



## Clinical trial results: Exploring Immune Effects of Oral Insulin in Relatives at Risk for Type 1 Diabetes Mellitus

### Summary

EudraCT number	2016-001923-30
Trial protocol	IT
Global end of trial date	13 March 2018

### Results information

Result version number	v1 (current)
This version publication date	14 August 2025
First version publication date	14 August 2025
Summary attachment (see zip file)	TN20.I.04.Adverse Event Summary Report (TN20.I.04.Adverse Event Summary Report.rtf)

### Trial information

#### Trial identification

Sponsor protocol code	TN-20
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02580877
WHO universal trial number (UTN)	-
Other trial identifiers	IND: 76419

Notes:

### Sponsors

Sponsor organisation name	TrialNet
Sponsor organisation address	3650 Spectrum Boulevard, Suite 100, Tampa, United States, 33612
Public contact	Erica Perri, TrialNet Coordinating Center, 813 3969543, erica.perri@epi.usf.edu
Scientific contact	Erica Perri, TrialNet Coordinating Center, 813 39669543, erica.perri@epi.usf.edu

Notes:

### Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 March 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 March 2018
Global end of trial reached?	Yes
Global end of trial date	13 March 2018
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the immune response to oral insulin in individuals at risk for type 1 diabetes, in order to determine whether it can modulate the autoimmune process that leads to the disease.

Protection of trial subjects:

The DSMB met regularly during the study and reviewed safety and related information.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 January 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Italy: 4
Country: Number of subjects enrolled	Australia: 6
Country: Number of subjects enrolled	United States: 79
Country: Number of subjects enrolled	Canada: 3
Worldwide total number of subjects	92
EEA total number of subjects	4

Notes:

### Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	75
Adolescents (12-17 years)	13
Adults (18-64 years)	4
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Participants were recruited from the TrialNet Natural History Study (TN01) and thus a relative of a proband with T1D..

### Pre-assignment

Screening details:

The initial testing for mIAA and other autoantibodies were done as part of TN01 screening. Those individuals who were mIAA positive were eligible for additional tests (OGTT) as part of TN01 Monitoring visit or this protocol as applicable.

### Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Oral Insulin daily (67.5 mg)

Arm description:

7.5 mg oral insulin crystals in capsules (by mouth or sprinkled on food) given daily for six months

67.5 mg oral insulin crystals daily: human insulin crystals in capsules

Arm type	Experimental
Investigational medicinal product name	Oral Insulin Crystals
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

67.5 mg oral insulin crystals in capsules (by mouth or sprinkled on food) given daily for six months

67.5 mg oral insulin crystals daily: human insulin crystals in capsules

<b>Arm title</b>	500 mg oral Insulin every other week
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Arm description:

500 mg oral insulin crystals in capsules (by mouth or sprinkled on food) given every other week for six months

Arm type	Experimental
Investigational medicinal product name	Oral Insulin Crystals
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

500 mg oral insulin crystals every other week: human insulin crystals in capsules (by mouth or sprinkled on food)

<b>Number of subjects in period 1</b>	Oral Insulin daily (67.5 mg)	500 mg oral Insulin every other week
Started	45	47
Completed	44	43
Not completed	1	4
Consent withdrawn by subject	1	3
Adverse event, non-fatal	-	1

## Baseline characteristics

### Reporting groups

Reporting group title	Oral Insulin daily (67.5 mg)
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Reporting group description:

7.5 mg oral insulin crystals in capsules (by mouth or sprinkled on food) given daily for six months

67.5 mg oral insulin crystals daily: human insulin crystals in capsules

Reporting group title	500 mg oral Insulin every other week
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Reporting group description:

500 mg oral insulin crystals in capsules (by mouth or sprinkled on food) given every other week for six months

Reporting group values	Oral Insulin daily (67.5 mg)	500 mg oral Insulin every other week	Total
Number of subjects	45	47	92
Age categorical			
Units: Subjects			
Children (2-11 years)	38	37	75
Adolescents (12-17 years)	6	7	13
Adults (18-64 years)	1	3	4
Age continuous			
Units: years			
median	8.9	7.9	
inter-quartile range (Q1-Q3)	3.8 to 28.1	3.0 to 43.6	-
Gender categorical			
Units: Subjects			
Female	20	21	41
Male	25	26	51
Relationship to person with type 1 diabetes			
Units: Subjects			
Sibling	34	29	63
Parent	6	12	18
Child	1	2	3
Other	4	4	8
Glucose Tolerance			
Units: Subjects			
Normal Glucose Tolerance	36	36	72
Abnormal Glucose Tolerance	9	11	20
HLA DR3			
Units: Subjects			
Absent	31	27	58
Present	14	19	33
Unknown	0	1	1
HLA DR4			
Units: Subjects			
Absent	22	15	37
Present	23	31	54
Unknown	0	1	1



## End points

### End points reporting groups

Reporting group title	Oral Insulin daily (67.5 mg)
Reporting group description: 7.5 mg oral insulin crystals in capsules (by mouth or sprinkled on food) given daily for six months	
67.5 mg oral insulin crystals daily: human insulin crystals in capsules	
Reporting group title	500 mg oral Insulin every other week
Reporting group description: 500 mg oral insulin crystals in capsules (by mouth or sprinkled on food) given every other week for six months	

### Primary: Change in GAD65 Autoantibody Titer

End point title	Change in GAD65 Autoantibody Titer <sup>[1]</sup>
End point description: Change in autoantibody (GAD65) biomarker of beta cell specific immune response	
End point type	Primary
End point timeframe: 13 and 26 weeks after first dose versus baseline	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analysis is available. The mean change in autoantibody titer was calculated individually for each treatment arm. The two treatment arms were not compared.

End point values	Oral Insulin daily (67.5 mg)	500 mg oral Insulin every other week		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	47		
Units: DK Units/mL				
log mean (confidence interval 95%)				
13 weeks	247 (168 to 363)	234 (138 to 396)		
26 weeks	193 (118 to 313)	196 (121 to 318)		

### Statistical analyses

No statistical analyses for this end point

### Primary: Change in MIAA Autoantibody Titer From Baseline

End point title	Change in MIAA Autoantibody Titer From Baseline <sup>[2]</sup>
End point description: Micro-islet autoantibodies (mIAA) autoantibody titers are a measure of of beta cell immune response	
End point type	Primary

End point timeframe:

13 and 26 weeks after first dose versus baseline

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analysis is available. The mean change in autoantibody titer was calculated individually for each treatment arm. The two treatment arms were not compared.

End point values	Oral Insulin daily (67.5 mg)	500 mg oral Insulin every other week		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	47		
Units: DK Units/mL				
log mean (confidence interval 95%)				
13 weeks	0.021 (0.016 to 0.028)	0.020 (0.015 to 0.028)		
26 weeks	0.020 (0.015 to 0.028)	0.017 (0.013 to 0.023)		

## Statistical analyses

No statistical analyses for this end point



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected over 1 year

Adverse event reporting additional description:

Additional information regarding all adverse event can be found in the attached document labeled TN20.I.04.Adverse Event Summary Report .

Assessment type	Systematic
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### Dictionary used

Dictionary name	CTCAE
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Dictionary version	4
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### Reporting groups

Reporting group title	Oral Insulin daily (67.5 mg)
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Reporting group description:

67.5 mg oral insulin crystals in capsules (by mouth or sprinkled on food) given daily for six months

67.5 mg oral insulin crystals daily: human insulin crystals in capsules

Reporting group title	500 mg oral Insulin every other week
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Reporting group description:

500 mg oral insulin crystals in capsules (by mouth or sprinkled on food) given every other week for six months

Serious adverse events	Oral Insulin daily (67.5 mg)	500 mg oral Insulin every other week	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Oral Insulin daily (67.5 mg)	500 mg oral Insulin every other week	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	25 / 45 (55.56%)	24 / 47 (51.06%)	
Surgical and medical procedures			
Surgical and medical procedures subjects affected / exposed	3 / 45 (6.67%)	1 / 47 (2.13%)	
occurrences (all)	4	1	
General disorders and administration site conditions			

Fever			
subjects affected / exposed	4 / 45 (8.89%)	1 / 47 (2.13%)	
occurrences (all)	6	1	
flu-like symptoms			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
General disorders and administrative site conditions			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Immune system disorders			
Allergic reaction			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Anaphylaxis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Menorrhagia			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Allergic rhinitis			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Bronchospasm			
subjects affected / exposed	2 / 45 (4.44%)	0 / 47 (0.00%)	
occurrences (all)	2	0	
Cough			
subjects affected / exposed	4 / 45 (8.89%)	1 / 47 (2.13%)	
occurrences (all)	4	1	
Nasal congestion			
subjects affected / exposed	1 / 45 (2.22%)	1 / 47 (2.13%)	
occurrences (all)	1	2	
Productive cough			

subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Sore throat			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Psychiatric disorders			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Investigations			
Neutrophil count decreased			
subjects affected / exposed	4 / 45 (8.89%)	4 / 47 (8.51%)	
occurrences (all)	7	8	
White blood cell decreased			
subjects affected / exposed	1 / 45 (2.22%)	1 / 47 (2.13%)	
occurrences (all)	2	1	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			

Blood and lymphatic system disorders subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1	0 / 47 (0.00%) 0	
Ear and labyrinth disorders Ear and labyrinth disorders subjects affected / exposed occurrences (all)  Middle ear inflammation subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0  0 / 45 (0.00%) 0	1 / 47 (2.13%) 1  4 / 47 (8.51%) 5	
Eye disorders Conjunctivitis subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	1 / 47 (2.13%) 1	
Gastrointestinal disorders Diarrhea subjects affected / exposed occurrences (all)  Gastrointestinal disorders subjects affected / exposed occurrences (all)  Gastrointestinal pain subjects affected / exposed occurrences (all)  Toothache subjects affected / exposed occurrences (all)  Vomiting subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0  1 / 45 (2.22%) 1  0 / 45 (0.00%) 0  1 / 45 (2.22%) 1  4 / 45 (8.89%) 4	1 / 47 (2.13%) 1  1 / 47 (2.13%) 1  1 / 47 (2.13%) 1  0 / 47 (0.00%) 0  2 / 47 (4.26%) 2	
Skin and subcutaneous tissue disorders Skin and subcutaneous tissue disorders subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1	1 / 47 (2.13%) 1	
Endocrine disorders			

Endocrine disorders subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 2	0 / 47 (0.00%) 0	
Hypothyroidism subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1	0 / 47 (0.00%) 0	
Musculoskeletal and connective tissue disorders Myalgia subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1	0 / 47 (0.00%) 0	
Infections and infestations Bronchial infection subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1	1 / 47 (2.13%) 1	
Infections and infestations subjects affected / exposed occurrences (all)	4 / 45 (8.89%) 5	2 / 47 (4.26%) 2	
Lung infection subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	1 / 47 (2.13%) 2	
Otitis externa subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	1 / 47 (2.13%) 1	
Otitis media subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1	2 / 47 (4.26%) 2	
Pharyngitis subjects affected / exposed occurrences (all)	7 / 45 (15.56%) 10	2 / 47 (4.26%) 2	
Sinusitis subjects affected / exposed occurrences (all)	4 / 45 (8.89%) 5	0 / 47 (0.00%) 0	
Soft tissue infection subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	1 / 47 (2.13%) 1	
Tooth infection			

subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1	0 / 47 (0.00%) 0	
Upper respiratory infection subjects affected / exposed occurrences (all)	3 / 45 (6.67%) 3	2 / 47 (4.26%) 2	
Metabolism and nutrition disorders Metabolism and nutrition disorders subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	1 / 47 (2.13%) 1	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported