The Swedish GAD-vaccination Trial: Outcomes of a Phase II Safety and Efficacy Trial with Diamyd™ for Preservation of Beta Cell Function in Children with Type 1 Diabetes.

J.Ludvigsson, R.Casas, O. Vaarala, G. Forsander, S.A.Ivarsson, C.Johansson, A.Lindh, N.O.Nilsson, J.Åman, E.Örtqvist, J.A.Robertson, Sweden

DIAMYD MEDICAL

Study: D/P2/04/3

©2006 Diamyd Medical AB, All rights reserved

Background

- Immune interventions at onset of diabetes in children so far have given
  - no or limited effect
  - too serious side effects
- GAD can prevent diabetes in experimental animals
- GAD vaccination (20 microgram) in LADA patients saved beta cell function (Agardh et al 2005)

©2006 Diamyd Medical AB, All rights reserved

Design of the Study

- Randomized, double blind, placebo-controlled clinical trial.
- Either placebo or 20 microg GAD (Diamyd™) sc at Days 1 and 30.
- Sustacal loads with determination of C-peptide (Delphia)
  - 0,30,60,90,120 minutes
  - day 1 and at 3 months, 9 months, 15 months
  - will continue at 21 and 30 months

Ludvigsson et al

©2006 Diamyd Medical AB, All rights reserved

Subjects and Inclusion Criteria

- 70 patients, male and female, with Type 1 diabetes
- 10 - 18 years at diagnosis of Type 1 diabetes and at first Diamyd vaccination. Disease duration 0-18 months at intervention.
- Fasting-C-peptide 0.1 nmol/l or more at screening.
- Positive for GAD65 auto-antibodies at screening.
- Written informed consent both from patients and both parents.

