Abstract:

OBJECTIVE: This randomized, four-arm, placebo-controlled, dose-ranging phase 2 trial was conducted to determine whether repeated subcutaneous injections of the altered peptide ligand, NBI-6024, designed to inhibit autoreactive T-cells, improves beta-cell function in patients with recently diagnosed type 1 diabetes. RESEARCH DESIGN AND METHODS: A total of 188 patients, aged 10-35 years, with recently diagnosed type 1 diabetes were randomly assigned for a treatment consisting of the subcutaneous administration of placebo or 1, 0.5, or 0.1 mg NBI-6024 at baseline, weeks 2 and 4, and then monthly until month 24. Fasting, peak, and area under the curve (AUC) C-peptide concentrations during a 2-h mixed-meal tolerance test were measured at 3-month intervals during treatment. Immune function parameters (islet antibodies and CD4 and CD8 T-cells) were also studied. RESULTS: The mean peak C-peptide concentration at 24 months after study entry showed no significant difference between the groups treated with 0.1 mg (0.59pmol/ml), 0.5 mg (0.57 pmol/ml), and 1.0 mg NBI-6024 (0.48 pmol/ml) and the placebo group (0.54 pmol/ml). Fasting, stimulated peak, and AUC C-peptide concentrations declined linearly in all groups by approximately 60% over the 24-month treatment period. The average daily insulin needs at month 24 were also
comparable between the four groups. No treatment-related changes in islet antibodies and T cell numbers were observed. CONCLUSIONS: Treatment with altered peptide ligand NBI-6024 at repeated doses of 0.1, 0.5, or 1.0 mg did not improve or maintain beta-cell function.