Tzield™ (teplizumab-mzwv) – New drug approval

- On November 17, 2022, the FDA announced the approval of Provention Bio's Tzield (teplizumab-mzwv), to delay the onset of Stage 3 type 1 diabetes (T1D) in adults and pediatric patients 8 years of age and older with Stage 2 T1D.

- T1D is an autoimmune disease that is caused by destruction of beta cells (cells that make insulin). Although it can appear at any age, T1D is usually diagnosed in children and young adults. A person is at higher risk for T1D if they have a parent, brother, or sister with T1D, although most patients do not have a family history.

    - Stage 2 T1D is defined by the presence of two or more T1D-related autoantibodies and dysglycemia.
    - Insulin therapy and glucose monitoring are currently the standard of care for treating clinical-stage, or Stage 3 T1D.

- Tzield is a novel CD3-directed monoclonal antibody. CD3 is a cell surface antigen present on T lymphocytes. Tzield may deactivate the immune cells that attack insulin-producing cells, while increasing the proportion of cells that help moderate the immune response.

- The efficacy of Tzield was established in a randomized, double-blind, event-driven, placebo-controlled study in 76 patients, 8 to 49 years of age with Stage 2 T1D. Patients were randomized to receive Tzield or placebo once daily by intravenous (IV) infusion for 14 days. The primary efficacy endpoint was the time from randomization to development of Stage 3 T1D diagnosis.

    - Stage 3 T1D was diagnosed in 20 (45%) of the Tzield-treated patients and in 23 (72%) of the placebo-treated patients.
    - A Cox proportional hazards model, stratified by age and oral glucose tolerance test status at randomization, demonstrated that the median time from randomization to Stage 3 T1D diagnosis was 50 months in the Tzield group and 25 months in the placebo group, for a difference of 25 months.
    - With a median follow-up time of 51 months, therapy with Tzield resulted in a statistically significant delay in the development of Stage 3 T1D (hazard ratio 0.41, 95% CI: 0.22, 0.78; p = 0.0066).

- Warnings and precautions for Tzield include cytokine release syndrome; serious infections; lymphopenia; hypersensitivity reactions; and vaccinations.

- The most common adverse reactions (> 10%) with Tzield use were lymphopenia, rash, leukopenia, and headache.

- Tzield is administered by IV infusion (over a minimum of 30 minutes), using a body surface area-based dosing, once daily for 14 consecutive days as follows:

    - Day 1: 65 mcg/m^2
    - Day 2: 125 mcg/m^2
    - Day 3: 250 mcg/m^2
    - Day 4: 500 mcg/m^2
    - Days 5 through 14: 1,030 mcg/m^2

- Refer to the Tzield drug label for complete dosing and administration recommendations.

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- Tzield will be priced at $13,850 a vial and $193,900 for the 14-day treatment regimen.
- Provention Bio's launch plans for Tzield are pending. Tzield will be available as a 2 mg/2 mL single-dose vial.