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IN PATIENTS AGED 8 AND OLDER WITH STAGE 2 AUTOIMMUNE TYPE 1 DIABETES (T1D),

YOU CAN'T CONTROL IF, BUT YOU MAY IMPACT

WHEN

Consider choosing TZIELD▼(teplizumab) to modify autoimmune T1D and help delay WHEN your patients progress[1]

INDICATION: TZIELD is indicated to delay the onset of Stage 3 T1D in adult and paediatric patients 8 years of age and older with Stage 2 T1D.[1]

This is intended for healthcare professionals in the United Kingdom only.

▼Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to the Sanofi drug safety department on Tel: 0800 0902 314. Alternatively, send via email to UK-drugsafety@sanofi.com

The Prescribing Information can be accessed at the end of this document.

Please see the Summary of Product Characteristics (SmPC) for the full Safety Information for TZIELD **here**.

MHRA, Medicines and Healthcare products Regulatory Agency; **SmPC,** Summary of Product Characteristics; **T1D,** Type 1 diabetes.

Patient outcomes may vary.
Not an actual patient.

Tzield® ▽
(teplizumab)

TZIELD is the first and only immunomodulator indicated to delay the onset of Stage 3 T1D in patients aged 8 years and older with Stage 2 T1D[1]

For the first time, the onset of symptomatic autoimmune T1D (Stage 3) can be delayed[1]

In the primary analysis of the TN-10 study:[1,2]

2x more time in presymptomatic Stage 2 autoimmune T1D with TZIELD vs placebo

Median time to diagnosis of Stage 3 autoimmune T1D:

TZIELD: 48.4 months
Placebo: 24.4 months

N=76; hazard ratio (HR) 0.41; 95% confidence interval (CI), 0.22–0.78; *P*=0.0066 by an adjusted Cox proportional-hazards model stratified by age and oral glucose tolerance test (OGTT) status at randomisation.[1,2]

Median follow-up time was 745 days (range: 74–2,683 days).[2]

Primary efficacy endpoint: Time from randomisation to diagnosis of Stage 3 clinical T1D.*[1]

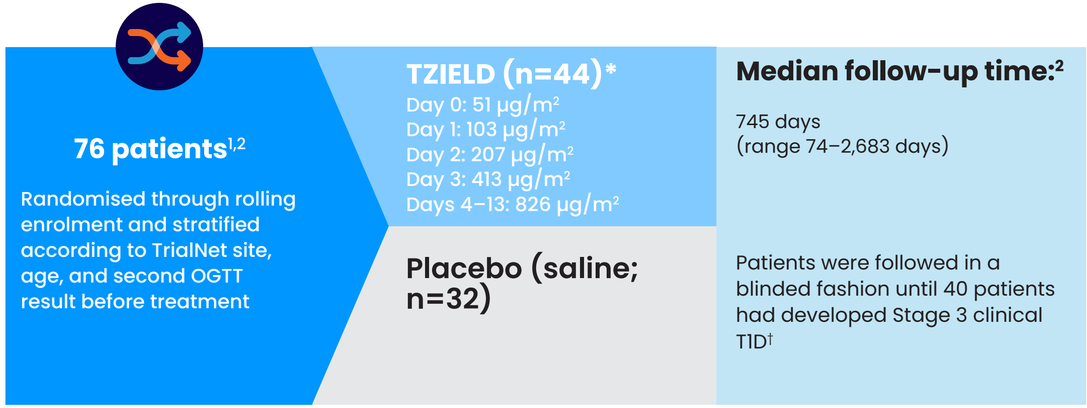
In TN-10, Stage 3 T1D was diagnosed in 20 (45%) patients treated with TZIELD and 23 (72%) patients treated with placebo.[1]

*Criteria for Stage 3 T1D were based on glucose testing or the presence of unequivocal hyperglycaemia or hyperglycaemic crisis.[2,3]
CI, confidence interval; **HR,** hazard ratio; **OGTT,** oral glucose tolerance test; **T1D,** Type 1 diabetes.

TrialNet-10 (TN-10) study design[2]

A phase 2, randomised, double-blind, event-driven, placebo-controlled study in 76 patients, 8–49 years of age, with Stage 2 T1D and who had a relative diagnosed with Stage 3 T1D.[1]

Stage 2 T1D is defined as having two or more pancreatic islet autoantibodies (glutamic acid decarboxylase 65 autoantibodies, insulin autoantibody, islet cell autoantibody, insulinoma-associated antigen 2 autoantibody, and zinc transporter 8 autoantibody) and dysglycaemia on OGTT.[1]



TZIELD dosing in the TN-10 trial is different to that recommended in the approved SmPC.[1,2] However, total drug exposure was comparable to that achieved with the recommended total TZIELD dosage.[1]

Primary efficacy endpoint:
Time from randomisation to diagnosis of Stage 3 clinical T1D.†[1]

*The recommended dosing as per the SmPC is 65 µg/m² on Day 1; 125 µg/m² on Day 2; 250 µg/m² on Day 3; 500 µg/m² on Day 4; and 1,030 µg/m² on Days 5 to 14.[1]

†Criteria for Stage 3 T1D were based on glucose testing or the presence of unequivocal hyperglycaemia or hyperglycaemic crisis.[2,3]

OGTT, oral glucose tolerance test; **SmPC,** Summary of Product Characteristics; **T1D,** Type 1 diabetes.

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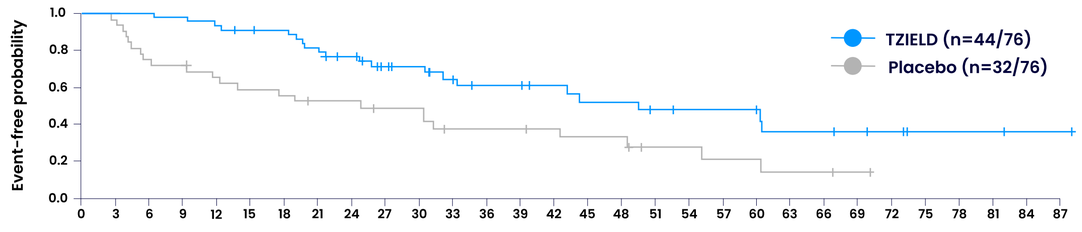
Effect of TZIELD on the development of T1D[1]

Kaplan-Meier curve of time to diagnosis of Stage 3 T1D[1]



Number of patients who are yet to experience Stage 3 type 1 diabetes onset

TZIELD	44	44	44	43	40	39	38	34	30	24	22	19	16	16	14	12	12	10	9	9	9	6	6	5	4	2	2	2	1	1
Placebo	32	31	24	23	20	18	17	15	15	13	13	9	9	9	8	7	7	4	4	3	3	2	2	1	0					

Cumulative number of patients who were diagnosed with Stage 3 type 1 diabetes

TZIELD	0	0	0	1	3	4	4	8	10	12	12	14	15	15	15	17	17	18	18	18	18	20	20	20	20	20	20	20	20	20
Placebo	0	1	8	9	11	13	14	15	15	16	16	19	19	19	19	20	20	21	21	22	22	23	23	23	23					

Adapted from TZIELD (teplizumab) UK SmPC. 2025.[1]

- HR 0.41; 95% CI, 0.22–0.78; *P*=0.0066 by an adjusted Cox proportional-hazards model stratified by age and OGTT status at randomisation
- Tick marks indicate censored data
- At the end of the trial, 25 TZIELD-treated patients did not have a Stage 3 autoimmune T1D diagnosis vs 9 with placebo[2]

Median time to diagnosis of Stage 3 autoimmune T1D:[1]

TZIELD: 48.4 months
Placebo: 24.4 months

CI, confidence interval; **HR,** hazard ratio; **OGTT,** oral glucose tolerance test; **T1D,** Type 1 diabetes.

The safety profile of TZIELD has been evaluated in a pool of adult and paediatric patients across five controlled clinical studies, four in Stage 3 T1D and one in Stage 2 T1D*[1]

Lymphopenia, leukopenia, neutropenia, decreased blood bicarbonate, and rash were the most frequently reported adverse reactions, which occurred at a higher frequency in the TZIELD group compared to the control group*[1]

Adverse reactions occurring in ≥5% of patients in the pooled safety analysis of clinical studies[1]

	Frequency		
System organ class	**Very common** (≥1/10)	**Common** (1/100 to <1/10)	**Not known**†
Blood and lymphatic system disorders	Lymphopenia Leukopenia Neutropenia Decreased haemoglobin Thrombocytopenia		
Immune system disorders		Cytokine release syndrome (CRS)	
Nervous system disorders	Headache		
Respiratory, thoracic and mediastinal disorders		Nasopharyngitis	
Gastrointestinal disorders	Nausea	Diarrhoea	Vomiting
Skin and subcutaneous tissue disorders	Rash Pruritus	Urticaria	Rash pruritic
General disorders and administration site conditions	Pyrexia	Chills	Fatigue Pain Illness
Investigations	Increased alanine aminotransferase (ALT) Increased aspartate aminotransferase (AST) Decreased blood bicarbonate Decreased blood calcium		

Adapted from TZIELD (teplizumab) UK SmPC. 2025.[1]

Refer to section 4.8 of the SmPC here for more information regarding these and other adverse reactions.

No drug interaction studies have been performed[1]

*Adverse reactions were evaluated in a pool of adult and paediatric patients across one phase 2 study in patients with Stage 2 autoimmune T1D (TN-10), three placebo-controlled studies in an unapproved population (Stage 3 T1D), and one open-label standard-of-care controlled study of TZIELD in an unapproved population (Stage 3 T1D).[1]

†Cannot be estimated from available data.

ALT, alanine aminotransferase; **AST,** aspartate aminotransferase; **CRS,** cytokine release syndrome; **SmPC,** Summary of Product Characteristics; **T1D,** Type 1 diabetes.

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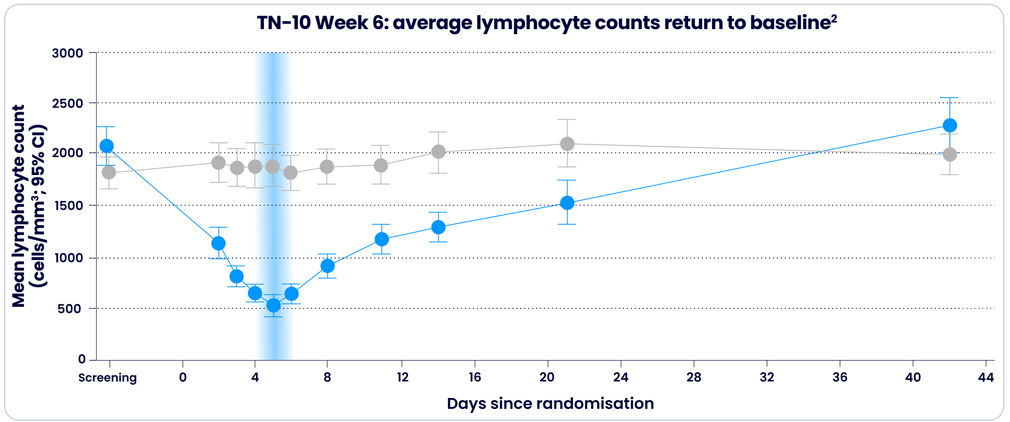
Serious adverse reactions have been reported with greater frequency in TZIELD-treated patients vs placebo-treated patients in TN-10[1]

Adverse reaction	TZIELD (n=44/76)	Placebo (n=32/76)
CRS	2%	0%
Serious infections*	9%	0%
Hypersensitivity reactions and serum sickness	2%	0%
Lymphopenia	73%	6%

Adapted from TZIELD (teplizumab) UK SmPC. 2025.[1]

Special warnings and precautions for use

Lymphopenia is an expected and very common adverse reaction to TZIELD that is often resolved by Week 6[1,2]



Adapted from Herold KC, et al. 2019.[2]

Refer to section 4.8 of the SmPC here for more information regarding these and other adverse reactions.

*Serious infections included cellulitis, gastroenteritis, pneumonia, and wound infection any time during or after the first dose of study treatment.[1]

CI, confidence interval; **CRS**, cytokine release syndrome.

Lymphopenia is an expected and very common adverse reaction to TZIELD that is often resolved by Week 6[1,2]

- In clinical trials, 80% of patients treated with TZIELD developed lymphopenia compared to 17% of patients in the control group
- Cases of lymphopenia usually occurred within the first few days of treatment
- Average lymphocyte count nadir occurred at Day 5 of treatment, with recovery and return to baseline by Week 6 in most patients
- Lymphopenia occurred in the absence of T-cell depletion

Guidance for lymphopenia[1]

- ✓ Monitor white blood cell counts during the 2-week treatment period
- ✓ If prolonged severe lymphopenia (<500 cells/µL, lasting one week or longer) develops, discontinue TZIELD

CRS was reported in 6% of TZIELD-treated patients[1]

- CRS manifestations in TZIELD-treated patients included fever, nausea, fatigue, headache, myalgia, arthralgia, increased ALT, increased AST, and increased total bilirubin, and typically occurred during the first 5 days of treatment[1]
- In clinical trials, CRS was reported in 6% of patients treated with TZIELD vs 1% of patients in the control group during the treatment period and through 28 days after the last study drug administration[1]
- 13% of these CRS cases were serious adverse reactions[1]

Mitigate CRS[1]

- Premedicate with antipyretics, antihistamines and/or antiemetics prior to TZIELD treatment for the first 5 days and as needed thereafter
- Monitor liver enzymes and bilirubin during treatment. Discontinue TZIELD treatment in patients who develop elevated ALT or AST more than five times the upper limit of normal (ULN) or bilirubin more than three times the ULN
- Treat symptoms of CRS with antipyretics, antihistamines and/or antiemetics. If severe CRS develops, consider pausing dosing for 1–2 days (and administer the remaining doses to complete the full 14-day course on consecutive days) or discontinuing treatment

ALT, alanine aminotransferase; **AST,** aspartate aminotransferase; **CRS,** cytokine release syndrome; **ULN,** upper limit of normal.

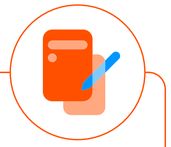
Tzield® (teplizumab)

Special warnings and precautions for use

Key information to support the use of TZIELD

Serious infections[1]

Bacterial and viral infections have occurred in TZIELD-treated patients including gastroenteritis, cellulitis, pneumonia, abscess and sepsis. In clinical trials, patients treated with TZIELD had a higher rate of serious infections (3.5%) than patients in the control group (2%).



Management considerations[1]

- Monitor patients for signs and symptoms of infection during and after TZIELD treatment. If serious infection develops, treat appropriately, and discontinue TZIELD

Concomitant immunosuppressive medication[1]

In T1D studies, the safety and efficacy of TZIELD in combination with immunosuppressive medication have not been evaluated. Caution should be exercised when considering concomitant use of immunosuppressive medication.

Hypersensitivity reactions[1]

Acute hypersensitivity reactions, including serum sickness, angioedema, urticaria, rash, vomiting and bronchospasm occurred in TZIELD-treated patients. Hypersensitivity reactions were reported with TZIELD in the TN-10 trial. Serum sickness was observed in 2% (1/44) of TZIELD-treated patients compared to 0% (0/32) of placebo-treated patients. See Rash and Hypersensitivity Reactions (section 4.8) of the SmPC for additional safety information from the five pooled clinical trials.

Management considerations[1]

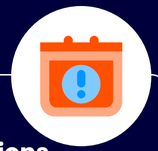
- If severe hypersensitivity reactions occur, discontinue use of TZIELD and treat promptly

Please see the SmPC for the full Safety Information for TZIELD **here**.

SmPC, Summary of Product Characteristics.

Vaccinations[1]

The safety of immunisation with live-attenuated vaccines in patients treated with TZIELD has not been studied. TZIELD may interfere with the immune response to vaccination and decrease vaccine efficacy.



Administer all age-appropriate vaccinations prior to starting TZIELD[1]

- Inactivated or messenger ribonucleic acid (mRNA) vaccinations are not recommended within the 2 weeks prior to TZIELD treatment, during treatment, or 6 weeks after completion of treatment
- Live-attenuated vaccinations are not recommended within the 8 weeks prior to TZIELD treatment, during treatment, or up to 52 weeks after treatment

List of excipients[1]

Dibasic sodium phosphate (E339)
Monobasic sodium phosphate (E339)
Polysorbate 80 (E433)
Sodium chloride
Water for injection

SmPC, Summary of Product Characteristics.

Incompatibilities[1]

In the absence of compatibility studies, TZIELD should not be mixed with other medicinal products. Do not add or simultaneously infuse other medicinal products through the same intravenous line. This medicinal product should be prepared and administered as instructed in section 4.2 and section 6.6 of the SmPC.

Pregnancy[1]

Available case reports from clinical trials with TZIELD are insufficient to identify a drug-associated risk of major birth defects, miscarriage or other adverse maternal or foetal outcomes. Although there are no data on TZIELD, monoclonal antibodies can be actively transported across the placenta, and TZIELD may cause immunosuppression in the utero-exposed infant. To minimise exposure to a foetus, avoid use of TZIELD during pregnancy and for at least 30 days prior to planned pregnancy.

Breastfeeding[1]

There are no data on the presence of TZIELD in human milk, effects on milk production, or effects on the breastfed child. As endogenous maternal immunoglobulin G (IgG) and monoclonal antibodies are transferred into human milk, a lactating woman may interrupt breastfeeding and pump and discard breast milk during treatment and for 20 days after TZIELD administration to minimise drug exposure to a breastfed child.

Fertility[1]

There are no clinical data available for TZIELD on the effects on fertility.

Effects on ability to drive and use machines[1]

Fatigue has been reported in patients taking TZIELD and this should be taken into account when driving or using machines.

Tzield® (teplizumab)

Consider taking control today and intervene with TZIELD to delay autoimmune T1D disease progression[1,2]

2x More time in presymptomatic Stage 2 autoimmune T1D with TZIELD vs placebo*[1,2]

TN-10 primary analysis

Median time to diagnosis of Stage 3 autoimmune T1D:†[1,2]

TZIELD: 48.4 months
Placebo: 24.4 months

The safety profile of TZIELD has been evaluated in a pool of adult and paediatric patients across five controlled clinical studies, four in Stage 3 T1D and one in Stage 2 T1D‡[1]

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References: 1. TZIELD® (teplizumab) UK Summary of Product Characteristics. 2025. **2.** Herold KC, et al. N Engl J Med. 2019; 381(7): 603–613. **3.** American Diabetes Association. Diabetes Care. 2019; 42(Suppl. 1): S13–S28.

Prescribing Information can be accessed by scanning or clicking this **QR code**:

Patient outcomes may vary.

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