Can A Drug That Delays The Onset Of Type 1 Diabetes Be A Success?

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Not to be confused with type 2 diabetes, the most common form of diabetes in which your body does not use insulin properly, type 1 diabetes is an autoimmune disease which causes the destruction of insulin producing pancreatic beta cells. Patients with type 1 diabetes require insulin injections for survival. While there are multiple drugs designed to treat type 2 diabetes, type 1 is controlled with insulin - an onerous burden especially when one considers that this disease often begins in childhood.

Given the autoimmune nature of type 1 diabetes, researchers have sought to control, or perhaps even halt, its progress by administering drugs that theoretically could block an overactive immune system from attacking the pancreas. Back in 2010, Lilly actually studied one of its drugs, teplizumab, an anti-CD3 antibody to see if it could do just that.

The development of type 1 diabetes is gradual and defined by three clinical stages. Stage 1 is asymptomatic, characterized by the presence of autoantibodies. Stage 2 is defined by an impaired metabolic response to a glucose load. Stage 3 is marked by insulin deficiency, hyperglycemia, and loss of beta cell function.

Lilly decided to study teplizumab in patients with early stage 3 disease and, while there was a glimmer of activity, the results were not significant. However, Dr. Jeffrey Bluestone of the Diabetes Center at UCSF, and collaborators at Provention Bio stayed with the idea. They focused on patients who were in type 1 stage 2 and characterized by a combination of unstable blood sugar and blood autoantibodies, a population that the investigators believed had a 75% chance of getting diabetes during the next five years. In the actual study, there were 44 patients who received teplizumab and 34 got placebo. Both groups were treated for 14 consecutive days with an IV infusion, then followed for five years. The results proved remarkable. Only 43% percent of those who received teplizumab progressed to diabetes after 5 years as opposed to 72% of those on placebo. The median time to diabetes was just over four years on teplizumab vs. two years on placebo.

Interestingly, the response to these results was muted. While a number of financial outlets commented favorably on this study, there was little coverage by the major news organizations like the New York Times, Washington Post, Wall Street Journal, etc. Perhaps that was due to the relatively early stage of this research and the fact that it was a small study.

But perhaps the lack of enthusiasm was due to broader concerns. How enthusiastic would parents be

about giving teplizumab to their children? Yes, the drug would stave off type 1 diabetes for two years, but would the impact that teplizumab have on the immune system expose their child to other adverse effects? Insulin has been prescribed for decades and its riskbenefit profile is well known. As their child would be transitioning to insulin therapy eventually, why not just go directly to insulin when the time comes?

To counteract such a concern, the FDA would undoubtedly set high safety bars for approval. While this is done for any drug, the fact that this would be given to many under the age of 12 during their formative years would heighten concerns about long-term safety.

Finally, and perhaps most importantly, payers will have a major say in this. What value is provided by a drug - likely to be a very expensive drug - that delays the onset of type 1 diabetes for a relatively short period of time? Economic benefits would have to be considerable for such a drug to be allowed on formularies.

There is no doubt that these results with teplizumab provide strong evidence (albeit indirect) about the pathogenesis of beta cell destruction and the potential to modify the course of type 1 diabetes. But are the teplizumab data compelling enough to change medical practice? That remains to be seen.

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