The Role of Immunomodulation Therapy in Autoimmune Diabetes

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Abstract

Type 1 diabetes (T1DM) is characterized by loss of virtually all endogenous insulin secretion. If residual insulin secretion is preserved, this will lead to improved metabolic balance, less acute and late complications, improved quality of life, and, in case of pronounced improvement of residual insulin secretion, complete remission and even cure of the disease.

Immune suppression or immune modulation have been demonstrated as a proof of principle to stop/decrease the destructive process and thereby preserve beta-cell function. Several methods to save residual beta-cell function have been tried for more than three decades with little or no evidence of efficacy. Positive effects have been seen mainly in adult patients but have been minimal or absent in children with diabetes. Furthermore, the safety of these immune interventions and/or their benefit to risk relationships have not been found to justify clinical use.

More specific immune modulation with anti-CD3 monoclonal antibodies has resulted in more encouraging postponement of C-peptide decline, but with frequent and serious adverse effects. Still more promising are the autoantigen therapies, of which glutamic acid decarboxylase (GAD) vaccination has shown significant preservation of residual insulin secretion in 10–18-year-old type 1 diabetes patients with recent onset. Efficacy was most impressive in the subgroup of patients with diabetes of short duration (<3 months). The treatment was simple, well tolerated, and showed no treatment-related adverse events. If these results can be confirmed, there is a realistic hope that GAD vaccination, perhaps in combination with vaccinations with other autoantigens and/or other therapies, will result in remission for some patients. The prospects of cure and prevention of T1DM will become less remote.

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Abbreviations: (AE) adverse event, (AUC) area under the curve, (GABA) gamma-aminobutyric acid, (GAD) glutamic acid decarboxylase, (GADA) glutamic acid decarboxylase autoantibodies, (IL) interleukin, (LADA) latent autoimmune diabetes in adults, (MMTT) mixed-meal tolerance test, (SAE) serious adverse event, (SPIDDM) slowly progressive insulin dependent diabetes mellitus, (SPS) stiff person syndrome, (T1DM) type 1 diabetes

Keywords: autoantigen treatment, C-peptide, glutamic acid decarboxylase vaccination, immune intervention, immunomodulation, type 1 diabetes

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