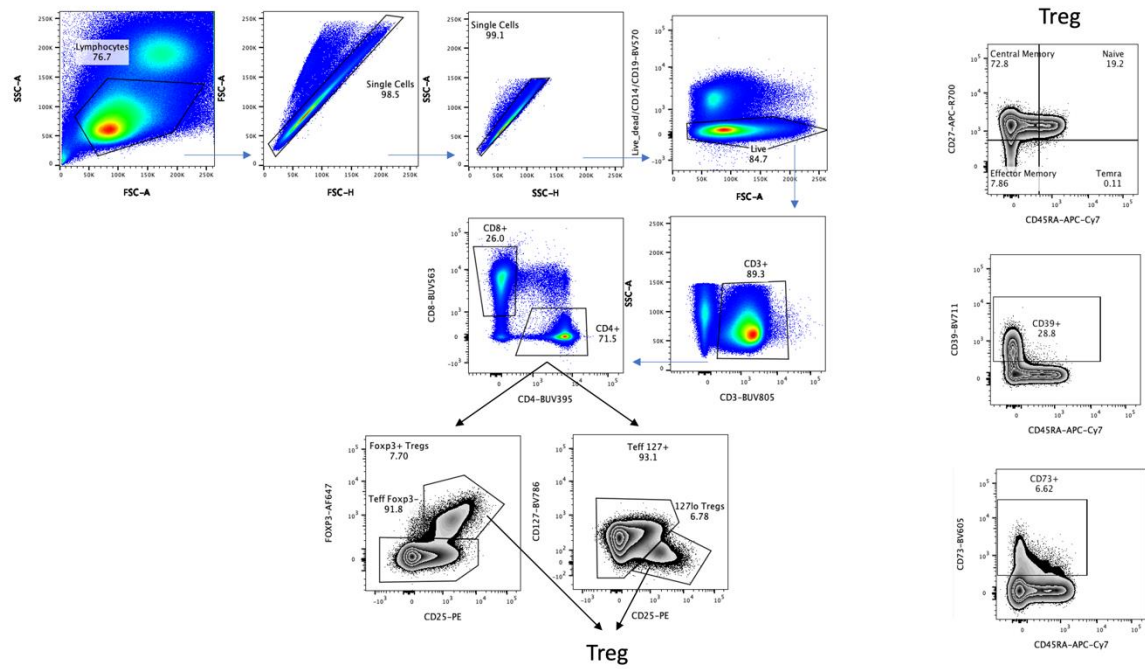
Subject	treatment	End visit	Sex
1	placebo	24w	F
2	placebo	21w	F
3	placebo	24w	M
4	placebo	24w	F
5	placebo	24w	F
6	MultipepT1De 10ug	24w	F
7	MultipepT1De 100ug	24w	F
8	MultipepT1De 100ug	24w	M
9	MultipepT1De 100ug	21w	F
10	MultipepT1De 500ug	24w	M

**Supplementary Table 4. Details of antibodies used to stain cryopreserved PBMCs for sorting Tregs for gene expression.**

Marker	Fluorochrome	Company	Clone
Live/Dead	Violet	Life Technologies	NA
CD3	APC-Cy7	Biolegend	OKT3
CD25	PE	BD	2A3
CD25	PE	BD	SK3
CD127	AF674	BD	HIL-7R-M21
CD4	FITC	BD	SK3
CD14	Pacific Blue	Invitrogen	TuK4

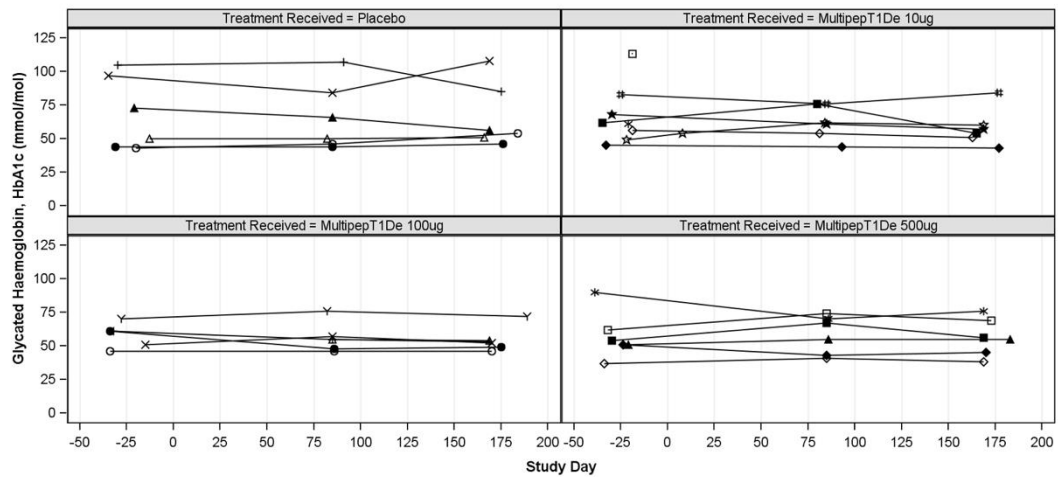
## Supplementary Figure 1. Gating strategy used for T cell immunophenotype panel.

Supplementary Figure 1

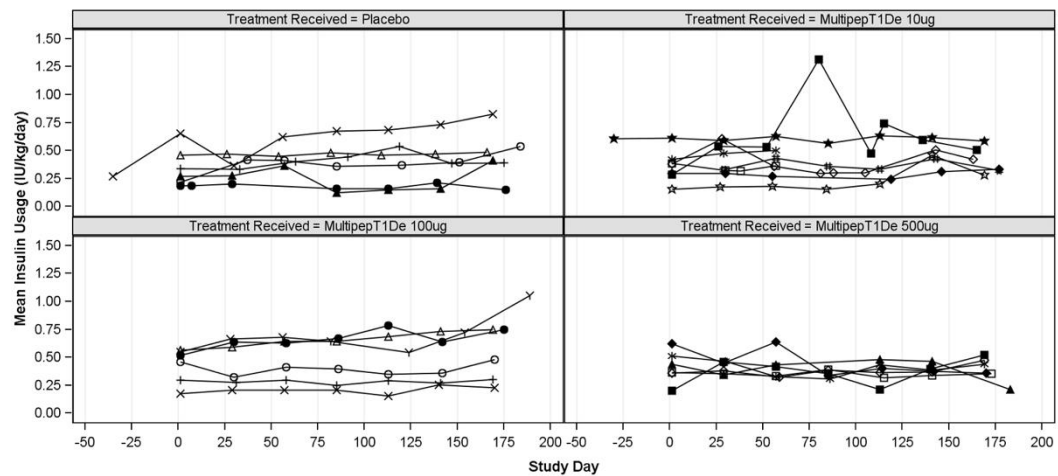


**Supplementary Figure 2.** Individual line plots of (A) glycated haemoglobin, HbA1c (mmol/mol) and (B) mean insulin usage (IU/kg/day) over time. Responses from each individual are joined by a line and different individuals within each cohort are indicated with a different symbol.

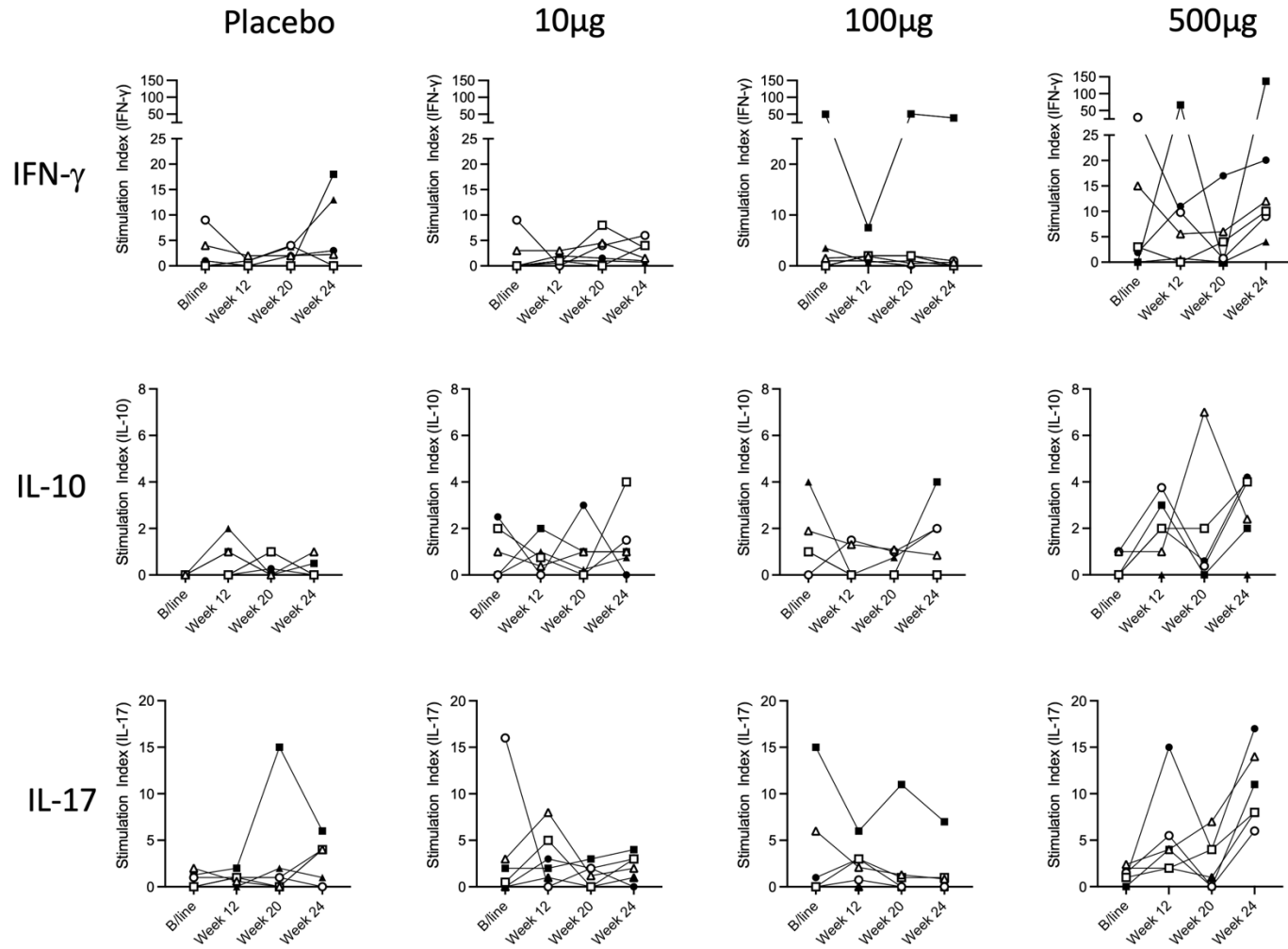
**A**



**B**



**Supplementary Figure 3.** Individual responses to proinsulin measured by ELISPOT measured at baseline, 12-, 20- and 24-weeks. Responses from each individual are joined by a line and different individuals within each cohort are indicated with a different symbol.



**Supplementary Figure 4.** Fold change in the frequency of FOXP3+ Treg at week 12 and 24 relative to baseline.