©2006 Diamyd Medical AB, All rights reserved

Baseline Data

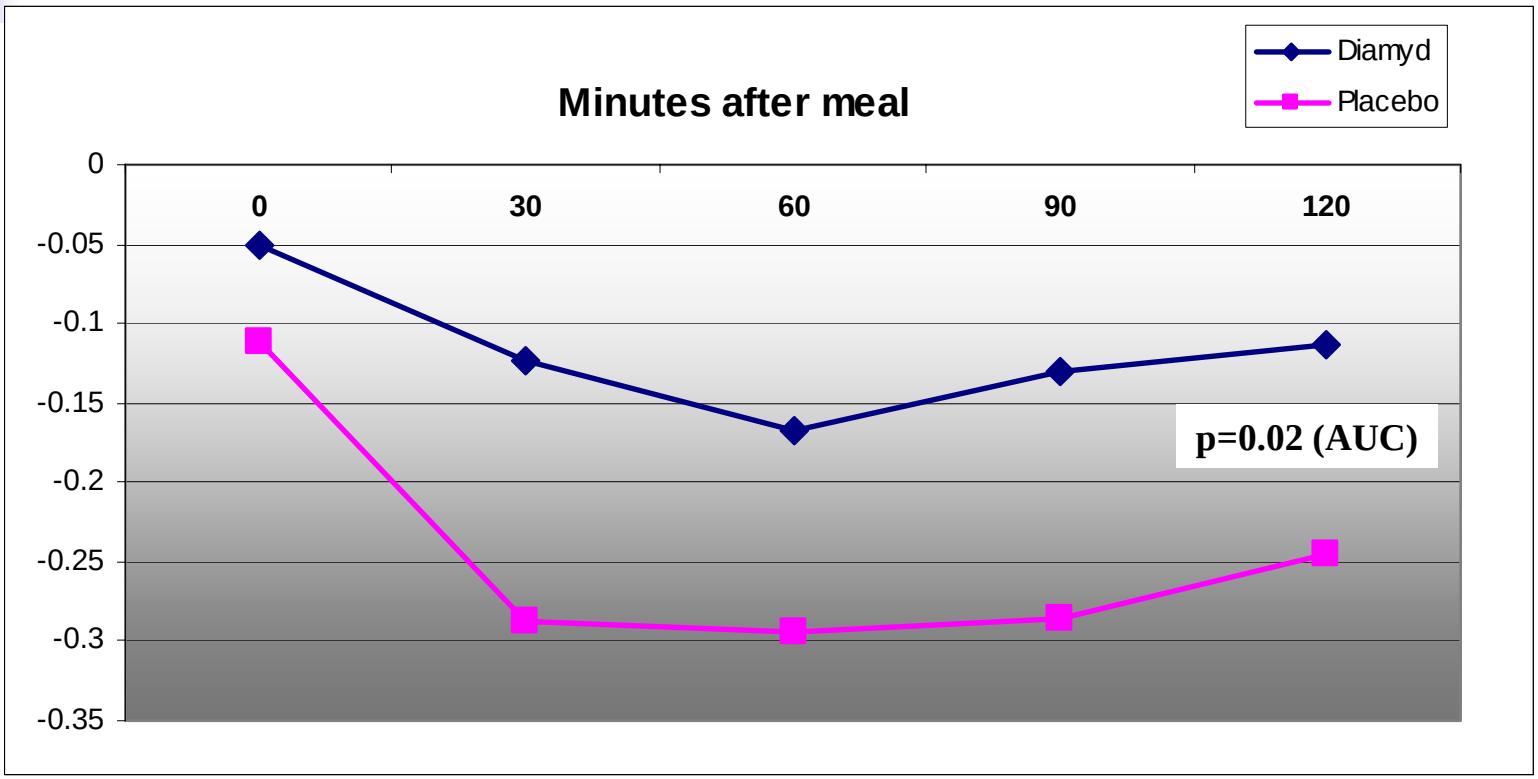
	GAD (Diamyd™)	Placebo
	Means ± SD	Means ± SD
Fasting s/C-peptide at screening, pmol/ml	0.337 ± 0.158	0.336 ± 0.178
C-peptide AUC Day 1, pmol/ml*2hour	1.239 ± 0.569	1.414 ± 0.867
Age, years	13.8 ± 2.3	12.8 ± 1.9
Duration of diabetes, (months) at intervention	9.9 ± 5.3	8.8 ± 5.4
GADA, Units (median)	500	500
GADA Day 1, % <500 U	42.9	32.4
GADA Day 1, % > 500 U	57.1	67.6

