Clinical trial results:
Pilot Trial to preserve residual insulin secretion in children and adolescents with recent onset Type 1 diabetes by using GAD-antigen (Diamyd) therapy in combination with Vitamin D and Ibuprofen .

Summary

EudraCT number	2012-003251-11
Trial protocol	SE
Global end of trial date	30 November 2016

Results information

Result version number	v1 (current)
This version publication date	14 June 2017
First version publication date	14 June 2017

Trial information

Trial identification

Sponsor protocol code	DIABGAD-1

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Div of Pediatrics, Dept of Clinical and Experimental Medicine, Faculty of Health Medicine
Sponsor organisation address	Linköping University, Linköping, Sweden, SE-581 85
Public contact	Johnny Ludvigsson, Linköping University, 46 13286854, Johnny.Ludvigsson@liu.se
Scientific contact	Johnny Ludvigsson, Linköping University, 46 13286854, Johnny.Ludvigsson@liu.se

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	30 November 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 November 2016
Global end of trial reached?	Yes
Global end of trial date	30 November 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- Evaluate the safety and influence of treatment with GAD-Alum (Diamyd) plus Vitamin D plus Ibuprofen on preservation of residual insulin secretion in recently-diagnosed Type 1 diabetes.
- Evaluate how the abovementioned treatments influencers the immune system of the patients and interact with any viral infections.
- Evaluate the safety and influence of treatment with double dose of GAD-Alum (Diamyd) plus Vitamin D on the immune system, viral infections and on preservation of residual insulin secretion in recently-diagnosed Type 1 diabetes

Protection of trial subjects:

After the injection of GAD-Alum (Diamyd)/Placebo at Visit 3 and 4, the patient was to remain in the vicinity of the study site for the next hour, and the injection site were examined by investigator/study nurse 1 hour post injection.

Background therapy:

Standard insulin treatment, education and psycho-social support for newly diagnosed Type 1 diabetes patients. All patients will continue to receive standard care for Type 1 diabetes during the study.

Evidence for comparator: -

Actual start date of recruitment	04 February 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Sweden: 64
Worldwide total number of subjects	64
EEA total number of subjects	64

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)	17
Adolescents (12-17 years)	47
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited from January 2013 to May 2014. Patients were recruited at 9 hospitals in Sweden.

Pre-assignment

Screening details:

Patients aged 10.00 to 17.99 years at the time of screening and with Type 1 diabetes according to the ADA classification with < 4 months diabetes duration at time of screening.

Period 1

Period 1 title	Baseline
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	Group A

Arm description:

Patients will be assigned to receive Ibuprofen as oral suspension; 400 mg every morning from Day 1 through 90 and from Day 1 through 450 also oral drops of Vitamin D 2000 IU per day (i.e. 25 drops per day). In addition 1 subcutaneous injection with 20 µg Diamyd and one with placebo given at two different sites in the stomach area, each on Days 15 and 45, i.e., prime and booster dose (providing a total dose of 40 µg Diamyd).

Arm type	Experimental
Investigational medicinal product name	D-vitamin Oil
Investigational medicinal product code	
Other name	Calciferol
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

The comercially available Vitamin D, calciferol. Vitamin D was administered as oral solution ; 2000 IU per day (i.e. 25 drops per day) from Day 1 through Day 450.

Investigational medicinal product name	Ibuprofen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

The commercially available ibuprofen.
Ibuprofen was administered as oral suspension; 400 mg every morning from Day 1 through 90.

Arm title	Group B

Arm description:

Patients will be assigned to receive placebo as oral suspension every morning from Day 1 through 90 and from Day 1 through 450 also oral drops of Vitamin D 2000 IU per day (i.e. 25 drops per day). In addition 1 subcutaneous injection with 20 µg Diamyd and one with placebo given at two different sites in the stomach area, each on Days 15 and 45, i.e., prime and booster dose (providing a total dose of 40 µg Diamyd).

Arm type	Experimental

Investigational medicinal product name	D-vitamin Oil
Investigational medicinal product code	
Other name	Calciferol
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

The comercially available Vitamin D, calciferol. Vitamin D was administered as oral solution ; 2000 IU per day (i.e. 25 drops per day) from Day 1 through Day 450.

Investigational medicinal product name	Placebo Ibuprofen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Placebo ibuprofen was administered as oral suspension; every morning from Day 1 through 90.

Arm title	Group C

Arm description:

Patients will be assigned to receive placebo as oral suspension every morning from Day 1 through 90 and from Day 1 through 450 also oral drops of Vitamin D 2000 IU per day (i.e. 25 drops per day). In addition 2 subcutaneous injections with 20 µg Diamyd given at two different sites in the stomach area, each on Days 15 and 45, i.e., prime and booster doses (providing a total dose of 80µg Diamyd).

Arm type	Experimental
Investigational medicinal product name	D-vitamin Oil
Investigational medicinal product code	
Other name	Calciferol
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

The comercially available Vitamin D, calciferol. Vitamin D was administered as oral solution ; 2000 IU per day (i.e. 25 drops per day) from Day 1 through Day 450.

Investigational medicinal product name	Placebo Ibuprofen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Placebo ibuprofen was administered as oral suspension; every morning from Day 1 through 90.

Arm title	Group D

Arm description:

Patients will be assigned to receive placebo as oral suspension every morning from Day 1 through 90 and placebo oral drops from Day 1 through 450, and 2 subcutaneous injections with placebo (given at two different sites in the stomach area), each on Days 15 and 45

Arm type	Placebo
Investigational medicinal product name	Placebo D-vitamin Oil
Investigational medicinal product code	
Other name	Calciferol
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Placebo was administered as oral solution i.e. 25 drops per day from Day 1 through Day 450.

Investigational medicinal product name	Placebo Ibuprofen
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Placebo ibuprofen was administered as oral suspension; every morning from Day 1 through 90.

Number of subjects in period 1	Group A	Group B	Group C
Started	16	16	16
Completed	16	16	16

Number of subjects in period 1	Group D
Started	16
Completed	16

Period 2

Period 2 title	Baseline to Month 30
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Assessor

Blinding implementation details:

The treatment code was broken 24 March 2015, and data from Visit 1 to Visit 6 (6 months) were made available to one representative from the Sponsor (unblinded statistician), and the drug supplier (Diamyd Medical). The study was kept blinded to patients, investigators and study personnel until study completion.

Arms

Are arms mutually exclusive?	Yes
Arm title	Group A

Arm description:

Patients will be assigned to receive Ibuprofen as oral suspension; 400 mg every morning from Day 1 through 90 and from Day 1 through 450 also oral drops of Vitamin D 2000 IU per day (i.e. 25 drops per day). In addition 1 subcutaneous injection with 20 µg Diamyd and one with placebo given at two different sites in the stomach area, each on Days 15 and 45, i.e., prime and booster dose (providing a total dose of 40 µg Diamyd).

Arm type	Experimental
Investigational medicinal product name	D-vitamin Oil
Investigational medicinal product code	
Other name	Calciferol
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

The comercially available Vitamin D, calciferol. Vitamin D was administered as oral solution ; 2000 IU per day (i.e. 25 drops per day) from Day 1 through Day 450.

Investigational medicinal product name	Ibuprofen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

The commercially available ibuprofen.
Ibuprofen was administered as oral suspension; 400 mg every morning from Day 1 through 90.

Investigational medicinal product name	Diamyd
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

1 x Diamyd injection.
Diamyd 20 µg was administered as subcutaneous injections on Days 15 and 45 (prime and booster dose).
The Diamyd® Drug Product was composed of the rhGAD65 protein formulated in a sterile, non-pyrogenic phosphate buffered saline containing the aluminum hydroxide adjuvant, Alhydrogel®.
Diamyd® was administered as a 0.5 mL subcutaneous injection.
Each injection contained 20 µg Diamyd® protein.

Investigational medicinal product name	Placebo Diamyd
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

1 x Diamyd placebo injection containing 0 ug Diamyd.
Diamyd placebo was administered as subcutaneous injections on Days 15 and 45 (prime and booster dose).
A sterile, non-pyrogenic phosphate buffered saline containing the aluminum hydroxide adjuvant, Alhydrogel®. 0.5 mL subcutaneous injection.

Arm title	Group B

Arm description:

Patients will be assigned to receive placebo ibuprofen as oral suspension every morning from Day 1 through 90 and from Day 1 through 450 also oral drops of Vitamin D 2000 IU per day (i.e. 25 drops per day). In addition 1 subcutaneous injection with 20 µg Diamyd and one with placebo given at two different sites in the stomach area, each on Days 15 and 45, i.e., prime and booster dose (providing a total dose of 40 µg Diamyd).

Arm type	Experimental
Investigational medicinal product name	D-vitamin Oil
Investigational medicinal product code	
Other name	Calciferol
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

The comercially available Vitamin D, calciferol. Vitamin D was administered as oral solution ; 2000 IU per day (i.e. 25 drops per day) from Day 1 through Day 450.

Investigational medicinal product name	Placebo Ibuprofen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Placebo ibuprofen was administered as oral suspension; every morning from Day 1 through 90.

Investigational medicinal product name	Diamyd
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

1 x Diamyd injection.
Diamyd 20 µg was administered as subcutaneous injections on Days 15 and 45 (prime and booster dose).
The Diamyd® Drug Product was composed of the rhGAD65 protein formulated in a sterile, non-pyrogenic phosphate buffered saline containing the aluminum hydroxide adjuvant, Alhydrogel®.
Diamyd® was administered as a 0.5 mL subcutaneous injection.
Each injection contained 20 µg Diamyd® protein.

Investigational medicinal product name	Placebo Diamyd
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

1 x Diamyd placebo injection containing 0 ug Diamyd.
Diamyd placebo was administered as subcutaneous injections on Days 15 and 45 (prime and booster dose).
A sterile, non-pyrogenic phosphate buffered saline containing the aluminum hydroxide adjuvant, Alhydrogel®. 0.5 mL subcutaneous injection.

Arm title	Group C

Arm description:

Patients will be assigned to receive placebo ibuprofen as oral suspension every morning from Day 1 through 90 and from Day 1 through 450 also oral drops of Vitamin D 2000 IU per day (i.e. 25 drops per day). In addition 2 subcutaneous injections with 20 µg Diamyd given at two different sites in the stomach area, each on Days 15 and 45, i.e., prime and booster doses (providing a total dose of 80µg Diamyd).

Arm type	Experimental
Investigational medicinal product name	Placebo Ibuprofen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Placebo ibuprofen was administered as oral suspension; every morning from Day 1 through 90.

Investigational medicinal product name	D-vitamin Oil
Investigational medicinal product code	
Other name	Calciferol
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

The comercially available Vitamin D, calciferol. Vitamin D was administered as oral solution ; 2000 IU per day (i.e. 25 drops per day) from Day 1 through Day 450.

Investigational medicinal product name	Diamyd
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

1 x Diamyd injection.

Diamyd 20 µg was administered as subcutaneous injections, on Days 15 and 45 (prime and booster dose).
The Diamyd® Drug Product was composed of the rhGAD65 protein formulated in a sterile, non-pyrogenic phosphate buffered saline containing the aluminum hydroxide adjuvant, Alhydrogel®.
Diamyd® was administered as a 0.5 mL subcutaneous injection.
Each injection contained 20 µg Diamyd® protein.

Investigational medicinal product name	Diamyd
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

1 x Diamyd injection.
Diamyd 20 µg was administered as subcutaneous injections on Days 15 and 45 (prime and booster dose).
The Diamyd® Drug Product was composed of the rhGAD65 protein formulated in a sterile, non-pyrogenic phosphate buffered saline containing the aluminum hydroxide adjuvant, Alhydrogel®.
Diamyd® was administered as a 0.5 mL subcutaneous injection.
Each injection contained 20 µg Diamyd® protein.

Arm title	Group D

Arm description:

Patients will be assigned to receive placebo ibuprofen as oral suspension every morning from Day 1 through 90 and placebo oral drops from Day 1 through 450, and 2 subcutaneous injections with placebo (given at two different sites in the stomach area), each on Days 15 and 45

Arm type	Placebo
Investigational medicinal product name	Placebo Ibuprofen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Placebo ibuprofen was administered as oral suspension; every morning from Day 1 through 90.

Investigational medicinal product name	Placebo D-vitamin Oil
Investigational medicinal product code	
Other name	Calciferol
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Placebo was administered as oral solution i.e. 25 drops per day from Day 1 through Day 450.

Investigational medicinal product name	Placebo Diamyd
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

1 x Diamyd placebo injection containing 0 ug Diamyd.
Diamyd placebo was administered as subcutaneous injections on Days 15 and 45 (prime and booster dose).
A sterile, non-pyrogenic phosphate buffered saline containing the aluminum hydroxide adjuvant, Alhydrogel®. 0.5 mL subcutaneous injection.

Investigational medicinal product name	Placebo Diamyd
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

1 x Diamyd placebo injection containing 0 ug Diamyd.
Diamyd placebo was administered as subcutaneous injections on Days 15 and 45 (prime and booster dose).
A sterile, non-pyrogenic phosphate buffered saline containing the aluminum hydroxide adjuvant, Alhydrogel®. 0.5 mL subcutaneous injection.

Number of subjects in period 2[1]	Group A	Group B	Group C
Started	16	16	16
Prime injection Diamyd/Placebo	16	16	16
Boost injection Diamyd/Placebo	16	16	15
Completed 6 month visit	16	16	15
Completed 15 month visit	15	16	15
Completed 30 month visit	15	16	15
Completed	15	16	15
Not completed	1	0	1
Consent withdrawn by subject	1	-	1
Physician decision	-	-	-

Number of subjects in period 2[1]	Group D
Started	15
Prime injection Diamyd/Placebo	15
Boost injection Diamyd/Placebo	15
Completed 6 month visit	13
Completed 15 month visit	13
Completed 30 month visit	13
Completed	13
Not completed	2
Consent withdrawn by subject	1
Physician decision	1

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: 1 patient in Group D completed Baseline but decided not to continue in the study after baseline visit.

Baseline characteristics

Reporting groups	
Reporting group title	Group A
Reporting group description:	
Patients will be assigned to receive Ibuprofen as oral suspension; 400 mg every morning from Day 1 through 90 and from Day 1 through 450 also oral drops of Vitamin D 2000 IU per day (i.e. 25 drops per day). In addition 1 subcutaneous injection with 20 µg Diamyd and one with placebo given at two different sites in the stomach area, each on Days 15 and 45, i.e., prime and booster dose (providing a total dose of 40 µg Diamyd).	
Reporting group title	Group B
Reporting group description:	
Patients will be assigned to receive placebo as oral suspension every morning from Day 1 through 90 and from Day 1 through 450 also oral drops of Vitamin D 2000 IU per day (i.e. 25 drops per day). In addition 1 subcutaneous injection with 20 µg Diamyd and one with placebo given at two different sites in the stomach area, each on Days 15 and 45, i.e., prime and booster dose (providing a total dose of 40 µg Diamyd).	
Reporting group title	Group C
Reporting group description:	
Patients will be assigned to receive placebo as oral suspension every morning from Day 1 through 90 and from Day 1 through 450 also oral drops of Vitamin D 2000 IU per day (i.e. 25 drops per day). In addition 2 subcutaneous injections with 20 µg Diamyd given at two different sites in the stomach area, each on Days 15 and 45, i.e., prime and booster doses (providing a total dose of 80µg Diamyd).	
Reporting group title	Group D
Reporting group description:	
Patients will be assigned to receive placebo as oral suspension every morning from Day 1 through 90 and placebo oral drops from Day 1 through 450, and 2 subcutaneous injections with placebo (given at two different sites in the stomach area), each on Days 15 and 45	

Reporting group values	Group A	Group B	Group C
Number of subjects	16	16	16
Age categorical 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)	5	4	6
Adolescents (12-17 years)	11	12	10
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	13.3	14.4	13.3
standard deviation	± 1.9	± 2.7	± 2.4
Gender categorical Units: Subjects			
Female	6	7	10
Male	10	9	6

Reporting group values	Group D	Total	
Number of subjects	16	64	
Age categorical 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)	2	17	
Adolescents (12-17 years)	14	47	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	14.2		
standard deviation	± 2.2	-	
Gender categorical Units: Subjects			
Female	9	32	
Male	7	32	

