Treatment of type 1 diabetes with teplizumab: clinical and immunological follow-up after 7 years from diagnosis.


Abstract

AIMS/HYPOTHESIS: The long-term effects of successful immune therapies for treatment of type 1 diabetes have not been well studied. The Autoimmunity-Blocking Antibody for Tolerance (AbATE) trial evaluated teplizumab, an Fc receptor non-binding humanised anti-CD3 monoclonal antibody in individuals with new-onset type 1 diabetes, and ended in 2011. Clinical drug-treated responders showed an increased frequency of 'partially exhausted' CD8+ T cells. We studied the clinical, immunological and metabolic status of participants after an average follow-up of 7 years.

METHODS: Participants with detectable C-peptide at year 2 of AbATE returned for follow-up. C-peptide responses were assessed by 4 h mixed-meal tolerance test. Autoantibodies and HbA1c levels were measured and average daily insulin use was obtained from patient logs. Peripheral blood mononuclear cells were analysed by flow cytometry and cytokine release.

RESULTS: Fifty-six per cent of the original participants returned. Three of the original control group who did not return had lost all detectable C-peptide by the end of the 2 year trial. The C-peptide responses to a mixed-meal tolerance test were similar overall in the drug vs control group of participants but were significantly improved, with less loss of C-peptide, in drug-treated responders identified at 1 year. However, the improvements in C-peptide response were not associated with
lower HbA$_{1c}$ levels or insulin use. Drug-treated responders showed a significantly increased frequency of programmed cell death protein 1-positive central memory and anergic CD8$^+$ T cells at follow-up.

**CONCLUSIONS/INTERPRETATION:** These findings suggest there is reduced decline in C-peptide and persistent immunological responses up to 7 years after diagnosis of diabetes in individuals who respond to teplizumab.

**TRIAL REGISTRATION:** ClinicalTrials.gov [NCT02067923](https://www.clinicaltrials.gov/ct2/show/NCT02067923?term=teplizumab); the protocol is available at [www.immunetolerance.org](http://www.immunetolerance.org) (ITN027AI).

**KEYWORDS:** Anergy; Anti-CD3; C-peptide; Exhaustion; T cells; Teplizumab; Type 1 diabetes

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