Format: Abstract

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

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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 HbA_{1c} 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; the protocol is available at www.immunetolerance.org (ITN027AI).

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

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