AIMS/HYPOTHESIS: The aim of the study was to examine the 48 month outcome of treating recent-onset type 1 diabetic patients for 6 days with humanised CD3-antibody, ChAglyCD3. METHODS: Eighty patients, aged 12-39 years, were recruited for a phase 2 multicentre trial and randomised to placebo (n=40) or ChAglyCD3 (n=40) treatment by a third party member; participants and care-givers were blinded. The change in insulin dose (U kg(-1)day(-1)) over 48 months was chosen as primary endpoint and compared in 31 placebo-and 33 ChAglyCD3-treated patients. Adverse events were followed in 35 and 38 patients, respectively. RESULTS: Treatment with ChAglyCD3 delayed the rise in insulin requirements of patients with recent-onset diabetes and reduced its amplitude over 48 months (+0.09 vs +0.32 U kg(-1)day(-1) in the placebo group). Using multivariate analysis this effect was correlated with higher baseline residual beta cell function and a younger age. It was associated with better outcome variables in subgroups selected according to these variables. In the ChAglyCD3 subgroup with higher initial beta cell function, 0/11 patients became C-peptide-negative over 48 months vs 4/9 in the corresponding placebo.
In the subgroup aged 80% decline within 24 months in the placebo subgroup < 27 years old), resulted in lower HbA1c concentrations and tended to reduce glycaemic variability (p = 0.08). No longterm adverse events were observed. CONCLUSIONS/INTERPRETATION: A 6 day ChAgyCD3 treatment can suppress the rise in insulin requirements of recent-onset type 1 diabetic patients over 48 months, depending on their age and initial residual beta cell function. In younger patients this effect is associated with reduced deterioration of metabolic variables. These observations help to define inclusion criteria for prevention trials. TRIAL REGISTRATION: ClinicalTrials.gov NCT00627146 FUNDING: Center grants from the Juvenile Diabetes Research Foundation (4-2001-434, 4-2005-1327) and grants from the Belgian Fund for Scientific Research-Flanders and from Brussels Free University-VUB.

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