

Immunomodulation in presymptomatic type 1 diabetes: The Teplizumab breakthrough

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Abstract

Type 1 diabetes is a progressive autoimmune disease characterized by the destruction of insulin-producing pancreatic beta cells. Stage 2 T1D represents a critical asymptomatic window defined by the presence of two or more islet autoantibodies and dysglycemia, carrying an active, near-inevitable risk of progression to insulin-dependent stage 3 clinical disease. Intervening at stage 2 offers a strategic opportunity to preserve remaining functional beta-cell mass and alter the natural history of the disease. Teplizumab is an Fc-receptor non-binding anti-CD3 monoclonal antibody, marking a paradigm shift by successfully targeting underlying pathophysiology during the asymptomatic phase of stage 2. Long-term follow-up data from the landmark TrialNet TN-10 randomized controlled trial reveal that a single 14-day intravenous course of Teplizumab demonstrated a median delay in the onset of clinical T1DM of 32.5 months compared to placebo, with sustained metabolic benefits. Mechanistically, modulates the TCR-CD3 complex, inducing a transient downmodulation of CD3, a partial depletion of circulating lymphocytes and a phenotypic shift toward cellular exhaustion in pathogenic CD8⁺ effector memory T cells. Concurrently, it preserves or expands protective CD4 regulatory T cells. The most common adverse events were transient lymphopenia (resolving within 1-2 weeks), maculopapular skin rash and mild self-limiting cytokine release syndrome. [*J Assoc Clin Endocrinol Diabetol Bangladesh*, 2026;5(Suppl 1): S23]

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