DIAMYD MEDICAL Study: D/P2/04/3

©2006 Diamyd Medical AB, All rights reserved

Ludvigsson et al

Change from Day 1 in C-Peptide after Sustacal Challenge; *9 Months*

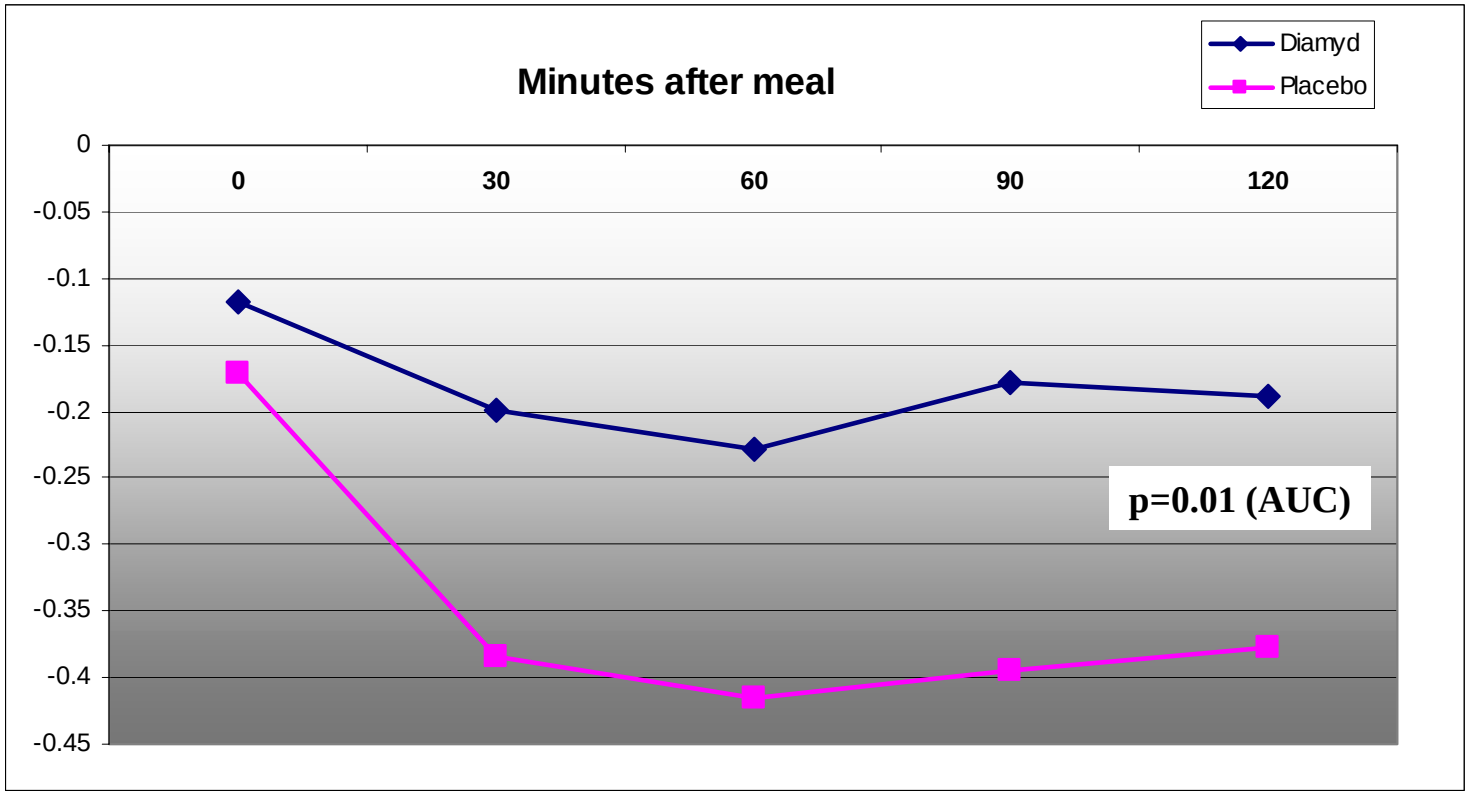


Conclusion: Over a 2 hour period after a meal, Diamyd™ treatment group's C-peptide production declined less than placebo group when compared to measurements obtained at day 1.

