Supplementary Information

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Supplementary Table 1. Summary of clinical end points for the GAD-alum treatment group compared to Placebo, in the Full Analysis Set and the subgroup defined by patients carrying the HLA DR3-DQ2.

			Full Analysis Set	HLA DR3-DQ2 subgroup
Change in stimulated C-peptide AUC from baseline GAD-alum / Placebo	Visit 6 Month 6	Estimated treatment ratio (95% CI)	1.111 (0.951; 1.298)	1.313 (0.953; 1.809)
		P value	0.1821	0.0948
	Visit 7 Month 15	Estimated treatment ratio (95% CI)	1.091 (0.845; 1.408)	1.557 (1.126; 2.153)
		P value	0.5009	0.0078
Change in IDAA1C from baseline GAD-alum / Placebo	Visit 6 Month 6	Estimated treatment difference (95% CI)	-0.153 (-0.732; 0.426)	-0.903 (-1.868; 0.062)
		P value	0.6013	0.0665
	Visit 7 Month 15	Estimated treatment difference (95% CI)	0.299 (-0.434; 1.031)	-0.692 (-1.868; 0.483)
		P value	0.4204	0.2449
Change in HbA1C from baseline GAD-alum / Placebo	Visit 6 Month 6	Estimated treatment difference (95% CI)	-3.027 (-6.643; 0.589)	-7.143 (-12.999; -1.287)
		P value	0.0999	0.0173
	Visit 7 Month 15	Estimated treatment difference (95% CI)	-0.908 (-5.525; 3.709)	-5.812 (-13.176; 1.552)
		P value	0.6975	0.1206
Change in daily exogenous insulin dose from baseline GAD-alum / Placebo	Visit 6 Month 6	Estimated treatment difference (95% CI)	0.018 (-0.066; 0.102)	-0.091 (-0.227; 0.045)
		P value	0.6694	0.1866
	Visit 7 Month 15	Estimated treatment difference (95% CI)	0.081 (-0.036; 0.198)	-0.058 (-0.241; 0.126)
		P value	0.1745	0.5331
Change in maximum stimulated C-peptide from baseline GAD-alum / Placebo	Visit 6 Month 6	Estimated treatment difference (95% CI)	0.041 (-0.092; 0.174)	0.210 (0.006; 0.413)
		P value	0.5422	0.0432
	Visit 7 Month 15	Estimated treatment difference (95% CI)	-0.005 (-0.139; 0.129)	0.131 (-0.075; 0.337)
		P value	0.9403	0.2104
Change in fasting C-peptide from baseline GAD-alum / Placebo	Visit 6 Month 6	Estimated treatment difference (95% CI)	0.050 (0.001; 0.099)	0.103 (0.029; 0.178)
		P value	0.0447	0.0071
	Visit 7 Month 15	Estimated treatment difference (95% CI)	-0.003 (-0.052; 0.047)	0.033 (-0.043; 0.109)
		P value	0.9155	0.3927
Maximum stimulated C-peptide >0.2 nmol/L	Visit 7 Month 15	GAD-alum n (%) Placebo n (%)	51 (92.7%) 37 (75.5%)	28 (96.6%) 12 (70.6%)
		GAD-alum 95% CI [a] Placebo 95% CI [a]	82.4 - 98.0 61.1 - 86.7	82.2 - 99.9 44.0 - 89.7
		P value [b]	0.0159	0.0284
Stimulated 90 Minutes C-peptide >0.2 nmol/L	Visit 7 Month 15	GAD-alum n (%) Placebo n (%)	48 (87.3%) 35 (71.4%)	28 (96.6%) 11 (64.7%)
		GAD-alum 95% CI [a] Placebo 95% CI [a]	75.5 - 94.7 56.7 - 83.4	82.2 - 99.9 38.3 - 85.8
		P value [b]	0.0445	0.0086

IDAA1C <= 9	Visit 7 Month 15	GAD-alum n (%) Placebo n (%)	32 (62.7%) 27 (61.4%)	22 (78.6%) 6 (40.0%)
		GAD-alum 95% CI [a] Placebo 95% CI [a]	48.1 - 75.9 45.5 - 75.6	59.0 - 91.7 16.3 - 67.7
		P value [b]	0.8883	0.0310

Change in C-peptide $AUC_{mean\ 0\text{-}120min}$.was analysed on the log scale and back transformed to original scale. Continuous variables were analysed using Mixed Model Repeated Measures [MMRM]). The model for analysis included fixed, categorical effects of treatment, randomization strata (GADA level), visit, Presence or not of HLA DR3-DQ2 haplotype and treatment by visit by HLA DR3-DQ2 haplotype interaction, as well as the continuous, fixed covariate of log-transformed baseline C-peptide $AUC_{mean\ 0\text{-}120min}$.

Least square means (95% confidence intervals) are given together with p-values from this model.
The MMRM did not converge when unstructured covariance structure was used. For this reason, compound symmetry structure was used instead.

[a] Clopper-Pearson's CI of patient proportion.
[b] P-value for Cochran-Mantel-Haenszel (non-zero correlation) (stratified by GAD65A level)

Supplementary Table 2 - Summary of Treatment Emergent Adverse Events (AE) observed in the two groups (GAD-alum and Placebo) between the baseline and Month 15 Visits (Safety Set).

Body System or Organ Class	GAD-alum (n=57) Total AEs: 28 (49.1%) 66		Placebo (n=52) Total AEs: 30 (57.7%) 66	
	Not related	Possibly/Probably Related	Not related	Possibly/Probably Related
Blood and lymphatic system disorders	2 (3.5%) 3		2 (3.8%) 2	
Cardiac disorders		1 (1.8%) 1		
Gastrointestinal disorders	2 (3.5%) 2		5 (9.6%) 7	
General disorders and administration site conditions	2 (3.5%) 2	1 (1.8%) 1	5 (9.6%) 6	2 (3.8%) 3
Hepatobiliary disorders			1 (1.9%) 1	
Immune system disorders			1 (1.9%) 1	
Infections and infestations	15 (26.3%) 24	2 (3.5%) 2	13 (25.0%) 21	1 (1.9%) 1
Injury, poisoning and procedural complications	4 (7.0%) 5		3 (5.8%) 3	
Investigations	1 (1.8%) 1	1 (1.8%) 1		
Metabolism and nutrition disorders	1 (1.8%) 1		2 (3.8%) 2	1 (1.9%) 1
Musculoskeletal and connective tissue disorders	4 (7.0%) 4		3 (5.8%) 5	1 (1.9%) 1
Nervous system disorders	3 (5.3%) 3		2 (3.8%) 2	
Psychiatric disorders	3 (5.3%) 3		1 (1.9%) 1	
Renal and urinary disorders			1 (1.9%) 1	
Reproductive system and breast disorders		1 (1.8%) 2	1 (1.9%) 1	1 (1.9%) 1
Respiratory, thoracic and mediastinal disorders	2 (3.5%) 3	1 (1.8%) 2	2 (3.8%) 2	
Skin and subcutaneous tissue disorders	5 (8.8%) 5	1 (1.8%) 1	2 (3.8%) 2	2 (3.8%) 2
Injection site reactions[a]		45 (78.9%) 414		39 (75.0%) 307

n (%) N : n (%) represents the number of patients with at least one AE (percentage) and N the total number of AEs.

[a] Injection site reactions were collected by the investigators at the clinics as well as reported by subjects in their diaries.

Supplementary Figure 1 – C-peptide $AUC_{mean\ 0\text{-}120\ min}$ over time.

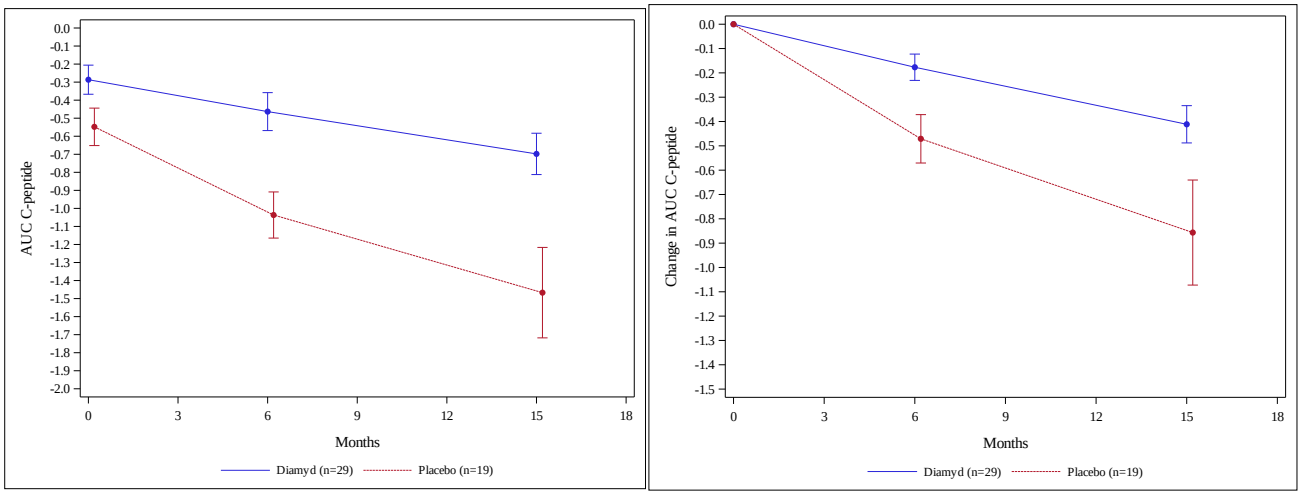

Figure 1. C-peptide $AUC_{mean\ 0\text{-}120\ min}$**.**

Log-transformed C-peptide $AUC_{mean\ 0\text{-}120\ min}$ during a Mixed-Meal Tolerance Test for the two treatment groups (GAD-alum and Placebo) in the prespecified subgroup HLA DR3-DQ2 **(left)**. Change from baseline of log-transformed C-peptide $AUC_{mean\ 0\text{-}120\ min}$ during a Mixed-Meal Tolerance Test for the two treatment groups (GAD-alum and Placebo) in the prespecified subgroup HLA DR3-DQ2 **(right)**. Error bars indicate standard deviation.