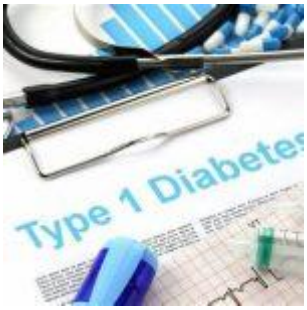
Disease-Modifying Immunotherapy in Type 1 Diabetes



Type 1 diabetes (T1D) is an autoimmune condition marked by the destruction of pancreatic beta cells, leading to insulin deficiency. Immunotherapies that modulate immune responses offer potential for altering T1D progression by preserving beta cell function and reducing insulin dependency. This systematic review evaluates various immunotherapies for T1D, examining their efficacy, safety, and implications for long-term diabetes management.

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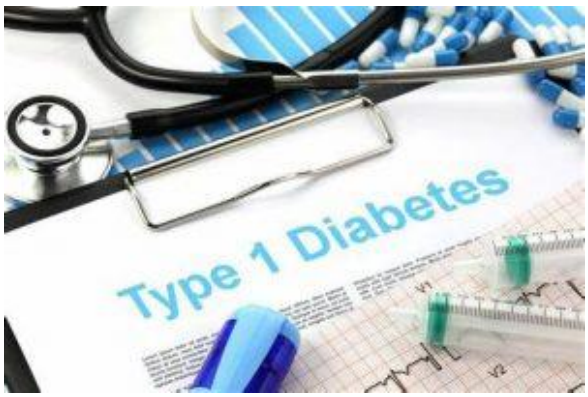
A meta-analysis included randomized controlled trials (RCTs) from PubMed, Embase, and Cochrane CENTRAL databases up to December 2023. Clinical trials were assessed if they reported on hypoglycaemia incidence or baseline changes in C-peptide levels, HbA1c, insulin dosage, and fasting plasma glucose (FPG). Thirty-four trials met inclusion criteria, providing insights into antigen-based and non-antigen-based immunotherapies, such as T cell-targeted therapies and TNF-α inhibitors.

Immunotherapy has shown modest but promising results in C-peptide preservation, particularly with non-antigen-based therapies. For instance, TNF-α inhibitors and T cell-targeted treatments demonstrated significant preservation of 2-hour and

4-hour C-peptide levels, critical markers of residual beta cell function. While antigen-based therapies, like oral insulin, showed limited improvement in beta cell function, these approaches demonstrated reduced daily insulin dosage.



No substantial improvements in HbA1c or FPG were observed with either non-antigen-based or antigen-based immunotherapies, suggesting that while these therapies may aid in preserving beta cell function, they may not directly influence glycaemic control. Additionally, immunotherapy did not increase hypoglycaemia risk, indicating favourable safety profiles.

Immunotherapy for T1D is advancing, though challenges remain in achieving lasting metabolic improvements. Non-antigen-based therapies, particularly TNF-α inhibitors and T cell-targeted approaches, show promise for preserving beta cell function. Immunotherapy's limited impact on HbA1c may result from immune mechanisms not directly targeted by current treatments, particularly the roles of innate immune cells like macrophages and dendritic cells in T1D pathogenesis.

The variability in response to immunotherapy may stem from patient-specific factors such as age, disease duration, and extent of beta cell preservation. Long-term follow-up is needed to understand immunotherapy's effects fully and to optimize dosing strategies that maintain efficacy while minimizing adverse effects.

Current immunotherapies represent an important step toward disease modification in T1D, but there remains a need to

refine these treatments for consistent and robust metabolic benefits. Further research into combined therapies targeting both adaptive and innate immunity may enhance the therapeutic potential of immunotherapy in T1D.

Journal article: **Lin, C., Hu, S., Cai, X., et al.** (2024). The opportunities and challenges of disease-modifying immunotherapy for type 1 diabetes: A systematic review and meta-analysis. Pharmacological Research, 203, 107157.

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