Transition From Research to Clinical Care

Lexie Chesshir, BSN, RN, CDCES
Childhood Diabetes Prevention Symposium
11/9/23
FDA NEWS RELEASE

FDA Approves First Drug That Can Delay Onset of Type 1 Diabetes

For Immediate Release: November 17, 2022

Today, the U.S. Food and Drug Administration approved Tzield (teplizumab-mzwv) injection to delay the onset of stage 3 type 1 diabetes in adults and pediatric patients 8 years and older who currently have stage 2 type 1 diabetes.

“Today’s approval of a first-in-class therapy adds an important new treatment option for certain at-risk patients,” said John Sharrett, M.D., director of the Division of Diabetes, Lipid Disorders, and Obesity in the FDA’s Center for Drug Evaluation and Research. “The drug’s potential to delay clinical diagnosis of type 1 diabetes may provide patients with months to years...
Teplizumab in Clinical Trials

**2005**  
ABATE  
New onset (8 wks)  
8-30 yo (n=52 tx drug)  
6 sites  
ITN, NIAID

**2006-13**  
DELAY (P2)  
Recent onset (4-12 mo)  
8-30 yo (n=34 tx w/ drug)  
4 sites  
JDRF, NIDDK

**2006-11**  
Protégé (P2/3)  
New onset (12 wks)  
8-35 yo (n=415 tx w/ drug)  
MacroGenics, JDRF, Eli Lilly  
Endpoints: TDD, HbA1c

**2009-12**  
Protégé Encore (P3)  
New onset (12 wks)  
8-35 yo (n~126 tx w/ drug)  
MacroGenics, Eli Lilly  
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DELAY (P2)  
Recent onset (4-12 mo)  
8-30 yo (n=34 tx w/ drug)  
4 sites  
JDRF, NIDDK

**2010-19**  
TN10 (P2)  
≥2 AB + dysglycemia on OGTT  
8-45 yo (n=44 tx w/drug)  
19 sites,  
NIDDK (TrialNet)

**2017-2023**  
PROTECT  
New onset (6 wks)  
8-17 yo (n=150 tx w/drug)  
Provention Bio

**2020-2024**  
TN10 Extension  
TN10, new onset (0-12 mo)  
8-45 yo  
5 sites  
Provention Bio

Slide adapted courtesy of Dr. Kimber Simmons, presented at ATDC and Diabetes Dialog 2023
Transitioning to Clinic

Research
• Protocol specific enrollment criteria
• Specific windows for visits
• Protocol specific daily dosing window
• CURP (CU Research Pharmacy)
• Protocol specific follow-up

Clinic
• Approvals through insurance
• Any form of dysglycemia
• Drug prepared by trained RN’s
• More flexible daily dosing windows
• In clinic follow-up
Hurdles and Benefits in Transitioning From Research to Clinic

- Research scheduling is more oriented around participant’s time while clinic scheduling tends to be more structured.

- Research Participants → Clinic Patient
  - Benefit from having historical AAB data
  - Collaborating with all BDC study teams to identify participants who are eligible for treatment

- Payment
# TN10 Research Schedule of Assessments

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Slide adapted courtesy of Dr. Kimber Simmons, presented at diabetes Dialog 2023
# Tzield in Clinical Care

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Hurdles in Transitioning from Research Nursing to Clinic Nursing

• Documentation
  • Creating new smart phrases/ dot phrases
  • Drug
  • Labels

• Communication
  • Mychart
  • Calls
Patient Identification: Islet Autoantibodies
Clinical Antibody Testing

• All 4 major type 1 diabetes related antibodies are available commercially.
• HCP responsible for ordering testing in high-risk individuals is not clearly defined.
• Many clinical assays use different methodology than research assays.
  • Difference in antibody affinities
  • Differences in sensitivity and specificities
  • Minimal standardization/optimization for commercial assays
# ASK the Experts Patient Screening and Confirmation Results

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Patient Identification: Dysglycemia
Stage of T1D by Monitoring Tool Used in Early T1D Clinic (n=24)

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Individuals in
Stage 1 (n=6), CGM time ≥ 140 mg/dl (7.8 mmol/L) 6 to 12%
Stage 2 (n=17), CGM time ≥ 140 mg/dl (7.8 mmol/L) 5 to 63%
Stage 3 (n=1), CGM time ≥ 140 mg/dl (7.8 mmol/L) 46%

Slide adapted by Dr. Kimber Simmons, presented at ATDC and Diabetes Dialog 2023.
Patient Identification: Dysglycemia Hurdles

- Patients with Stage 2 T1D varies by method used to categorize.
- Dysglycemia criteria are different between TN10 and ADA staging.
- Dysglycemia required for approval varies among payers.
- OGTTs are not routinely done in many practices (especially pediatric).
- Stage 2 T1D not yet part of ICD10 codes in EPIC.
Treatment Administration
Mixing of Teplizumab

- Prepared by RNs with a double check system in place
- Preparation takes about 10-15 min
- Dosage doubles each day until day 5 which then is max dosage.
Teplizumab Route of Administration

- Placement of PICC/midline often requires scheduling flexibility
- HCP team needs to be able to address/have a plan for any issues
- Risk of infection so need to complete infectious work up with fevers
Teplizumab Administration Location

14-day infusion over at least 30 minutes with 1 hour observation

- Limited weekend coverage
- Standard of care for pediatric infusions in other disease states is administration in medical setting.

Infusion Center  Observation/outpatient hospital bed  Home infusion

Slide adapted courtesy of Dr. Kimber Simmons, presented at ATDC and Diabetes Dialog 2023
Impact on Patient
Not Everyone Will Respond to Teplizumab

- Numbers are small so should not be translated into clinical decision making.
- High cost and burden for patients that are non-responders.
- HLA and c-peptide not routinely clinically ordered/available.
BDC Early T1D Clinical Experience

- Opened Early T1D clinic 12/9/2022
- 27 clinical staging visits for multiple T1D related autoantibody positive individuals with concern for dysglycemia to date.
  - 10 children (ages 10-17 years)
  - 14 adults (18-50 years)

Slide adapted courtesy of Dr. Kimber Simmons, presented at ATDC and Diabetes Dialog 2023.
Over Half of Stage 2 Patients Evaluated for Tzield Have Been Approved for Treatment

Slide adapted courtesy of Dr. Kimber Simmons, presented at Diabetes Dialog 2023.
### BDC Infusion Experience

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In Summary

• Establishing a process for type 1 diabetes related autoantibody screening in high-risk individuals needs to be implemented and may look different for each clinical team.

• Full metabolic testing is important to identify those who may be eligible for treatment.

• Successful administration requires that the ordering provider and team are comfortable with management of all infusion related issues.

• Laboratory evaluation should be focused on keeping a patient safe with attention to warning and precautions in published prescribing information.

• Participation in registries will be important for understanding real-world impact of treatment.