Transition From Research to Clinical Care

Lexie Chesshir, BSN, RN, CDCES

Childhood Diabetes Prevention Symposium

11/9/23

Barbara Davis Center for Diabetes
UNIVERSITY OF COLORADO **ANSCHUTZ MEDICAL CAMPUS**

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 Sharretts, 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

Content current as of:
11/17/2022

Regulated Product(s)
Drugs

Follow FDA
Follow @US_FDA
Follow FDA
Follow @FDAmedia

Teplizumab in Clinical Trials

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

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

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

2009-12
Protégé Encore (P3)
New onset (12 wks)
8-35 yo (n~126 tx w/ drug)
MacroGenics, Eli Lilly
Endpoints: TDD, HbA1c

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

Barbara Davis Center for Diabetes
UNIVERSITY OF COLORADO ANSCHUTZ MEDICAL CAMPUS

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

Visit number	-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Study drug[1]		X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Chemistries [2,3]	X	X	X	X	X	X	X	X					X		X	
INR[2]	X	X	X	X	X	X	X						X		X	
CBC with diff[2]	X	X	X	X	X	X	X	X		X			X		X	X
Liver Function[2,3]	X	X	X	X	X	X	X	X					X		X	
mAb levels[4]		X										X	X	X	X	
Anti-teplizumab response	X															
EBV and CMV viral loads[5]	X															X
EBV/CMV serology	X															
History/Physical exam[6]	X	X					X					X			X	X
Oral Glucose Tolerance[7]	X	X														
HIV, HepB and C serology	X															
PPD test	X															
Urine pregnancy test	X	X														
HbA1c	X															
Mechanistic assessments[8]		X														X
glycemic status[9]	X															
EKG		X														

Barbara Davis Center for Diabetes
UNIVERSITY OF COLORADO **ANSCHUTZ MEDICAL CAMPUS**

Slide adapted courtesy of Dr. Kimber Simmons, presented at diabetes Dialog 2023

Tzield in Clinical Care

Visit number	-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Study drug[1]		X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Chemistries [2,3]	X	X	X	X	X	X	X	X					X		X	
INR[2]	X	X	X	X	X	X	X						X		X	
CBC with diff[2]	X	X	X	X	X	X	X	X		X			X	X	X	X
Liver Function[2,3]	X	X	X	X	X	X	X	X		X			X	X	X	X
mAb levels[4]		X										X	X	X	X	
Anti-teplizumab response	X															
EBV and CMV viral loads[5]	X															X
EBV/CMV serology	X															
History/Physical exam[6]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Oral Glucose Tolerance[7]	X	X														
HIV, HepB and C serology	X															
PPD test	X															
Urine pregnancy test	X	X														
HbA1c	X															
Mechanistic assessments[8]		X														X
glycemic status[9]	X															
EKG		X														

Barbara Davis Center for Diabetes
UNIVERSITY OF COLORADO **ANSCHUTZ MEDICAL CAMPUS**

Slide adapted by Dr. Kimber Simmons, presented at Diabetes Dialog 2023

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

Barbara Davis Center for Diabetes
UNIVERSITY OF COLORADO **ANSCHUTZ MEDICAL CAMPUS**

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

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

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

ASK the Experts Patient Screening and Confirmation Results

	Screened – (n=12)	Screened single + (n=17)	Screened multiple + (n=23)
Confirmation test –	**12 (100%)**	13 (76.5%)	11 (47.8%)
Confirmation test single +	0	**3 (17.6%)**	2 (8.7%)
Confirmation test multiple +	0	1 (5.9%)	**10 (43.5%)**

Barbara Davis Center for Diabetes
UNIVERSITY OF COLORADO **ANSCHUTZ MEDICAL CAMPUS**

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

Patient Identification: Dysglycemia

Stage of T1D by Monitoring Tool Used in Early T1D Clinic (n=24)

	Stage 1	Stage 2	Stage 3
HbA1c	11	13	0
Fasting Blood Glucose	17	4	3
2-Hour OGTT Glucose	9	8	7

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.

Slide adapted by Dr. Kimber Simmons, presented at ATDC and Diabetes Dialog 2023

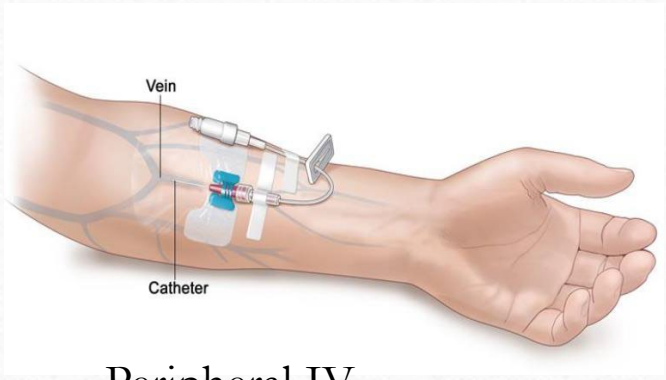
Treatment Administration

Mixing of Teplizumab

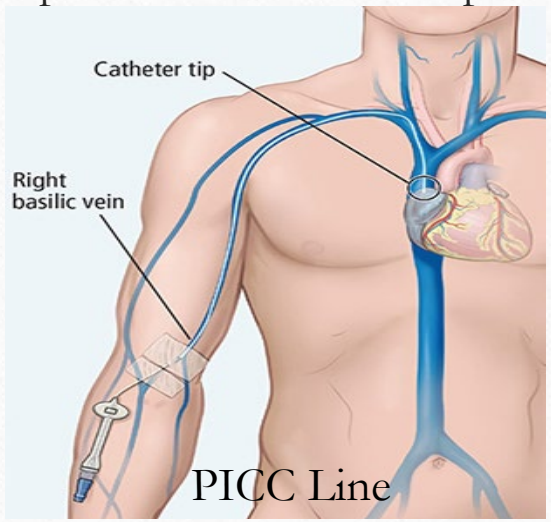
- Prepared by RNs with a double check system in place
- Preparation takes about 10-15 min
- Dosage doubles each day until day 5 which then is max dosage.

Teplizumab Route of Administration

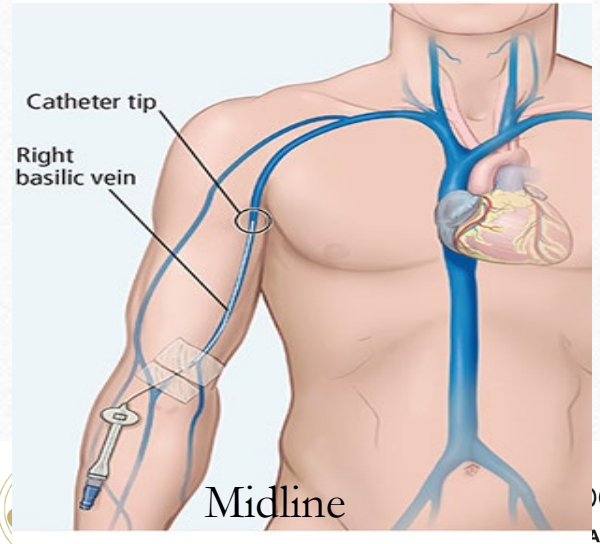
- Placement of PICC/midline often requires scheduling flexibility
- HCP team needs to be able to address/have a plan for any issues
- Risk of infection so need to complete infectious work up with fevers



Peripheral IV



PICC Line



Midline

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

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

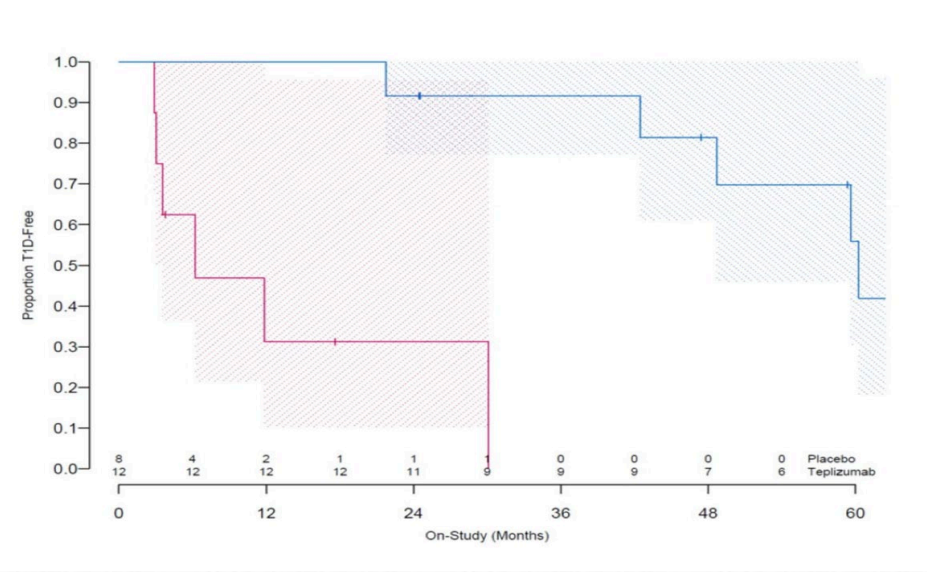
Barbara Davis Center for Diabetes
UNIVERSITY OF COLORADO **ANSCHUTZ MEDICAL CAMPUS**

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

Impact on Patient

Not Everyone Will Respond to Teplizumab

----- = teplizumab, ----- = placebo



- 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.

Barbara Davis Center for Diabetes
UNIVERSITY OF COLORADO **ANSCHUTZ MEDICAL CAMPUS**

Slide adapted courtesy of Dr. Kimber Simmons, presented by ATDC and Diabetes Dialog 2023

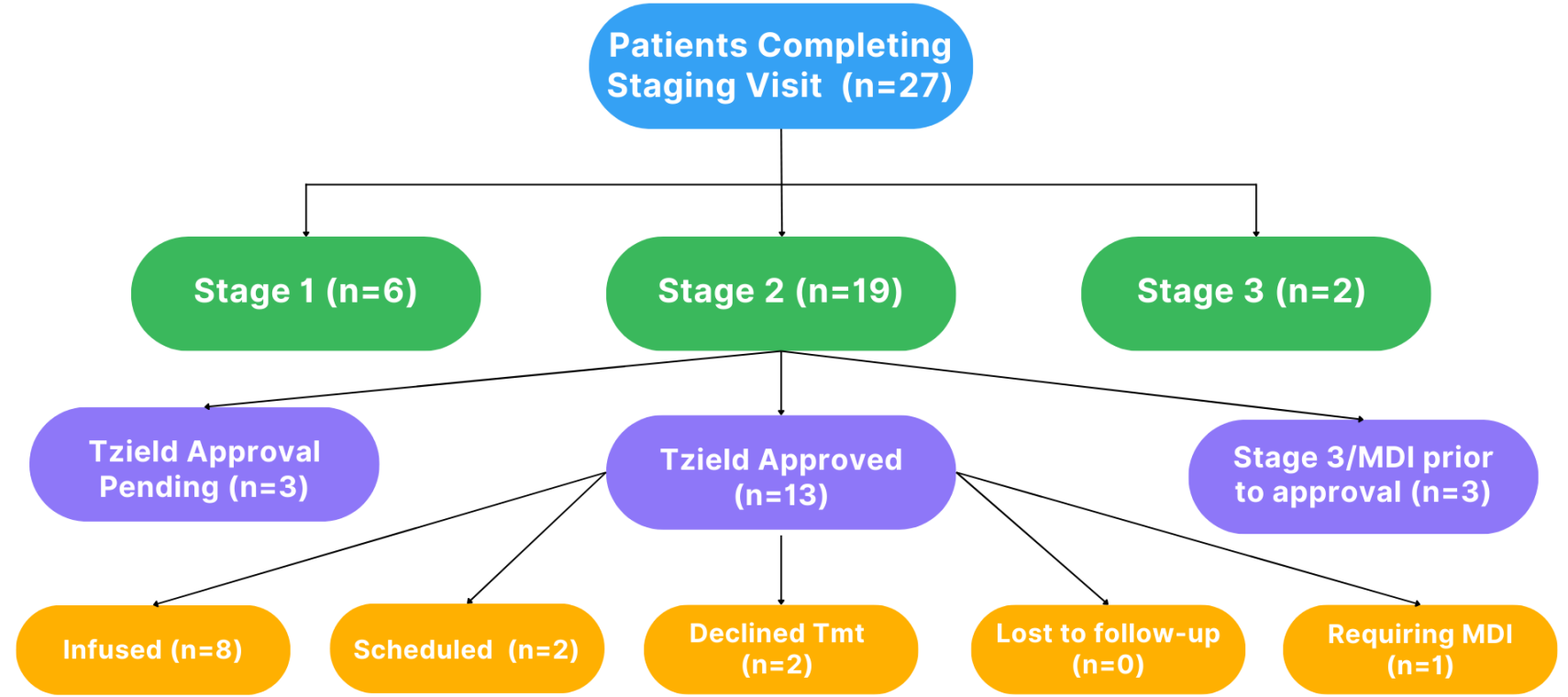
BDC Early T1D Clinical Experience

- 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)

Barbara Davis Center for Diabetes
UNIVERSITY OF COLORADO ANSCHUTZ MEDICAL CAMPUS

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

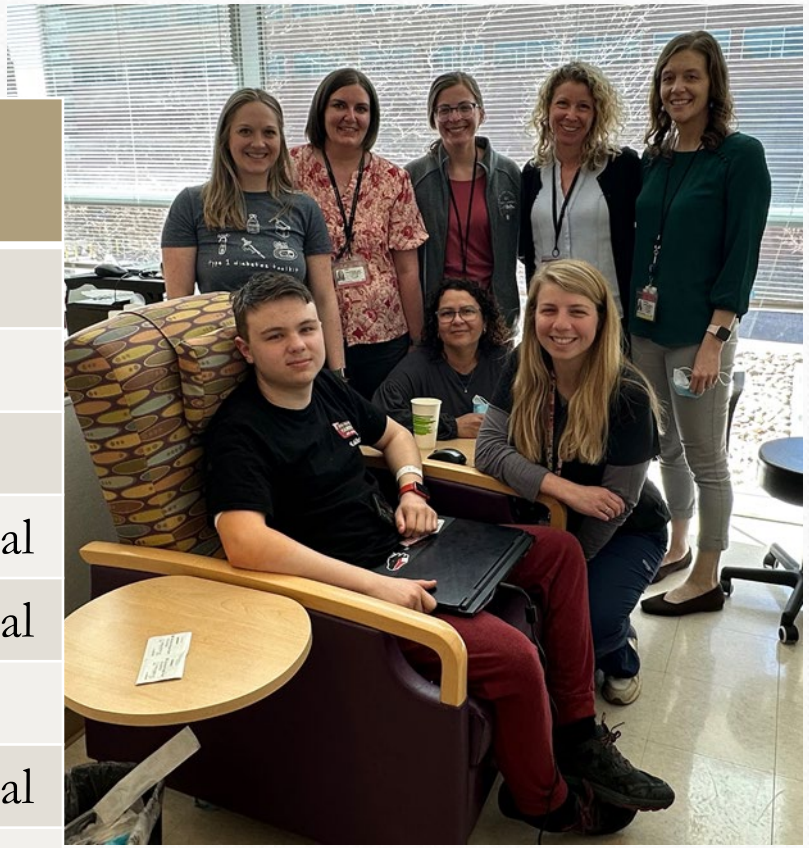


Barbara Davis Center for Diabetes
UNIVERSITY OF COLORADO ANSCHUTZ MEDICAL CAMPUS

Slide adapted courtesy of Dr. Kimber Simmons, presented at Diabetes Dialog 2023.

BDC Infusion Experience

Age	Sex	Race	BMI, %tile	Tanner Stage	Referral Source
16	M	NHW	26.1 (90.5%tile)	5	TrialNet
10	M	NHW	17.5 (55.9%tile)	1	TrialNet
14	M	NHW	21.9 (75.1%tile)	4	ASK
28	F	HIS	25.6	NA	Community Referral
32	M	NHW	22.6	NA	Community Referral
19	F	NHW	28.5 (91.0%tile)	5	ASK
18	M	Asian	20.8 (27.6%tile)	5	Community Referral
25	M	NHW	19.8	NA	Community Referral



Barbara Davis Center for Diabetes
UNIVERSITY OF COLORADO ANSCHUTZ MEDICAL CAMPUS

Slide adapted courtesy of Dr. Kimber Simmons, presented at Diabetes Dialog 2023.

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.

Barbara Davis Center for Diabetes
UNIVERSITY OF COLORADO ANSCHUTZ MEDICAL CAMPUS

Slide adapted courtesy of Dr. Kimber Simmons, presented at Diabetes Dialog 2023