Take advantage of T.I.M.E.

Four steps to help you identify patients that may benefit from disease management before onset of Stage 3 T1D.

T1ME TO SCREEN

Trace familial risk

Talk to first-degree relatives about screening[1]

Your patients' first-degree relatives—parents, siblings, children—should understand the importance of screening for type 1 diabetes (T1D).

These first-degree relatives have a higher risk of T1D than the general population.

Up to 15x greater risk of developing T1D[2]

Discuss the importance of familial screening with your patients.

Identify ≥2 pancreatic islet autoantibodies

Screen for pancreatic islet autoantibodies (AAbs)

AAbs are a defining characteristic and reliable indicator of T1D at any stage of disease.[2]

Identifying ≥2 positive AAbs from the following list confirms a diagnosis of T1D[2]:

- Glutamic acid decarboxylase 65 autoantibody **(GADA)**
- Insulinoma-associated antigen 2 autoantibody **(IA-2A)**
- Insulin autoantibody **(IAA)**
- Islet cell autoantibody **(ICA)**
- Zinc transporter-8 autoantibody **(ZnT8A)**

There are several ways to screen for T1D; each is a blood test that screens for specific autoantibodies.

Open to Learn More ▶

Stages of T1D

Use **T.I.M.E.** to help stage patients.

T1D is an autoimmune disease with 3 distinct stages, each with detectable characteristics[3]**:**

STAGE 1[3]

- ⚠ ≥2 AAbs
- Normoglycemia
- No symptoms

STAGE 2[3]

- ⚠ ≥2 AAbs
- ⚠ Dysglycemia
- No symptoms

STAGE 3[3]

- ⚠ ≥2 AAbs
- ⚠ Hyperglycemia
- ⚠ Symptoms

Monitor for dysglycemia

Follow up and monitor for dysglycemia

Dysglycemia is defined as a recurring fluctuation of glucose levels (outside of normal range). Signs of dysglycemia include[4,5]:

Impaired Fasting Glucose (IFG) and/or **Impaired Glucose Tolerance (IGT)**

Fasting Plasma Glucose (FPG) 100–125 mg/dL

2-H Plasma Glucose (2-H PG) 140–199 mg/dL during OGTT

30-/60-/90-minute PG ≥200 mg/dL during OGTT

A1c 5.7–6.54% or **≥10% increase** consecutive A1c levels

Frequency[1]

There are currently no uniform guidelines for monitoring individuals in early-stage T1D.

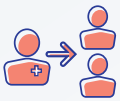
- **In office:** Standard monitoring includes a 2-hour OGTT and an A1c test every 6 months
- **At home:** Fasting and 1- or 2-hour postprandial glucose levels with finger-stick glucose monitoring or use of continuous glucose monitor (CGM). At-home monitoring is not diagnostic.

In patients with ≥2 AAbs, dysglycemia without overt hyperglycemia* indicates Stage 2 T1D.[1]

*Overt hyperglycemia means a clear clinical diagnosis could be made (ie, patient in a hyperglycemic crisis or with classic symptoms of hyperglycemia; PG of ≥200 mg/dL) or 2 abnormal screening test results, either from the same sample or in 2 separate test samples.[4]

Educate patients and families

Educate patients and families on what's next[1]**:**



Expand the care team by referring patients to professionals who can support mental health and other needs

Advise patients and caregivers to be vigilant for symptoms of hyperglycemia and diabetic ketoacidosis (DKA)

Discuss the potential benefits and risks of pharmacological intervention if eligible

T.I.M.E. can help you determine patient eligibility for a potential treatment option.

Autoantibody screening options*

	TEST	WHERE	ACCESS	GADA	IA-2A	IAA	ICA	ZnT8A
Commercial Labs[1]	Blood draw	Local commercial lab (eg, Labcorp, Quest Diagnostics) or healthcare provider's office	Most commercial insurance plans in the US cover the cost of AAb screening in whole or in part	●	●	●	●	●
TrialNet[1]	Blood draw or finger stick	TrialNet location, event, or health fair. Patients can also receive a test kit to use at home or bring to Labcorp or Quest Diagnostics	Free screening for relatives of people diagnosed with T1D who are interested in participating in clinical studies	●	●	●	●	●
Autoimmunity Screening for Kids (ASK)[6-8]	Blood draw or finger stick	Barbara Davis Center for Diabetes in Aurora and additional Colorado locations, and at-home screening kits for families	Free screening available to all US residents aged 1 year and older with or without a family history of T1D	●	●	●		●
Online Ordering[9,10]	Finger stick	Testing kits can be sent by vendors such as Enable Biosciences through online ordering	A low-cost option (typically less than $100) for families with or without a history of T1D	●	●	●		

This may not be an exhaustive list of available screening options. The appropriateness of any AAb screening test and the validity of the test results are up to the requesting physician to determine.

Commercial lab order codes*

Potential considerations following results

- **If ≤1 autoantibody detected[1]:**
  - Additional screening may be needed for high-risk patients
- **If ≥2 autoantibodies detected[1]:**
  - Explain the significance of the results to your patient and their family
  - Perform a confirmatory test within 2 to 6 weeks as standard practice
  - Gain commitment of periodic follow-up testing

It is recommended to screen for the entire panel of AAbs to ensure that individuals with T1D are able to be diagnosed properly.

