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FDA approves first drug that can delay onset of type 1 diabetes

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The Food and Drug Administration (FDA) has approved Tzield (teplizumab-mzwv) injection to delay the onset of stage 3 type 1 diabetes (T1D) in adults and pediatric patients 8 years and older who have stage 2 T1D.

Tzield (pronounced TEE-zeeld) is the first disease-modifying therapy for T1D, a debilitating disease that occurs when the immune system attacks and destroys the body's insulin-producing cells, leading to dependence on exogenous insulin therapy for survival.

Although Tzield does not prevent or cure T1D, treatment can delay the need for exogenous insulin therapy and its associated risks and intensive regimen. This delay is clinically meaningful, particularly because T1D often presents in patients younger than 10 years who may face challenges with complex disease management.

T1D affects about 1.6 million Americans and generally progresses through three stages (http://bit.ly/3gHPGyf). Stage 1 occurs when a patient develops two or more autoreactive antibodies to pancreatic islet cells. By stage 2, patients have lost enough insulin-producing cells to result in abnormal glucose levels (dysglycemia) but do not yet meet the criteria for diabetes. Stage 2 T1D is associated with a 75% risk of progression to a T1D diagnosis (stage 3) within four to five years and a lifetime risk of nearly 100% (Insel RA, et al. *Diabetes Care*. 2015;38:1964-1974). Stage 3 occurs when patients develop overt hyperglycemia, typically with signs and symptoms of diabetes (increased thirst, increased urination, blurred vision, weight loss, fatigue).

While a family history of T1D substantially increases a patient's risk, approximately 90% of patients with new-onset T1D do not have a family history of T1D (Sims EK, et al. *Diabetes*. 2022;71:610-623).

Tzield is a CD3-directed antibody that binds to and may deactivate pancreatic beta cell auto-reactive T lymphocytes. Tzield is administered by intravenous infusion once daily for 14 consecutive days.

Patients are eligible for Tzield when they have laboratory evidence of at least two positive pancreatic beta cell autoantibodies and dysglycemia. As the gold standard in diabetes diagnosis, an oral glucose tolerance test is recommended to confirm presence of dysglycemia.

Tzield's safety and efficacy were evaluated in a randomized, double-blind, event-driven, placebo-controlled trial with 76 patients with stage 2 T1D (http://bit.ly/3Uhl3NI). The primary measure of efficacy was the time from randomization to stage 3 T1D diagnosis.

Over a median follow-up of 51 months, 45% of the 44 patients who received Tzield were diagnosed with stage 3 T1D compared to 72% of the 32 patients who received a placebo. The mid-range time from randomization to stage 3 T1D diagnosis was 50 months for patients who received Tzield and 25 months for those who received a placebo, representing a statistically significant delay in stage 3 T1D diagnosis of approximately two years (Herold KC, et al. *N Engl J Med*. 2019;381:603-613).

Confirmatory evidence of effectiveness was provided by a meta-analysis of five trials that demonstrated a statistically significant reduction in the decline of C-peptide, a measure of endogenous insulin secretion,

when teplizumab was administered to patients with new or recent onset stage 3 T1D.

The most common side effects of Tzield include lymphopenia, rash, leukopenia and headache. Use of Tzield comes with warnings and precautions about the risks of cytokine release syndrome, serious infections, lymphopenia and hypersensitivity reactions, as well as the need to administer age-appropriate vaccinations prior to starting Tzield and avoid concurrent use of live, inactivated and mRNA vaccines.

The FDA's Office of Pediatric Therapeutics and Office of New Drug's Division of Pediatrics and Maternal Health and Division of Diabetes, Lipid Disorders, and Obesity contributed to this article.

Resource

Prescribing information for Tzield