Intralymphatic GAD-Alum (Diamyd®) improves hyperglycemia and glycemic control in Type 1 diabetes patients carrying HLA DR3-DQ2 - Exploratory analysis of continuous glucose monitoring data from the DIAGNODE-2 phase IIb clinical trial

Johnny Ludvigsson [1], Christoph Nowak[2,3], Ulf Hannelius[3]

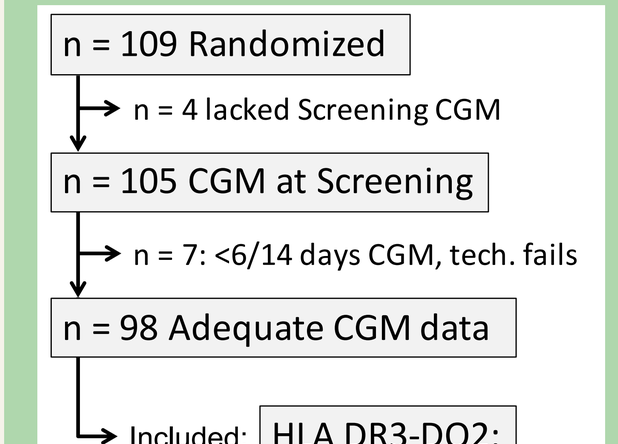
1. Linköping University, Crown Princess Victoria Children´s Hospital and Division of Pediatrics, Dept of Biomedical and Clinical Sciences, Linköping, Sweden. 2. Karolinska Institutet, Department of Neurobiology, Care Sciences and Society, Huddinge, Sweden, 3 Diamyd Medical AB, Stockholm, Swedens. Contact: Johnny.Ludvigsson@liu.se

Background & Aim

Residual beta cell function is crucial for the prevention of acute and late complications in Type 1 diabetes. Most immune interventions have failed with minimal or transient efficacy and/or unacceptable side effects. Autoantigen therapy with recombinant human GAD65 in alum (GAD-alum/Diamyd®) given intralymphatically in combination with Vitamin D has shown promising results in patients with the HLA DR3-DQ2 haplotype (Ludvigsson et al. Diab Care 2021, PMID 34021020). Here, we explore the efficacy of intralymphatic GAD-alum combined with vitamin D on blood glucose recorded by 14-day continuous glucose monitoring (CGM).

Material & Methods

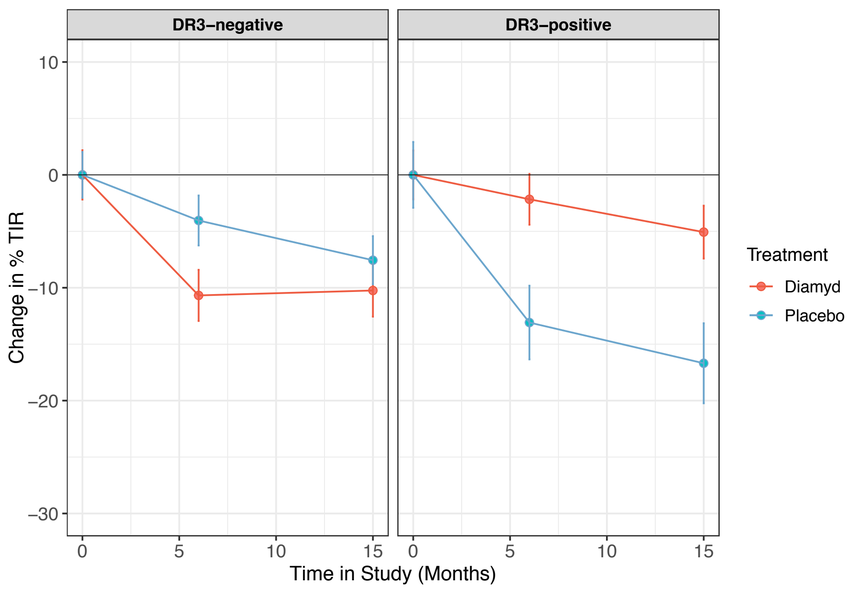
- DIAGNODE-2 (NCT03345004): multicenter, placebo-controlled phase IIb RCT including recent-onset T1D patients aged 12–24y with GADA and fasting C-peptide >0.12 nmol/L
- 3 intralymphatic injections of 4 µg GAD-alum and oral vitamin D, or placebo
- Significant efficacy for C-peptide preservation and trend for better HbA1c in genetic subgroup carrying HLA DR3-DQ2
- Change from baseline analysed by MMRM adjusted for subject, baseline value, visit, treatment, DR3 and baseline*visit and treatment*visit*DR3 interactions



Results

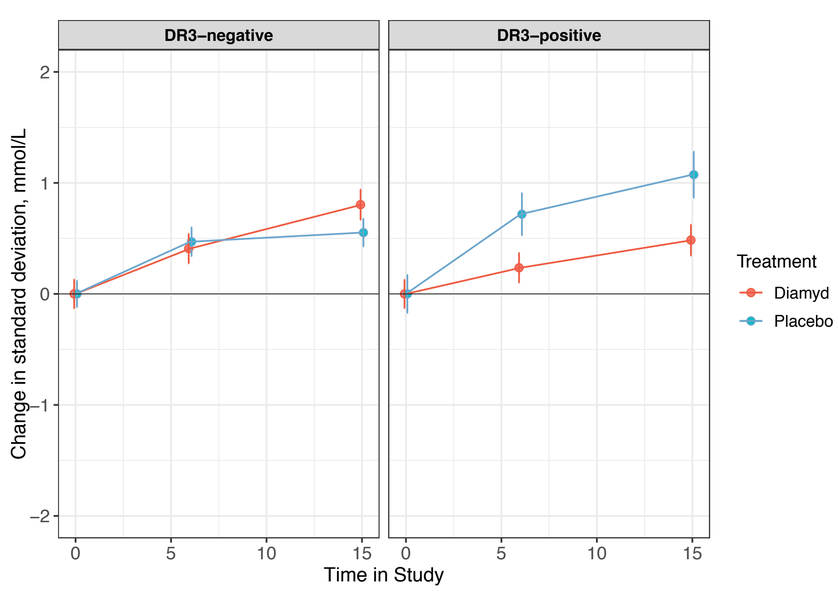
% Time in range (4-10 mmol/L, 70-180 mg/dL)

Significant benefit Diamyd vs. Placebo (DR3-DQ2) at 6M (p=.0072) and 15M (p=.0075)



Glucose, standard deviation (mmol/L)

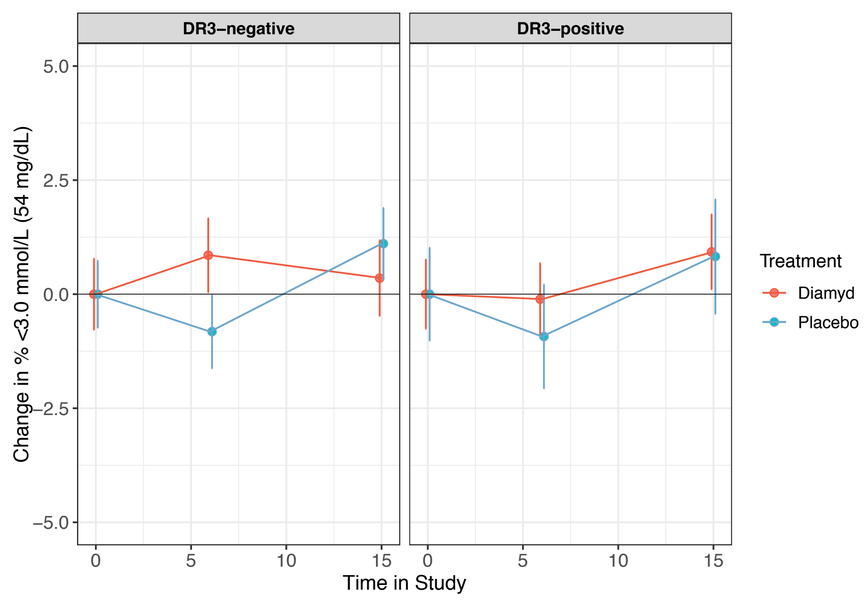
Significant benefit Diamyd vs. Placebo (DR3-DQ2) at 6M (p=.0420) and 15M (p=.0219)



Change from baseline as predicted by MMRM analysis, error bar = standard error

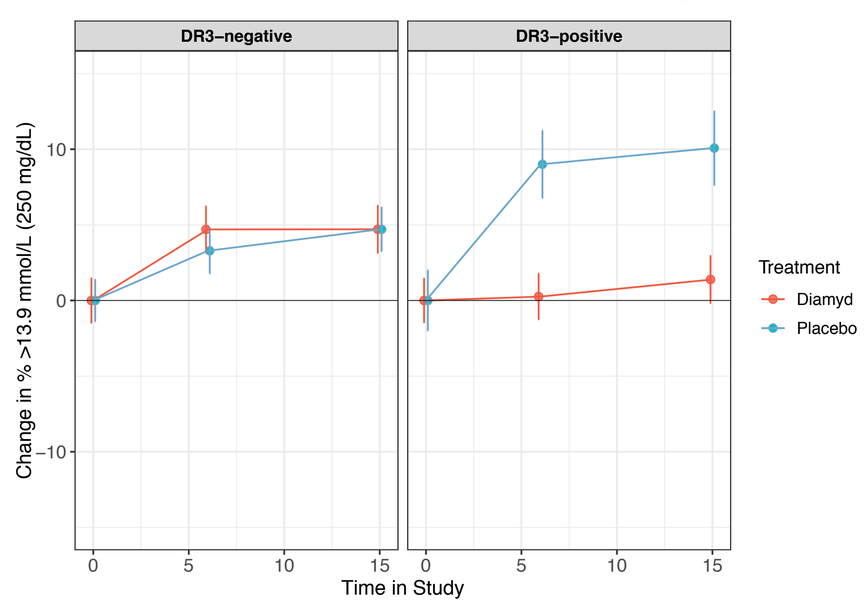
% Time in level 2 hypoglycemia (<3.0 mmol/L)

No difference Diamyd vs. Placebo (DR3-DQ2) at 6M (p=.5543) and 15M (p=.9457)



% Time in hyperglycemia >13.9 mmol/L (250 mg/dL)

Significant benefit Diamyd vs. Placebo (DR3-DQ2) at 6M (p=.0016) and 15M (p=.0036)



Acknowledgements

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Conclusions

Intralymphatic GAD-alum (Diamyd®) improves glycemic control and hyperglycemia in individuals with recently diagnosed T1D carrying HLA DR3-DQ2 regarding change from baseline compared to placebo.