These commercial labs offer screening tests and panels that cover all 5 pancreatic islet autoantibodies.

Scan codes below and enter the appropriate test/panel codes to order for your patients.

Quest Diagnostics[11]

Test/panel names and order codes	
GAD65, IA-2, and Insulin Autoantibody	**10584**
Zinc Transporter 8 (ZnT8) Antibody	**93022**
Islet Cell Antibody Screen with Reflex to Titer	**36741**

Labcorp[12]

Test/panel names and order codes	
Diabetes Autoimmune Profile	**504050**
Antipancreatic Islet Cells	**160721**

*This is a list of type 1 diabetes codes available as of April 4, 2023; appropriate codes can vary by patient, setting of care, and payer. Correct coding is the responsibility of the provider submitting the claim for the item or service. Provention Bio does not make any representation or guarantees concerning reimbursement or coverage for any service or item.

REFERENCES: 1. Scheiner G, et al. *ADCES Pract*. 2022:20-25. **2.** Couper JJ, et al. *Pediatr Diabetes*. 2018;19(suppl 27):20-27. **3.** Insel RA, et al. *Diabetes Care*. 2015;38(10):1964-1974. **4.** ElSayed NA, et al. *Diabetes Care*. 2023;46(suppl 1):S10-S40. **5.** Type 1 Diabetes TrailNet. Version June 2014. Accessed May 5, 2023. https://clinicaltrials.gov/ProvidedDocs/61/NCT01030861/Prot_000.pdf **6.** ASK. Accessed March 31, 2023. https://redcap.ucdenver.edu/surveys/?s=YLWCN8MT9R **7.** ASK. Accessed March 31, 2023. https://www.askhealth.org/locations **8.** McQueen RB, et al. *Diabetes Care*. 2020;43(7):1496-1503. **9.** Enable Biosciences. Accessed March 31, 2023. https://type1testing.enablebiosciences.com/order-form-2 **10.** Enable Biosciences. Accessed March 31, 2023. https://blog.enablebiosciences.com/2023/01/19/the-role-of-autoantibodies-in-type-1-diabetes/ **11.** Quest Diagnostics. Accessed March 31, 2023. https://testdirectory.questdiagnostics.com/test/home **12.** Labcorp. Accessed March 31, 2023. https://specialtytesting.labcorp.com/test-menu/search

Tzield®
(teplizumab-mzwv)
Injection | 2 mg/2mL

Learn more about a treatment option for your appropriate patients with Stage 2 T1D

Scan code

INDICATION

TZIELD is a CD3-directed monoclonal antibody indicated to delay the onset of Stage 3 type 1 diabetes (T1D) in adults and pediatric patients aged 8 years and older with Stage 2 T1D.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

- **Cytokine Release Syndrome (CRS):** CRS occurred in TZIELD-treated patients during the treatment period and through 28 days after the last drug administration. Prior to TZIELD treatment, premedicate with antipyretics, antihistamines and/or antiemetics, and treat similarly if symptoms occur during treatment. If severe CRS develops, consider pausing dosing for 1 day to 2 days and administering the remaining doses to complete the full 14-day course on consecutive days; or discontinue treatment. Monitor liver enzymes during treatment. Discontinue TZIELD treatment in patients who develop elevated alanine aminotransferase or aspartate aminotransferase more than 5 times the upper limit of normal (ULN) or bilirubin more than 3 times ULN.
- **Serious Infections:** Use of TZIELD is not recommended in patients with active serious infection or chronic infection other than localized skin infections. Monitor patients for signs and symptoms of infection during and after TZIELD administration. If serious infection develops, treat appropriately, and discontinue TZIELD.
- **Lymphopenia:** Lymphopenia occurred in most TZIELD-treated patients. For most patients, lymphocyte levels began to recover after the fifth day of treatment and returned to pretreatment values within two weeks after treatment completion and without dose interruption. Monitor white blood cell counts during the treatment period. If prolonged severe lymphopenia develops (<500 cells per mcL lasting 1 week or longer), discontinue TZIELD.
- **Hypersensitivity Reactions:** Acute hypersensitivity reactions including serum sickness, angioedema, urticaria, rash, vomiting and bronchospasm occurred in TZIELD-treated patients. If severe hypersensitivity reactions occur, discontinue TZIELD and treat promptly.
- **Vaccinations:** The safety of immunization with live-attenuated (live) vaccines with TZIELD-treated patients has not been studied. TZIELD may interfere with immune response to vaccination and decrease vaccine efficacy. Administer all age-appropriate vaccinations prior to starting TZIELD.
  - Administer live vaccines at least 8 weeks prior to treatment. Live vaccines are not recommended during treatment, or up to 52 weeks after treatment.
  - Administer inactivated (killed) vaccines or mRNA vaccines at least 2 weeks prior to treatment. Inactivated vaccines are not recommended during treatment or 6 weeks after completion of treatment.

ADVERSE REACTIONS

Most common adverse reactions (>10%) were lymphopenia, rash, leukopenia, and headache.

USE IN SPECIFIC POPULATIONS

- **Pregnancy:** May cause fetal harm.
- **Lactation:** A lactating woman may consider pumping and discarding breast milk during and for 20 days after TZIELD administration.

Please read the accompanying Prescribing Information, including Medication Guide.

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