Clinical trial results:
A Phase 2, Randomised, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy, Safety, Tolerability, and Pharmacokinetics of Different Doses of MEDI0382 in Overweight and Obese Subjects with Type 2 Diabetes Mellitus

Summary

EudraCT number	2017-002025-38
Trial protocol	DE
Global end of trial date	23 January 2018

Results information

Result version number	v4 (current)
This version publication date	18 December 2019
First version publication date	14 February 2019
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	D5670C00011

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03244800
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	MedImmune Limited
Sponsor organisation address	Milstein Building, Granta Park,, Cambridge, United Kingdom, CB21 6GH
Public contact	Victoria Parker, MedImmune Limited, +44 747 1357152, information.center@astrazeneca.com
Scientific contact	Victoria Parker, MedImmune Limited, +44 747 1357152, information.center@astrazeneca.com

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	23 January 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	23 January 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the effects of MEDI0382 titrated up to a dose level of 300 µg on glucose control and body weight versus placebo after 49 days of treatment (Cohort 1 only).

Protection of trial subjects:

The conduct of this study met all the local legal and regulatory requirements. The study was conducted in accordance with ethical principles that have their origin in the Declaration of Helsinki and was consistent with the International Council for Harmonisation (ICH) Guidelines on Good Clinical Practice (GCP). Participating participants signed the informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 September 2017
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	Germany: 65
Worldwide total number of subjects	65
EEA total number of subjects	65

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	45
From 65 to 84 years	20

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted across 5 sites in Germany between 04Sep2017 and 23Jan2018.

Pre-assignment

Screening details:

A total of 120 participants consented to participate in the study. Of which 55 were screen failures; 65 participants were randomised (46 to MEDI0382 and 19 to placebo).

Period 1

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

Blinding implementation details:

This was a double-blind study (MEDI0382 and placebo are identically labeled and indistinguishable in appearance). Neither the participant nor any of the investigator or sponsor staff who are involved in the treatment or clinical evaluation of the participants were aware of the treatment received.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo Cohort 1

Arm description:

Participants received placebo matching with MEDI0382 subcutaneously (SC) once daily for 49 days.

Arm type	Placebo
Investigational medicinal product name	Placebo Cohort 1
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection, Sterile concentrate
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received placebo matching with MEDI0382 subcutaneously (SC) once daily for 49 days.

Arm title	MEDI0382 Cohort 1

Arm description:

Participants received subcutaneous injection of MEDI0382 once daily for 49 days as Dose 1 for 7 days, followed by Dose 2 for 7 days, Dose 3 for 7 days, and Dose 4 for 28 days.

Arm type	Experimental
Investigational medicinal product name	MEDI0382 Cohort 1
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Sterile concentrate
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received subcutaneous injection of MEDI0382 once daily for 49 days as Dose 1 for 7 days, followed by Dose 2 for 7 days, Dose 3 for 7 days, and Dose 4 for 28 days.

Arm title	Placebo Cohort 2

Arm description:

Participants received placebo matching with MEDI0382 SC once daily for 49 days.

Arm type	Placebo

Investigational medicinal product name	Placebo Cohort 2
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection, Sterile concentrate
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received placebo matching with MEDI0382 SC once daily for 49 days.

Arm title	MEDI0382 Cohort 2

Arm description:

Participants received subcutaneous injection of MEDI0382 once daily for 49 days as Dose 1 for 14 days, followed by Dose 2 for 14 days, Dose 3 for 14 days, and Dose 4 for 7 days.

Arm type	Experimental
Investigational medicinal product name	MEDI0382 Cohort 2
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Sterile concentrate
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received subcutaneous injection of MEDI0382 once daily for 49 days as Dose 1 for 14 days, followed by Dose 2 for 14 days, Dose 3 for 14 days, and Dose 4 for 7 days.

Number of subjects in period 1	Placebo Cohort 1	MEDI0382 Cohort 1	Placebo Cohort 2
Started	13	26	6
Completed	13	25	6
Not completed	0	1	0
Adverse event, non-fatal	-	1	-
Withdrew treatment	-	-	-

Number of subjects in period 1	MEDI0382 Cohort 2
Started	20
Completed	18
Not completed	2
Adverse event, non-fatal	1
Withdrew treatment	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo Cohort 1
Reporting group description:	
Participants received placebo matching with MEDI0382 subcutaneously (SC) once daily for 49 days.	
Reporting group title	MEDI0382 Cohort 1
Reporting group description:	
Participants received subcutaneous injection of MEDI0382 once daily for 49 days as Dose 1 for 7 days, followed by Dose 2 for 7 days, Dose 3 for 7 days, and Dose 4 for 28 days.	
Reporting group title	Placebo Cohort 2
Reporting group description:	
Participants received placebo matching with MEDI0382 SC once daily for 49 days.	
Reporting group title	MEDI0382 Cohort 2
Reporting group description:	
Participants received subcutaneous injection of MEDI0382 once daily for 49 days as Dose 1 for 14 days, followed by Dose 2 for 14 days, Dose 3 for 14 days, and Dose 4 for 7 days.	

Reporting group values	Placebo Cohort 1	MEDI0382 Cohort 1	Placebo Cohort 2
Number of subjects	13	26	6
Age categorical Units: Subjects			
Adults (18-64 years)	11	18	4
From 65-84 years	2	8	2
Age Continuous Units: Years			
arithmetic mean	60.2	58.7	60.3
standard deviation	± 5.6	± 8.5	± 9.5
Sex: Female, Male Units: Subjects			
Female	4	7	1
Male	9	19	5
Race/Ethnicity, Customized Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	13	26	6
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaskan Native Asian	0	0	0
Black or African American	0	0	0
Native Hawaiian or Other Pacific Islander	0	1	0
White	13	25	6
Other	0	0	0

Reporting group values	MEDI0382 Cohort 2	Total	
Number of subjects	20	65	

Age categorical Units: Subjects			
Adults (18-64 years)	12	45	
From 65-84 years	8	20	
Age Continuous Units: Years			
arithmetic mean	61.9		
standard deviation	± 6.0	-	
Sex: Female, Male Units: Subjects			
Female	10	22	
Male	10	43	
Race/Ethnicity, Customized Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	20	65	
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaskan Native Asian	0	0	
Black or African American	0	0	
Native Hawaiian or Other Pacific Islander	0	1	
White	20	64	
Other	0	0	

Subject analysis sets

Subject analysis set title	Placebo
Subject analysis set type	Full analysis

Subject analysis set description:

Participants who received placebo matching with MEDI0382 subcutaneously (SC) once daily for 49 days.

Subject analysis set title	MEDI0382
Subject analysis set type	Full analysis

Subject analysis set description:

Participants who received subcutaneous injection of MEDI0382 once daily for 49 days.

Reporting group values	Placebo	MEDI0382	
Number of subjects	19	46	
Age categorical Units: Subjects			
Adults (18-64 years)			
From 65-84 years			
Age Continuous Units: Years			
arithmetic mean	60.2	60.1	
standard deviation	± 6.8	± 7.6	
Sex: Female, Male Units: Subjects			
Female			
Male			

Race/Ethnicity, Customized Units: Subjects			
Hispanic or Latino Not Hispanic or Latino			
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaskan Native Asian Black or African American Native Hawaiian or Other Pacific Islander White Other			

End points

End points reporting groups

Reporting group title	Placebo Cohort 1
Reporting group description:	
Participants received placebo matching with MEDI0382 subcutaneously (SC) once daily for 49 days.	
Reporting group title	MEDI0382 Cohort 1
Reporting group description:	
Participants received subcutaneous injection of MEDI0382 once daily for 49 days as Dose 1 for 7 days, followed by Dose 2 for 7 days, Dose 3 for 7 days, and Dose 4 for 28 days.	
Reporting group title	Placebo Cohort 2
Reporting group description:	
Participants received placebo matching with MEDI0382 SC once daily for 49 days.	
Reporting group title	MEDI0382 Cohort 2
Reporting group description:	
Participants received subcutaneous injection of MEDI0382 once daily for 49 days as Dose 1 for 14 days, followed by Dose 2 for 14 days, Dose 3 for 14 days, and Dose 4 for 7 days.	
Subject analysis set title	Placebo
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants who received placebo matching with MEDI0382 subcutaneously (SC) once daily for 49 days.	
Subject analysis set title	MEDI0382
Subject analysis set type	Full analysis
Subject analysis set description:	
Participants who received subcutaneous injection of MEDI0382 once daily for 49 days.	

Primary: Cohort 1: Percent Change From Baseline in Plasma Glucose Area Under the Concentration-time Curve From Time 0 to 4 hours (AUC0-4h) by Mixed-meal Tolerance Test (MMTT) to Day 49

End point title	Cohort 1: Percent Change From Baseline in Plasma Glucose Area Under the Concentration-time Curve From Time 0 to 4 hours (AUC0-4h) by Mixed-meal Tolerance Test (MMTT) to Day 49[1]
End point description:	
The MMTT test involved the consumption of a standardised liquid meal within 5 minutes and timed serial blood samples obtained for the measurement of glucose and parameters related to glucose metabolism through 240 minutes after consumption of the standardised meal (with no additional food intake during this time). The percent change in the MMTT plasma glucose AUC 0-4h from the baseline (Day -1) to Day 49 is reported. Pharmacodynamic (PD) population included all participants who received at least one dose of study drug and had at least one post-baseline MMTT PD sample or PD evaluation.	
End point type	Primary
End point timeframe:	
Zero minutes before and 15, 30, 45, 60, 90, 120, 180, and 240 minutes after consumption of the standardised liquid meal	

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

End point values	Placebo Cohort 1	MEDI0382 Cohort 1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	26		
Units: Percent change				
least squares mean (confidence interval 95%)	6.32 (-0.74 to 13.38)	-21.52 (-26.51 to -16.54)		

Statistical analyses

Statistical analysis title	Cohort 1: Statistical analysis
Comparison groups	Placebo Cohort 1 v MEDI0382 Cohort 1
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA

Primary: Cohort 1: Percent Change From Baseline in Body Weight to Day 50

End point title	Cohort 1: Percent Change From Baseline in Body Weight to Day 50[2]

End point description:

The percent change in body weight from baseline to Day 50 is reported. Intent-to-treat (ITT) population included all participants who received any study drug and were analyzed according to their randomized treatment group.

