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Psoriasis drug shows promising results for treating type 1 diabetes

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A drug formerly used to treat the skin disorder psoriasis has shown encouraging results in a phase 2 trial to assess its effectiveness in treating type 1 diabetes, according to new research published in *The Lancet Diabetes and Endocrinology*.

Type 1 diabetes is an autoimmune condition where the body's immune system mistakenly attacks insulin-producing cells in the pancreas, resulting in insulin deficiency and an inability to regulate blood sugar. The condition is thought to affect around 400,000 people in the UK; patients require lifelong treatment with insulin injections, and are at substantially increased risk of illness and death related to their condition.

Trials in the 1980s and 1990s explored the possibility of using immune-supressing drugs to treat type 1 diabetes, but the risks of long-term immunosuppressant therapy outweighed the benefits. However, in recent years, immune-suppressing drugs have been developed that have a much more specific effect on the immune system cells that cause problems in autoimmune disorders, while preserving the immune cells which are essential for normal immune functioning.

Alefacept (marketed as Amevive) is one such drug, which has been used for around a decade to successfully treat the skin condition psoriasis (also thought to be an autoimmune disorder, where the immune system attacks healthy skin cells). Results from clinical trials in psoriasis have shown that alefacept works by attacking specific types of T cells (themselves a type of white blood cell) – effector memory (Tem) cells

and, to a lesser extent, central memory (Tcm) cells – which are involved in the body's mistaken attack against itself.

Since type 1 diabetes involves Tem cells and Tcm cells attacking insulin-producing cells in the pancreas, a team of researchers led by Professor Mark Rigby of Indiana University and the Riley Hospital for Children in Indianapolis, USA, investigated whether alefacept had any effect on patients newly diagnosed with type 1 diabetes in a study run by the US National Institutes of Health's Immune Tolerance Network.

Between March 2011 and March 2012, 49 individuals from across 14 different clinical centres in the USA were enrolled into the trial, although this was less than the planned 66 participants because alefacept was withdrawn by its manufacturer in December 2011. 33 participants received weekly injections of alefacept for 12 weeks, followed by a break of 12 weeks, and then 12 further weekly doses. 16 participants received a placebo according to the same schedule.

The trial's primary outcome was a measure of how well the pancreas could secrete insulin in response to food, two hours after eating. The researchers found no significant difference between the two groups according to this measure, but there were some notable differences between the groups when the secondary outcomes were analysed. Using the same measure of insulin secretion four hours after eating, there was a significant difference between the study and control group: the group who received alefacept showed preserved insulin secretion, whereas insulin secretion in the placebo group decreased.

Moreover, 12 months after starting treatment, insulin use in the placebo group was significantly higher than in the study group, and those who received alefacept showed no significant increase in insulin use over the course of the trial, whereas those in the placebo group did. These results suggest that treatment with alefacept preserved the body's ability to

produce its own insulin. Participants receiving alefacept also had fewer episodes of hypoglycaemia (low blood glucose levels), which are a common and dangerous occurrence in patients requiring insulin shots.

Importantly, alefacept was found to deplete potentially disease-causing Tem cells and Tcm cells while leaving protective regulatory T cells unaffected. Thus, the selective actions of this drug on the immune system might be an improvement over earlier drugs that induced general immune suppression.

According to Professor Rigby, "Alefacept is the first targeted biological drug assessed in patients with new-onset type 1 diabetes that significantly depleted the T cells which attack the pancreas in type 1 diabetes, while preserving other immune cells which are important for pancreatic function. Although the primary endpoint was not met, several key secondary endpoints were significantly different between treatment groups, suggesting that alefacept might preserve pancreas cell function during the first 12 months after diagnosis. Targeting memory T cells might be a useful strategy in type 1 diabetes, but longer follow-up is required to confirm the preliminary signal of efficacy observed at 12 months in the T1DAL trial."

Writing in a linked Comment, Dr Kevan Herold of Yale University, New Haven, USA, says "These new results, together with the findings from recent trials of a CD3 monoclonal antibody, are leading to mechanism-based strategies to restore the balance between those cells needed for protection against pathogens and those that maintain tolerance to self, rather than broadly eliminating immune cells. It is important to underscore these small successes since, as in other fields such as oncology and infectious diseases, the small achievements acquire greater significance when they are combined. In this regard, the withdrawal of pharmaceutical companies from this and other trials, even before the final outcomes of trials were realised, was disappointing—particularly as

we move closer to finally reaching the ultimate goal: to prevent, stop, and even reverse type 1 diabetes."

More information: www.thelancet.com/journals/lan … (13)70111-6/abstract

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