



Clinical trial results:

Fr1da Insulin Intervention - Mechanistic study using oral insulin for immune and treatment efficacy in secondary prevention of type 1 diabetes

Summary

| | |
|--------------------------|-------------------|
| EudraCT number | 2015-003028-30 |
| Trial protocol | DE |
| Global end of trial date | 30 September 2024 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 11 February 2026 |
| First version publication date | 11 February 2026 |

Trial information

Trial identification

| | |
|-----------------------|-----------|
| Sponsor protocol code | 808040019 |
|-----------------------|-----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02620072 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Technical University Munich, School of Medicine |
| Sponsor organisation address | Ismaninger Str. 22, Munich, Germany, 81675 |
| Public contact | Univ.-Prof. Dr. Anette-G. Ziegler, Forschergruppe Diabetes, Klinikum rechts der Isar, Technische Universität München, +49 8931872896, anette-g.ziegler@helmholtz-muenchen.de |
| Scientific contact | Univ.-Prof. Dr. Anette-G. Ziegler, Forschergruppe Diabetes, Klinikum rechts der Isar, Technische Universität München, +49 8931872896, anette-g.ziegler@helmholtz-muenchen.de |

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? | No |

Notes:

Results analysis stage

| | |
|--|-------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 22 May 2025 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 30 September 2024 |
| Global end of trial reached? | Yes |
| Global end of trial date | 30 September 2024 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To determine the immune efficacy, and treatment efficacy of daily high dose oral insulin (up to 67.5 mg) in children aged 2 years to 12 years with multiple islet autoantibodies in a secondary intervention study. Immune efficacy is defined as a change in the immune response to the treatment, which is associated with a reduction in the progression to dysglycemia or diabetes. Treatment efficacy is a treatment related reduction in the rate of progression to dysglycemia or diabetes.

Protection of trial subjects:

- Blood glucose, insulin and c-peptide values were measured before and 30, 60, and 120 minutes after study drug was administered during the baseline and 3 month visit. Capillary blood glucose was measured with a glucose meter. Families were instructed to report suspected hypoglycemic events
- Systematic adverse event (AE) assessment at all study visits
- Allergy surveillance: parents instructed to monitor and report signs of allergic reactions (e.g. conjunctivitis, rhinitis, urticaria, anaphylaxis).
- Blood sampling: safety blood draw at visit 1 and visit 5

Background therapy:

no background therapy

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 11 December 2015 |
| 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 | Germany: 220 |
| Worldwide total number of subjects | 220 |
| EEA total number of subjects | 220 |

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 | 0 |

| | |
|---------------------------|-----|
| months) | |
| Children (2-11 years) | 220 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Potential trial participants have been identified through screening for islet auto-antibodies in the Fr1da study (majority) or in any other screening program in Germany (i.e. Munich Cohort Studies). Recruitment started in December 2015 and lasted until June 2021.

Pre-assignment

Screening details:

The Fr1da study offers islet auto-antibody testing to all children in Bavaria at the age of 2 - 10 years in the context of compulsory medical preventive check-ups. The Fr1da screening enables detection of type 1 diabetes at an early stage and is conducted by Helmholtz Munich in cooperation with the association of pediatricians.

Period 1

| | |
|------------------------------|---|
| Period 1 title | Overall trial (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Data analyst, Carer, Assessor |

Arms

| | |
|------------------------------|--------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Oral Insulin |

Arm description:

Children in the oral insulin group received increasing dose of daily oral insulin: 7.5 mg (3 months), rising to 67.5 mg (9 months).

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

Dosage and administration details:

Children received increasing dose of daily oral insulin: 7.5 mg (3 months), rising to 67.5 mg (9 months). The insulin crystals (7.5 mg rH-insulin crystals or 67.5 mg rH-insulin crystals) are formulated together with filling substance (microcrystalline cellulose to a total weight of 200 mg) and contained in hard gelatine capsules.

The study treatment was self-administered by participants or by the child's parents or guardians as content of one capsule per day. The study treatment will be given orally as a powder spread on a small quantity meal serving e.g. with yoghurt, tea spoon of water etc.

Treatment was administered daily preferably in the morning (7-10am) after feeding for 12 months.

| | |
|------------------|---------|
| Arm title | Placebo |
|------------------|---------|

Arm description:

Children in the placebo group will receive 12 months of daily oral placebo.

| | |
|--|----------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Placebo was the filling substance microcrystalline cellulose (200 mg) contained in hard gelatine capsules. The study treatment was self-administered by participants or by the child's parents or guardians as

content of one capsule per day. The study treatment was given orally as a powder spread on a small quantity meal serving e.g. with yoghurt, tea spoon of water etc. Treatment was administered daily preferably in the morning (7-10am) after feeding for 12 months.

| Number of subjects in period 1 | Oral Insulin | Placebo |
|---------------------------------------|--------------|---------|
| Started | 110 | 110 |
| Completed | 90 | 89 |
| Not completed | 20 | 21 |
| Consent withdrawn by subject | 4 | 7 |
| other reason & non-compliance | 13 | 11 |
| Lost to follow-up | 3 | 3 |

Baseline characteristics

Reporting groups

| | |
|---|--------------|
| Reporting group title | Oral Insulin |
| Reporting group description: Children in the oral insulin group received increasing dose of daily oral insulin: 7.5 mg (3 months), rising to 67.5 mg (9 months). | |
| Reporting group title | Placebo |
| Reporting group description: Children in the placebo group will receive 12 months of daily oral placebo. | |

| Reporting group values | Oral Insulin | Placebo | Total |
|--|--------------|---------|-------|
| Number of subjects | 110 | 110 | 220 |
| Age categorical | | | |
| children at median age 4.8 years | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 110 | 110 | 220 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 0 | 0 | 0 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 59 | 53 | 112 |
| Male | 51 | 57 | 108 |

Subject analysis sets

| | |
|---|--|
| Subject analysis set title | Full Analysis Set (Intention-to-treat) |
| Subject analysis set type | Full analysis |
| Subject analysis set description: All randomised children who received ≥ 1 dose of study medication | |
| Subject analysis set title | Safety analysis set |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: All children who received ≥ 1 dose, analyzed per actual treatment | |

| Reporting group values | Full Analysis Set (Intention-to-treat) | Safety analysis set | |
|----------------------------------|--|---------------------|--|
| Number of subjects | 220 | 220 | |
| Age categorical | | | |
| children at median age 4.8 years | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | |

| | | | |
|---|-----|-----|--|
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 220 | 220 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 0 | 0 | |
| From 65-84 years | 0 | 0 | |
| 85 years and over | 0 | 0 | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | | | |
| Male | | | |

End points

End points reporting groups

| | |
|---|--|
| Reporting group title | Oral Insulin |
| Reporting group description: Children in the oral insulin group received increasing dose of daily oral insulin: 7.5 mg (3 months), rising to 67.5 mg (9 months). | |
| Reporting group title | Placebo |
| Reporting group description: Children in the placebo group will receive 12 months of daily oral placebo. | |
| Subject analysis set title | Full Analysis Set (Intention-to-treat) |
| Subject analysis set type | Full analysis |
| Subject analysis set description: All randomised children who received ≥ 1 dose of study medication | |
| Subject analysis set title | Safety analysis set |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: All children who received ≥ 1 dose, analyzed per actual treatment | |

Primary: Primary: Immune Response (efficacy)

| | |
|--|-------------------------------------|
| End point title | Primary: Immune Response (efficacy) |
| End point description: Of the first 90 randomised children, 86 received at least one dose of treatment or placebo and their immune response results were recorded, therefore they are considered as part of the full analysis sample for the primary endpoint analysis. | |
| End point type | Primary |
| End point timeframe: From baseline, children were monitored for a minimum of 36 months and up to approximately 90 months or until diagnosis of diabetes | |

| End point values | Oral Insulin | Placebo | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 44 | 42 | | |
| Units: Subjects | 11 | 13 | | |