End point type	Primary

End point timeframe:

Day 1 through Day 50

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

End point values	Placebo Cohort 1	MEDI0382 Cohort 1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	26		
Units: Percent change				
least squares mean (confidence interval 95%)	-0.21 (-1.88 to 1.46)	-3.59 (-4.77 to -2.41)		

Statistical analyses

Statistical analysis title	Cohort 1: Statistical analysis
Comparison groups	Placebo Cohort 1 v MEDI0382 Cohort 1

Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	ANCOVA

Secondary: Cohort 1: Change From Baseline in Glycated Haemoglobin (HbA1c) to Day 49

End point title	Cohort 1: Change From Baseline in Glycated Haemoglobin (HbA1c) to Day 49[3]

End point description:

The change from baseline in Glycated haemoglobin (HbA1c) to Day 49 is reported. ITT population included all participants who received any study drug and were analyzed according to their randomized treatment group.

End point type	Secondary

End point timeframe:

Baseline (Day -1) through Day 49

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

End point values	Placebo Cohort 1	MEDI0382 Cohort 1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	26		
Units: Percentage change				
least squares mean (confidence interval 90%)	-0.07 (-0.27 to 0.14)	-0.67 (-0.82 to -0.53)		

Statistical analyses

Statistical analysis title	Cohort 1: Statistical analysis
Comparison groups	Placebo Cohort 1 v MEDI0382 Cohort 1
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA

Secondary: Cohort 1: Change From Baseline in Fasting Plasma Glucose to Day 49

End point title	Cohort 1: Change From Baseline in Fasting Plasma Glucose to Day 49[4]

End point description:

The changes in the fasting plasma glucose level during the study period from baseline to Day 49 is

reported. ITT population included all participants who received any study drug and were analyzed according to their randomized treatment group.

End point type	Secondary

End point timeframe:

Baseline (Day -1) through Day 49

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

End point values	Placebo Cohort 1	MEDI0382 Cohort 1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	26		
Units: mg/dL				
least squares mean (confidence interval 90%)	-2.31 (-12.74 to 8.13)	-35.37 (-42.75 to -27.99)		

Statistical analyses

Statistical analysis title	Cohort 1: Statistical analysis
Comparison groups	Placebo Cohort 1 v MEDI0382 Cohort 1
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA

Secondary: Cohort 1: Change From Baseline in Body Weight to Day 50

End point title	Cohort 1: Change From Baseline in Body Weight to Day 50[5]

End point description:

The changes in the body weight during the study period from baseline to Day 50 is reported. ITT population included all participants who received any study drug and were analyzed according to their randomized treatment group.

End point type	Secondary

End point timeframe:

Day 1 through Day 50

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

End point values	Placebo Cohort 1	MEDI0382 Cohort 1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	26		
Units: Kilogram				
least squares mean (confidence interval 90%)	-0.08 (-1.45 to 1.28)	-3.41 (-4.37 to -2.44)		

Statistical analyses

Statistical analysis title	Cohort 1: Statistical analysis
Comparison groups	Placebo Cohort 1 v MEDI0382 Cohort 1
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	ANCOVA

Secondary: Cohort 1: Percentage of Participants Achieving Greater Than or Equal to 5% Body Weight Loss from Baseline to Day 50

End point title	Cohort 1: Percentage of Participants Achieving Greater Than or Equal to 5% Body Weight Loss from Baseline to Day 50[6]

End point description:

Participants achieving greater than or equal to 5% body weight loss from baseline to Day 50 is reported. ITT population included all participants who received any study drug and were analyzed according to their randomized treatment group.

End point type	Secondary

End point timeframe:

Day 1 through Day 50

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

End point values	Placebo Cohort 1	MEDI0382 Cohort 1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	26		
Units: Percentage of Participants				
number (not applicable)	7.7	42.3		

Statistical analyses

Statistical analysis title	Cohort 1: Statistical analysis
Comparison groups	Placebo Cohort 1 v MEDI0382 Cohort 1

Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.04
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	10.76
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.61
upper limit	72.03

Secondary: Percent Change From Baseline in MMTT Plasma Glucose AUC 0-4h to Day 7

End point title	Percent Change From Baseline in MMTT Plasma Glucose AUC 0-4h to Day 7

End point description:

The MMTT test involved the consumption of a standardised liquid meal within 5 minutes and timed serial blood samples obtained for the measurement of glucose and parameters related to glucose metabolism through 240 minutes after consumption of the standardised meal (with no additional food intake during this time). The percent change in the MMTT plasma glucose AUC 0-4h from the baseline (Day -1) evaluation to Day 7 is reported. The PD population included all participants who received at least one dose of study drug and had at least one post-baseline MMTT PD sample or PD evaluation. The number of participants analyzed at the specified time point for this outcome measure are reported.

End point type	Secondary

End point timeframe:

Zero minutes before and 15, 30, 45, 60, 90, 120, 180, and 240 minutes after consumption of the standardised liquid meal

End point values	Placebo Cohort 1	MEDI0382 Cohort 1	Placebo Cohort 2	MEDI0382 Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	26	6	19
Units: Percent change				
arithmetic mean (standard deviation)	-2.02 (± 11.70)	-27.17 (± 9.83)	1.77 (± 23.43)	-31.80 (± 7.16)

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 1 and Cohort 2: Number of Participants With Treatment-emergent Adverse Events (TEAEs) and Treatment-emergent Serious Adverse Events (TESAEs)

End point title	Cohort 1 and Cohort 2: Number of Participants With Treatment-emergent Adverse Events (TEAEs) and Treatment-emergent Serious Adverse Events (TESAEs)

End point description:

An adverse event (AE) is any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. An SAE is an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. Treatment-emergent are the events between first doses of study drug through 7 to 14 days after the last dose of study drug (approximately 64 days). As-treated population included all participants who received any study drug and were analyzed according to the treatment they received.