©2006 Diamyd Medical AB, All rights reserved

Ludvigsson et al

Change from Day 1 in C-Peptide after Sustacal Challenge; *15 Months*

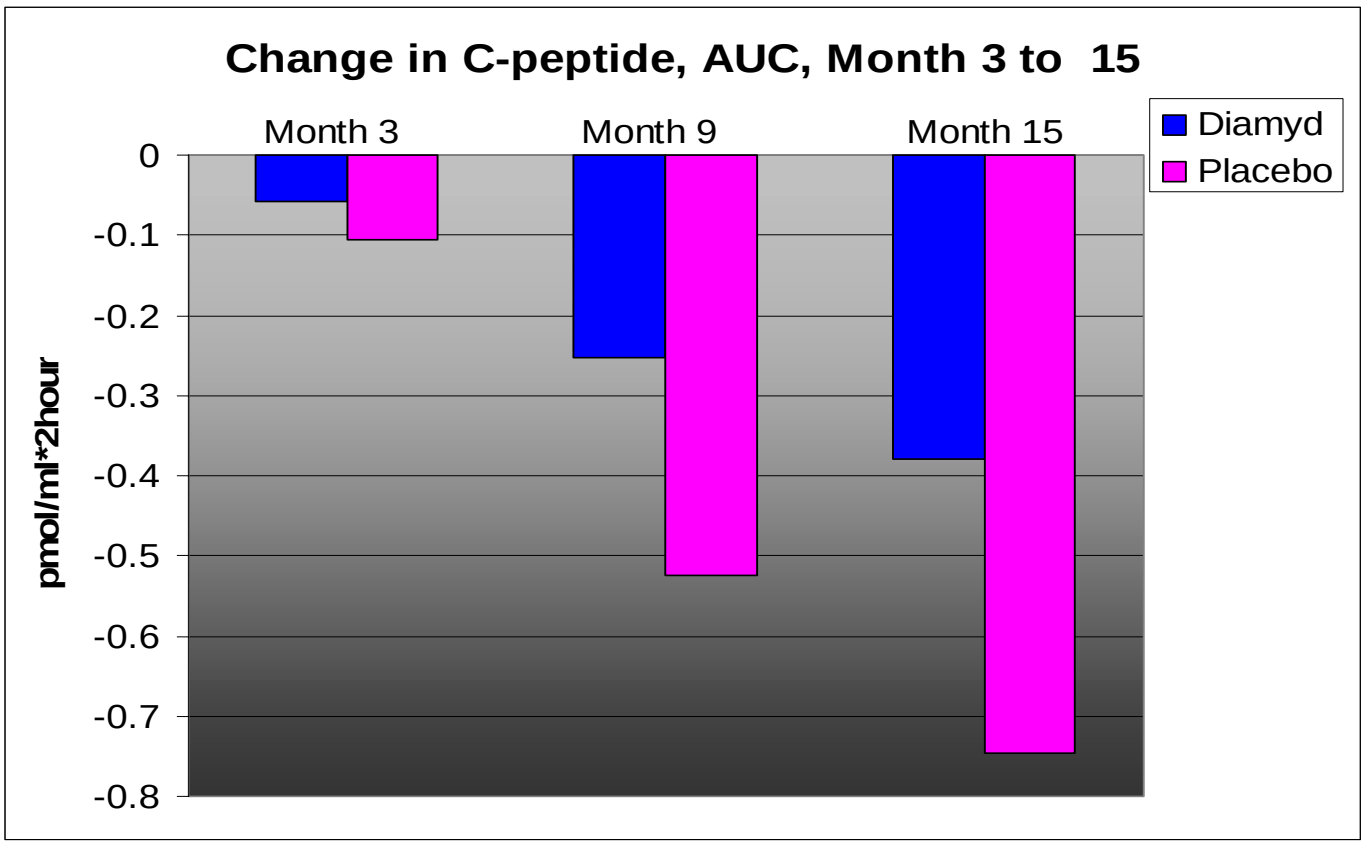


Conclusion: Over a 2 hour period after a meal, Diamyd™ treatment group's C-Peptide production declined less than placebo group when compared to measurements obtained at day 1.

©2006 Diamyd Medical AB, All rights reserved

Ludvigsson et al

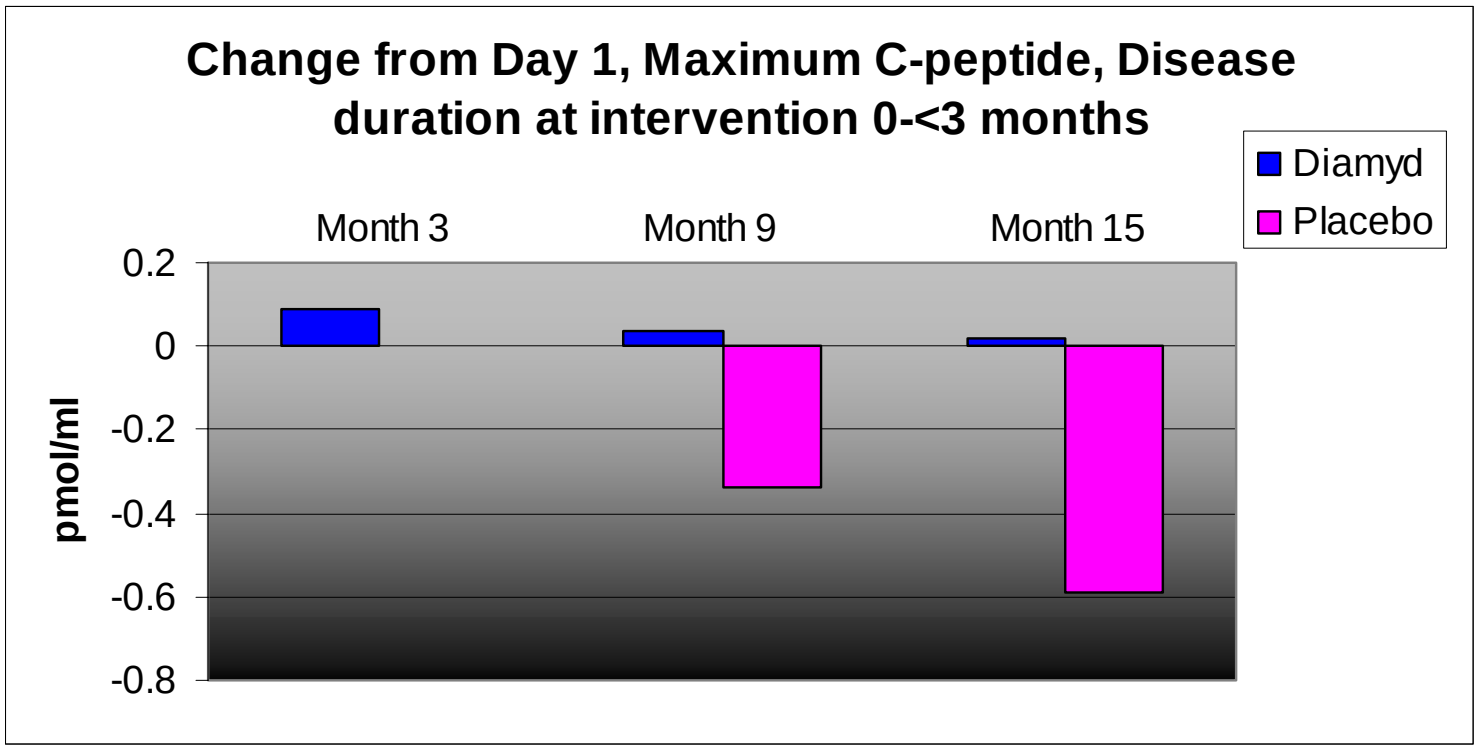
Change in C-Peptide, AUC



©2006 Diamyd Medical AB, All rights reserved