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | Primary Immune Response per Treatment Arm |
| Comparison groups | Placebo v Oral Insulin |

| | |
|---|--------------------|
| Number of subjects included in analysis | 86 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.63 |
| Method | Fisher exact |
| Parameter estimate | Hazard ratio (HR) |
| Confidence interval | |
| level | 95 % |
| Variability estimate | Standard deviation |

Primary: Co-primary: Treatment efficacy

| | |
|--|--------------------------------|
| End point title | Co-primary: Treatment efficacy |
| End point description: | |
| <p>The co-primary outcome was the elapsed time from randomisation treatment assignment to the development of persistent dysglycemia or diabetes onset.</p> <p>Dysglycemia was determined based on abnormal glucose values during oral glucose tolerance tests (OGTT), while diabetes onset followed ADA diagnostic criteria. The analysis was conducted in the full intention-to-treat (ITT) population (n = 220) and evaluated using time-to-event methods, with participants censored at their last assessment if no event occurred.</p> | |
| End point type | Primary |
| End point timeframe: | |
| <p>From baseline, children were monitored for a minimum of 36 months and up to approximately 90 months or until diagnosis of diabetes</p> | |

| End point values | Oral Insulin | Placebo | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 110 | 110 | | |
| Units: Subjects | 46 | 41 | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Time to dysglycemia or diabetes progression |
| Comparison groups | Oral Insulin v Placebo |
| Number of subjects included in analysis | 220 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.74 |
| Method | Wald-Test |
| Parameter estimate | Hazard ratio (HR) |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.66 |
| upper limit | 1.73 |

| | |
|----------------------|--------------------|
| Variability estimate | Standard deviation |
|----------------------|--------------------|

Secondary: Type 1 Diabetes (T1D)

| | |
|-----------------|-----------------------|
| End point title | Type 1 Diabetes (T1D) |
|-----------------|-----------------------|

End point description:

Time to onset of clinical type 1 diabetes, defined according to ADA criteria. Diagnosis requires confirmation on two separate occasions (≥ 1 day apart) based on one or more of the following:

Fasting plasma glucose ≥ 126 mg/dL (7.0 mmol/L),
 2-hour plasma glucose ≥ 200 mg/dL (11.1 mmol/L) during OGTT,
 Random plasma glucose ≥ 200 mg/dL (11.1 mmol/L) with classic symptoms (polyuria, polydipsia, weight loss).

Participants were followed from randomisation until diagnosis or last contact with the trial center.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From baseline, children were monitored for a minimum of 36 months and up to approximately 90 months or until diagnosis of diabetes

| End point values | Oral Insulin | Placebo | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 110 | 110 | | |
| Units: Subjects | 38 | 36 | | |

Statistical analyses

| | |
|---|-------------------------|
| Statistical analysis title | Time to T1D progression |
| Comparison groups | Oral Insulin v Placebo |
| Number of subjects included in analysis | 220 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.9182 |
| Method | Wald-test |
| Parameter estimate | Cox proportional hazard |
| Point estimate | 1.024 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.649 |
| upper limit | 1.616 |

Secondary: Immune response outcomes -IAA

| | |
|-----------------|-------------------------------|
| End point title | Immune response outcomes -IAA |
|-----------------|-------------------------------|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From baseline, children were monitored for a minimum of 36 months and up to approximately 90 months or until diagnosis of diabetes

| End point values | Oral Insulin | Placebo | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 44 | 42 | | |
| Units: subjects | 9 | 9 | | |

Statistical analyses

| | | | | |
|---|---|--|--|--|
| Statistical analysis title | Insulin auto-antibodies response analysis | | | |
| Comparison groups | Oral Insulin v Placebo | | | |
| Number of subjects included in analysis | 86 | | | |
| Analysis specification | Pre-specified | | | |
| Analysis type | superiority | | | |
| P-value | = 0.9558 | | | |
| Method | Logrank | | | |
| Parameter estimate | Hazard ratio (HR) | | | |
| Point estimate | 0.974 | | | |
| Confidence interval | | | | |
| level | 95 % | | | |
| sides | 2-sided | | | |
| lower limit | 0.387 | | | |
| upper limit | 2.455 | | | |
| Variability estimate | Standard deviation | | | |

Secondary: Immune reponse outcome: Salivary IgA

| | |
|-----------------|--------------------------------------|
| End point title | Immune reponse outcome: Salivary IgA |
|-----------------|--------------------------------------|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From baseline, children were monitored for a minimum of 36 months and up to approximately 90 months or until diagnosis of diabetes

| End point values | Oral Insulin | Placebo | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 40 | 42 | | |
| Units: Subjects | 2 | 2 | | |

Statistical analyses

| Statistical analysis title | Salivary IgA Response analysis |
|---|--------------------------------|
| Comparison groups | Oral Insulin v Placebo |
| Number of subjects included in analysis | 82 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.9338 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.087 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.153 |
| upper limit | 7.715 |
| Variability estimate | Standard deviation |

Secondary: Immune response outcome: CD4+ T-cell

| | |
|--|--------------------------------------|
| End point title | Immune response outcome: CD4+ T-cell |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| From baseline, children were monitored for a minimum of 36 months and up to approximately 90 months or until diagnosis of diabetes | |

| End point values | Oral Insulin | Placebo | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 38 | 38 | | |
| Units: subjects | 2 | 3 | | |

Statistical analyses

| Statistical analysis title | CD4+ T-cell response analysis |
|----------------------------|-------------------------------|
| Comparison groups | Placebo v Oral Insulin |

| | |
|---|--------------------|
| Number of subjects included in analysis | 76 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.6587 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.67 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.112 |
| upper limit | 4.01 |
| Variability estimate | Standard deviation |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were assessed every three months during the 12-month treatment phase and subsequently at 6-month intervals until 90 months after baseline or until the development of type 1 diabetes.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 14.1 |

Reporting groups

| | |
|--------------------------------|--------------|
| Reporting group title | Oral Insulin |
| Reporting group description: - | |
| Reporting group title | Placebo |
| Reporting group description: - | |

| Serious adverse events | Oral Insulin | Placebo | |
|---|-----------------|-----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 4 / 110 (3.64%) | 1 / 110 (0.91%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | | | |
| Injury, poisoning and procedural complications | | | |
| Injury, poisoning and procedural complications | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | 0 / 110 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Cardiac disorder | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | 0 / 110 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Gastrointestinal disorder | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | 0 / 110 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|---|-----------------|-----------------|--|
| Respiratory, thoracic and meidatinal disorder | | | |
| subjects affected / exposed | 1 / 110 (0.91%) | 1 / 110 (0.91%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Infection and infestation | | | |
| subjects affected / exposed | 4 / 110 (3.64%) | 1 / 110 (0.91%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Oral Insulin | Placebo | |
|---|-------------------|-------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 98 / 110 (89.09%) | 96 / 110 (87.27%) | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Neoplasms benign, malignant and unspecified | | | |
| subjects affected / exposed | 2 / 110 (1.82%) | 0 / 110 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Surgical and medical procedures | | | |
| Surgical and medical procedures | | | |
| subjects affected / exposed | 2 / 110 (1.82%) | 0 / 110 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| General disorders and administration site conditions | | | |
| General disorders ans administration site conditions | | | |
| subjects affected / exposed | 35 / 110 (31.82%) | 35 / 110 (31.82%) | |
| occurrences (all) | 63 | 50 | |
| Immune system disorders | | | |
| Immune system disorders | | | |
| subjects affected / exposed | 5 / 110 (4.55%) | 3 / 110 (2.73%) | |
| occurrences (all) | 5 | 3 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|--|-------------------------|-------------------------|--|
| subjects affected / exposed occurrences (all) | 25 / 110 (22.73%) 72 | 32 / 110 (29.09%) 71 | |
| Investigations Investigations subjects affected / exposed occurrences (all) | 1 / 110 (0.91%) 1 | 1 / 110 (0.91%) 1 | |
| Injury, poisoning and procedural complications Injury, poisoning and procedural complications subjects affected / exposed occurrences (all) | 8 / 110 (7.27%) 13 | 6 / 110 (5.45%) 6 | |
| Congenital, familial and genetic disorders Congenital, familial and genetic disorders subjects affected / exposed occurrences (all) | 1 / 110 (0.91%) 1 | 1 / 110 (0.91%) 1 | |
| Cardiac disorders Cardiac disorder subjects affected / exposed occurrences (all) | 1 / 110 (0.91%) 1 | 0 / 110 (0.00%) 0 | |
| Nervous system disorders Nervous system disorders subjects affected / exposed occurrences (all) | 5 / 110 (4.55%) 7 | 7 / 110 (6.36%) 9 | |
| Blood and lymphatic system disorders Blood and lymphatic system disorders subjects affected / exposed occurrences (all) | 3 / 110 (2.73%) 4 | 0 / 110 (0.00%) 0 | |
| Ear and labyrinth disorders Ear and labyrinth disorders subjects affected / exposed occurrences (all) | 0 / 110 (0.00%) 0 | 4 / 110 (3.64%) 5 | |
| Gastrointestinal disorders Gastrointestinal disorders subjects affected / exposed occurrences (all) | 39 / 110 (35.45%) 59 | 26 / 110 (23.64%) 47 | |
| Skin and subcutaneous tissue disorders | | | |

| | | | |
|--|--------------------------|--------------------------|--|
| Skin and subcutaneous tissue disorders subjects affected / exposed occurrences (all) | 6 / 110 (5.45%) 8 | 6 / 110 (5.45%) 8 | |
| Endocrine disorders Endocrine disorders subjects affected / exposed occurrences (all) | 0 / 110 (0.00%) 0 | 1 / 110 (0.91%) 2 | |
| Musculoskeletal and connective tissue disorders Musculoskeletal and connective tissue disorders subjects affected / exposed occurrences (all) | 3 / 110 (2.73%) 4 | 3 / 110 (2.73%) 4 | |
| Infections and infestations Infections and infestations subjects affected / exposed occurrences (all) | 86 / 110 (78.18%) 252 | 78 / 110 (70.91%) 202 | |
| Metabolism and nutrition disorders Metabolism and nutrition disorders subjects affected / exposed occurrences (all) | 2 / 110 (1.82%) 2 | 0 / 110 (0.00%) 0 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|---|
| 04 December 2015 | Shelf life extension of IMP |
| 22 September 2016 | Protocol Version 3.0: additional endpoint dysglycemia and Increase in the number of participants from 62 to 220 |
| 22 February 2018 | Shelf life extension of IMP |
| 22 May 2019 | Protocol Version 4.1 -Extension of recruitment period from 30 months to 56 months -Extension of study duration -new definition of AE-reporting timelines -Changes in study objective and primary /secondary outcome -Modifications to the statistical rationale for sample size calculation. |
| 15 April 2020 | Update IB Version 2.0 Protocol Version 5.0 |
| 15 January 2021 | Protocol Version 6 -Revision of inconsistencies regarding the objective and outcomes -Update timelines for end of study |
| 07 September 2021 | Protocol Version 7 -Interim analysis for first 90 study participants |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

A limitation of the design is the short treatment duration, which prevents conclusions regarding potential long-term therapeutic effects. Since treatment was largely in individuals while they had stage 1 type 1 diabetes, it is unknown whether hig

Notes:

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/41563349>