End points

End points reporting groups

Reporting group title	Group A

Reporting group description:

Patients will be assigned to receive Ibuprofen as oral suspension; 400 mg every morning from Day 1 through 90 and from Day 1 through 450 also oral drops of Vitamin D 2000 IU per day (i.e. 25 drops per day). In addition 1 subcutaneous injection with 20 µg Diamyd and one with placebo given at two different sites in the stomach area, each on Days 15 and 45, i.e., prime and booster dose (providing a total dose of 40 µg Diamyd).

Reporting group title	Group B

Reporting group description:

Patients will be assigned to receive placebo as oral suspension every morning from Day 1 through 90 and from Day 1 through 450 also oral drops of Vitamin D 2000 IU per day (i.e. 25 drops per day). In addition 1 subcutaneous injection with 20 µg Diamyd and one with placebo given at two different sites in the stomach area, each on Days 15 and 45, i.e., prime and booster dose (providing a total dose of 40 µg Diamyd).

Reporting group title	Group C

Reporting group description:

Patients will be assigned to receive placebo as oral suspension every morning from Day 1 through 90 and from Day 1 through 450 also oral drops of Vitamin D 2000 IU per day (i.e. 25 drops per day). In addition 2 subcutaneous injections with 20 µg Diamyd given at two different sites in the stomach area, each on Days 15 and 45, i.e., prime and booster doses (providing a total dose of 80µg Diamyd).

Reporting group title	Group D

Reporting group description:

Patients will be assigned to receive placebo as oral suspension every morning from Day 1 through 90 and placebo oral drops from Day 1 through 450, and 2 subcutaneous injections with placebo (given at two different sites in the stomach area), each on Days 15 and 45

Reporting group title	Group A

Reporting group description:

Patients will be assigned to receive Ibuprofen as oral suspension; 400 mg every morning from Day 1 through 90 and from Day 1 through 450 also oral drops of Vitamin D 2000 IU per day (i.e. 25 drops per day). In addition 1 subcutaneous injection with 20 µg Diamyd and one with placebo given at two different sites in the stomach area, each on Days 15 and 45, i.e., prime and booster dose (providing a total dose of 40 µg Diamyd).

Reporting group title	Group B

Reporting group description:

Patients will be assigned to receive placebo ibuprofen as oral suspension every morning from Day 1 through 90 and from Day 1 through 450 also oral drops of Vitamin D 2000 IU per day (i.e. 25 drops per day). In addition 1 subcutaneous injection with 20 µg Diamyd and one with placebo given at two different sites in the stomach area, each on Days 15 and 45, i.e., prime and booster dose (providing a total dose of 40 µg Diamyd).

Reporting group title	Group C

Reporting group description:

Patients will be assigned to receive placebo ibuprofen as oral suspension every morning from Day 1 through 90 and from Day 1 through 450 also oral drops of Vitamin D 2000 IU per day (i.e. 25 drops per day). In addition 2 subcutaneous injections with 20 µg Diamyd given at two different sites in the stomach area, each on Days 15 and 45, i.e., prime and booster doses (providing a total dose of 80µg Diamyd).

Reporting group title	Group D

Reporting group description:

Patients will be assigned to receive placebo ibuprofen as oral suspension every morning from Day 1 through 90 and placebo oral drops from Day 1 through 450, and 2 subcutaneous injections with placebo (given at two different sites in the stomach area), each on Days 15 and 45

Primary: Change in AUC for C-peptide from baseline to month 6

End point title	Change in AUC for C-peptide from baseline to month 6[1]

End point description:

End point type	Primary

End point timeframe:

From baseline to 6 months

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: The clinical study protocol defined statistical methods for efficacy data regarding C-peptide and immune system as well as Adverse events and other safety data as being composed of summary tables with descriptive statistics.

End point values	Group A	Group B	Group C	Group D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	15	14	10
Units: AUC for C-peptide (nmol/L				
arithmetic mean (standard deviation)	-0.264 (± 0.231)	-0.114 (± 0.164)	-0.19 (± 0.161)	0.008 (± 0.271)

Statistical analyses

No statistical analyses for this end point

Primary: Change in AUC for C-peptide from baseline to month 15

End point title	Change in AUC for C-peptide from baseline to month 15[2]

End point description:

End point type	Primary

End point timeframe:

From baseline to Month 15

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: The clinical study protocol defined statistical methods for efficacy data regarding C-peptide and immune system as well as Adverse events and other safety data as being composed of summary tables with descriptive statistics.

End point values	Group A	Group B	Group C	Group D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	15	14	10
Units: AUC for C-peptide (nmol/L)				
arithmetic mean (standard deviation)	-0.362 (± 0.243)	-0.195 (± 0.167)	-0.277 (± 0.216)	-0.273 (± 0.245)

Statistical analyses

No statistical analyses for this end point

Primary: Change in AUC for C-peptide from baseline to month 30

End point title	Change in AUC for C-peptide from baseline to month 30[3]

End point description:

End point type	Primary

End point timeframe:

Baseline to Month 30

Notes:

[3] - 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: The clinical study protocol defined statistical methods for efficacy data regarding C-peptide and immune system as well as Adverse events and other safety data as being composed of summary tables with descriptive statistics.

End point values	Group A	Group B	Group C	Group D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	14	14	11
Units: AUC for C-peptide (nmol/L)				
arithmetic mean (standard deviation)	-0.512 (± 0.318)	-0.383 (± 0.161)	-0.458 (± 0.209)	-0.405 (± 0.257)

Statistical analyses

No statistical analyses for this end point

Primary: Change in mean fasting C-peptide, baseline to month 6

End point title	Change in mean fasting C-peptide, baseline to month 6[4]

End point description:

End point type	Primary

End point timeframe:

Baseline to Visit 6

Notes:

[4] - 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: The clinical study protocol defined statistical methods for efficacy data regarding C-peptide and immune system as well as Adverse events and other safety data as being composed of summary tables with descriptive statistics.

End point values	Group A	Group B	Group C	Group D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	15	14	10
Units: Mean fasting C-peptide (nmol/L)				
arithmetic mean (standard deviation)	-0.108 (± 0.195)	-0.015 (± 0.143)	-0.068 (± 0.133)	0.023 (± 0.191)

Statistical analyses

No statistical analyses for this end point

Primary: Change in mean fasting C-peptide, baseline to month 15

End point title	Change in mean fasting C-peptide, baseline to month 15[5]

End point description:

End point type	Primary

End point timeframe:

Baseline to month 15

Notes:

[5] - 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: The clinical study protocol defined statistical methods for efficacy data regarding C-peptide and immune system as well as Adverse events and other safety data as being composed of summary tables with descriptive statistics.

End point values	Group A	Group B	Group C	Group D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	15	14	10
Units: Mean fasting C-peptide (nmol/L)				
arithmetic mean (standard deviation)	-0.131 (± 0.166)	-0.061 (± 0.143)	-0.142 (± 0.133)	-0.039 (± 0.185)

Statistical analyses

No statistical analyses for this end point

Primary: Change in mean fasting C-peptide, baseline to month 30

End point title	Change in mean fasting C-peptide, baseline to month 30[6]

End point description:

End point type	Primary

End point timeframe:

Baseline to month 30

Notes:

[6] - 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: The clinical study protocol defined statistical methods for efficacy data regarding C-peptide and immune system as well as Adverse events and other safety data as being composed of summary tables with descriptive statistics.

End point values	Group A	Group B	Group C	Group D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	14	14	11
Units: Mean fasting C-peptide (nmol/L)				
arithmetic mean (standard deviation)	-0.194 (± 0.204)	-0.134 (± 0.133)	-0.203 (± 0.124)	-0.13 (± 0.117)

Statistical analyses

No statistical analyses for this end point

Primary: Change in HbA1c from baseline to month 15

End point title	Change in HbA1c from baseline to month 15[7]

End point description:

End point type	Primary

End point timeframe:

Baseline to 15 Months

Notes:

[7] - 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: The clinical study protocol defined statistical methods for efficacy data regarding C-peptide and immune system as well as Adverse events and other safety data as being composed of summary tables with descriptive statistics.

End point values	Group A	Group B	Group C	Group D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	15	14	10
Units: HbA1c (mmol/mol)				
arithmetic mean (standard deviation)	5.455 (± 7.751)	5.667 (± 15.407)	5.643 (± 9.951)	6.5 (± 10.967)

Statistical analyses

No statistical analyses for this end point

Primary: Change in HbA1c from baseline to month 30

End point title	Change in HbA1c from baseline to month 30[8]

End point description:

End point type	Primary

End point timeframe:

Baseline to Month 30.

Notes:

[8] - 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: The clinical study protocol defined statistical methods for efficacy data regarding C-peptide and immune system as well as Adverse events and other safety data as being composed of summary tables with descriptive statistics.

End point values	Group A	Group B	Group C	Group D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	14	14	11
Units: HbA1c (mmol/mol)				
arithmetic mean (standard deviation)	12.4 (± 5.816)	13.286 (± 15.563)	7.286 (± 11.323)	10.909 (± 16.837)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events were recorded by the physician at every visit throughout the study.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20

Reporting groups

Reporting group title	Group A

Reporting group description:

Patients will be assigned to receive Ibuprofen as oral suspension; 400 mg every morning from Day 1 through 90 and from Day 1 through 450 also oral drops of Vitamin D 2000 IU per day (i.e. 25 drops per day). In addition 1 subcutaneous injection with 20 µg Diamyd and one with placebo given at two different sites in the stomach area, each on Days 15 and 45, i.e., prime and booster dose (providing a total dose of 40 µg Diamyd).

Reporting group title	Group B

Reporting group description:

Patients will be assigned to receive placebo as oral suspension every morning from Day 1 through 90 and from Day 1 through 450 also oral drops of Vitamin D 2000 IU per day (i.e. 25 drops per day). In addition 1 subcutaneous injection with 20 µg Diamyd and one with placebo given at two different sites in the stomach area, each on Days 15 and 45, i.e., prime and booster dose (providing a total dose of 40 µg Diamyd).

Reporting group title	Group C

Reporting group description:

Patients will be assigned to receive placebo as oral suspension every morning from Day 1 through 90 and from Day 1 through 450 also oral drops of Vitamin D 2000 IU per day (i.e. 25 drops per day). In addition 2 subcutaneous injections with 20 µg Diamyd given at two different sites in the stomach area, each on Days 15 and 45, i.e., prime and booster doses (providing a total dose of 80µg Diamyd).

Reporting group title	Group D

Reporting group description:

Patients will be assigned to receive placebo as oral suspension every morning from Day 1 through 90 and placebo oral drops from Day 1 through 450, and 2 subcutaneous injections with placebo (given at two different sites in the stomach area), each on Days 15 and 45

Serious adverse events	Group A	Group B	Group C
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 16 (0.00%)	3 / 16 (18.75%)	2 / 16 (12.50%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Upper limb fracture			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Group D		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 15 (13.33%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Upper limb fracture			

subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperglycaemia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Group A	Group B	Group C
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 16 (75.00%)	15 / 16 (93.75%)	16 / 16 (100.00%)
Surgical and medical procedures			
Breast operation			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Injection site oedema			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	1 / 16 (6.25%)
occurrences (all)	0	2	1
Injection site rash			
subjects affected / exposed	1 / 16 (6.25%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	1	2	0
Injection site reaction			
subjects affected / exposed	5 / 16 (31.25%)	4 / 16 (25.00%)	6 / 16 (37.50%)
occurrences (all)	8	5	7
Pyrexia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2
Injection site pain			
subjects affected / exposed	0 / 16 (0.00%)	2 / 16 (12.50%)	1 / 16 (6.25%)
occurrences (all)	0	3	1
Injection site nodule			
subjects affected / exposed	2 / 16 (12.50%)	1 / 16 (6.25%)	2 / 16 (12.50%)
occurrences (all)	2	1	2
Injection site erythema			
subjects affected / exposed	1 / 16 (6.25%)	1 / 16 (6.25%)	3 / 16 (18.75%)
occurrences (all)	1	1	3
Injection site swelling			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	2
Injection site haematoma			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Peripheral swelling			

subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	2
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Obsessive-compulsive disorder			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Attention deficit/hyperactivity disorder			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Investigations			
Blood cholesterol increased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Haemoglobin decreased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Back injury			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Road traffic accident			

subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Dermatitis contact			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Tachycardia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Juvenile myoclonic epilepsy			
subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Abdominal pain			

subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Abdominal pain upper			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Gastritis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Diarrhoea			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Coeliac disease			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Toothache			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Pruritus genital			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Rash papular			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0

Acne			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Microalbuminuria			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Hypothyroidism			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Muscle twitching			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Costochondritis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Viral infection			
subjects affected / exposed	1 / 16 (6.25%)	2 / 16 (12.50%)	1 / 16 (6.25%)
occurrences (all)	1	2	1
Ear infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	2	0	0
Pharyngitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	3	0
Urinary tract infection			

subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	6 / 16 (37.50%)	7 / 16 (43.75%)	7 / 16 (43.75%)
occurrences (all)	10	8	8
Tonsillitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Pseudocroup			
subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis			
subjects affected / exposed	1 / 16 (6.25%)	2 / 16 (12.50%)	1 / 16 (6.25%)
occurrences (all)	1	3	1
Tinea infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Cystitis			
subjects affected / exposed	0 / 16 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Conjunctivitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Varicella			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Rhinitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2
Borrelia infection			

subjects affected / exposed	1 / 16 (6.25%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Infectious mononucleosis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1

Non-serious adverse events	Group D		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 15 (93.33%)		
Surgical and medical procedures			
Breast operation			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Injection site oedema			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Injection site rash			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Injection site reaction			
subjects affected / exposed	6 / 15 (40.00%)		
occurrences (all)	7		
Pyrexia			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Injection site pain			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Injection site nodule			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	3		
Injection site erythema			

subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Injection site swelling			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Injection site haematoma			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Peripheral swelling			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Oropharyngeal pain			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Obsessive-compulsive disorder			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Attention deficit/hyperactivity disorder			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Investigations			
Blood cholesterol increased			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Haemoglobin decreased			

subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Back injury			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Road traffic accident			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Fall			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Dermatitis contact			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	2		
Ligament sprain			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Tachycardia			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	2		
Juvenile myoclonic epilepsy			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Abdominal pain			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Abdominal pain upper			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Gastritis			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Diarrhoea			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Coeliac disease			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Toothache			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Pruritus genital			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Rash papular			

subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Eczema			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Acne			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Renal and urinary disorders			
Microalbuminuria			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Hypothyroidism			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Muscle twitching			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Costochondritis			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Infections and infestations			
Viral infection			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		
Ear infection			
subjects affected / exposed	0 / 15 (0.00%)		
occurrences (all)	0		

Pharyngitis				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences (all)	0			
Upper respiratory tract infection				
subjects affected / exposed	3 / 15 (20.00%)			
occurrences (all)	4			
Urinary tract infection				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences (all)	0			
Nasopharyngitis				
subjects affected / exposed	4 / 15 (26.67%)			
occurrences (all)	4			
Tonsillitis				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences (all)	1			
Viral upper respiratory tract infection				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences (all)	0			
Pseudocroup				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences (all)	0			
Gastroenteritis				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences (all)	1			
Tinea infection				
subjects affected / exposed	1 / 15 (6.67%)			
occurrences (all)	1			
Influenza				
subjects affected / exposed	3 / 15 (20.00%)			
occurrences (all)	3			
Cystitis				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences (all)	0			
Conjunctivitis				
subjects affected / exposed	0 / 15 (0.00%)			
occurrences (all)	0			

Varicella subjects affected / exposed occurrences (all) Rhinitis subjects affected / exposed occurrences (all) Borrelia infection subjects affected / exposed occurrences (all) Infectious mononucleosis subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0 0 / 15 (0.00%) 0 0 / 15 (0.00%) 0 0 / 15 (0.00%) 0		
Metabolism and nutrition disorders Hypoglycaemia subjects affected / exposed occurrences (all)	0 / 15 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported