

Screening and prevention of type 1 diabetes

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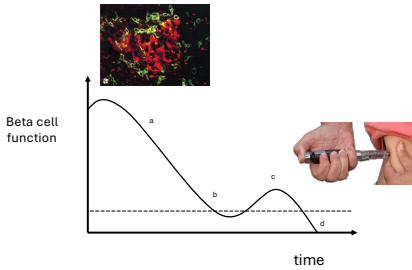
University of Birmingham
The Queen Elizabeth Hospital,
Birmingham

Diabetes Update 2025

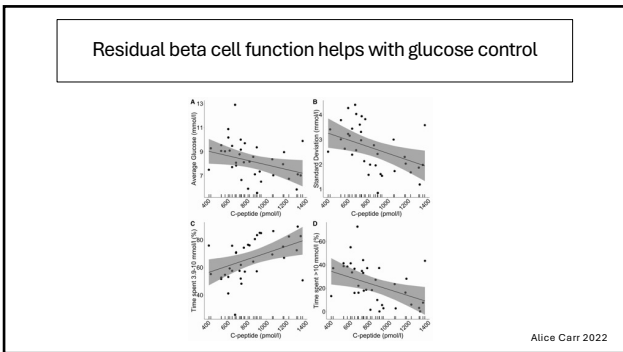


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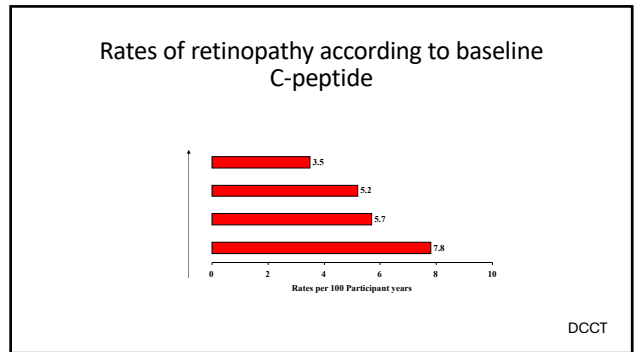
Natural history of T1D



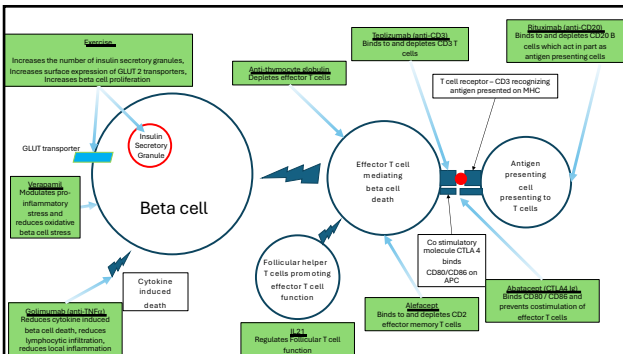
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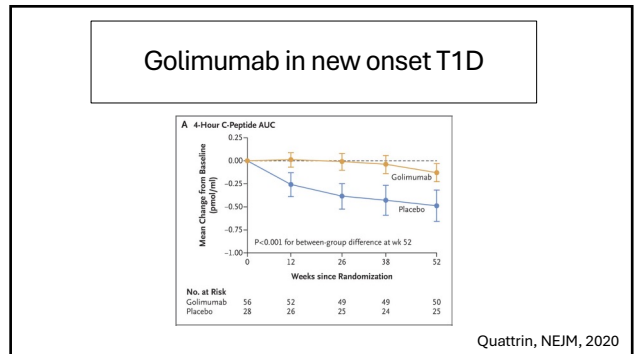
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ORIGINAL ARTICLE

An Anti-CD3 Antibody, Teplizumab, in Relatives at Risk for Type 1 Diabetes

- 76 first degree relatives at risk of T1D (Stage 2)
- Age 8-49 (most under 18 years)
- 2-week intervention with daily IV infusion of anti CD3
- 6 monthly OGTT for 5 years

Herold NEJM 2019

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Suppressing the immune system in those at risk of T1D

Hazard ratio 0.41
 Rates of diagnosis/year 15% vs 36%
 Median time to diagnosis 48 months vs 24 months

Herold NEJM 2019
Sims Sci Trans Med 2021

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Adverse Event Category	Teplizumab		Placebo	
	Events (N=112)	Participants (N=44)	Events (N=23)	Participants (N=23)
	no.	no. (%)	no.	no. (%)
Blood or bone marrow†	45	31 (70)	2	2 (9)
Dermatologic or skin†	17	14 (32)	1	1 (5)
Flu	11	5 (11)	5	2 (9)
Infection	8	5 (11)	5	3 (13)
Gastrointestinal	5	4 (9)	3	3 (13)
Metabolic or laboratory	7	4 (9)	2	2 (9)
Pulmonary or upper respiratory	6	4 (9)	0	0
Constitutional symptoms	2	2 (5)	0	0
Allergy or immunologic	2	2 (5)	0	0
Cardiac, general	1	1 (2)	1	1 (5)
Endocrine	0	0	2	2 (9)
Vascular	1	1 (2)	1	1 (5)
Neurologic	1	1 (2)	0	0
Other or viral	1	1 (2)	0	0
Musculoskeletal or soft tissue	2	1 (2)	0	0
Hepatobiliary or pancreatic	0	0	1	1 (5)
Symptoms	1	1 (2)	0	0
Hemorrhage or bleeding	1	1 (2)	0	0

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FIRST EVER TREATMENT TO DELAY TYPE 1 DIABETES IS LICENSED IN THE US

2022-11-17

The US Food and Drugs Administration (FDA) has approved the world's first ever immunotherapy for type 1 diabetes, teplizumab, also called Tzield. This is the biggest treatment breakthrough for the condition since the discovery of insulin 100 years ago.

Show me more

Is there a cure for diabetes?

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NICE review - ongoing

NICE National Institute for Health and Care Excellence

Guidance | Standards and indicators | Life sciences | British National Formulary (BNF) | British National Formulary for Children (BNFC) | Clinical Knowledge Summaries (CKS) | About

Home > NICE Guidance > Conditions and diseases > Diabetes and other endocrinal, nutritional and metabolic conditions > Diabetes

Teplizumab for delaying the onset of stage 3 type 1 diabetes in people 8 years and over with stage 2 type 1 diabetes [ID6259]

In development [GID-TA10981] Expected publication date: 16 July 2025

Project information | Project documents

Suggested remit: To appraise the clinical and cost effectiveness of teplizumab within its marketing authorisation for delaying the onset of type 1 diabetes in people aged 8 and over at risk of developing the condition.

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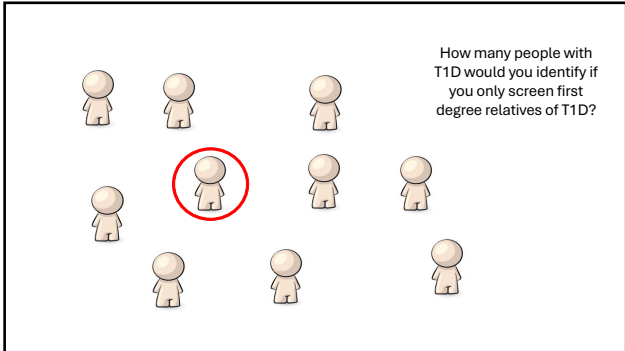
Medicines tested in new onset T1D that have potential for T1D delay

A: Azathioprine
 B: IFN alpha
 C: Autologous DCs
 D: Anti TNF
 E: ATG
 F: Teplizumab
 G: Verapamil
 H: Basiliximab
 I: Cyclosporin

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Can we identify people who will benefit from disease modifying therapy?

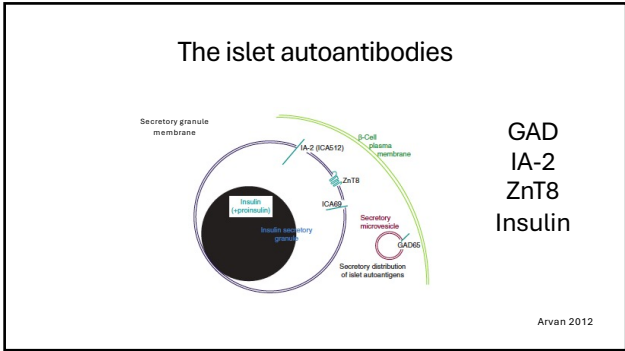
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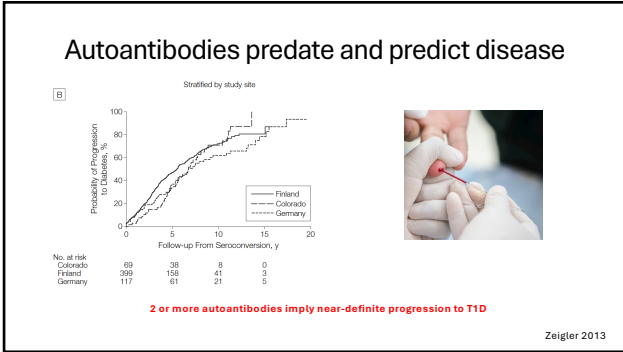
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The role of antibodies

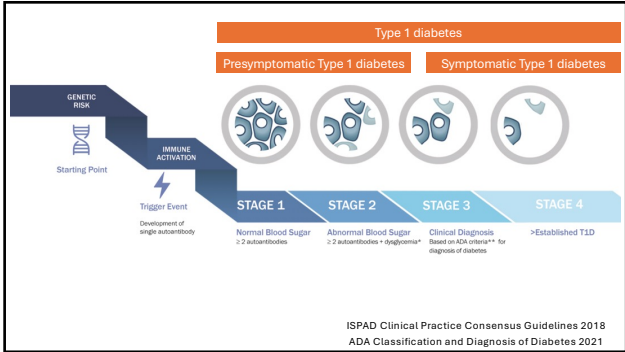
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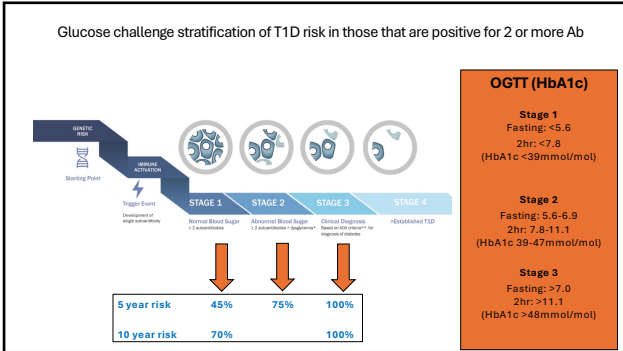
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ELSA

International SNOMED Code 'Presymptomatic type 1 diabetes'

- Suggested term:** Presymptomatic type 1 diabetes
- Summary of request:** Presymptomatic type 1 diabetes is a recognised precursor to type 1 diabetes, which does not require insulin treatment but there is no clinical code.
- The code was released by SNOMED International October 2023
- 1290118005 | Presymptomatic diabetes mellitus type 1 (disorder).**

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Benefits of early detection of T1D

More frequent check-ups

Monitoring

Start Treatment sooner

Improve HbA1c for >5 years after diagnosis

Prevent your child getting unwell

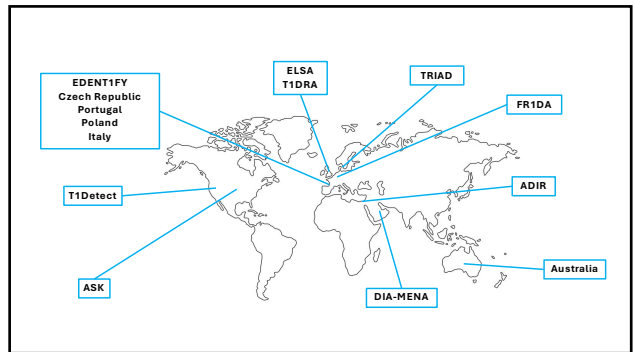
Reduce diabetes ketoacidosis

Access to promising new treatments

Teplizumab and other therapies

FR1DA, Ziegler 2020, Duca 2018, Herold 2019.

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Patient groups
Clinical benefits
Research interest

Cost
Distress
Practicalities

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ELSA

The ELSA Study

Population	Children aged 3-13 years
Intervention	Screening trial
Comparator	Usual care
Outcomes	Feasibility and Acceptability

NIHR | National Institute for Health Research

DIABETES UK
KNOW DIABETES. FIGHT DIABETES.

Breakthrough T1D™
Formerly IDP

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GP practices

Community Pharmacies for recruitment

Recruitment through schools

Community Research Nurses

Online and home testing

'Piggy backing' e.g. vaccine programme

NIHR Clinical Research Network West Midlands

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ELSA

Community Connexions

ELSA Community clinics

NHS South Central Ambulance Service

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Screening test – Dried Blood Spot

Clinical Immunology Services

Venous sample → DBS

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Dried Blood Spot: Antibodies

Serum confirmation: Antibodies

T1D staging

Education

Interview

Monitoring

Clinical trials

Study End

Study End

Figure created using Camia: <https://www.camia.com/>

RSR-3 screen: GAD, IA2, ZnT8

GAD, IA2, ZnT8, + IAA

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ELSA

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Shankar Kanumakala
Daniela Eleri

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'A smooth landing'

- 5-year-old girl
- Parent T1D
- ELSA study results
 - IA2, GAD, ZnT8 positive
 - Subsequent HbA1c 41mmol/mol
 - OGTT 0 mins: 6.1mmol/L, 120 mins 9.5mmol/L
- 2 PAU attendance reviews before needing insulin
- Treatment onset (3 months after screening)
 - HbA1c 50mmol/mol
 - 0.5U FIASP with evening meal
 - No basal insulin
- Current treatment (6 months after screening)
 - 0.5U FIASP with breakfast and 1U with evening meal
 - No basal insulin

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Diabetologia
https://doi.org/10.1007/s00125-024-6929-5

CONSENSUS REPORT

Consensus guidance for monitoring individuals with islet autoantibody-positive pre-stage 3 type 1 diabetes

Moche Phillips^{1,2}, Peter Achenbach^{3,4}, Ananta Addala^{5,6}, Anastasia Albanese-O'Neill⁷, Taneli Battelino^{8,9}, Koenraad J. Beil¹⁰, Rachel J. Bevan^{11,12}, Ego Bonifacio^{13,14}, Helen M. Colburn^{15,16}, Jennifer J. Cooper^{17,18,19}, Maria E. Craig^{20,21}, Thomas Danne²², Carine de Beaufort^{23,24,25}, Klavenn Dove²⁶, Kimberly A. Driemel^{27,28}, Sanjay Datta²⁹, Ouzge Ebekiova³⁰, Helena Elding Larsson^{31,32}, Daniel J. Felton³³, Brigitte I. Froehner³⁴, Robert A. Gabbay³⁵, Mary P. Gallagher³⁶, Carla J. Greenbaum³⁷, Kurt J. Griffin³⁸, William Hagopian³⁹, Michael J. Halperin⁴⁰, Christel Heudecker^{41,42}, Emile Hendrickx⁴³, Richard G. Hoel^{44,45}, Lucille Hughes⁴⁶, Jitaba M. Ismail⁴⁷, Laura M. Jacobsen⁴⁸, Suzanne B. Johnson⁴⁹, Leslie E. Kolb⁵⁰, Olga Kordonouri⁵¹, Karin Lange⁵², Robert M. Lamb⁵³, Axel Lemmas^{54,55}, Ingrid Litman⁵⁶, Markus Lundgren^{57,58}, David M. Maahs⁵⁹, M. Loredana Marcovecchio⁶⁰, Chantal Mathieu⁶¹, Kellie M. Miller⁶², Holly K. O'Donnell⁶³, Tal Oron⁶⁴, Shivraj P. Patel⁶⁵, Rodica Pop-Bucur⁶⁶, Mariani J. Reaver⁶⁷, Stephen S. Rich⁶⁸, Desmond A. Schatz⁶⁹, Ritika Schulman-Rosenbaum⁷⁰, Kimber M. Simmons⁷¹, Emily K. Sims⁷², Jay S. Skyler⁷³, Lara S. Seals⁷⁴, Cate Spaak⁷⁵, Andra K. Stack⁷⁶, Nicholas P. B. Thomas⁷⁷, Kumari N. Tonyushkin⁷⁸, Ritva Veijola⁷⁹, John M. Weir^{80,81}, Diane K. Wheeler⁸², Jamie B. Wood⁸³, Anette-Gabriele Ziegler⁸⁴, Linda A. DiMeo⁸⁵

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Highlighting the new consensus guidelines for managing people at risk of, and with early-stage type 1 diabetes. Relevance to clinical care in the UK

- Frequency and intensity of follow up for adults and children with pre-T1D, glucose monitoring, safety, insulin initiation
- Urgent need to educate health care professional colleagues around pre-T1D
- Pre-T1D best managed in secondary care
- Potential need for psychosocial support
- Need for more research

Narendran et al 2025, Diabetic Medicine

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Early T1 Diabetes Service

Who we can see

- Clinical service open nationally
- Virtual/In-person
- Shared care with local teams
- Early T1D (Stage 1/2/3a)
 - ≥ 2 islet Aab (GAD/IAA2/ZnT8/IA 2A)
 - Not requiring insulin or very early need for insulin

How to refer

- Young People (< 16 years): Renuka Dias
 - r.dias1@nhs.net
 - www.diabetesadministrators@nhs.net
 - 0121 333 8188
- Adults (>16 years): Parth Narendran
 - Parth.Narendran@uhb.nhs.uk
 - Wendy.read@uhb.nhs.uk (sec)
 - 0121 3714407

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Teplizumab in Clinical Care

- 14 children identified through ELSA as eligible for Teplizumab through 11 sites
- Supporting teams to deliver
- Weekly Friday meetings to discuss strategies and options
- Pharmacy: shared BCH DTC application
- Protocol for delivery: Shared US
- Funding and bed options
- BCH experience

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First of disease modifying therapy in the UK clinical setting

14 yr male; Father has T1D

- AAB GAD 65, ZnT8 +ve, OGTT (ELSA)

	2023	2024
Timepoint	Glucose mmol/l	Glucose mmol/l
0	4.8	4.6
120	9.1	10.1
HbA1c	26	29 (rise of 11.1% in 8 months)

Approved for Teplizumab treatment under Sanofi MAP September 2024
<https://www.sanofi.com/en/your-health/healthcare-professional-support/sanofi-manage-access-program>

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Teplizumab in Practice

- Delivered on CRF
 - Able to offer a skilled and experienced team of nurses who have delivered new drugs as part of research for many years
 - No bed pressures compared to normal ward beds
- Clinical Experience
 - No rashes/fever
 - Minimal neutropenia
 - Significant lymphopenia (nadir 0.6)
 - IV access issues initially

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Screening?
ADA 2.7 Autoantibody-based screening for presymptomatic type 1 diabetes should be offered to those with a family history of type 1 diabetes or otherwise known elevated genetic risk.

Practicalities of 14-day infusion?

Which centres?

Follow up?

Effect on clinical workload?

Equitable access?

NHSE
Professional organisations
Patient organisations

Preparing for disease modifying drugs in the UK

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Summary

Early identification of T1D has clinical advantages

Disease modifying drugs are coming

UK needs to prepare!

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ELSA Study Team

<p>University of Birmingham: Sarah Nadeem Lauren Quinn Sheila Greenfield Ian Litchfield Barbara Hudson Angila Rachna Sue Irwin</p>	<p>Professor of diabetes medicine Doctoral Fellow Professor of Qualitative Research Research Fellow DSN DSN DSN</p>	<p>University of Warwick: Felicity Boardman Matthew Randell</p>	<p>Professor in medicine ethics and society PhD candidate</p>
<p>CIS: Alan Richter Tim Plant Chris Bentley Sian Faustini Frank (Hui Fai)</p>	<p>Professor of clinical immunology CIS Laboratory Manager Research technician Research fellow Research technician</p>	<p>University of Bristol: Kathleen Gillespie</p>	<p>Professor of Diabetes</p>
<p>NHSC/CRN: Trevor Allen Emma Goodwin Julie Timmins Carly Tibbins</p>	<p>GP and Clinical Research Specialty Lead Research Delivery Manager, Diabetes Early Contact Research Support Officer Senior Research Nurse PPI Engagement Officer</p>	<p>Birmingham Community Healthcare: Christine Burt Fatima Zakia Ulfan-Siddika Jo Garatang</p>	<p>Research First: Sai Orreew, Gosh Heritage, Hollie Webb, Ryan Chahal, Joe Humphries, Nadège Houdouji-Javaux, Andy Knight, Linda Gardner, Shula Murphy, Ben Bahador</p>
<p>Paediatricians: Tim Bennett Rosalva Dias</p>	<p>Professor of Paediatrics Consultant Paediatrician, BCH ELSA Paediatricians</p>	<p>PPI Co-applicants: Christina Gardner Clair McGarr Amanda Lopley</p>	<p>Morph and Native</p>

All the parents and stakeholders who contributed to this study

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