Ludvigsson et al

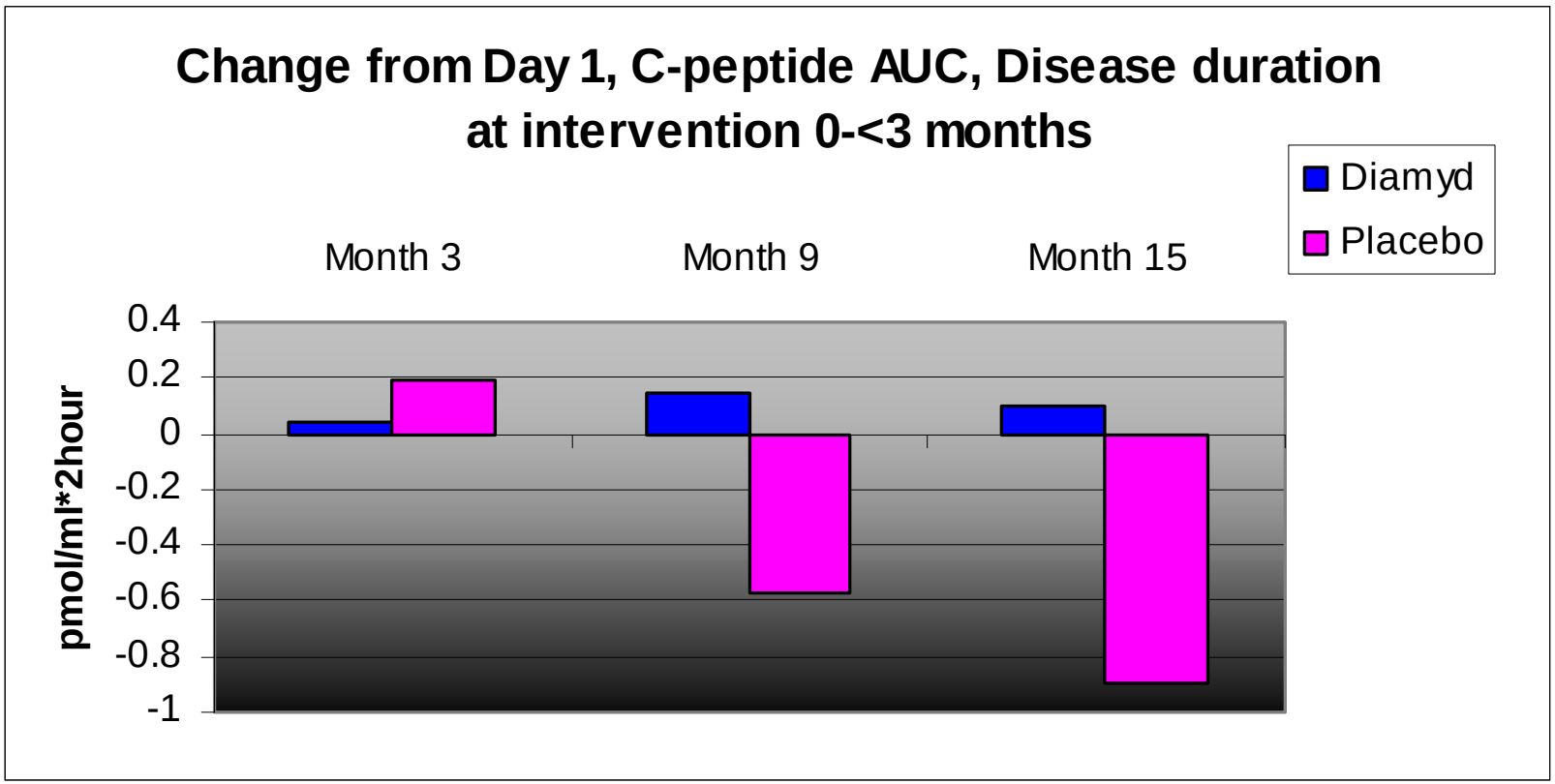
No decline of Max C-Peptide when GAD given to patients with <3 months disease duration



Ludvigsson et al

©2006 Diamyd Medical AB, All rights reserved

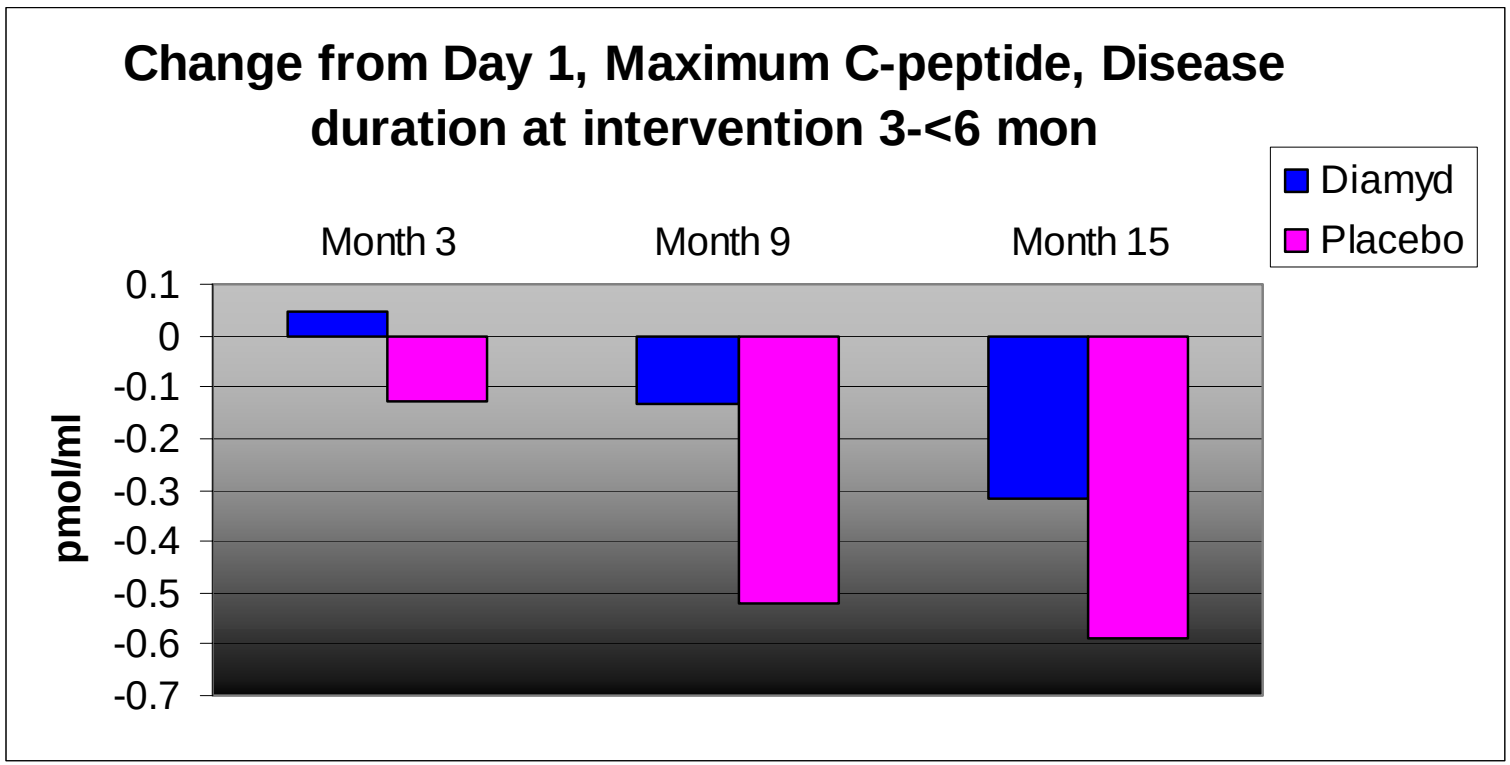
No decline of C-Peptide AUC when GAD given to patients with <3 months disease duration



Ludvigsson et al

©2006 Diamyd Medical AB, All rights reserved

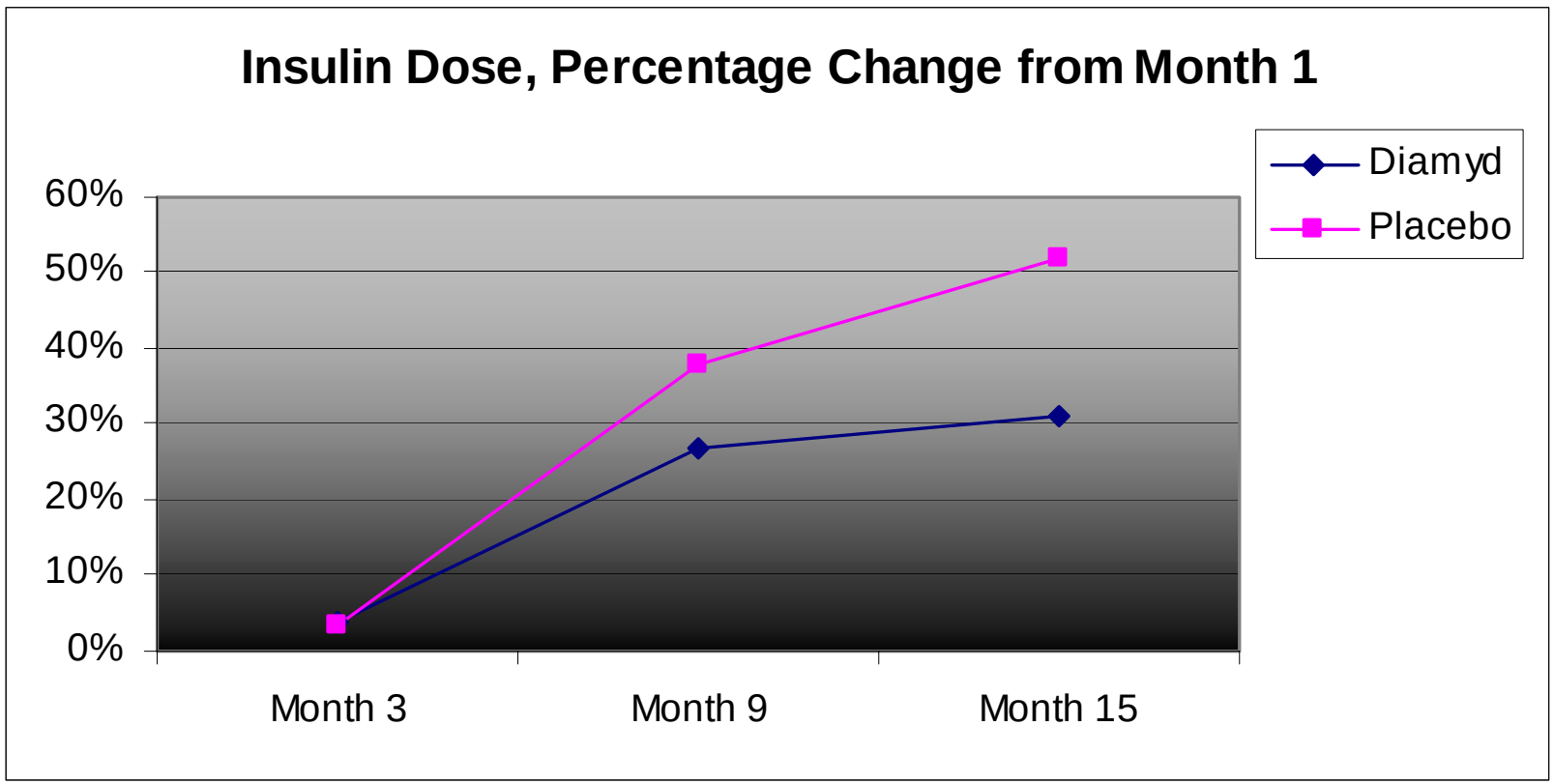
Less C-peptide decline also in patients treated with 3-6 months disease duration



Ludvigsson et al

©2006 Diamyd Medical AB, All rights reserved

Less increase of insulin dose in the GAD intervention group



©2006 Diamyd Medical AB, All rights reserved

Adverse Events

	Diamyd™	Placebo
Connective tissue	3	6
Nervous system	3	3
Immune System	2	1
Blood	1	1
Serious AE	1	3

There were no treatment-related Serious Adverse Events.

©2006 Diamyd Medical AB, All rights reserved

Conclusions

- GAD 65 has demonstrated efficacy in slowing the decline of C-peptide Levels after sustacal load.
- GAD 65 therapy proposes a novel, first-in-class therapy for slowing the progression of autoimmune Type 1 diabetes.
- GAD 65 offers a compelling therapeutic option for type 1 diabetes due to ease of use and patient acceptance.

©2006 Diamyd Medical AB, All rights reserved