End point type	Secondary

End point timeframe:

From Day 1 through 7 to 14 days after the last dose of study drug (approximately 64 days)

End point values	Placebo Cohort 1	MEDI0382 Cohort 1	Placebo Cohort 2	MEDI0382 Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	26	6	20
Units: Participants				
TEAEs	6	22	3	15
TESAEs	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 1 and Cohort 2: Number of Participants With Abnormal Vital Signs Reported as TEAEs

End point title	Cohort 1 and Cohort 2: Number of Participants With Abnormal Vital Signs Reported as TEAEs

End point description:

Treatment-emergent adverse events observed in participants with clinically significant vital signs abnormalities are reported. Vital sign parameters included blood pressure, heart rate, body temperature, and respiration rate. As-treated population included all participants who received any study drug and were analyzed according to the treatment they received.

End point type	Secondary

End point timeframe:

From Day 1 through 7 to 14 days after the last dose of study drug (approximately 64 days)

End point values	Placebo Cohort 1	MEDI0382 Cohort 1	Placebo Cohort 2	MEDI0382 Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	26	6	20
Units: Participants	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 1 and Cohort 2: Number of Participants With Abnormal Electrocardiogram Reported as TEAEs

End point title	Cohort 1 and Cohort 2: Number of Participants With Abnormal Electrocardiogram Reported as TEAEs

End point description:

Treatment-emergent adverse events observed in participants with clinically significant ECG abnormalities are reported. As-treated population included all participants who received any study drug and were analyzed according to the treatment they received.

End point type	Secondary

End point timeframe:

From Day 1 through 7 to 14 days after the last dose of study drug (approximately 64 days)

End point values	Placebo Cohort 1	MEDI0382 Cohort 1	Placebo Cohort 2	MEDI0382 Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	26	6	20
Units: Participants	0	0	0	1

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 1 and Cohort 2: Number of Participants With Clinical Laboratory Abnormalities Reported as TEAEs

End point title	Cohort 1 and Cohort 2: Number of Participants With Clinical Laboratory Abnormalities Reported as TEAEs

End point description:

An abnormal laboratory finding which required an action or intervention by the investigator, or a finding judged by the investigator as medically significant is reported as an AE. Laboratory evaluations included haematology, serum chemistry, and urinalysis. As-treated population included all participants who received any study drug and were analyzed according to the treatment they received.

End point type	Secondary

End point timeframe:

From Day 1 through 7 to 14 days after the last dose of study drug (approximately 64 days)

End point values	Placebo Cohort 1	MEDI0382 Cohort 1	Placebo Cohort 2	MEDI0382 Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	26	6	20
Units: Participants				
Thrombocytopenia	0	0	0	1
Hypoglycaemia	0	1	0	1

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 1 and Cohort 2: Number of Participants With Injection Site Erythema

End point title	Cohort 1 and Cohort 2: Number of Participants With Injection Site Erythema

End point description:

The injection site reactions observed during study visits are reported. Injection site reactions included (but are not limited to) local erythema, pain, tenderness, induration, swelling, pruritus, ulceration, and pigmentation. As-treated population included all participants who received any study drug and were analyzed according to the treatment they received.

End point type	Secondary

End point timeframe:

From Day 1 through 7 to 14 days after the last dose of study drug (approximately 64 days)

End point values	Placebo Cohort 1	MEDI0382 Cohort 1	Placebo Cohort 2	MEDI0382 Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	26	6	20
Units: Participants	0	0	0	5

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 1: Area Under the Concentration-time Curve During the Dosing Interval (AUCt) of MEDI0382

End point title	Cohort 1: Area Under the Concentration-time Curve During the Dosing Interval (AUCt) of MEDI0382[7]

End point description:

The area under the concentration-time curve during the dosing interval of MEDI0382 is reported. Pharmacokinetic (PK) population included all participants who received at least 1 dose of study drug and had at least 1 post-baseline PK sample with a value above lower limit of quantification. The 'n' denotes the number of participants analysed for specified time points.

End point type	Secondary

End point timeframe:

Cohort 1: Predose and 1, 2, 4, 6, 8, and 12 hours postdose on Days 22 and 49

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the

baseline period.

End point values	MEDI0382 Cohort 1			
Subject group type	Reporting group			
Number of subjects analysed	26			
Units: ng*hr/mL				
geometric mean (full range (min-max))				
Day 22 (n=18)	226.31 (103.95 to 488.98)			
Day 49 (n=24)	248.83 (86.57 to 558.57)			

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 2: Area Under the Concentration-time Curve During the Dosing Interval (AUCt) of MEDI0382

End point title	Cohort 2: Area Under the Concentration-time Curve During the Dosing Interval (AUCt) of MEDI0382[8]

End point description:

The area under the concentration-time curve during the dosing interval of MEDI0382 is reported. PK population included all participants who received at least 1 dose of study drug and had at least 1 post-baseline PK sample with a value above lower limit of quantification. The 'n' denotes the number of participants analysed for specified time points.

End point type	Secondary

End point timeframe:

Cohort 2: Predose and 1, 2, 4, 6, 8, and 12 hours postdose on Days 1, 7, and 14

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

End point values	MEDI0382 Cohort 2			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: ng*hr/mL				
geometric mean (full range (min-max))				
Day 1 (n=8)	38.67 (34.05 to 47.25)			
Day 7 (n=13)	37.51 (8.99 to 69.82)			
Day 14 (n=15)	46.75 (26.38 to 65.61)			

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 1: Maximum Observed Concentration (Cmax) of MEDI0382

End point title	Cohort 1: Maximum Observed Concentration (Cmax) of MEDI0382[9]

End point description:

The maximum observed concentration of MEDI0382 is reported. PK population included all participants who received at least 1 dose of study drug and had at least 1 post-baseline PK sample with a value above lower limit of quantification. The 'n' denotes the number of participants analysed for specified time points.

End point type	Secondary

End point timeframe:

Cohort 1: Predose and 1, 2, 4, 6, 8, and 12 hours postdose on Days 22 and 49

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

End point values	MEDI0382 Cohort 1			
Subject group type	Reporting group			
Number of subjects analysed	26			
Units: ng/mL				
geometric mean (full range (min-max))				
Day 22 (n=25)	13.24 (4.89 to 30.3)			
Day 49 (n=24)	14.8 (5.76 to 33.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 2: Maximum Observed Concentration (Cmax) of MEDI0382

End point title	Cohort 2: Maximum Observed Concentration (Cmax) of MEDI0382[10]

End point description:

The maximum observed concentration of MEDI0382 is reported. PK population included all participants who received at least 1 dose of study drug and had at least 1 post-baseline PK sample with a value above lower limit of quantification. The 'n' denotes the number of participants analysed for specified time points.

End point type	Secondary

End point timeframe:

Cohort 2: Predose and 1, 2, 4, 6, 8, and 12 hours postdose on Days 1, 7, and 14

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

End point values	MEDI0382 Cohort 2			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: ng/mL				
geometric mean (full range (min-max))				
Day 1 (n=20)	2.00 (1.09 to 3.25)			
Day 7 (n=20)	2.53 (0.85 to 4.14)			
Day 14 (n=19)	2.65 (1.50 to 3.77)			

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 1: Time to Reach Maximum Observed Concentration (Tmax) of MEDI0382

End point title	Cohort 1: Time to Reach Maximum Observed Concentration (Tmax) of MEDI0382[11]

End point description:

The time to reach the maximum observed concentration of MEDI0382 is reported. PK population included all participants who received at least 1 dose of study drug and had at least 1 post-baseline PK sample with a value above lower limit of quantification. The 'n' denotes the number of participants analysed for specified time points.

End point type	Secondary

End point timeframe:

Cohort 1: Predose and 1, 2, 4, 6, 8, and 12 hours postdose on Days 22 and 49

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

End point values	MEDI0382 Cohort 1			
Subject group type	Reporting group			
Number of subjects analysed	26			
Units: Hours				
median (full range (min-max))				
Day 22 (n=25)	6 (4 to 12)			
Day 49 (n=24)	4 (2 to 8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 2: Time to Reach Maximum Observed Concentration (Tmax) of

MEDI0382

End point title	Cohort 2: Time to Reach Maximum Observed Concentration (Tmax) of MEDI0382[12]

End point description:

The time to reach the maximum observed concentration of MEDI0382 is reported. PK population included all participants who received at least 1 dose of study drug and had at least 1 post-baseline PK sample with a value above lower limit of quantification. The 'n' denotes the number of participants analysed for specified time points.

End point type	Secondary

End point timeframe:

Cohort 2: Predose and 1, 2, 4, 6, 8, and 12 hours postdose on Days 1, 7, and 14

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

End point values	MEDI0382 Cohort 2			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: Hours				
median (full range (min-max))				
Day 1 (n=20)	8 (4 to 12)			
Day 7 (n=20)	6 (0 to 8)			
Day 14 (n=19)	6 (4 to 12)			

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 1: Terminal Half life (t1/2) of MEDI0382

End point title	Cohort 1: Terminal Half life (t1/2) of MEDI0382[13]

End point description:

The t1/2 is the time measured for the concentration to decrease by one half after the dose of MEDI0382. PK population included all participants who received at least 1 dose of study drug and had at least 1 post-baseline PK sample with a value above lower limit of quantification. The 'n' denotes the number of participants analysed for specified time points.

End point type	Secondary

End point timeframe:

Cohort 1: Predose and 1, 2, 4, 6, 8, and 12 hours postdose on Days 22 and 49

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

End point values	MEDI0382 Cohort 1			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Hours				
geometric mean (full range (min-max))				
Day 22 (n=1)	9.67 (9.67 to 9.67)			
Day 49 (n=5)	8.4 (7.7 to 9.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 2: Terminal Half life (t1/2) of MEDI0382

End point title	Cohort 2: Terminal Half life (t1/2) of MEDI0382[14]

End point description:

The t1/2 is the time measured for the concentration to decrease by one half after the dose of MEDI0382. PK population included all participants who received at least 1 dose of study drug and had at least 1 post-baseline PK sample with a value above lower limit of quantification. The 'n' denotes the number of participants analysed for specified time points.

