Clinical trial results:
- PRE-POINT-EARLY STUDY -
Pilot study using oral insulin at early age for immune efficacy in primary prevention of type 1 diabetes

Summary

EudraCT number	2014-005287-15
Trial protocol	DE
Global end of trial date	21 December 2017

Results information

Result version number	v1 (current)
This version publication date	22 August 2020
First version publication date	22 August 2020

Trial information

Trial identification

Sponsor protocol code	808040017

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02547519
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Technische Universität München; Fakultät für Medizin
Sponsor organisation address	Ismaninger Str. 22, Munich, Germany, 81675
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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	21 May 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 December 2017
Global end of trial reached?	Yes
Global end of trial date	21 December 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine whether daily administration of up to 67.5 mg insulin to young children aged 6 months to 2 years with high genetic risk for T1D induces immune responses to insulin with features of immune regulation.

Protection of trial subjects:

Local anesthetics (EMLA) to reduce pain during blood draws

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 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: 44
Worldwide total number of subjects	44
EEA total number of subjects	44

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)	38
Children (2-11 years)	6
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: -

Pre-assignment

Screening details:

Children from age 6 months to 2 years who have at least one first degree relative with type 1 diabetes diagnosed before age 40 years.

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:

Human Insulin (7.5 mg, 22.5 mg, 67.5 mg per day) is given orally daily together with food for the duration of the study.

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:

Content of one capsule (7.5 mg, 22.5 mg or 67.5 mg Human insulin) is given orally daily together with food for the duration of the study.

Arm title	Placebo

Arm description:

Content of one capsule is given orally daily together with food for the duration of the study.

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 is given orally daily together with food for the duration of the study.

Number of subjects in period 1	Oral Insulin	Placebo
Started	22	22
Completed	21	20
Not completed	1	2
Adverse event, non-fatal	-	1
Dropped out due to illness of the sibling twin	1	-
due to social/familiar problems	-	1

Baseline characteristics

Reporting groups

Reporting group title	Oral Insulin

Reporting group description:

Human Insulin (7.5 mg, 22.5 mg, 67.5 mg per day) is given orally daily together with food for the duration of the study.

Reporting group title	Placebo

Reporting group description:

Content of one capsule is given orally daily together with food for the duration of the study.

Reporting group values	Oral Insulin	Placebo	Total
Number of subjects	22	22	44
Age categorical Units: Subjects			
Infants and toddlers (28 days-23 months)	20	18	38
Children (2-11 years)	2	4	6
Gender categorical Units: Subjects			
female	7	10	17
male	15	12	27

Subject analysis sets

Subject analysis set title	INS AA genotype oral insulin
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Frequency of immune responses was compared between treatment groups in subjects with susceptible INS AA genotype.

Subject analysis set title	INS AA genotype placebo
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Frequency of immune responses was compared between treatment groups in subjects with susceptible INS AA genotype.

Subject analysis set title	Safety / Insulin
Subject analysis set type	Safety analysis

Subject analysis set description:

There was no difference between Placebo and Insulin group in:
- blood glucose,
- Insulin,
- C-Peptide values,
- the Insulin / C-Peptide ratio or
- the areas under the concentration time curve for glucose, Insulin or C-Peptide.

Subject analysis set title	Safety / Placebo
Subject analysis set type	Safety analysis

Subject analysis set description:

There was no difference between Placebo and Insulin group in:
- blood glucose,
- Insulin,
- C-Peptide values,

- the Insulin / C-Peptide ratio or
- the areas under the concentration time curve for glucose, Insulin or C-Peptide.

Reporting group values	INS AA genotype oral insulin	INS AA genotype placebo	Safety / Insulin
Number of subjects	11	11	22
Age categorical			
Units: Subjects			
Infants and toddlers (28 days-23 months)	10	9	
Children (2-11 years)	1	2	
Gender categorical			
Units: Subjects			
female	2	6	
male	9	5	

Reporting group values	Safety / Placebo		
Number of subjects	21		
Age categorical			
Units: Subjects			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Gender categorical			
Units: Subjects			
female			
male			

End points

End points reporting groups

Reporting group title	Oral Insulin

Reporting group description:

Human Insulin (7.5 mg, 22.5 mg, 67.5 mg per day) is given orally daily together with food for the duration of the study.

Reporting group title	Placebo

Reporting group description:

Content of one capsule is given orally daily together with food for the duration of the study.

Subject analysis set title	INS AA genotype oral insulin
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Frequency of immune responses was compared between treatment groups in subjects with susceptible INS AA genotype.

Subject analysis set title	INS AA genotype placebo
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Frequency of immune responses was compared between treatment groups in subjects with susceptible INS AA genotype.

Subject analysis set title	Safety / Insulin
Subject analysis set type	Safety analysis

Subject analysis set description:

There was no difference between Placebo and Insulin group in:
- blood glucose,
- Insulin,
- C-Peptide values,
- the Insulin / C-Peptide ratio or
- the areas under the concentration time curve for glucose, Insulin or C-Peptide.

Subject analysis set title	Safety / Placebo
Subject analysis set type	Safety analysis

Subject analysis set description:

There was no difference between Placebo and Insulin group in:
- blood glucose,
- Insulin,
- C-Peptide values,
- the Insulin / C-Peptide ratio or
- the areas under the concentration time curve for glucose, Insulin or C-Peptide.

Primary: Immune response

End point title	Immune response

End point description:

Immune response was defined as an increase in serum IgG antibodies to insulin, salivary IgA antibodies to insulin, or serum IAA and a CD4+ T cell response was defined as a stimulation index (SI) above 3 that was more than 2-fold increased over baseline.

End point type	Primary

End point timeframe:

12 months (from baseline until end of treatment)

End point values	Oral Insulin	Placebo	INS AA genotype oral insulin	INS AA genotype placebo
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	22	21	11	11
Units: subjects	12	14	9	7

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Oral Insulin
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.54 [1]
Method	Fisher exact

Notes:

[1] - The difference in the frequency of observed positive outcomes between the 2 treatment arms was not significant.

Statistical analysis title	Statistical Analysis 2
Comparison groups	INS AA genotype placebo v INS AA genotype oral insulin
Number of subjects included in analysis	22
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.64
Method	Fisher exact

Secondary: Gene expression of insulin responsive CD4+ T-Cells at 12 months

End point title	Gene expression of insulin responsive CD4+ T-Cells at 12 months

End point description:

Gene expression values of insulin responsive CD4+ T-cells was measured as FOXP3 Treg/IFNg cell ratio

End point type	Secondary

End point timeframe:

at 12 months

End point values	Oral Insulin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1	4		
Units: --				
median (inter-quartile range (Q1-Q3))	1.00 (1.00 to 1.00)	6.44 (4.61 to 14.00)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Antibody Response to insulin

End point title	Antibody Response to insulin

End point description:

End point type	Other pre-specified

End point timeframe:

12 months (Baseline to End of treatment)

End point values	Oral Insulin	Placebo	INS AA genotype oral insulin	INS AA genotype placebo
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	22	21	11	11
Units: subjects	9	7	8	2

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Oral Insulin v Placebo
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.36
Method	Fisher exact

Statistical analysis title	Statistical Analysis 2
Comparison groups	INS AA genotype oral insulin v INS AA genotype placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.03 [2]
Method	Fisher exact

Notes:
[2] - The difference in observed positive outcomes between the two treatment arms was significant.

Other pre-specified: CD4+ T-Cell Response to insulin

End point title	CD4+ T-Cell Response to insulin

End point description:

End point type	Other pre-specified

End point timeframe:
12 months (Baseline until End of Treatment)

End point values	Oral Insulin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	21		
Units: subjects	4	8		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Oral Insulin v Placebo
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.19
Method	Fisher exact

Other pre-specified: LOG2 CD4+ T-Cell Values at 9 months

End point title	LOG2 CD4+ T-Cell Values at 9 months

End point description:

End point type	Other pre-specified

End point timeframe:
at 9 months

End point values	Oral Insulin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	21		
Units: SI (stimulation index)				
median (inter-quartile range (Q1-Q3))	0.54 (-0.09 to 0.99)	0.55 (0.20 to 0.93)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: LOG2 CD4+ T-Cell Values at 12 months

End point title	LOG2 CD4+ T-Cell Values at 12 months

End point description:

End point type	Other pre-specified

End point timeframe:

at 12 months

End point values	Oral Insulin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	18		
Units: SI (stimulation index)				
median (inter-quartile range (Q1-Q3))	-0.04 (-0.47 to 0.21)	0.50 (-0.07 to 0.87)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: IGE Analysis Placebo versus Verum at 12 month

End point title	IGE Analysis Placebo versus Verum at 12 month

End point description:

End point type	Other pre-specified

End point timeframe:

At 12 month visit

End point values	Safety / Insulin	Safety / Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	22	21		
Units: Subjects	17	17		

Statistical analyses

Statistical analysis title	Analyse 1
Comparison groups	Safety / Insulin v Safety / Placebo
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.174
Method	Wilcoxon (Mann-Whitney)

Other pre-specified: Safety

End point title	Safety

End point description:

End point type	Other pre-specified

End point timeframe:

Complete study duration

End point values	Safety / Insulin	Safety / Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	22	21		
Units: Subjects	8	1		

Statistical analyses

Statistical analysis title	Analysis 1 / Skin and subcutaneus tissue disorders
Comparison groups	Safety / Insulin v Safety / Placebo
Number of subjects included in analysis	43
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.011
Method	Logrank

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were recorded throughout the study; documentation and assessment of AEs and SAEs occurred during 3 monthly visits.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Reference placebo, filled with microcrystalline cellulose as filling substance, orally, once daily for the duration of the study

Reporting group title	Verum

Reporting group description:

Human Insulin (7.5mg, 22.5mg, 67.5mg), orally, once daily for the duration of the study

Serious adverse events	Placebo	Verum	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 21 (4.76%)	3 / 22 (13.64%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
burns second degree			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stair fall			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Invagination			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			

Pneumonia right basal lobe			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive Pneumonia / Bronchitis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis with dehydration			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	Verum	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 21 (90.48%)	21 / 22 (95.45%)	
Investigations			
Temperature elevation			
subjects affected / exposed	1 / 21 (4.76%)	1 / 22 (4.55%)	
occurrences (all)	1	1	
Injury, poisoning and procedural complications			
Burns second degree			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Falling down			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Fibula fracture			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Wasp sting			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	

Congenital, familial and genetic disorders			
Hydrozele			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Surgical and medical procedures			
Inguinal hernia repair			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Routine vaccination			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Orchiopexy			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Pancytopenia			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Lymphadenitis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
General malaise			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	3	
Fever			
subjects affected / exposed	11 / 21 (52.38%)	14 / 22 (63.64%)	
occurrences (all)	18	26	
Fatigue			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Immune system disorders			
Peanut allergy			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			

Diarrhoea			
subjects affected / exposed	2 / 21 (9.52%)	8 / 22 (36.36%)	
occurrences (all)	2	10	
Invagination of intestine			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Threw up			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Stomatitis/Stomatitis aphtosa			
subjects affected / exposed	1 / 21 (4.76%)	1 / 22 (4.55%)	
occurrences (all)	1	1	
Teething/Teething pain			
subjects affected / exposed	2 / 21 (9.52%)	2 / 22 (9.09%)	
occurrences (all)	3	5	
Vomiting			
subjects affected / exposed	3 / 21 (14.29%)	4 / 22 (18.18%)	
occurrences (all)	3	6	
Tooth pain			
subjects affected / exposed	2 / 21 (9.52%)	2 / 22 (9.09%)	
occurrences (all)	3	6	
Respiratory, thoracic and mediastinal disorders			
Cough/Coughing			
subjects affected / exposed	4 / 21 (19.05%)	6 / 22 (27.27%)	
occurrences (all)	6	14	
Runny nose			
subjects affected / exposed	1 / 21 (4.76%)	5 / 22 (22.73%)	
occurrences (all)	1	5	
Sore throat			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Reactive airways disease			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			

Diaper rash			
subjects affected / exposed	0 / 21 (0.00%)	2 / 22 (9.09%)	
occurrences (all)	0	4	
Eczema			
subjects affected / exposed	1 / 21 (4.76%)	2 / 22 (9.09%)	
occurrences (all)	1	2	
Erythema/Erythema facial			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	2	
Exanthema			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Pruritus			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Urticaria			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	2	
Infections and infestations			
Acute gastroenteritis/Gastroenteritis/Gastroenteritis and fungal infection			
subjects affected / exposed	7 / 21 (33.33%)	12 / 22 (54.55%)	
occurrences (all)	7	20	
Bronchitis/Bronchitis viral			
subjects affected / exposed	6 / 21 (28.57%)	6 / 22 (27.27%)	
occurrences (all)	7	7	
Common cold			
subjects affected / exposed	13 / 21 (61.90%)	10 / 22 (45.45%)	
occurrences (all)	25	28	
Conjunctivitis			
subjects affected / exposed	5 / 21 (23.81%)	5 / 22 (22.73%)	
occurrences (all)	5	6	
Gingivitis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
hand-mouth-feet disease			

subjects affected / exposed	3 / 21 (14.29%)	2 / 22 (9.09%)	
occurrences (all)	3	2	
croup			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Erysipelas			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences (all)	2	0	
Febrile cold (excl flu like illness)			
subjects affected / exposed	1 / 21 (4.76%)	2 / 22 (9.09%)	
occurrences (all)	1	2	
Impetigo			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Otitis / Otitis media			
subjects affected / exposed	4 / 21 (19.05%)	0 / 22 (0.00%)	
occurrences (all)	5	0	
Pneumonia/Obstructive pneumonia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences (all)	3	0	
Respiratory tract infection bacterial			
subjects affected / exposed	1 / 21 (4.76%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Rhinitis			
subjects affected / exposed	4 / 21 (19.05%)	4 / 22 (18.18%)	
occurrences (all)	11	4	
Viral infection			
subjects affected / exposed	0 / 21 (0.00%)	2 / 22 (9.09%)	
occurrences (all)	0	2	
Oral infection			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Tonsillitis			
subjects affected / exposed	0 / 21 (0.00%)	2 / 22 (9.09%)	
occurrences (all)	0	3	
Herpes simplex			

subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
no appetite			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
dehydration			
subjects affected / exposed	0 / 21 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 August 2015	Investigator's Brochure (IB): Chapter 6 of the IB has been revised and updated. Furthermore, the results, especially the safety data, of the completed Pre-POINT study were described in more detail. Study protocol: (1) The benefit-risk analysis in chapter 2.6.1 and 2.6.2 was described in more detail with regard to the current results of the Pre-POINT study and other studies with oral insulin for the prevention of type 1 diabetes (DPT-1 study and TN07-TrialNet Oral Insulin Study) and analyzed with regard to the benefit-risk ratio on this basis. (2) The dosage information from international units has been added in Chapters 2.8 and 6.1.1. (3) It is also included in the study protocol that the study physician clearly indicates the risk of approximately 10% of patients suffering from type 1 diabetes during the consenting process (Chapter 7.2). Patient information and patient informed consent: The information on current study results was revised and presented in more detail.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported