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Real-world experiences of adult individuals or caregivers of children who received teplizumab treatment in stage 2 type 1 diabetes

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Abstract

Aims: This study surveyed individuals and caregivers of children who received teplizumab at stage 2 type 1 diabetes (T1D) to garner real-world experiences and their health outlook for the future following treatment with the first approved disease-modifying immune therapy for delaying the onset of Stage 3 T1D.

Materials and Methods: This was a cross-sectional, observational, online survey (conducted September–October 2024) of adults (≥18 years) and caregivers of children (8–17 years) who received teplizumab while participating in the US COMPASS patient support program. Questions pertained to demographics, health history, T1D screening, the decision to take teplizumab, treatment, post-treatment experience, outlook on prognosis and self-reported health status. All data were summarized using descriptive statistics.

Results: A total of 47/116 invited individuals responded (30 adults, 17 caregivers of children). Almost half of respondents had a family history of T1D, and 36% reported autoimmune comorbidities. The top reason for both screening for T1D and receiving teplizumab was for a chance at delaying Stage 3 T1D. Although respondents expressed continued concern over diabetes progression, 87% felt grateful to receive teplizumab, 72% felt it would help slow down the disease, 60% felt it would make T1D easier to manage and most (>80%) would recommend treatment/make the same decision for another family member.

Conclusions: Individuals living with or caring for someone who received teplizumab felt grateful for the opportunity to delay disease or make it easier to manage following teplizumab, with most agreeing they would recommend teplizumab and make the same decision for family in their situation.

Plain Language Summary

Type 1 diabetes (T1D) happens when the body destroys cells in the pancreas that make insulin. This ultimately causes high blood sugar. People with T1D often worry about the long-term effects of the disease. Teplizumab is the first FDA-approved treatment that delays the onset of high blood sugar in people in the early stages of T1D—when there are signs of cell damage and mild increases in blood sugar. We surveyed adults ($N = 30$) and caregivers ($N = 17$) of children treated with teplizumab about their journey before and after treatment. More than half of adults were initially told they might have a different type of diabetes, usually type 2, before being accurately diagnosed with early-stage T1D. Doctors specializing in diabetes were most often the ones who recommended screening for T1D. The most common reason to screen was a chance for more time before the onset of high blood sugar. Greater than 80% of people were grateful they or their child had the opportunity to receive teplizumab, and most would recommend it to others in a similar situation. After receiving teplizumab, most people still worried about their blood sugar and measured it frequently. Most thought that teplizumab would delay the disease progression to symptoms, and more than half thought teplizumab would make T1D easier to manage. These findings are the first to describe the journey of adults and caregivers of children treated with teplizumab, their reasons for screening, and their beliefs about the future.

KEYWORDS

attitudes, observational study, patient-reported outcomes, perceptions, real-world evidence, type 1 diabetes

1 | INTRODUCTION

In November 2022, teplizumab was approved in the United States to delay the onset of Stage 3 (clinical) type 1 diabetes (T1D) in individuals aged ≥8 years with stage 2 T1D, making it the first disease-modifying immune therapy for T1D.[1] Teplizumab is a humanized monoclonal antibody that binds to CD3 (a cell surface antigen on T lymphocytes) and exhausts autoreactive T lymphocytes.[2–4] Teplizumab is administered by intravenous infusion once daily for 30 min over 14 consecutive days.[2] In the pivotal, phase 2, placebo-controlled, double-blind trial, teplizumab delayed the progression to Stage 3 T1D in individuals with stage 2 T1D by 24 months versus placebo (median follow-up of ~24.5 months).[5,6] A recent extended analysis (median follow-up of 80.5 months) confirmed these results and found teplizumab delayed the median time to Stage 3 by 25 months.[7] Some teplizumab-treated individuals had persisting effects, and after 5 years of follow-up, 39% of drug-treated individuals had not progressed to Stage 3 T1D compared with 19% of individuals on placebo.[7] Delaying onset of Stage 3 T1D provides more time without the burdensome self-management routine required for individuals on insulin therapy and time for youth to mature cognitively and emotionally to be better able to manage Stage 3 while clinical tools for managing T1D continue to improve.

Currently, there are no studies documenting the real-world experiences or perspectives of adult individuals or caregivers of children who have received teplizumab to delay Stage 3 T1D.[8] The present study described the characteristics of adult patients and caregivers of youth who received teplizumab, their experiences with screening for pre-symptomatic T1D and with teplizumab treatment, as well as their feelings and health outlook post-teplizumab. This study is the first to report the experiences and feelings of individuals and caregivers of individuals treated with teplizumab after being approved for clinical use in the United States.

2 | MATERIALS AND METHODS

2.1 | Study design

In this cross-sectional observational study, participants in the United States who were enrolled in the Sanofi teplizumab-mzwv COMPASS patient support program ('COMPASS') and who had valid

documentation of consent to be recontacted for participation in future studies were invited to participate in an online survey via email outreach. COMPASS is a personalized program, supported by Sanofi, that facilitates access to teplizumab through provision of tools and educational resources related to teplizumab. COMPASS also provides information about the copay program, which may cover some or all of the cost of teplizumab as well as financial assistance options that may be available to individuals. Institutional review board approval for the study was obtained from the Western Institutional Review Board Copernicus Group. This study complied with the principles of the Declaration of Helsinki. Participants were required to provide informed consent to participate in this study. Participants also had the option to provide consent to have their sensitive demographic data translated into a non-identifiable code to allow linking of the survey findings to other sources of non-identifiable information in future analyses. The data presented in this report focus on the findings from the survey.

2.2 | Participants

Participants were adults (≥18 years of age) or adult caregivers of a child (8–17 years of age) who received treatment with teplizumab, reside in the United States, are fluent in English and provided informed consent for participation in this study. All 116 individuals from COMPASS who provided consent to be recontacted for participation in future studies and had valid contact information were invited to participate in the survey.

2.3 | Study procedures and data collected

Respondents completed an online survey developed in collaboration with behavioural scientists with expertise in T1D and patient-reported outcomes that was hosted on the IQVIA Connection™ platform. The survey was designed to take approximately 30 min and was open for 1 month from 26 September 2024, through 27 October 2024. The survey collected information on demographics (of the adults, children and caregivers), health history (of the adults and children), T1D screening, teplizumab treatment, experiences post-teplizumab treatment, outlook on the disease prognosis and health status (of the adults and caregivers) as measured by the 5-level EQ-5D (EQ-5D-5L; EuroQol Research Foundation, Rotterdam, The Netherlands), which is a validated patient-reported outcome measure. Survey items on knowledge, feelings, decisions and outlook pertained to those of the adults and caregivers.

To respond to survey items (other than the EQ-5D-5L), participants indicated their level of agreement with a statement or the importance of a certain factor using a 5-point Likert scale (e.g., 'strongly disagree' to 'strongly agree'); a slider from 1 to 10 to indicate how often they felt a certain way; or selected their response(s) from a list of two or more response options. For the EQ-5D-5L, the participants assessed five dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression) using a 5-point Likert scale (for more detailed methods on the EQ-5D-5L, refer to the Table 1 footnotes).[9] The full survey (excluding the EQ-5D-5L) is included in the Supplemental Appendix.

2.4 | Statistical analysis

Participants who met all inclusion criteria and completed at least one survey item were included in the full analysis set. Continuous and categorical data were described using descriptive statistics. For conditional survey items, the denominator was the number of participants who were eligible to complete the item. Subgroups were examined by participant type (adults vs. caregivers) and by family history of T1D (those who reported a family history vs. those who did not). Fisher's exact test was conducted post hoc for specific survey items to compare the proportion who agreed/strongly agreed versus the proportion who did not among the levels for each subgroup.

3 | RESULTS

3.1 | Demographics and clinical characteristics

Among those enrolled in COMPASS who had consented to be recontacted for future studies ($N = 119$; three with invalid contact details), the mean (SD) age of the children and adults who had received teplizumab was 26.6 (16.6) years; 52.1% (62/119) were ≥18 years, 24.4% (29/119) were 12–17 years and 23.5% (28/119) were 8–11 years. Additionally, 52.1% (62/119) of these children and adults who had received teplizumab and were invited to participate were female.

Forty-seven participants responded to the survey out of 116 invited (40.5% response rate), including 30 adults and 17 caregivers of children. Demographic and clinical characteristics of the adults, children and caregivers are shown in Table 1. At the time of the survey, all respondents had been treated with teplizumab within the past year (Table 2). Most adults and caregiver respondents were female, though there were more paediatric males than females who received the therapy. Of the children and adult participants, approximately half were female, similar to the children and adults invited to participate in the study. Likewise, most participants (30/47) were ≥18 years of age. Of the survey respondents, all were White and the vast majority were not of Hispanic or Latino ethnicity. About half of the respondents had a family history of T1D, among whom 69.6% (16/23) had a first-degree relative with T1D. Comorbid autoimmune conditions were reported by 10/30 adult respondents and for 7/17 children. Adults and children had family members with a broad history of autoimmune conditions, including hypothyroidism, celiac disease, rheumatoid arthritis, hyperthyroidism, juvenile rheumatoid arthritis, vitiligo, Sjögren's syndrome and systemic lupus erythematosus. Adults and caregivers provided favourable ratings for their own health on average, using the visual analogue scale of the EQ-5D-5L (Table 1; the EQ-5D-5L descriptive system is shown in Table S1).

TABLE 1 Demographics and clinical characteristics of the full respondent analysis set.

Parameter, *n* (%)	All individuals receiving teplizumab *N* = 47	All respondents *N* = 47	Adult respondents *N* = 30	Children receiving teplizumab *N* = 17	Caregiver respondents *N* = 17
Age (years)					
Mean (SD)	27.21 (16.26)	38.53 (12.72)	35.63 (14.61)	12.35 (2.37)	43.65 (5.87)
Median	22.0	39.0	32.5	12.0	43.0
Min/Max	9/67	18/67	18/67	9/17	33/56
Sex					
Male	22 (46.8%)	14 (29.8%)	12 (40.0%)	10 (58.8%)	2 (11.8%)
Female	25 (53.2%)	33 (70.2%)	18 (60.0%)	7 (41.2%)	15 (88.2%)
Ethnicity					
Hispanic or Latino	3 (6.4%)	2 (4.3%)	1 (3.3%)	2 (11.8%)	1 (5.9%)
Not Hispanic or Latino	44 (93.6%)	45 (95.7%)	29 (96.7%)	15 (88.2%)	16 (94.1%)
Race					
White	47 (100.0%)	47 (100.0%)	30 (100.0%)	17 (100.0%)	17 (100.0%)
Black or African American	0	0	0	0	0
Asian	0	0	0	0	0
Annual family income					
<$50 000	–	6 (12.8%)	4 (13.3%)	–	2 (11.8%)
$50 000–$75 000	–	2 (4.3%)	1 (3.3%)	–	1 (5.9%)
$75 001–$100 000	–	6 (12.8%)	4 (13.3%)	–	2 (11.8%)
$100 001–$150 000	–	5 (10.6%)	5 (16.7%)	–	0
>$150 000	–	19 (40.4%)	10 (33.3%)	–	9 (52.9%)
Prefer not to answer	–	9 (19.1%)	6 (20.0%)	–	3 (17.6%)
Education					
Some high school, no diploma	–	1 (2.1%)	1 (3.3%)	–	0
High school diploma or GED	–	3 (6.4%)	2 (6.7%)	–	1 (5.9%)
Some college, no degree	–	7 (14.9%)	6 (20.0%)	–	1 (5.9%)
Trade, technical or vocational training	–	1 (2.1%)	0	–	1 (5.9%)
Associate's degree	–	4 (8.5%)	3 (10.0%)	–	1 (5.9%)
Bachelor's degree	–	13 (27.7%)	6 (20.0%)	–	7 (41.2%)
Graduate degree	–	18 (38.3%)	12 (40.0%)	–	6 (35.3%)
Employment[a]					
Employed full-time	–	24 (51.1%)	16 (53.3%)	–	8 (47.1%)
Employed part-time	–	5 (10.6%)	2 (6.7%)	–	3 (17.6%)
Self-employed	–	3 (6.4%)	2 (6.7%)	–	1 (5.9%)
Unemployed (looking for work)	–	3 (6.4%)	3 (10.0%)	–	0
Unemployed (not looking for work)	–	10 (21.3%)	6 (20.0%)	–	4 (23.5%)
Unable to work	–	2 (4.3%)	1 (3.3%)	–	1 (5.9%)
Insurance					
Do not have health insurance	–	1 (2.1%)	0	–	1 (5.9%)
Private insurance[b]	–	27 (57.4%)	16 (53.3%)	–	11 (64.7%)
Own private insurance[c]	–	9 (19.1%)	7 (23.3%)	–	2 (11.8%)
Public insurance[d]	–	8 (17.0%)	5 (16.7%)	–	3 (17.6%)
Tricare	–	1 (2.1%)	1 (3.3%)	–	0
I don't know	–	1 (2.1%)	1 (3.3%)	–	0

TABLE 1 (Continued)

Parameter, *n* (%)	All individuals receiving teplizumab *N* = 47	All respondents *N* = 47	Adult respondents *N* = 30	Children receiving teplizumab *N* = 17	Caregiver respondents *N* = 17
Family history of T1D					
Yes	23 (48.9%)	–	16 (53.3%)	7 (41.2%)	–
No	23 (48.9%)	–	13 (43.3%)	10 (58.8%)	–
I don't know	1 (2.1%)	–	1 (3.3%)	0	–
Degree relative with T1D[e]	*N* = 23		*N* = 16	*N* = 7	
First-degree	16 (69.6%)	–	10 (62.5%)	6 (85.7%)	–
Second-degree	10 (43.5%)	–	6 (37.5%)	4 (57.1%)	–
Not sure	1 (4.3%)	–	1 (6.3%)	0	–
Missing/not asked	24	–	14	10	–
Autoimmune condition					
Celiac disease	5 (10.6%)	–	1 (3.3%)	4 (23.5%)	–
Addison's disease	1 (2.1%)	–	0	1 (5.9%)	–
Hyperthyroidism	2 (4.3%)	–	2 (6.7%)	0	–
Hypothyroidism	11 (23.4%)	–	7 (23.3%)	4 (23.5%)	–
Vitiligo	1 (2.1%)	–	1 (3.3%)	0	–
None	27 (57.4%)	–	18 (60.0%)	9 (52.9%)	–
I don't know	3 (6.4%)	–	2 (6.7%)	1 (5.9%)	–
Family member with an autoimmune condition					
Celiac disease	4 (8.5%)	–	2 (6.7%)	2 (11.8%)	–
Addison's disease	0	–	0	0	–
Hyperthyroidism	4 (8.5%)	–	2 (6.7%)	2 (11.8%)	–
Hypothyroidism	11 (23.4%)	–	8 (26.7%)	3 (17.6%)	–
Juvenile rheumatoid arthritis	2 (4.3%)	–	1 (3.3%)	1 (5.9%)	–
Rheumatoid arthritis	4 (8.5%)	–	3 (10.0%)	1 (5.9%)	–
Vitiligo	2 (4.3%)	–	1 (3.3%)	1 (5.9%)	–
Sjögren's syndrome	2 (4.3%)	–	1 (3.3%)	1 (5.9%)	–
Systemic lupus erythematosus	2 (4.3%)	–	1 (3.3%)	1 (5.9%)	–
None	23 (48.9%)	–	15 (50.0%)	8 (47.1%)	–
I don't know	4 (8.5%)	–	2 (6.7%)	2 (11.8%)	–
Informed may have another type of diabetes[f]					
Yes	20 (42.6%)	–	17 (56.7%)	3 (17.6%)	–
No	27 (57.4%)	–	13 (43.3%)	14 (82.4%)	–
If yes	*N* = 20	–	*N* = 17	*N* = 3	–
T2D	17 (85.0%)	–	14 (82.4%)	3 (100.0%)	–
Gestational diabetes	2 (10.0%)	–	2 (11.8%)	0	–
Other	1 (5.0%)	–	1 (5.9%)	0	–
Missing/not asked	27	–	13	14	–
Time to figure out you (or the child you care for) did not have another type of diabetes[g]	*N* = 20	–	*N* = 17	*N* = 3	–
<6 months	12 (60.0%)	–	10 (58.8%)	2 (66.7%)	–
6–12 months	4 (20.0%)	–	3 (17.6%)	1 (33.3%)	–
>12 months	2 (10.0%)	–	2 (11.8%)	0	–
I don't know	2 (10.0%)	–	2 (11.8%)	0	–
Missing/not asked	27	–	13	14	–

(Continues)

TABLE 1 (Continued)

Parameter, *n* (%)	All individuals receiving teplizumab *N* = 47	All respondents *N* = 47	Adult respondents *N* = 30	Children receiving teplizumab *N* = 17	Caregiver respondents *N* = 17
Use of medications for diabetes other than teplizumab					
Yes	16 (34.0%)	–	12 (40.0%)	4 (23.5%)	–
No	31 (66.0%)	–	18 (60.0%)	13 (76.5%)	–
Medications for diabetes other than teplizumab	*N* = 16		*N* = 12	*N* = 4	
OADs to lower blood glucose	10 (62.5%)	–	9 (75.0%)	1 (25.0%)	–
Insulin	9 (56.3%)	–	5 (41.7%)	4 (100.0%)	–
Injectable GLP-1 RA	1 (6.3%)	–	1 (8.3%)	0	–
Other/I don't know	0	–	0	0	–
Missing/not asked	31	–	18	13	–
How good/bad is your health today, EQ-5D-5L[h,i]					
Mean (SD)	–	79.09 (13.37)	79.33 (11.67)	–	78.65 (16.34)
Median	–	80.0	80.0	–	82.0
Min/Max	–	46.0/100.0	46.0/99.0	–	50.0/100.0
EQ-5D-5L index (US)[j]					
Mean (SD)	–	0.92 (0.12)	0.93 (0.08)	–	0.91 (0.17)
Median	–	0.943	0.943	–	0.943
Min/Max	–	0.29/1.00	0.65/1.00	–	0.29/1.00

Note: Data reported in the above table are not an exhaustive list of the options available to respondents to select as answers. Some zero-response values are omitted. Missing/not asked data are included only if non-zero.

Abbreviations: GED, general educational development; GLP-1 RA, glucagon-like peptide-1 receptor agonist; Max, maximum; Min, minimum; *N*, number of observations; OAD, oral antidiabetes drug; SD, standard deviation; T1D, type 1 diabetes; T2D, type 2 diabetes.

[a]Full-time was defined as 40+ h per week; part-time <40 h per week.

[b]Private carriers including Kaiser, Aetna, Blue Shield, etc.

[c]Private carriers through job, school or the Affordable Care Act/Healthcare.gov.

[d]Medicare, Medicaid, California Children's Services, Massachusetts Health, Children's Health Insurance Program, etc.

[e]First-degree relatives would include mothers, fathers, siblings; while second-degree relatives would include grandparents, aunts, uncles, cousins, nieces, nephews, half-siblings, for example. Multiple response options were permitted.

[f]The full question was, 'Before being told you were in early stages of type 1 diabetes, has a doctor ever told you they thought you (or the child you care for) may have another type of diabetes?'

[g]The full question was, 'How long did it take for your doctor to figure out you (or the child you care for) did not have that type of diabetes?' This was a follow-up question to the question in footnote 'f'.

[h]Visual analogue scale based on 100-point scale anchored at 0 ('the worst health you can imagine') and 100 ('the best health you can imagine').

[i]Participants assessed five dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression) using a 5-point Likert scale ranging from 'no problems' to 'extreme problems'; these responses collectively formed a health state. For each health state, an index value was assigned representing the country-specific utility value (to allow for calculations of quality-adjusted life years; in this survey, the US-based value set was utilized, ranging from −0.573 to 1, where 1 is 'perfect health,' 0 is 'death,' and <0 represents 'worse than death' using societal preference weights).[9] For the EQ-5D-5L, participants also rated their own health along a 100-point scale anchored at 0 ('the worst health you can imagine') and 100 ('the best health you can imagine').

[j]Health Utility Indexes range from −0.573 (worse than death) to 1 (perfect health).

More than half of adult respondents had been told they may have another type of diabetes, most often type 2 diabetes (T2D), before they were told they were in the early stages of T1D. This was less common among children (Table 1). Notably, respondents with a family history of T1D were less likely to be told they had another type of diabetes, with 78.6% (11/14) of adults and 30.0% (3/10) of children lacking family history of T1D being told they may have another type of diabetes, compared to 37.5% (6/16) of adults and 0 (0/7) children with family history of T1D.

3.2 | Respondents' experience with T1D screening and the decision to screen

There were varying degrees of knowledge about screening for T1D autoantibodies across respondents, including by family history of T1D or participant type (adult vs. caregiver). Among caregivers, 58.8% (10/17) agreed or strongly agreed with the statement 'I was aware I could get screened for T1D before I chose to do so', which was higher than the percentage of adults who agreed or strongly agreed (26.7%

TABLE 2 Respondents' experience leading up to teplizumab treatment.

Parameter, *n* (%)	All respondents *N* = 47	Adult respondents *N* = 30	Caregiver respondents *N* = 17
How long has it been since you/your child have been treated?			
<3 months	18 (38.3%)	12 (40.0%)	6 (35.3%)
3–6 months	15 (31.9%)	12 (40.0%)	3 (17.6%)
7–12 months	14 (29.8%)	6 (20.0%)	8 (47.1%)
>12 months	0	0	0
What was the main way you learned about teplizumab? Please pick all that apply			
Child's doctor	14 (29.8%)	1 (3.3%)	13 (76.5%)
My doctor	24 (51.1%)	23 (76.7%)	1 (5.9%)
Social media	5 (10.6%)	3 (10.0%)	2 (11.8%)
Mainstream media/magazine	2 (4.3%)	1 (3.3%)	1 (5.9%)
Other	7 (14.9%)	4 (13.3%)	3 (17.6%)
What kind of doctor prescribed teplizumab to you (or your child)?			
Paediatrician	0	0	0
Primary care provider/general practitioner	1 (2.1%)	1 (3.3%)	0
Adult endocrinologist	22 (46.8%)	22 (73.3%)	0
Paediatric endocrinologist	21 (44.7%)	4 (13.3%)	17 (100.0%)
Nurse practitioner or physician assistant	2 (4.3%)	2 (6.7%)	0
I don't know	1 (2.1%)	1 (3.3%)	0
Before teplizumab, how worried were you that you/your child would not tolerate the medication?			
Very worried	12 (25.5%)	7 (23.3%)	5 (29.4%)
A little worried	33 (70.2%)	22 (73.3%)	11 (64.7%)
Not worried at all	2 (4.3%)	1 (3.3%)	1 (5.9%)

Note: Data reported in the above table are not an exhaustive list of the options available to respondents to select as answers. Some zero-response values are omitted. All questions presented in this table were answered by all participants. There are no missing data.

[8/30], $p = 0.031$; Table S2). For the same statement, 52.2% (12/23) of respondents reporting a family history of T1D agreed or strongly agreed that they were aware, compared with only 25.0% (6/24) of those without a family history of T1D ($p = 0.053$). Respondents reporting a family history of T1D were generally more likely than those without a family history of the disease to have knowledge and awareness surrounding screening through a research study (34.8% [8/23] vs. 4.2% [1/24], $p = 0.009$) or knowledge about T1D through friends and family (82.6% [19/23] vs. 20.8% [5/24], $p < 0.0001$). Caregivers were more likely than adults to have knowledge regarding screening through a research study (35.3% [6/17] vs. 10.0% [3/30], $p = 0.044$) but were not more likely than adults to have knowledge through family and friends (58.8% [10/17] vs. 46.7% [14/30], $p = 0.310$; Table S2). Recommendations to screen for both adult and child participants typically came from an endocrinologist (27.7% adult endocrinologist [13/47], 21.3% paediatric endocrinologist [10/47]), with infrequent recommendations from paediatricians and adult primary care providers and some respondents deciding to get screened on their own (Table S3). Screening among adults was most often prescribed through a doctor's office (30.0%, 9/30), whereas in the paediatric setting it was most often prescribed in the hospital or doctor's office (7/17 respondents each, 41.2%) (Table S3). When asked about reasons for screening for T1D, most respondents endorsed the chance at more time before they or their child got T1D and wanting to know their risk for T1D as 'important' or 'very important' (Figure 1; Table S4). Additional reasons that more than half the respondents endorsed as 'important' or 'very important' in deciding to screen for T1D included wanting to contribute to T1D research and being worried about diabetic ketoacidosis (Figure 1; Table S4). Notably, less than a quarter of participants endorsed wanting time to learn about T1D before being diagnosed as an 'important' or 'very important' reason in their decision to screen for T1D.

3.3 | Views and expectations associated with teplizumab

3.3.1 | Pre-treatment

Most respondents learned about teplizumab through their doctor, and physicians prescribing teplizumab were generally endocrinologists (Table 2). When asked about their feelings on how worried they were that they or their child would not tolerate the medication, most respondents reported feeling 'a little worried', with fewer being 'very

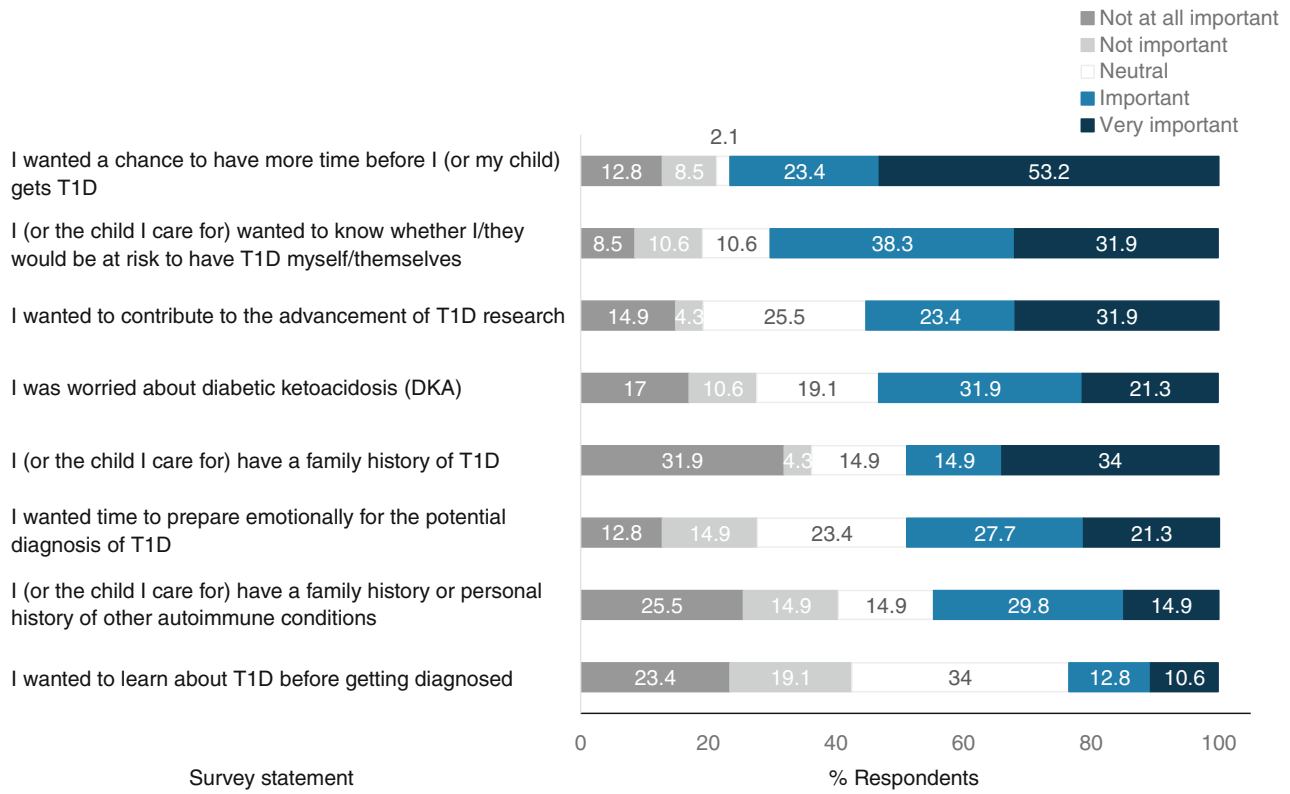

FIGURE 1 Respondents' reasons behind the decision to get screened for type 1 diabetes (T1D).* The percent respondents ($N = 47$ total, both adults and caregiver respondents are plotted) rating their feelings towards the plotted statement pertaining to their decision to get screened for T1D as very important, important, neutral, not important or not at all important are shown here. *All questions presented in this figure were answered by all participants. There are no missing data.

worried' about how they would tolerate teplizumab (Table 2). Despite this, over half of respondents reported that they 'agreed' or 'strongly agreed' that the decision to take teplizumab was easy (19.1% [9/47] disagreed and 4.3% [2/47] strongly disagreed) (Figure 2; Table S5).

3.3.2 | Post-treatment

A vast majority endorsed that they 'agreed' or 'strongly agreed' with the statement 'I am glad I (or my child) did the teplizumab infusion', and likewise most reported that they 'agreed' or 'strongly agreed' that they would recommend teplizumab to others in their situation (Figure 2; Table S5). Although most respondents were glad about their decision to take teplizumab, participants reported continued concern and worry about developing T1D. Most participants reported that they 'disagreed' or 'strongly disagreed' with the statements 'I think less about my (or the child I care for) blood glucose' (74.5%, 35/47), 'I worry less about what I (or the child) is eating' (68.1%, 32/47), 'I am less worried about (me or the child I care for) getting T1D' (63.8%, 30/47), 'I think less about diabetes' (61.7%, 29/47) and 'I check my (or the child I care for) blood glucose less often' (61.7%, 29/47) (Table S6). Nonetheless, almost a third (31.9%, 15/47) of respondents reported they 'agreed' or 'strongly agreed' with the statement 'I feel more relaxed', whereas 23.4% (11/47) disagreed and 6.4% (3/47) strongly disagreed. Interestingly, more caregivers were in agreement with this statement (52.9%, 9/17) compared to adults who received teplizumab (20.0%, 6/30). A greater percentage of caregivers endorsed they 'agreed' or 'strongly agreed' with the statement 'My (or the child I care for) blood glucose has improved' compared to adults (52.9% [9/17] of caregivers vs. 33.3% [10/30] of adults) (Table S6). Most respondents were grateful for the opportunity to receive teplizumab—41/47 (87.2%) respondents ranked the statement with an 8 or higher on a scale of 1–10, with 10 being they 'feel this way a lot', and 31/47 (66.0% of the total respondents) ranking it a 10 (Table S7). Insulin treatment post-teplizumab is shown in Table S8.

3.3.3 | Monitoring for disease progression

Most individuals were monitoring their glucose after receiving teplizumab, primarily with continuous glucose monitoring (CGM; 59.6% [28/47] currently used CGM all the time, 17.0% [8/47] used it some of the time; Table S9). Those not using CGM were typically using doctor-ordered tests to check their average blood glucose over the past few months (HbA1c) (72.7% of those not using CGM, 8/11 respondents). Most respondents (83.0%, 39/47) agreed/strongly agreed they take comfort knowing their/their child's blood glucose levels, with almost half (48.9%, 23/47) agreeing/strongly agreeing that

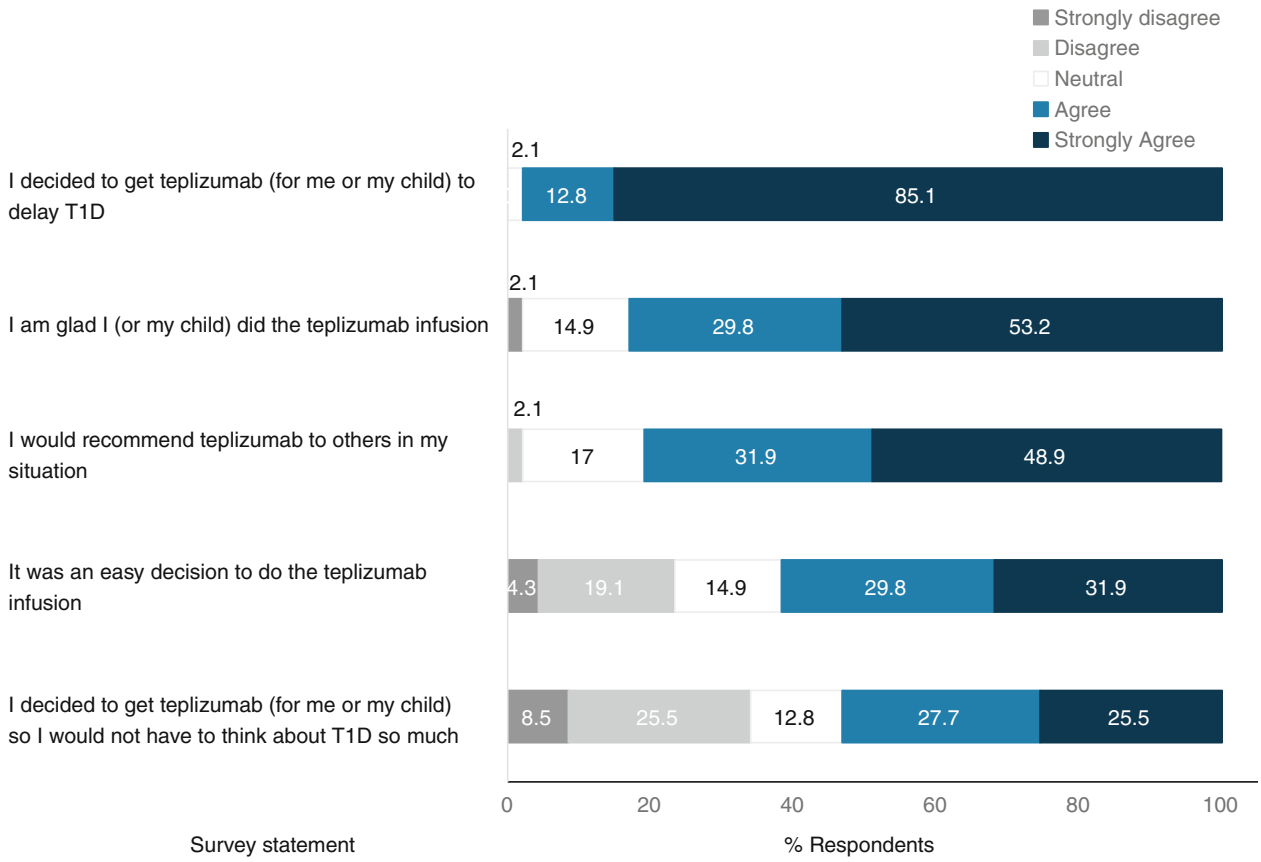

FIGURE 2 Views and expectations associated with teplizumab.* The percent respondents ($N = 47$ total, both adults and caregiver respondents are plotted) that strongly agreed, agreed, felt neutral about, disagreed or strongly disagreed with the plotted statement pertaining to their views and expectations about teplizumab are shown here. *All questions presented in this figure were answered by all participants. There are no missing data. T1D, type 1 diabetes.

they monitored their blood glucose more often than asked to by their physician, especially in adult respondents (Table S10).

When individuals/caregivers were asked about their current outlook towards T1D prognosis, most respondents believed that they would still get clinical Stage 3 T1D eventually, and a majority of respondents endorsed that they 'agreed' or 'strongly agreed' that teplizumab would delay when they or their child would get clinical Stage 3 T1D (4.3% disagreed and 4.3% strongly disagreed, 2/47 each) and more than half endorsed that they 'agreed' or 'strongly agreed' it would make the disease easier to manage (8.5% [4/47] disagreed and 4.3% [2/47] strongly disagreed; Figure 3; Table S11). All respondents endorsed they 'agreed' or 'strongly agreed' that they would keep seeing their doctor for their T1D, and almost all reported that they 'agreed' or 'strongly agreed' that they would make the same decision in the future about teplizumab should another family member need treatment.

4 | DISCUSSION

Despite impressive advancements in insulin therapies and technology (i.e., insulin delivery systems and glucose monitoring), clinical T1D remains a burdensome disease for individuals and caregivers. The impact of this disease is reflected by the ubiquity of diabetes distress among respondents, which describes the expected emotional reaction to the burden of living with and managing a chronic disease like T1D. Given the challenges in managing T1D, the potential to prevent or delay disease onset is a paradigm shift in approaching this condition. Teplizumab represents the first opportunity to treat the underlying autoimmune mechanism of T1D, as opposed to its metabolic consequences.[6]

This survey represents the first direct capture of the perspectives of individuals or caregivers of those treated with teplizumab. Overall, survey respondents endorsed delaying clinical T1D onset as an important determinant in the decision to screen for T1D and pursue teplizumab therapy. Importantly, approximately half of caregivers reported feeling more relaxed since their child's treatment with teplizumab. A possible explanation for this is that pre-symptomatic T1D is often experienced as unpredictable and uncontrollable; treatment with teplizumab may provide some sense of control in a situation perceived as largely outside of one's control. When caregivers were asked if they feel they have more control over T1D, more participants felt this way than not (Table S7). However, following teplizumab therapy, anxiety and worry about developing T1D remained high; individuals in

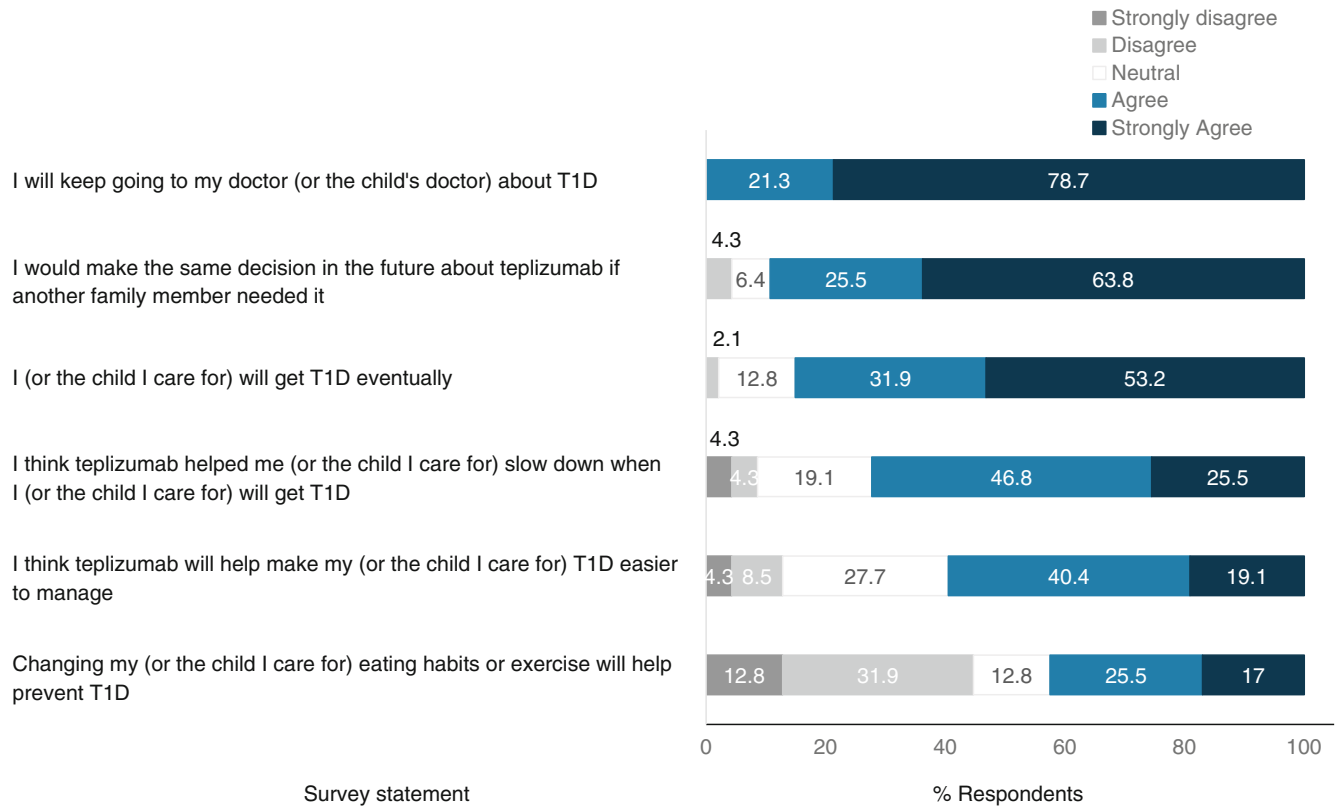

FIGURE 3 Respondents' current outlook and views on disease prognosis.* The percent respondents ($N = 47$ total, both adults and caregiver respondents are plotted) that strongly agreed, agreed, felt neutral about, disagreed or strongly disagreed with the plotted statement pertaining to their current outlook and views towards disease prognosis are shown here. *All questions presented in this figure were answered by all participants. There are no missing data. T1D, type 1 diabetes.

pre-symptomatic stages of T1D continued to wonder when they would progress to clinical disease and remained vigilant with glucose monitoring post-teplizumab therapy. Despite respondents remaining worried about progression to Stage 3 T1D, most were highly satisfied with their decision to be treated (or have their child treated) with teplizumab. Furthermore, most felt teplizumab would not only delay T1D progression but also would ease clinical management. These survey findings delineate important areas of discussion for healthcare providers to have with potential teplizumab recipients.

The characteristics of individuals in this study are consistent with known risk factors for T1D,[10–16] and the representation of both adults and children is consistent with the fact that pre-symptomatic T1D may occur at any age.[17–19] In this survey, consistent with what has been reported in the literature,[20] 46.7% (14/30) of adults were initially told they may have T2D. This initial misdiagnosis may have delayed the correct diagnosis of half of the adults in this survey and supports the recommendation that islet cell autoantibodies should be utilized by providers to distinguish stage 2 T1D from pre-T2D in people with glucose abnormalities. Likewise, in the present study, having a medical and/or family history of other autoimmune diseases and family history of T1D was common, which in clinical practice may help identify individuals at risk for T1D.[10–16] Individuals with other autoimmune diseases likely had a unique perspective towards screening and treatment, as they were not new to the medical system or to monitoring their health. Therefore, medical history and family history may have played a role in a respondent's decision to screen for T1D or take teplizumab.

Medical and family history of autoimmune disease may also have played a part in individuals seeking care from endocrinologists. In the present study, recommendations for T1D screening more commonly came from specialists than primary care providers. Endocrinologists are well positioned to recommend T1D screening for those in their care with other autoimmune diseases and to family members of individuals with T1D or other autoimmune diseases. However, primary care providers have access to greater numbers of individuals who may benefit from T1D screening given that ~90% of those with new-onset clinical T1D do not have a first-degree relative with the disease.[21,22] Therefore, awareness of the mechanics, benefits and interpretation of results related to screening among primary care providers should be improved so that more individuals are correctly identified in the pre-symptomatic stages of T1D and have the chance to delay clinical T1D onset and preserve beta-cell function.

There are limitations and strengths of this study. First, 47 participants is a relatively small group (~10% of people who have been treated with teplizumab through the end of 2024) and it is possible that the characteristics of the sample are not representative of those who have received teplizumab outside of a clinical trial. As more individuals are able to access this disease-modifying therapy, it will be important

to re-examine characteristics. Second, the demographics of the sample are not consistent with what is known about individuals who develop T1D. This may limit the generalizability of the views expressed in this study. Specifically, there was a higher proportion of adult females (60.0%, 18/30) treated with teplizumab than adult males (40.0%, 12/30); however, in adults, the incidence of T1D has been found to be somewhat higher in males.[23] Most caregivers were female (88.2%, 15/17) as well; the higher proportion of female respondents overall is consistent with females being more likely to respond to surveys and with the high proportion of hypothyroidism in this study.[24,25] Furthermore, all of the individuals in this study were White, which represents a limitation given T1D occurs across races,[26] and respondents tended to have a high socioeconomic status. Therefore, the views of male caregivers or those with greater socioeconomic burden were largely not represented. These demographic factors should be considered when interpreting the results of this survey, as a high level of education and access to private insurance may have influenced decisions regarding treatment. Similarly, individuals who were actively worried about and monitoring their/their child's disease may have been more highly motivated to respond to the survey. Notably, the full demographics and characteristics (outside of age and gender) of those people invited to the survey that did not respond cannot be compared in this analysis, given they did not answer the survey or provide consent for participation. Third, this study asked participants to reflect on their experience and report thoughts and feelings retrospectively, which could introduce bias as participants' recall may be influenced by their current feelings after receiving teplizumab. Also, the survey did not ask whether caregivers had T1D themselves. Based on responses, 6/17 (35.3%) children had first-degree relatives with T1D. If we assume that caregivers were first-degree relatives (which is not guaranteed), then at least 11/17 (64.7%) caregivers did not have T1D. Additionally, the survey was not sent at a standardized timepoint after teplizumab infusion. While most respondents reported having received teplizumab in the last 3 months, levels of worry could potentially change over time. Although the study only utilized one validated patient-reported outcome (EQ-5D-5L), this survey was designed intentionally to obtain descriptive views and experiences of individuals specifically receiving teplizumab. Strengths of the study included the high percentage (40.5%, 47/116) of respondents among individuals who were invited to participate compared to other online surveys[27–29] and the low amount of missing data. Planned publications will more precisely explore and understand individuals' experiences with insulin usage and other diabetes medications pre- and post-teplizumab treatment. Future studies are needed to further assess patient-reported outcomes from the teplizumab treatment and to compare the perspectives of those treated with teplizumab to those not treated with teplizumab.

In conclusion, this survey provided the first chance to capture the perspectives of individuals who received teplizumab clinically to delay onset of Stage 3 T1D, some of whom were initially misdiagnosed with T2D. Based on the responses, an important talking point for healthcare providers when discussing T1D screening is the possibility to delay Stage 3 T1D clinical onset. Healthcare providers may also wish to discuss how individuals who have received teplizumab have reported a positive outlook regarding the disease following treatment, with most expressing they thought teplizumab would delay progression to Stage 3 and make their T1D easier to manage. Furthermore, most were glad they had received teplizumab and would recommend it to others in their situation, but remained anxious about when they might progress to Stage 3. These real-world findings are the first to demonstrate the value of teplizumab treatment from the perspectives of adults and caregivers of those who have received the treatment, which can guide physicians in discussions with individuals in their care who may benefit from T1D screening or teplizumab treatment.

AUTHOR CONTRIBUTIONS

Design: Holly K. O'Donnell, Korey K. Hood, Kimber M. Simmons, Terry Dex, Mattias Wieloch and Julia Zaccai. Conduct/data collection: France Ginchereau Sowell and James Turnbull. Analysis: Robert Hill and Jennifer D'Souza. Writing manuscript: Holly K. O'Donnell, Kimber M. Simmons, Stephen E. Gitelman, Terry Dex, Robert Hill, Mattias Wieloch, Julia Zaccai, Jennifer D'Souza, France Ginchereau Sowell, James Turnbull and Korey K. Hood.

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CONFLICT OF INTEREST STATEMENT

Holly K. O'Donnell has served on an advisory board and as a consultant for Sanofi, and has received support from the National Institutes of Health (NIH), Breakthrough T1D and The Helmsley Charitable Trust for research studies. Kimber M. Simmons has served on advisory boards for Provention Bio, Sanofi and Shoreline Biosciences and has received support from the NIH and Provention Bio for roles as an investigator in clinical trials. Stephen E. Gitelman has served on advisory boards for Abata Therapeutics, Genentech, GentiBio, Provention Bio, SAB Biotherapeutics, Sana Biotechnology, Sanofi and Shoreline Biosciences; has received support from the NIH, Provention Bio and Sanofi for roles as an investigator in clinical trials; and serves on data and safety monitoring boards for Diamyd Medical, Breakthrough T1D and INNODIA. Terry Dex, Mattias Wieloch and Julia Zaccai are employees of Sanofi and may hold stock in Sanofi. Robert Hill is an employee of Cytel and was on contract with Sanofi at the time of this study. Jennifer D'Souza, France Ginchereau Sowell and James Turnbull are employees of IQVIA and may hold stock in IQVIA. Korey K. Hood has received consulting fees from Sanofi, Havas Health and MannKind and received a research grant from Embecta.

PEER REVIEW

The peer review history for this article is available at https://www.webofscience.com/api/gateway/wos/peer-review/10.1111/dom.16246.

DATA AVAILABILITY STATEMENT

Qualified researchers may request access to data. Further details on Sanofi's data sharing criteria, eligible studies and process for requesting access can be found at: https://www.vivli.org/.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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