# Clinical trial results:
# An Exploratory Phase 2, Randomised, Double-blind, Placebo-controlled, and Open-label Active Comparator Study to Evaluate the Effect of MEDI0382 on Hepatic Glycogen Metabolism in Overweight and Obese Subjects with Type 2 Diabetes Mellitus

## Summary

| | |
|---|---|
| EudraCT number | 2017-005081-22 |
| Trial protocol | SE GB |
| Global end of trial date | 26 August 2021 |

### Results information

| | |
|---|---|
| Result version number | v3 (current) |
| This version publication date | 26 February 2025 |
| First version publication date | 27 April 2022 |
| Version creation reason | |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | D5670C00022 |

### Additional study identifiers

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

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | AstraZeneca Clinical Study Information Center |
| Sponsor organisation address | One Medimmune Way, Gaithersburg, United States, 20878 |
| Public contact | Medical Monitor, AstraZeneca Clinical Study Information Center, +1 877-240-9479, information.center@astrazeneca.com |
| Scientific contact | Medical Monitor, AstraZeneca Clinical Study Information Center, +1 877-240-9479, 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 | 16 September 2021 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 26 August 2021 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To assess the effect of MEDI0382 on hepatic glycogen levels versus placebo after 28 days (Part A) and 35 days (Part B) of treatment

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with GCP and the applicable regulatory requirement(s).

Background therapy:

MEDI0382 is a synthetic peptide with both glucagon-like peptide-1 (GLP-1) and glucagon receptor agonist activity which is under development for the treatment of T2DM and non-alcoholic steatohepatitis (NASH). GLP-1 receptor agonists are established treatments for T2DM that improve glycaemic control, delay gastric emptying, and depress appetite leading to modest, but often non-sustained weight loss (typically 3% versus baseline at one year). Glucagon has similar effects to GLP-1 on gastric emptying and appetite, and has also been shown to promote increased energy expenditure (Lynch et al, 2014; Habegger et al, 2013). Oxyntomodulin, a naturally occurring peptide with GLP-1 and glucagon receptor co-agonist activity, has been shown to promote weight loss through effects on appetite and energy expenditure (Wynne et al, 2006) and co-infusion of GLP-1 and glucagon has synergistic effects on reducing food intake and promoting weight loss in human subjects (Bagger et al, 2015).

Evidence for comparator:

Liraglutide is an analog with 97% homology to human glucagon-like peptide (GLP-1) and acts as a GLP-1 receptor agonist. Several large, randomized, multicenter phase 3 trials evaluated the efficacy and safety of liraglutide by comparing monotherapy and combination therapy with other antidiabetic medications in adult patients with type 2 diabetes. The Liraglutide Effect and Action in Diabetes (LEAD) program demonstrated that liraglutide, when used alone or in combination with other antidiabetic medications, effectively controls hyperglycemia (glycosylated hemoglobin [A1C] reductions up to 1.6%) and assists patients in meeting established glycemic targets. Compared with certain other classes of antidiabetic agents, liraglutide is associated with a lower risk of hypoglycemia. Liraglutide has also been associated with weight loss (1.8 to 3.4 kg) and improved patient satisfaction and health-related quality of life.

| | |
|---|---|
| Actual start date of recruitment | 31 May 2018 |
| 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 | Netherlands: 16 |
| Country: Number of subjects enrolled | Sweden: 35 |
| Worldwide total number of subjects | 51 |
| EEA total number of subjects | 51 |

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) | 21 |
| From 65 to 84 years | 30 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

A total of 51 participants (total for Part A [21 participants] and B [30 participants]) participated in the study from 31 May 2018 (date first participant enrolled) to 14 April 2021 (date of last participant last visit) at one site in Sweden for Part A, and 2 sites (one in Sweden and one in the Netherlands) for Part B.

### Pre-assignment

Screening details:

A total of 95 participants consented to participate in the study (36 from Part A and 59 from Part B) from one site in Sweden for Part A, and 2 sites (one in Sweden and one in the Netherlands) for Part B. Of these, 15 participants from Part A and 29 participants from Part B were considered screen failures.

### Pre-assignment period milestones

| | |
|---|---|
| Number of subjects started | 51 |
| Number of subjects completed | 51 |

### Period 1

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

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | MEDI0382 (Part A) |

Arm description: -

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Cotadutide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

MEDI0382 100 µg for 7 days, followed by 200 µg for 7 days, followed by 300 µg for 14 days once daily in the morning via SC injection as

| | |
|---|---|
| **Arm title** | Placebo (Part A) |

Arm description: -

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

Dosage and administration details:

Placebo for 28 days

| | |
|---|---|
| **Arm title** | Liraglutide (Part B) |

| | |
|---|---|
| Arm description: - | |
| Arm type | Active comparator |
| Investigational medicinal product name | Victoza |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Open label liraglutide 0.6 mg for 7 days, followed by 1.2 mg for 7 days, followed by 1.8 mg for 21 days

| | |
|---|---|
| **Arm title** | MEDI0382 (Part B) |
| Arm description: - | |
| Arm type | Experimental |
| Investigational medicinal product name | Cotadutide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

MEDI0382 50 µg for 7 days, followed by 100 µg for 7 days, followed by 200 µg for 7 days, followed by 300 µg for 14 days

| | |
|---|---|
| **Arm title** | Placebo (Part B) |
| Arm description: - | |
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Placebo for 35 days

| **Number of subjects in period 1** | MEDI0382 (Part A) | Placebo (Part A) | Liraglutide (Part B) |
|---|---|---|---|
| Started | 12 | 9 | 10 |
| Completed | 12 | 9 | 10 |

| **Number of subjects in period 1** | MEDI0382 (Part B) | Placebo (Part B) |
|---|---|---|
| Started | 9 | 11 |
| Completed | 9 | 11 |

## Period 2

| | |
|---|---|
| Period 2 title | Treatment Period |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Carer, Data analyst, Assessor |

## Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | MEDI0382 (Part A) |

Arm description: -

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Cotadutide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

MEDI0382 100 µg for 7 days, followed by 200 µg for 7 days, followed by 300 µg for 14 days once daily in the morning via SC injection as

| | |
|---|---|
| **Arm title** | Placebo (Part A) |

Arm description: -

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

Dosage and administration details:

Placebo for 28 days

| | |
|---|---|
| **Arm title** | Liraglutide (Part B) |

Arm description: -

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | Victoza |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Open label liraglutide 0.6 mg for 7 days, followed by 1.2 mg for 7 days, followed by 1.8 mg for 21 days

| | |
|---|---|
| **Arm title** | MEDI0382 (Part B) |

Arm description: -

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Cotadutide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

MEDI0382 50 µg for 7 days, followed by 100 µg for 7 days, followed by 200 µg for 7 days, followed by 300 µg for 14 days

| **Arm title** | Placebo (Part B) |
|---|---|
| Arm description: - | |
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Placebo for 35 days

| **Number of subjects in period 2** | MEDI0382 (Part A) | Placebo (Part A) | Liraglutide (Part B) |
|---|---|---|---|
| Started | 12 | 9 | 10 |
| Completed | 12 | 9 | 10 |

| **Number of subjects in period 2** | MEDI0382 (Part B) | Placebo (Part B) |
|---|---|---|
| Started | 9 | 11 |
| Completed | 9 | 11 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | MEDI0382 (Part A) |
| Reporting group description: - | |
| Reporting group title | Placebo (Part A) |
| Reporting group description: - | |
| Reporting group title | Liraglutide (Part B) |
| Reporting group description: - | |
| Reporting group title | MEDI0382 (Part B) |
| Reporting group description: - | |
| Reporting group title | Placebo (Part B) |
| Reporting group description: - | |

| Reporting group values | MEDI0382 (Part A) | Placebo (Part A) | Liraglutide (Part B) |
|---|---|---|---|
| Number of subjects | 12 | 9 | 10 |
| Age Categorical<br>Units: Subjects | | | |
| aged ≥ 18 years | 12 | 9 | 10 |
| Gender Categorical<br>Units: Subjects | | | |
| Female | 5 | 3 | 4 |
| Male | 7 | 6 | 6 |

| Reporting group values | MEDI0382 (Part B) | Placebo (Part B) | Total |
|---|---|---|---|
| Number of subjects | 9 | 11 | 51 |
| Age Categorical<br>Units: Subjects | | | |
| aged ≥ 18 years | 9 | 11 | 51 |
| Gender Categorical<br>Units: Subjects | | | |
| Female | 3 | 2 | 17 |
| Male | 6 | 9 | 34 |

| Subject analysis sets | |
|---|---|
| Subject analysis set title | As-treated population |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: | |
| Participants who received any study IP were included in the as-treated population and participants were analysed according to the treatment they actually received. | |
| Subject analysis set title | Intent-to-treat population |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: | |
| Participants who received any study IP were included in the ITT population and participants were analysed according to their randomised treatment group. | |

| **Reporting group values** | As-treated population | Intent-to-treat population | |
|---|---|---|---|
| Number of subjects | 51 | 51 | |
| Age Categorical<br>Units: Subjects | | | |
| aged ≥ 18 years | 51 | 51 | |
| Gender Categorical<br>Units: Subjects | | | |
| Female | 17 | 17 | |
| Male | 34 | 34 | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | MEDI0382 (Part A) |
| Reporting group description: - | |
| Reporting group title | Placebo (Part A) |
| Reporting group description: - | |
| Reporting group title | Liraglutide (Part B) |
| Reporting group description: - | |
| Reporting group title | MEDI0382 (Part B) |
| Reporting group description: - | |
| Reporting group title | Placebo (Part B) |
| Reporting group description: - | |
| Reporting group title | MEDI0382 (Part A) |
| Reporting group description: - | |
| Reporting group title | Placebo (Part A) |
| Reporting group description: - | |
| Reporting group title | Liraglutide (Part B) |
| Reporting group description: - | |
| Reporting group title | MEDI0382 (Part B) |
| Reporting group description: - | |
| Reporting group title | Placebo (Part B) |
| Reporting group description: - | |
| Subject analysis set title | As-treated population |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: | |
| Participants who received any study IP were included in the as-treated population and participants were analysed according to the treatment they actually received. | |
| Subject analysis set title | Intent-to-treat population |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: | |
| Participants who received any study IP were included in the ITT population and participants were analysed according to their randomised treatment group. | |

### Primary: Change in hepatic glycogen concentration adjusted for liver volume as measured by MRS at T = 4 hours post standardised morning meal from baseline (Day -1) to the end of 28 days of treatment (Part A only)

| | |
|---|---|
| End point title | Change in hepatic glycogen concentration adjusted for liver volume as measured by MRS at T = 4 hours post standardised morning meal from baseline (Day -1) to the end of 28 days of treatment (Part A only) |
| End point description: | |
| To assess the effect of MEDI0382 on hepatic glycogen levels postprandially versus placebo after 28 days of treatment | |
| End point type | Primary |
| End point timeframe: | |
| from baseline (Day -1) to the end of 28 days of treatment (Part A only) | |

| End point values | MEDI0382 (Part A) | Placebo (Part A) | Intent-to-treat population | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 12 | 9 | 21[1] | |
| Units: mmol/L | | | | |
| least squares mean (confidence interval 90%) | | | | |
| Change from baseline | -100.2 (-150.2 to -50.1) | 5.5 (-47.2 to 58.3) | -105.7 (-178.8 to -32.6) | |

Notes:

[1] - Part A Only MEDI0382 (Part A) vs. Placebo (Part A)

## Statistical analyses

| Statistical analysis title | Primary Analysis (Part A) |
|---|---|

Statistical analysis description:

To assess the effect of cotadutide on hepatic glycogen levels versus placebo after 28 days (Part A)

| | |
|---|---|
| Comparison groups | MEDI0382 (Part A) v Placebo (Part A) |
| Number of subjects included in analysis | 21 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.023 |
| Method | ANCOVA |
| Parameter estimate | Least square mean difference |
| Point estimate | -105.7 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -178.8 |
| upper limit | -32.6 |

## Primary: Percentage change in fasting hepatic glycogen concentration adjusted for liver volume as measured by MRS at T = 24 hours post standardised morning meal from baseline (Day 1) to the end of 35 days of treatment (Day 36) (Part B)

| | |
|---|---|
| End point title | Percentage change in fasting hepatic glycogen concentration adjusted for liver volume as measured by MRS at T = 24 hours post standardised morning meal from baseline (Day 1) to the end of 35 days of treatment (Day 36) (Part B) |

End point description:

| | |
|---|---|
| End point type | Primary |

End point timeframe:

from baseline (Day 1) to the end of 35 days of treatment (Day 36) (Part B)

| End point values | MEDI0382 (Part B) | Placebo (Part B) | Intent-to-treat population | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 9 | 11 | 20[2] | |
| Units: percent change from baseline | | | | |
| least squares mean (confidence interval 90%) | -27.02 (-38.04 to -16.01) | -1.15 (-11.09 to 8.79) | -25.87 (-40.88 to -10.86) | |

Notes:

[2] - Part B Only MEDI0382 (Part B) vs. Placebo (Part B)

### Statistical analyses

| Statistical analysis title | Primary Analysis Part B |
|---|---|

Statistical analysis description:

To assess the effect of cotadutide on hepatic glycogen levels versus placebo after 35 days (Part B) of treatment

| Comparison groups | MEDI0382 (Part B) v Placebo (Part B) v Intent-to-treat population |
|---|---|
| Number of subjects included in analysis | 40 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.008 |
| Method | ANCOVA |
| Parameter estimate | Least square mean difference |
| Point estimate | -25.87 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -40.88 |
| upper limit | -10.86 |

## Secondary: Percentage change in fasting hepatic glycogen concentration adjusted for liver volume as measured by MRS at T = 24 hours post standardised morning meal from baseline (Day 1) to the end of 35 days of treatment (Day 36, Part B only)

| End point title | Percentage change in fasting hepatic glycogen concentration adjusted for liver volume as measured by MRS at T = 24 hours post standardised morning meal from baseline (Day 1) to the end of 35 days of treatment (Day 36, Part B only) |
|---|---|

End point description:

To assess the effect of MEDI0382 on hepatic glycogen levels versus liraglutide after 35 days of treatment (Part B only)

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

End point timeframe:

Fom baseline (Day -1) to Day 35

| End point values | Liraglutide (Part B) | MEDI0382 (Part B) | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 10 | 9 | | |
| Units: Percentage change from baseline | | | | |
| least squares mean (confidence interval 90%) | -5.33 (-13.97 to 3.32) | -27.31 (-36.42 to -18.20) | | |

**Statistical analyses**

| Statistical analysis title | Comparing groups: MEDI0382 vs Liraglutide |
|---|---|
| Comparison groups | Liraglutide (Part B) v MEDI0382 (Part B) |
| Number of subjects included in analysis | 19 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.008 |
| Method | ANCOVA |
| Parameter estimate | Least Square Mean difference |
| Point estimate | -21.99 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -34.55 |
| upper limit | -9.43 |

**Secondary: Change of hepatic fat fraction from baseline as measured by magnetic resonance imaging (Day -1) to the end of 35 days of treatment (Part B only)**

| End point title | Change of hepatic fat fraction from baseline as measured by magnetic resonance imaging (Day -1) to the end of 35 days of treatment (Part B only) |
|---|---|
| End point description: | |
| To assess the effect of cotadutide on hepatic fat fraction versus placebo after 35 days of treatment (Part B only) | |
| End point type | Secondary |
| End point timeframe: | |
| Day -1 to Day 36 | |

| End point values | Liraglutide (Part B) | MEDI0382 (Part B) | Placebo (Part B) | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 10 | 9 | 11 | |
| Units: Percent | | | | |
| least squares mean (confidence interval 90%) | -15.40 (-21.09 to -9.72) | -26.26 (-51.13 to -1.39) | 8.79 (-10.46 to 28.05) | |

**Statistical analyses**

| **Statistical analysis title** | Comparing groups: MEDI0382 vs Liraglutide |
|---|---|
| Comparison groups | Liraglutide (Part B) v MEDI0382 (Part B) |
| Number of subjects included in analysis | 19 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.03 |
| Method | ANCOVA |
| Parameter estimate | Least Square Mean difference |
| Point estimate | -11.72 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -20.13 |
| upper limit | -3.3 |

| **Statistical analysis title** | Comparing groups: MEDI0382 vs Placebo |
|---|---|
| Comparison groups | MEDI0382 (Part B) v Placebo (Part B) |
| Number of subjects included in analysis | 20 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.07 |
| Method | ANCOVA |
| Parameter estimate | Least Square Mean difference |
| Point estimate | -35.06 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -66.54 |
| upper limit | -3.58 |

| **Secondary: Development of Anti-drug antibody/antibodies (ADA)** | |
|---|---|
| End point title | Development of Anti-drug antibody/antibodies (ADA) |
| End point description:<br>To characterise the immunogenicity profile of cotadutide titrated up to a dose level of 300 µg | |
| End point type | Secondary |

End point timeframe:

Baseline to (Follow-up Period) 28 days post last dose + (3-month poststudy)

| End point values | MEDI0382 (Part A) | Placebo (Part A) | Liraglutide (Part B) | MEDI0382 (Part B) |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 12 | 9 | 10 | 9 |
| Units: Participants | | | | |
| Baseline ADA result | 0 | 0 | 0 | 0 |
| ADA result for Day 28 (Part A) and Day 35 (Part B) | 1 | 0 | 0 | 3 |
| Follow-up ADA result | 0 | 0 | 0 | 3 |
| Post Study ADA result | 0 | 0 | 0 | 1 |

| End point values | Placebo (Part B) | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 11 | | | |
| Units: Participants | | | | |
| Baseline ADA result | 0 | | | |
| ADA result for Day 28 (Part A) and Day 35 (Part B) | 0 | | | |
| Follow-up ADA result | 0 | | | |
| Post Study ADA result | 0 | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Measures of safety and tolerability of daily SC doses of MEDI0382 titrated up to a dose level of 300µg (Parts A and B) by assessment of Number of Participants with Treatment Emergent Adverse Events (TEAEs) as assessed by CTCAE V4.0

| End point title | Measures of safety and tolerability of daily SC doses of MEDI0382 titrated up to a dose level of 300µg (Parts A and B) by assessment of Number of Participants with Treatment Emergent Adverse Events (TEAEs) as assessed by CTCAE V4.0 |
|---|---|

End point description:

Safety and tolerability of daily SC doses of MEDI0382 by assessment of the following using CTCAE V4.0:The number of Treatment Emergent Adverse events (TEAEs)

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

End point timeframe:

Post dosing (Day 1) to final follow-up (28 Days post last dose)

| End point values | MEDI0382 (Part A) | Placebo (Part A) | Liraglutide (Part B) | MEDI0382 (Part B) |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 12 | 9 | 10 | 9 |
| Units: participants | | | | |
| At least one event | 11 | 7 | 8 | 7 |
| At least one IP related event | 7 | 5 | 7 | 7 |

| End point values | Placebo (Part B) | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 11 | | | |
| Units: participants | | | | |
| At least one event | 6 | | | |
| At least one IP related event | 3 | | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Measures of safety and tolerability of daily SC doses of MEDI0382 titrated up to a dose level of 300µg (Parts A and B) by assessment of Number of Participants with Treatment Emergent Serious Adverse Events (TESAEs) as assessed by CTCAE V4.0

| End point title | Measures of safety and tolerability of daily SC doses of MEDI0382 titrated up to a dose level of 300µg (Parts A and B) by assessment of Number of Participants with Treatment Emergent Serious Adverse Events (TESAEs) as assessed by CTCAE V4.0 |
|---|---|

End point description:

Safety and tolerability of daily SC doses of MEDI0382 by assessment of the following using CTCAE V4.0:The number of Treatment-Emergent Serious Adverse Events (TESAEs)

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

End point timeframe:

Post dosing (Day 1) to final follow-up (28 Days post last dose)

| End point values | MEDI0382 (Part A) | Placebo (Part A) | Liraglutide (Part B) | MEDI0382 (Part B) |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 12 | 9 | 10 | 9 |
| Units: Participants | | | | |
| Treatment Emergent Serious Adverse Events(TESAEs) | 0 | 0 | 0 | 0 |

| End point values | Placebo (Part B) | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 11 | | | |
| Units: Participants | | | | |
| Treatment Emergent Serious Adverse Events(TESAEs) | 0 | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Measures of safety and tolerability of daily SC doses of MEDI0382 titrated up to a dose level of 300µg (Parts A and B) by assessment of changes in heart rate and blood pressure (BP)

| End point title | Measures of safety and tolerability of daily SC doses of MEDI0382 titrated up to a dose level of 300µg (Parts A and B) by assessment of changes in heart rate and blood pressure (BP) |
|---|---|

End point description:

Number of subjects with clinically significant changes in heart rate (BPM) or systolic and diastolic blood pressure (mmHg)

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

End point timeframe:

Post dosing (Day 1) to final follow-up (28 Days post last dose)

| End point values | MEDI0382 (Part A) | Placebo (Part A) | Liraglutide (Part B) | MEDI0382 (Part B) |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 12 | 9 | 10 | 9 |
| Units: Participants | | | | |
| clinically significant changes in heartrate or BP | 0 | 0 | 0 | 0 |

| End point values | Placebo (Part B) | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 11 | | | |
| Units: Participants | | | | |
| clinically significant changes in heartrate or BP | 0 | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Measures of safety and tolerability of daily SC doses of MEDI0382 titrated up to a dose level of 300µg (Parts A and B) by assessment of changes in ECG

| End point title | Measures of safety and tolerability of daily SC doses of MEDI0382 titrated up to a dose level of 300µg (Parts A and B) by assessment of changes in ECG |
|---|---|

End point description:

Number of subjects with an ECG determined to be abnormal and clinically significant

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

End point timeframe:

Post dosing (Day 1) to final follow-up (28 Days post last dose)

| End point values | MEDI0382 (Part A) | Placebo (Part A) | Liraglutide (Part B) | MEDI0382 (Part B) |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 12 | 9 | 10 | 9 |
| Units: participants | | | | |
| ECG deemed abnormal and clinically significant | 0 | 0 | 0 | 0 |

| End point values | Placebo (Part B) | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 11 | | | |
| Units: participants | | | | |
| ECG deemed abnormal and clinically significant | 0 | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Measures of safety and tolerability of daily SC doses of MEDI0382 titrated up to a dose level of 300µg (Parts A and B) by assessment of changes in haematology (Haem) and clinical (Clin) chemistry (Chem) parameters (Paras)

| End point title | Measures of safety and tolerability of daily SC doses of MEDI0382 titrated up to a dose level of 300µg (Parts A and B) by assessment of changes in haematology (Haem) and clinical (Clin) chemistry (Chem) parameters (Paras) |
|---|---|

End point description:

Number of subjects with clinically significant (sig) changes in haematology and or clinical chemistry parameters

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

End point timeframe:

Post dosing (Day 1) to final follow-up (28 Days post last dose)

| End point values | MEDI0382 (Part A) | Placebo (Part A) | Liraglutide (Part B) | MEDI0382 (Part B) |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 12 | 9 | 10 | 9 |
| Units: Participants | | | | |
| clin sig changes in haem or clin chem paras | 0 | 0 | 0 | 0 |

| End point values | Placebo (Part B) | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 11 | | | |
| Units: Participants | | | | |
| clin sig changes in haem or clin chem paras | 0 | | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Post dosing (Day 1) to final follow-up (28 Days post last dose)

Adverse event reporting additional description:

Adverse events were coded with MedDRA version 21.0 or higher. Analysis of AEs included the type, incidence, severity and relationship to study IP summarised by MedDRA SOC and PT by study part treatment group as well as for combined study parts.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 21 |

### Reporting groups

| | |
|---|---|
| Reporting group title | MEDI0382 (Part A) |
| Reporting group description: - | |
| Reporting group title | Placebo (Part B) |
| Reporting group description: - | |
| Reporting group title | MEDI0382 (Part B) |
| Reporting group description: - | |
| Reporting group title | Placebo (Part A) |
| Reporting group description: - | |
| Reporting group title | Liraglutide (Part B) |
| Reporting group description: - | |

| Serious adverse events | MEDI0382 (Part A) | Placebo (Part B) | MEDI0382 (Part B) |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 11 (0.00%) | 0 / 9 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |

| Serious adverse events | Placebo (Part A) | Liraglutide (Part B) | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 10 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |

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

| **Non-serious adverse events** | MEDI0382 (Part A) | Placebo (Part B) | MEDI0382 (Part B) |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 11 / 12 (91.67%) | 6 / 11 (54.55%) | 7 / 9 (77.78%) |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 11 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chills | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 0 / 11 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Fatigue | | | |
| subjects affected / exposed | 6 / 12 (50.00%) | 0 / 11 (0.00%) | 3 / 9 (33.33%) |
| occurrences (all) | 7 | 0 | 3 |
| Early satiety | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 11 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Feeling cold | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 11 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Injection site erythema | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 11 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Injection site haematoma | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 11 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Injection site rash | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 11 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Malaise | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 0 / 11 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 2 | 0 | 1 |
| Pain | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 11 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pyrexia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 11 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 1 | 0 | 1 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Productive cough | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 11 (9.09%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 11 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nasal congestion | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 11 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Epistaxis | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 1 / 11 (9.09%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Dry throat | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 11 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Cough | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 1 / 11 (9.09%) | 1 / 9 (11.11%) |
| occurrences (all) | 1 | 1 | 1 |
| Rhinalgia | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 11 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Psychiatric disorders | | | |
| Daydreaming | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 11 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Apathy | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 11 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Insomnia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 11 (0.00%) | 2 / 9 (22.22%) |
| occurrences (all) | 0 | 0 | 2 |
| Irritability | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 11 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Investigations | | | |
| Heart rate increased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 11 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Procedural pain | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 11 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Head injury | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 11 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fall | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 11 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac disorders | | | |
| Palpitations | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 11 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 11 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 3 / 12 (25.00%) | 1 / 11 (9.09%) | 1 / 9 (11.11%) |
| occurrences (all) | 3 | 1 | 1 |
| Headache | | | |
| subjects affected / exposed | 5 / 12 (41.67%) | 1 / 11 (9.09%) | 1 / 9 (11.11%) |
| occurrences (all) | 11 | 2 | 1 |
| Eye disorders | | | |
| Vision blurred | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 11 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Visual impairment | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 11 (9.09%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gastrointestinal disorders | | | |
| Breath odour | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 11 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 11 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Abdominal pain lower | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 11 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 1 / 11 (9.09%) | 0 / 9 (0.00%) |
| occurrences (all) | 5 | 1 | 0 |
| Abdominal distension | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 11 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Abdominal discomfort | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 0 / 11 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Constipation | | | |
| subjects affected / exposed | 3 / 12 (25.00%) | 0 / 11 (0.00%) | 2 / 9 (22.22%) |
| occurrences (all) | 3 | 0 | 2 |
| Vomiting | | | |
| subjects affected / exposed | 5 / 12 (41.67%) | 0 / 11 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 8 | 0 | 3 |
| Nausea | | | |
| subjects affected / exposed | 8 / 12 (66.67%) | 0 / 11 (0.00%) | 5 / 9 (55.56%) |
| occurrences (all) | 11 | 0 | 7 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 11 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dyspepsia | | | |
| subjects affected / exposed | 6 / 12 (50.00%) | 0 / 11 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 10 | 0 | 0 |

| | | | |
|---|---|---|---|
| Dry mouth | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 11 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 11 (9.09%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 1 | 2 |
| Skin and subcutaneous tissue disorders | | | |
| Hyperhidrosis | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 0 / 11 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 2 | 0 | 1 |
| Renal and urinary disorders | | | |
| Pollakiuria | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 2 / 11 (18.18%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 11 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Torticollis | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 11 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 11 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 11 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Otitis media acute | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 11 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 11 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all) | 0 | 0 | 1 |
| Viral upper respiratory tract infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 11 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Food craving | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 11 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Decreased appetite | | | |
| subjects affected / exposed | 3 / 12 (25.00%) | 0 / 11 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |

| **Non-serious adverse events** | Placebo (Part A) | Liraglutide (Part B) | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 7 / 9 (77.78%) | 8 / 10 (80.00%) | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 0 | 2 | |
| Chills | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 0 | 1 | |
| Fatigue | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | 1 / 10 (10.00%) | |
| occurrences (all) | 2 | 1 | |
| Early satiety | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Feeling cold | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Injection site erythema | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Injection site haematoma | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Injection site rash | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Malaise | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 10 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Pain | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Productive cough | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Nasal congestion | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Dry throat | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Cough | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Rhinalgia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Psychiatric disorders | | | |

| | | | |
|---|---|---|---|
| Daydreaming | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Apathy | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Insomnia | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Irritability | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Investigations | | | |
| Heart rate increased | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 0 | 1 | |
| Injury, poisoning and procedural complications | | | |
| Procedural pain | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 0 | 1 | |
| Head injury | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 0 | 1 | |
| Fall | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Cardiac disorders | | | |
| Palpitations | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 0 | 2 | |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Nervous system disorders | | | |
| Dizziness | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 9 (0.00%) | 2 / 10 (20.00%) | |
| occurrences (all) | 0 | 2 | |
| Headache | | | |
| subjects affected / exposed | 3 / 9 (33.33%) | 1 / 10 (10.00%) | |
| occurrences (all) | 3 | 3 | |
| Eye disorders | | | |
| Vision blurred | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Visual impairment | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Gastrointestinal disorders | | | |
| Breath odour | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 0 | 1 | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Abdominal pain lower | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 0 | 1 | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Constipation | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 2 / 10 (20.00%) | |
| occurrences (all) | 0 | 2 | |
| Vomiting | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 10 (10.00%) | |
| occurrences (all) | 1 | 1 | |
| Nausea | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | 1 / 10 (10.00%) | |
| occurrences (all) | 4 | 3 | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 2 / 10 (20.00%) | |
| occurrences (all) | 0 | 3 | |
| Dyspepsia | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | 1 / 10 (10.00%) | |
| occurrences (all) | 3 | 2 | |
| Dry mouth | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | 0 / 10 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Hyperhidrosis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Renal and urinary disorders | | | |
| Pollakiuria | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 10 (10.00%) | |
| occurrences (all) | 0 | 1 | |
| Torticollis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Infections and infestations | | | |

| | | | |
|---|---|---|---|
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Otitis media acute | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 10 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Metabolism and nutrition disorders | | | |
| Food craving | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 10 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Decreased appetite | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 2 / 10 (20.00%) | |
| occurrences (all) | 1 | 2 | |

## 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