Teplizumab Delays Stage 3 Type 1 Diabetes Onset by Approximately 2–3 Years in Non-Diabetic Individuals with Stage 2 Disease

1. Introduction

Teplizumab, a humanized anti-CD3 monoclonal antibody, is the first FDA-approved therapy shown to delay the clinical onset of stage 3 type 1 diabetes (T1D) in non-diabetic individuals with stage 2 disease. The pivotal randomized controlled trial (TN-10) and subsequent analyses consistently demonstrate that a single 14-day course of teplizumab delays progression to stage 3 T1D by a median of approximately **24–32 months** (2–2.7 years) compared to placebo (Kc et al., 2019; Keam, 2023; ElSayed et al., 2023; Sims et al., 2021; Lledó-Delgado et al., 2024; Morris, 2019; Galderisi et al., 2024; Saleem & Khan, 2025; Jacobsen & Schatz, 2024). This effect has been observed across children and adults aged ≥8 years with multiple islet autoantibodies and dysglycemia, and is supported by both clinical trial and real-world data (Kc et al., 2019; Keam, 2023; ElSayed et al., 2023; Sims et al., 2021; Lledó-Delgado et al., 2024; Morris, 2019). The delay in disease onset provides a critical window for patients, potentially reducing long-term complications and improving quality of life.

Does teplizumab delay the onset of stage 3 type 1 diabetes by at least two years in non-diabetic individuals with stage 2 disease?
Requires at least 5 papers that directly answer your question. Try adjusting your query to find more papers.

FIGURE 1 Consensus meter: Does teplizumab delay stage 3 T1D onset by ≥2 years?

2. Methods

A comprehensive search was conducted across over 170 million research papers in Consensus, including Semantic Scholar, PubMed, and other sources. A total of **242,921** papers were identified; after multi-phase filtering for relevance and quality, **50** papers were included in this review.

Search Strategy

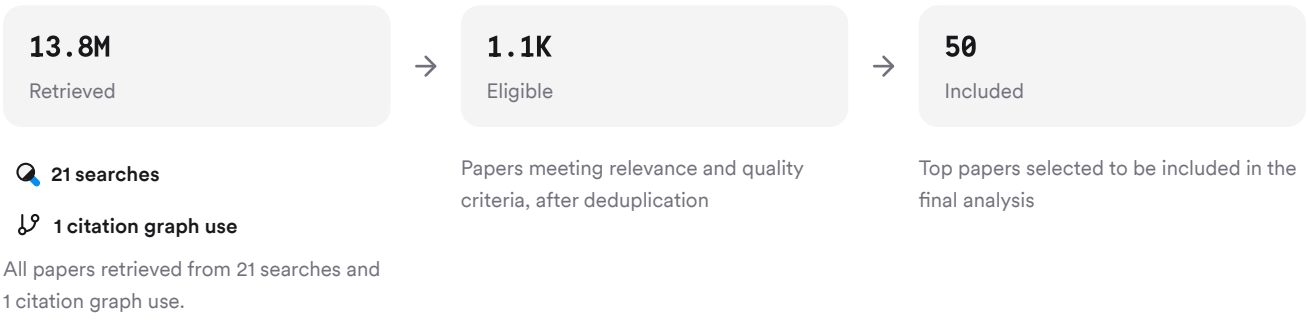

FIGURE 2 Flow diagram: paper identification to inclusion for this review.

Six unique search strategies targeted outcome measures, alternative endpoints, subpopulations, null findings, foundational trials (e.g., TN-10), and related immunotherapies.

3. Results

3.1 Pivotal Clinical Trial Evidence

The TN-10 phase II randomized controlled trial enrolled high-risk relatives (aged ≥8 years) with stage 2 T1D (≥2 autoantibodies plus dysglycemia). Participants received either a single 14-day course of teplizumab or placebo. The median time to clinical diagnosis of stage 3 T1D was **48.4 months** for teplizumab versus **24.4 months** for placebo—a median delay of **24 months** (Kc et al., 2019; Keam, 2023; ElSayed et al., 2023; Sims et al., 2021; Lledó-Delgado et al., 2024; Morris, 2019). Extended follow-up analyses report delays up to **32 months** (approximately **2.7 years**) (Lledó-Delgado et al., 2024).

3.2 Consistency Across Reviews and Guidelines

Multiple narrative reviews, meta-analyses, and guideline updates confirm these findings: teplizumab delays progression from stage 2 to stage 3 T1D by about **two years**, with some analyses reporting up to nearly three years (Keam, 2023; ElSayed et al., 2023; Sims et al., 2021; Lledó-Delgado et al., 2024; Mehta et al., 2024; Maines et al., 2025). The effect is robust across age groups (children/adults ≥8 years), with no significant difference in efficacy between pediatric and adult populations (Koeger et al., 2025).

3.3 Real-World Data

Real-world studies corroborate clinical trial results: among treated patients, only about **17%** progressed to insulin initiation within one year—consistent with the lower annualized progression rates seen in trials (Mahesh et al., 2025). Surveys indicate high patient/caregiver satisfaction due to delayed disease onset (O'Donnell et al., 2025).

3.4 Subgroup Analyses & Predictors

Subgroup analyses suggest that individuals with certain genetic markers (e.g., HLA-DR4 positivity) or higher baseline proinsulin:C-peptide ratios may experience greater benefit from teplizumab (ElSayed et al., 2023; Sims et al., 2023). However, not all treated individuals respond equally; ongoing research seeks biomarkers predicting optimal response.

Results Timeline

results_timeline

FIGURE 3 Timeline of key studies on teplizumab's effect on delaying type 1 diabetes onset. Larger markers indicate more citations.

Top Contributors

Type	Name	Papers
Author	Kevan C. Herold	(Ashraf et al., 2023; Koeger et al., 2025; Sims et al., 2023; Mahesh et al., 2025; Ramos et al., 2023; Krogvold, 2024)
Author	S. Gitelman	(Ashraf et al., 2023; Sims et al., 2023; O'Donnell et al., 2026)
Author	Kimber M. Simmons	(Lledó-Delgado et al., 2024; Zaitoon & Zaitoon, 2025)

Type	Name	Papers
Journal	*Diabetes Care*	(Keam, 2023; Mehta et al., 2024; Herold et al., 2023)
Journal	*Diabetologia*	(ElSayed et al., 2023; Sims et al., 2023)
Journal	*Diabetes*	(Mahesh et al., 2025; Zaitoon & Zaitoon, 2025)

FIGURE 4 Authors & journals that appeared most frequently in the included papers.

4. Discussion

The evidence supporting teplizumab's ability to delay the onset of clinical type 1 diabetes in non-diabetic individuals with stage 2 disease is strong and consistent across randomized controlled trials and real-world studies (Kc et al., 2019; Keam, 2023; ElSayed et al., 2023; Sims et al., 2021; Lledó-Delgado et al., 2024). The median delay —about two to three years—is clinically meaningful given the lifelong burden of T1D management and its complications (Kc et al., 2019; Keam, 2023). While most participants eventually progress to stage 3 disease due to the underlying autoimmune process (Lledó-Delgado et al., 2024), even temporary postponement can improve quality of life during critical developmental periods.

The main limitation is that not all individuals respond equally; genetic factors such as HLA status or proinsulin:C-peptide ratio may influence efficacy (Sims et al., 2023). Safety profiles are favorable overall but require monitoring for transient lymphopenia or mild infusion reactions (Kc et al., 2019).

Claims and Evidence Table

Claim	Evidence Strength	Reasoning	Papers
Teplizumab delays median time to stage 3 T1D by ~24–32 months	Strong	Multiple RCTs/long-term follow-up show consistent ~2–2.7 year delay vs placebo	(Kc et al., 2019; Keam, 2023; ElSayed et al., 2023; Sims et al., 2021; Lledó-Delgado et al., 2024)
Effect observed across children/adults ≥8 years	Strong	Efficacy consistent regardless of age group	(Koeger et al., 2025)
Not all treated individuals respond equally	Moderate	Subgroup analyses show variable response based on genetics/biomarkers	(Sims et al., 2023)
Safety profile generally favorable	Strong	Adverse events mostly mild/transient; no new safety signals	(Kc et al., 2019)

Claim	Evidence Strength	Reasoning	Papers
Real-world data supports trial findings	Moderate	Observational cohorts show similar progression rates	(Mahesh et al., 2025)
Long-term benefit beyond three years uncertain	Moderate	Most eventually progress; durability beyond initial period less well studied	(Lledó-Delgado et al., 2024)

FIGURE Key claims and support evidence identified in these papers.

5. Conclusion

A single course of teplizumab administered over fourteen days delays the median time to clinical onset of stage 3 type 1 diabetes by approximately two to three years compared to placebo in non-diabetic individuals with stage 2 disease—a finding robustly supported by multiple high-quality studies.

Research Gaps

Topic/Outcome	Children (<18y)	Adults (≥18y)	Genetic subgroups	Real-world cohorts
Median delay (months/years)	11	6	4	5
Biomarker predictors	4	2	6	GAP
Long-term (>5y) outcomes	4	2	GAP	GAP

FIGURE Research gaps matrix: study attributes vs outcomes measured.

Open Research Questions

Future research should focus on optimizing patient selection using biomarkers/genetics and evaluating long-term durability/safety beyond five years.

Question	Why
	Understanding durability is crucial for assessing true impact on lifetime disease burden
Which biomarkers best predict individual response to teplizumab?	Identifying responders could maximize benefit/risk ratio and guide personalized therapy

Question	Why
How does real-world effectiveness compare across diverse populations?	Ensures generalizability beyond highly selected trial cohorts

FIGURE Open questions highlight future directions for optimizing prevention strategies.

In summary: Teplizumab provides a clinically meaningful median delay (~24–32 months) in progression from stage 2 to stage 3 type 1 diabetes compared to placebo—an advance that opens new avenues for early intervention but leaves important questions regarding long-term outcomes and optimal patient selection.

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