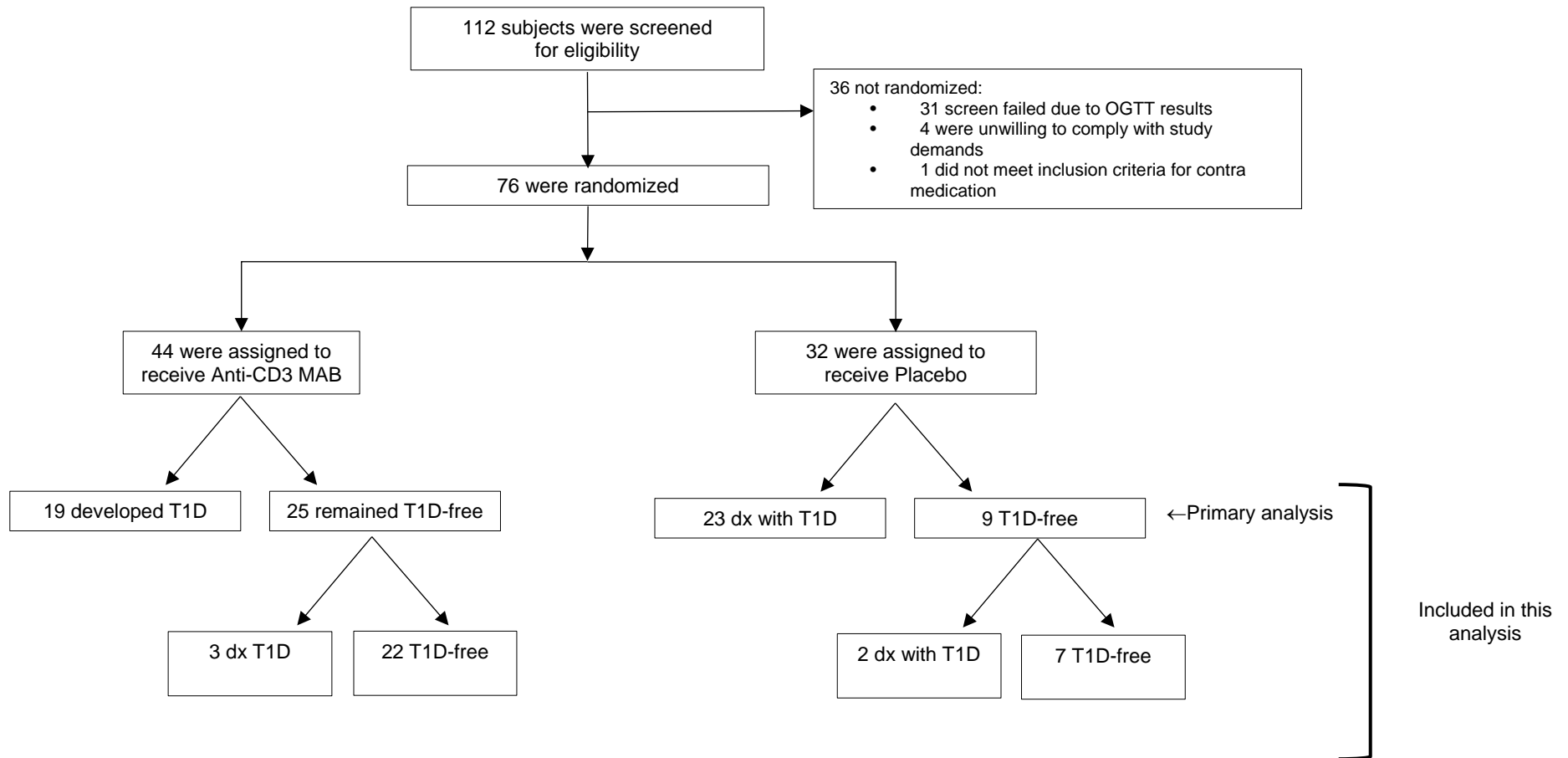


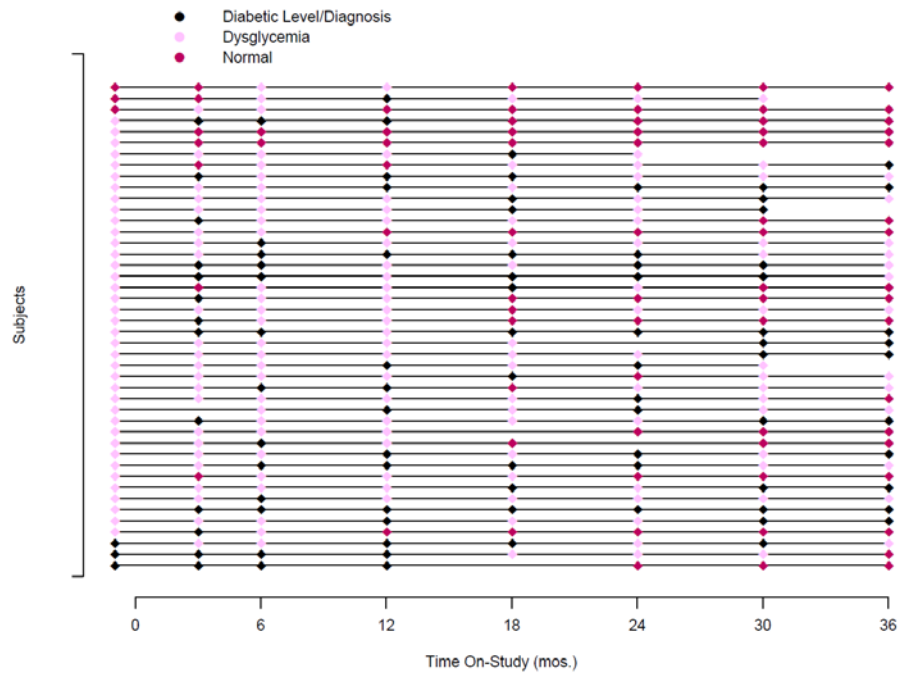
Figure S1



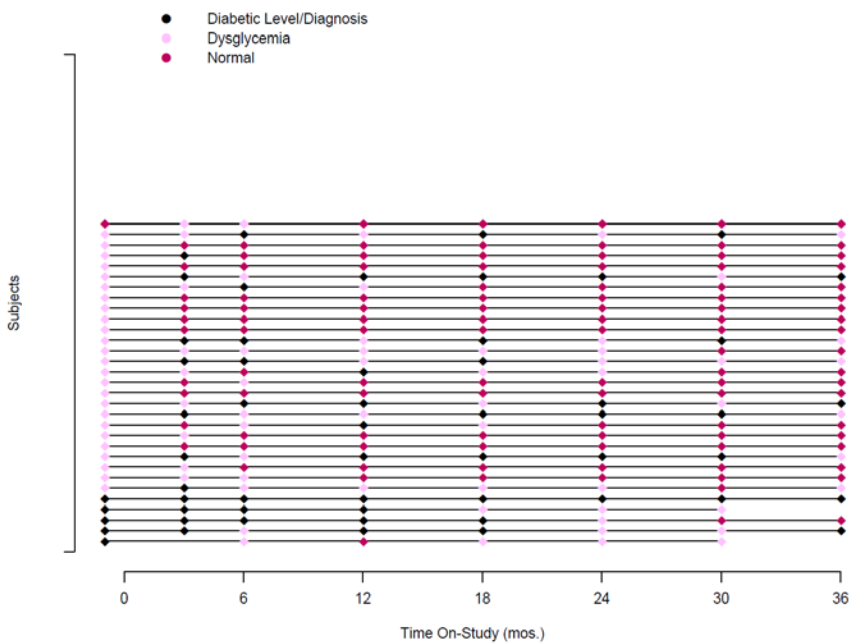
Supplemental Figure 1: Consort diagram

Figure S2

A Teplizumab treated participants

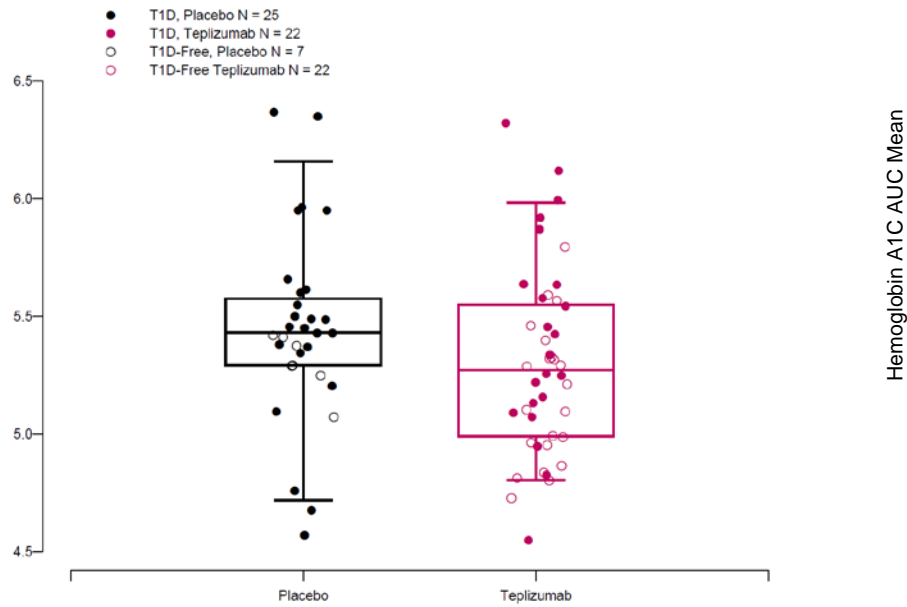


B Placebo treated participants

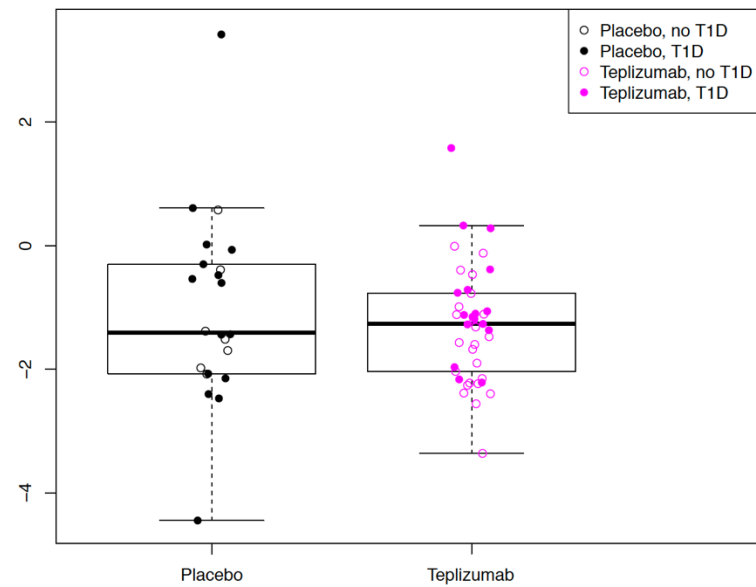


Supplemental Figure 2: Results of OGTT tests over the first 36 months in (A) teplizumab and (B) placebo treated participants: Each line represents a participant. The symbols indicate the time of OGTT testing. The results are indicated as: ●=diabetic level/diagnosis, ●=dysglycemia, ●=normal

A

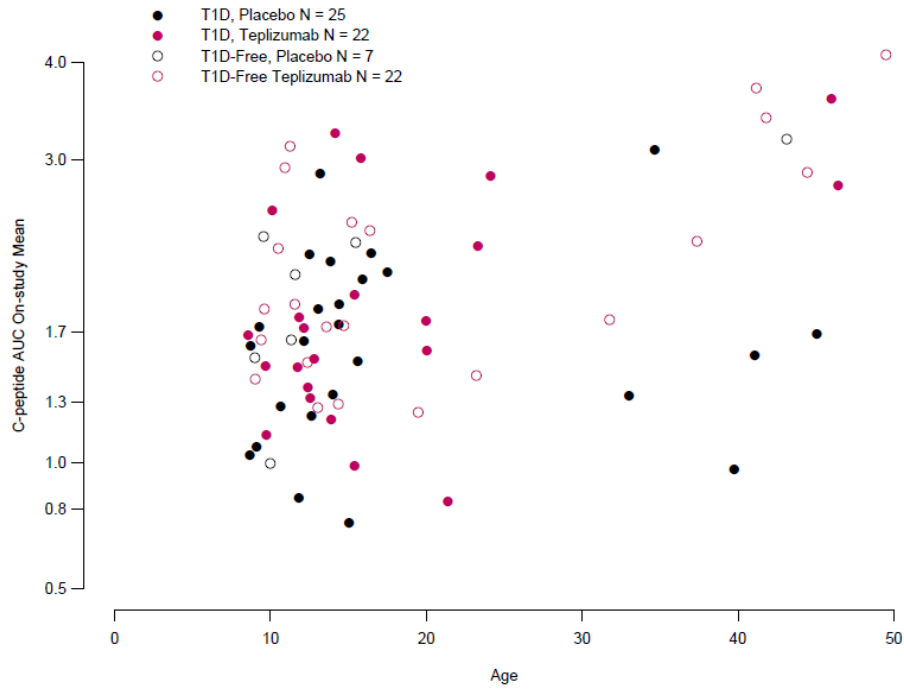


B



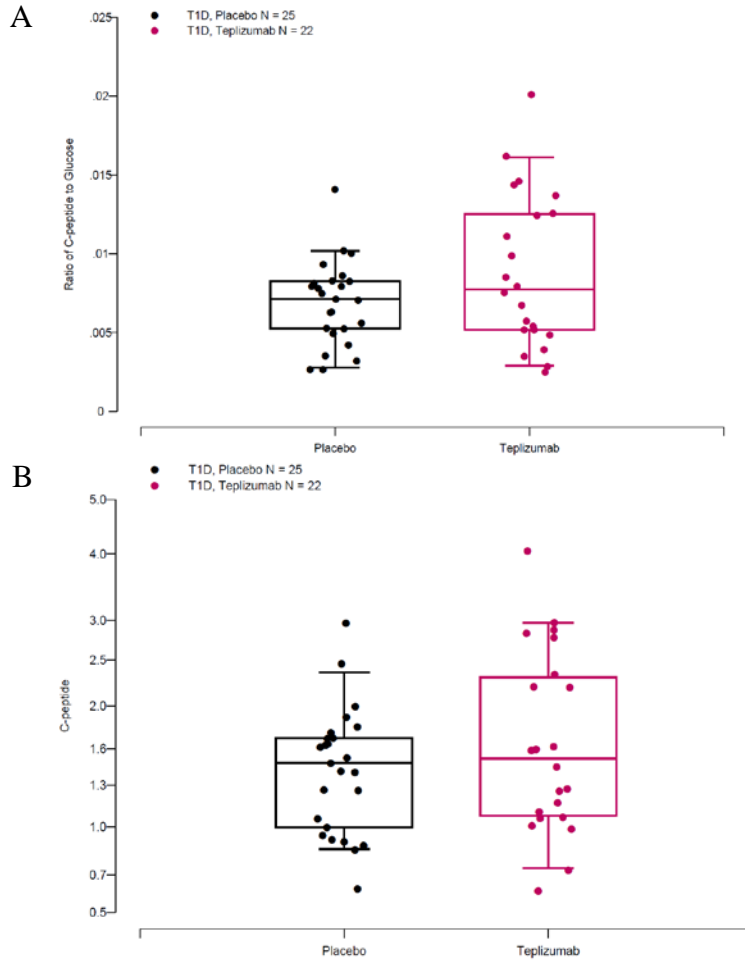
Supplemental Figure 3: Average on-study Hemoglobin A1c levels and Proinsulin:C-peptide ratios showed no significant differences between the treatment groups: A. Boxplot displaying median and interquartile ranges for average on-study Hemoglobin A1c AUC for participants from placebo and teplizumab treated groups. ANCOVA model incorporating baseline value, age, and treatment group showed no significant impact of treatment group ($p=0.14$). **B.** On-study PI:C ratio was calculated using on treatment values and showed no significant differences between groups. ($n=22$ in placebo and 41 in teplizumab, $p=0.31$, Wilcoxon rank sum test)

Figure S4



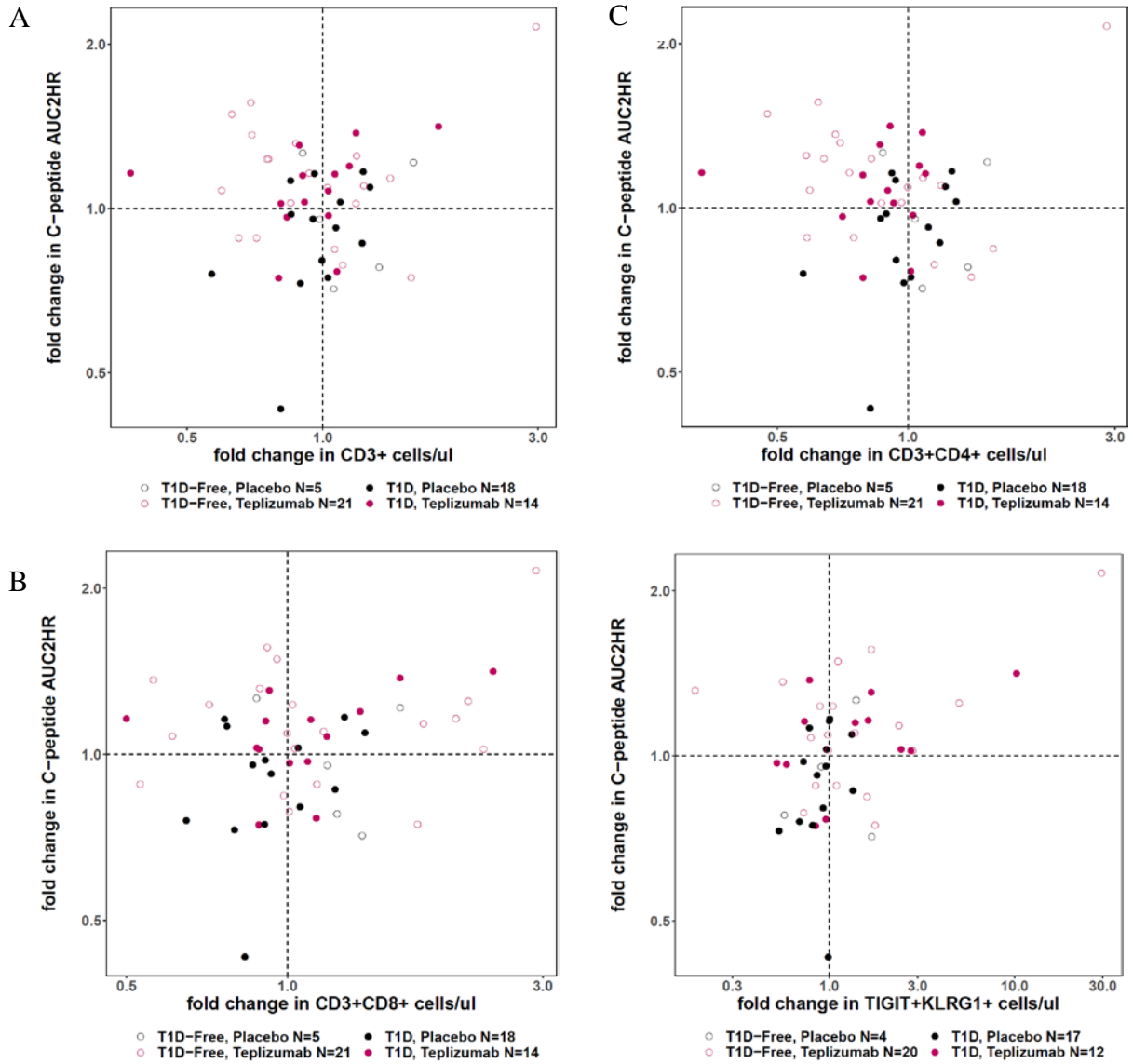
Supplemental Figure 4. Relationship of Average on Study C-peptide AUC with Age and Average on Study Glucose AUC. Scatterplot of age vs. on-study C-peptide AUC ($r=0.44$, $p=0.0001$)

Figure S5



Supplemental Figure 5. C-peptide values are similar between treatment groups at the time of diagnosis. A. C-peptide AUC/Glucose AUC at the time of clinical diagnosis of T1D. B. C-peptide AUC at the time of clinical diagnosis of T1D. Values were obtained from the first of two consecutive diagnostic OGTTs consistent with a classification of T1D.

Figure S6



Supplemental Figure 6. Changes in the number of circulating T cells at month 3 and C-peptide AUC at month 6. A: CD3+ T cells, Pearson $r=0.19$, $p=0.28$; B: CD3+CD4+ T cells, $r=0.01$, $p=0.97$; C: CD3+CD8+ T cells, $r=0.24$, $p=0.17$; D: CD3+CD8+CD45RO+TIGIT+KLRG1+ T cells, $r=0.4$, $p=0.02$

Supplemental Table 1: ANCOVA Model of On-study Glucose AUC Mean (transformed scale: natural log (ln))

Covariate	Coefficient	Standard Error	t-test	p-value
(Intercept)	3.11	0.592	5.25	< 0.0001
Glucose (baseline)	0.408	0.117	3.50	0.0008
Age	-0.000309	0.00143	-0.215	0.83
Teplizumab treatment	-0.0776	0.0335	-2.32	0.02

Predicted means for Teplizumab and Placebo groups are 164 and 177 mg/dL, respectively (baseline glucose and age set to the cohort mean) – Teplizumab mean is 92.5% of the placebo mean.

Supplemental Table 2: ANCOVA Model of On-study A1c AUC Mean (Ln-Ln transform)

Covariate	Coefficient	Standard Error	t-test	p-value
(Intercept)	0.0981	0.0483	2.03	0.05
A1c (baseline)	0.863	0.0968	8.92	< 0.0001
Age	-0.000226	0.000307	-0.736	0.46
Teplizumab treatment	-0.011	0.00715	-1.53	0.13

Supplemental Table 3: ANCOVA Model of On-study C-peptide AUC Mean (ln(x+1) transform)

Covariate	Coefficient	Standard Error	t-test	p-value
(Intercept)	0.116	0.0601	1.92	0.06
C-peptide (baseline)	0.78	0.0575	13.6	< 0.0001
Age	0.00346	0.00124	2.79	0.007
Teplizumab treatment	0.0768*	0.0271	2.83	0.006

*Predicted means for Teplizumab and Placebo groups are 1.94 and 1.72 nano-moles/L, respectively (baseline C-peptide and age set to the cohort mean)

Supplemental Table 4. Comparison of C-peptide AUC means among teplizumab and placebo

Treatment Group	TN-10 or Control Subject	Baseline		3 months		6 months	
		Mean	Std. Dev.	Mean	Std. Dev.	Mean	Std. Dev.
Placebo	TN-10*	1.91 (32)	0.704	1.78 (30)	0.712	1.81 (25)	0.855
	Control	2.41 (32)	0.822	--	--	--	--
Teplizumab	TN-10*	1.99 (44)	0.833	2.07 (43)	0.742	2.15 (44)	0.780
	Control	2.31 (44)	0.672	--	--	--	--

groups and matched islet autoantibody negative relatives (non-transformed values)

*Data shown as means (number of participants at indicated timepoint). Control Subject data is based on cross-sectional OGTTs obtained in islet autoantibody relatives matched by sex and age. For subjects < 19 years, age was matched within 6 months. Subjects \geq 19 were matched within +/- 2 years with the exception of 5 subjects, which required +/- 6 years. *The C-peptide values in the TN-10 participants were lower the matched autoantibody- controls ($p=0.001$, Wilcoxon).

Supplemental Table 5: Effect of HLA genotype and ZnT8 positivity on average C-peptide AUC

Factor	Main Effect Coefficient (p-value*)	Interaction Effect Coefficient (p-value)
HLA-DR3	0.00783 (p = 0.79)	-0.0431 (p = 0.44)
HLA-DR4	-0.0311 (0.27)	-0.0122 (p = 0.84)
ZnT8 positive/negative	-0.00814 (p = 0.80)	0.0129 (p = 0.84)

* interaction term was not included

Supplemental Table 6. ANCOVA analysis of C-peptide AUC slope Over 1st 6 months on Study

Covariate	Coefficient	Standard Error	t-test	p-value
Intercept	-0.0234	0.00715	-3.27	0.00166
Pre-slope	-0.078	0.0438	-1.78	0.0795
Age	0.000469	0.000284	1.65	0.103
Teplizumab treatment	0.0219	0.00662	3.31	0.00149

Supplemental Table 7: T cell phenotype flow cytometry panel

Markers	Format	Clone	Vendor
CD56	BUV395	NCAM16.2	Becton Dickinson
CD45RA	BUV737	HI100	Becton Dickinson
Ki67	BV421	Ki-67	BioLegend
CCR7	BV510	G043H7	BioLegend
CD3	BV605	OKT3	BioLegend
PD1	BV650	EH12.2H7	BioLegend
CD127	BV711	A019D5	BioLegend

CD45R0	BV786	UCHL1	Becton Dickinson
CD4	BB515	RPA-T4	Becton Dickinson
Eomes	PE	WD1928	eBiosciences
FoxP3	PE-CF594	259D/C7	Becton Dickinson
KLRG1	PE-Vio770	REA261	Miltenyi
TIGIT	APC	MBSA43	eBioscience
CD8	Ax700	SK1	BioLegend
CD57	APC-Vio770	REA769	Miltenyi
L/D	BUV496	NA	Becton Dickinson

Supplemental Table 8: Intracellular cytokine staining flow cytometry panel

Markers	Format	Clone	Vendor
IL-17	BV421	BL168	BioLegend
CD45RA	BV605	HI100	BioLegend
GrzmB	BV510	GB11	Becton Dickinson
PD-1	BV650	EH12.2H7	BioLegend
CD3	BUV737	UCHT1	Becton Dickinson
TNF α	APC	MAb11	BioLegend
CD127	BV785	A019D5	BioLegend
CD4	Ax700	RPA-T4	BioLegend
IFN γ	BV711	B27	Becton Dickinson
FoxP3	PE-CF594	259D/C7	Becton Dickinson
KLRG1	FITC	SA231A2	BioLegend
TIGIT	PE-Cy7	A15153G	BioLegend
CD8	BUV395	RPA-T8	Becton Dickinson
IL-2	BB700	MQ1-17H12	Becton Dickinson
L/D	BUV496	NA	Becton Dickinson