End point type	Secondary

End point timeframe:

Cohort 2: Predose and 1, 2, 4, 6, 8, and 12 hours postdose on Days 1, 7, and 14

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

End point values	MEDI0382 Cohort 2			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: Hours				
geometric mean (full range (min-max))				
Day 1 (n=3)	9.7 (8.9 to 10.2)			
Day 7 (n=3)	8.8 (8.6 to 9.0)			
Day 14 (n=4)	9.4 (8.7 to 10.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 1: Accumulation Ratio (Racc) of MEDI0382

End point title	Cohort 1: Accumulation Ratio (Racc) of MEDI0382[15]

End point description:

The Racc was calculated using the AUC method which account for the overall exposure measured using the specified time points on Day 22 and Day 49. PK population included all participants who received at least 1 dose of study drug and had at least 1 post-baseline PK sample with a value above lower limit of quantification. The data for number of participants analysed for specified time point are reported.

End point type	Secondary

End point timeframe:

Cohort 1: Predose and 1, 2, 4, 6, 8, and 12 hours postdose on Days 22 and 49

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

End point values	MEDI0382 Cohort 1			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: Ratio				
geometric mean (full range (min-max))				
Day 49	1.46 (1.13 to 2.98)			

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 2: Accumulation Ratio (Racc) of MEDI0382

End point title	Cohort 2: Accumulation Ratio (Racc) of MEDI0382[16]

End point description:

The Racc was calculated using the AUC method which account for the overall exposure measured using the specified time points on Day 1, Day 7 and Day 14. Racc was calculated using the formulas: Racc of Day 7 = AUCt of Day 7/AUCt of Day 1; Racc of Day 14 = AUCt of Day 14/AUCt of Day 1. PK population included all participants who received at least 1 dose of study drug and had at least 1 post-baseline PK sample with a value above lower limit of quantification. The 'n' denotes the number of participants analysed for specified time points.

End point type	Secondary

End point timeframe:

Cohort 2: Predose and 1, 2, 4, 6, 8, and 12 hours postdose on Days 1, 7, and 14

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

End point values	MEDI0382 Cohort 2			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: Ratio				
geometric mean (full range (min-max))				
Day 7 (n=13) Day 14 (n=13)	1.36 (1.2 to 1.6) 1.46 (1.2 to 1.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 1: Trough Plasma Concentration (Ctrough) of MEDI0382

End point title	Cohort 1: Trough Plasma Concentration (Ctrough) of

End point description:

Trough plasma concentration is the measured concentration from the plasma concentration-time data at the end of a dosing interval at steady state. PK population included all participants who received at least 1 dose of study drug and had at least 1 post-baseline PK sample with a value above lower limit of quantification. The 'n' denotes the number of participants analysed for specified time points.

End point type	Secondary

End point timeframe:

Cohort 1: Predose and 1, 2, 4, 6, 8, and 12 hours postdose on Days 22 and 49

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

End point values	MEDI0382 Cohort 1			
Subject group type	Reporting group			
Number of subjects analysed	26			
Units: ng/mL				
geometric mean (full range (min-max))				
Day 22 (n=25) Day 49 (n=24)	3.566 (0.50 to 9.27) 5.762 (1.53 to 11.80)			

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 2: Trough Plasma Concentration (Ctrough) of MEDI0382

End point title	Cohort 2: Trough Plasma Concentration (Ctrough) of

End point description:

Trough plasma concentration is the measured concentration from the plasma concentration time data at the end of a dosing interval at steady state. For Cohort 2, no participants were analyzed at Day 1 (n=0) because the values were below the limit of quantification for each participant. Therefore, reported by an arbitrary value (99999) which indicates data not available for Day 1 as zero participants were evaluable for this time point. PK population included all participants who received at least 1 dose of study drug and had at least 1 post-baseline PK sample with a value above lower limit of quantification. The 'n' denotes the number of participants analysed for specified time points.

End point type	Secondary

End point timeframe:

Cohort 2: Predose and 1, 2, 4, 6, 8, and 12 hours postdose on Days 1, 7, and 14

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

End point values	MEDI0382 Cohort 2			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: ng/mL				
geometric mean (full range (min-max))				
Day 1 (n=0)	99999 (99999 to 99999)			
Day 7 (n=19)	1.147 (0.79 to 2.36)			
Day 14 (n=19)	1.147 (0.69 to 1.92)			

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 1 and Cohort 2: Number of Participants With Positive Anti-drug Antibodies (ADA) to MEDI0382

End point title	Cohort 1 and Cohort 2: Number of Participants With Positive Anti-drug Antibodies (ADA) to MEDI0382

End point description:

Participants with positive serum antibodies to MEDI0382 are reported. As-treated population included all participants who received any study drug and were analyzed according to the treatment they received. The 'n' denotes the number of participants analysed for specified time points.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Day 29, Day 50, and Follow-up Visit 2 (28 days after the last dose [approximately 64 days])

End point values	Placebo Cohort 1	MEDI0382 Cohort 1	Placebo Cohort 2	MEDI0382 Cohort 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	26	6	20
Units: Participants				
Baseline (ADA positive) (n=13, 26, 6, 20)	0	0	0	0
Day 29 (ADA positive) (n=13, 26, 6, 18)	0	4	0	1
Day 50 (ADA positive) (n=13, 25, 6, 18)	0	7	0	2
Follow-up Visit 2 (ADA positive) (n=13, 24, 6, 20)	1	6	0	6

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From Day 1 through 7 to 14 days after the last dose of study drug (approximately 64 days)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups	
Reporting group title	Placebo Cohort 1
Reporting group description:	
Participants received placebo matching with MEDI0382 subcutaneously (SC) once daily for 49 days.	
Reporting group title	MEDI0382 Cohort 1
Reporting group description:	
Participants received subcutaneous injection of MEDI0382 once daily for 49 days as Dose 1 for 7 days, followed by Dose 2 for 7 days, Dose 3 for 7 days, and Dose 4 for 28 days.	
Reporting group title	Placebo Cohort 2
Reporting group description:	
Participants received placebo matching with MEDI0382 SC once daily for 49 days.	
Reporting group title	MEDI0382 Cohort 2
Reporting group description:	
Participants received subcutaneous injection of MEDI0382 once daily for 49 days as Dose 1 for 14 days, followed by Dose 2 for 14 days, Dose 3 for 14 days, and Dose 4 for 7 days.	

Serious adverse events	Placebo Cohort 1	MEDI0382 Cohort 1	Placebo Cohort 2
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 13 (0.00%)	0 / 26 (0.00%)	0 / 6 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	MEDI0382 Cohort 2		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Placebo Cohort 1	MEDI0382 Cohort 1	Placebo Cohort 2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 13 (46.15%)	22 / 26 (84.62%)	3 / 6 (50.00%)
General disorders and administration site conditions			
Face oedema			
subjects affected / exposed	0 / 13 (0.00%)	1 / 26 (3.85%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Fatigue			
subjects affected / exposed	1 / 13 (7.69%)	1 / 26 (3.85%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Induration			
subjects affected / exposed	0 / 13 (0.00%)	0 / 26 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injection site erythema			
subjects affected / exposed	0 / 13 (0.00%)	0 / 26 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injection site haematoma			
subjects affected / exposed	0 / 13 (0.00%)	0 / 26 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injection site reaction			
subjects affected / exposed	0 / 13 (0.00%)	0 / 26 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 13 (0.00%)	1 / 26 (3.85%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Medical device site pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 26 (3.85%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Medical device site swelling			
subjects affected / exposed	0 / 13 (0.00%)	1 / 26 (3.85%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Oedema peripheral			
subjects affected / exposed	0 / 13 (0.00%)	1 / 26 (3.85%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Pyrexia			

subjects affected / exposed	0 / 13 (0.00%)	1 / 26 (3.85%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Vessel puncture site haematoma			
subjects affected / exposed	0 / 13 (0.00%)	1 / 26 (3.85%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	0 / 13 (0.00%)	0 / 26 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 13 (0.00%)	1 / 26 (3.85%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Epistaxis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 26 (3.85%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Nasal obstruction			
subjects affected / exposed	0 / 13 (0.00%)	0 / 26 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 26 (3.85%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Loss of libido			
subjects affected / exposed	0 / 13 (0.00%)	1 / 26 (3.85%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 13 (7.69%)	0 / 26 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Procedural nausea			
subjects affected / exposed	0 / 13 (0.00%)	1 / 26 (3.85%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			

Tachycardia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 26 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 13 (0.00%)	1 / 26 (3.85%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	0 / 13 (0.00%)	2 / 26 (7.69%)	2 / 6 (33.33%)
occurrences (all)	0	2	2
Tremor			
subjects affected / exposed	0 / 13 (0.00%)	0 / 26 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 26 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Visual impairment			
subjects affected / exposed	0 / 13 (0.00%)	0 / 26 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 13 (0.00%)	0 / 26 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 26 (3.85%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Abdominal wall haematoma			
subjects affected / exposed	1 / 13 (7.69%)	0 / 26 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	0 / 13 (0.00%)	4 / 26 (15.38%)	0 / 6 (0.00%)
occurrences (all)	0	4	0
Diarrhoea			
subjects affected / exposed	1 / 13 (7.69%)	3 / 26 (11.54%)	0 / 6 (0.00%)
occurrences (all)	1	4	0

Dyspepsia			
subjects affected / exposed	0 / 13 (0.00%)	4 / 26 (15.38%)	0 / 6 (0.00%)
occurrences (all)	0	8	0
Eructation			
subjects affected / exposed	0 / 13 (0.00%)	3 / 26 (11.54%)	0 / 6 (0.00%)
occurrences (all)	0	4	0
Flatulence			
subjects affected / exposed	0 / 13 (0.00%)	1 / 26 (3.85%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	0 / 13 (0.00%)	5 / 26 (19.23%)	0 / 6 (0.00%)
occurrences (all)	0	8	0
Parotid gland enlargement			
subjects affected / exposed	0 / 13 (0.00%)	0 / 26 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Regurgitation			
subjects affected / exposed	0 / 13 (0.00%)	0 / 26 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tongue discomfort			
subjects affected / exposed	0 / 13 (0.00%)	0 / 26 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 13 (0.00%)	2 / 26 (7.69%)	0 / 6 (0.00%)
occurrences (all)	0	3	0
Vomiting			
subjects affected / exposed	0 / 13 (0.00%)	3 / 26 (11.54%)	0 / 6 (0.00%)
occurrences (all)	0	6	0
Skin and subcutaneous tissue disorders			
Dermatitis contact			
subjects affected / exposed	0 / 13 (0.00%)	1 / 26 (3.85%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Erythema			
subjects affected / exposed	0 / 13 (0.00%)	0 / 26 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			

subjects affected / exposed	0 / 13 (0.00%)	0 / 26 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 13 (0.00%)	1 / 26 (3.85%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Skin reaction			
subjects affected / exposed	0 / 13 (0.00%)	1 / 26 (3.85%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Nocturia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 26 (3.85%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 13 (7.69%)	0 / 26 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	2
Osteoarthritis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 26 (3.85%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Pain in extremity			
subjects affected / exposed	0 / 13 (0.00%)	1 / 26 (3.85%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 26 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nasal herpes			
subjects affected / exposed	0 / 13 (0.00%)	1 / 26 (3.85%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 26 (3.85%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 26 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			

subjects affected / exposed	3 / 13 (23.08%)	3 / 26 (11.54%)	0 / 6 (0.00%)
occurrences (all)	4	4	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 13 (15.38%)	13 / 26 (50.00%)	0 / 6 (0.00%)
occurrences (all)	2	17	0
Gout			
subjects affected / exposed	0 / 13 (0.00%)	1 / 26 (3.85%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hypoglycaemia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 26 (3.85%)	0 / 6 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	MEDI0382 Cohort 2		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 20 (75.00%)		
General disorders and administration site conditions			
Face oedema			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Induration			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Injection site erythema			
subjects affected / exposed	5 / 20 (25.00%)		
occurrences (all)	7		
Injection site haematoma			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Injection site reaction			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	2		
Malaise			

subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Medical device site pain			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Medical device site swelling			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Oedema peripheral			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Vessel puncture site haematoma			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Epistaxis			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Nasal obstruction			
subjects affected / exposed	0 / 20 (0.00%)		
occurrences (all)	0		
Oropharyngeal pain			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Psychiatric disorders			

Loss of libido subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0		
Injury, poisoning and procedural complications Contusion subjects affected / exposed occurrences (all) Procedural nausea subjects affected / exposed occurrences (all)	 0 / 20 (0.00%) 0 0 / 20 (0.00%) 0		
Cardiac disorders Tachycardia subjects affected / exposed occurrences (all)	 1 / 20 (5.00%) 1		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Tremor subjects affected / exposed occurrences (all)	 1 / 20 (5.00%) 1 4 / 20 (20.00%) 6 1 / 20 (5.00%) 5		
Blood and lymphatic system disorders Thrombocytopenia subjects affected / exposed occurrences (all)	 1 / 20 (5.00%) 1		
Eye disorders Visual impairment subjects affected / exposed occurrences (all)	 1 / 20 (5.00%) 1		
Gastrointestinal disorders Abdominal discomfort subjects affected / exposed occurrences (all) Abdominal pain	 1 / 20 (5.00%) 1 		

subjects affected / exposed	0 / 20 (0.00%)			
occurrences (all)	0			
Abdominal wall haematoma				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences (all)	0			
Constipation				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	1			
Diarrhoea				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	1			
Dyspepsia				
subjects affected / exposed	2 / 20 (10.00%)			
occurrences (all)	3			
Eructation				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences (all)	0			
Flatulence				
subjects affected / exposed	0 / 20 (0.00%)			
occurrences (all)	0			
Nausea				
subjects affected / exposed	7 / 20 (35.00%)			
occurrences (all)	11			
Parotid gland enlargement				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	1			
Regurgitation				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	1			
Tongue discomfort				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	2			
Toothache				
subjects affected / exposed	1 / 20 (5.00%)			
occurrences (all)	1			
Vomiting				

subjects affected / exposed occurrences (all)	4 / 20 (20.00%) 11		
Skin and subcutaneous tissue disorders Dermatitis contact subjects affected / exposed occurrences (all) Erythema subjects affected / exposed occurrences (all) Hyperhidrosis subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all) Skin reaction subjects affected / exposed occurrences (all)	 0 / 20 (0.00%) 0 1 / 20 (5.00%) 1 1 / 20 (5.00%) 1 0 / 20 (0.00%) 0 0 / 20 (0.00%) 0		
Renal and urinary disorders Nocturia subjects affected / exposed occurrences (all)	 0 / 20 (0.00%) 0		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) Osteoarthritis subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all)	 0 / 20 (0.00%) 0 0 / 20 (0.00%) 0 0 / 20 (0.00%) 0		
Infections and infestations Conjunctivitis subjects affected / exposed occurrences (all)	 1 / 20 (5.00%) 1		

Nasal herpes subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0		
Rhinitis subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0		
Urinary tract infection subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 2		
Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	3 / 20 (15.00%) 4		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0		
Gout subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0		
Hypoglycaemia subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 July 2017	The original protocol was amended to modify exploratory objectives, clinical laboratory test, exclusion criteria, procedures, prohibited concomitant medications, reduction in blood volume, and to correct typographical errors.
17 October 2017	The protocol amendment 2 was made to modify the procedures, table footnotes, time frame for serious adverse events, updated with the definition of postmenopausal to correct a previous oversight, and clarification on maternal exposure.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported