



Clinical trial results:

A Phase II, 12-week, double-blind, randomised, parallel group, multi-centre, international trial to assess the effect on glycaemic control of five doses of HM11260C versus placebo or open-label liraglutide in subjects with type 2 diabetes

Summary

| | |
|--------------------------|-------------------|
| EudraCT number | 2013-003625-29 |
| Trial protocol | HU SE CZ NL DE ES |
| Global end of trial date | 12 December 2014 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 02 November 2016 |
| First version publication date | 02 November 2016 |

Trial information

Trial identification

| | |
|-----------------------|------------|
| Sponsor protocol code | HM-EXC-203 |
|-----------------------|------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02057172 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Hanmi Pharmaceutical Co., Ltd. |
| Sponsor organisation address | 14, Wiryeseong-daero, Songpa-gu, Seoul, Korea, Republic of, 05545 |
| Public contact | Jahoon Kang, Executive Director of Clinical Research and Development, Hanmi Pharmaceutical Co., Ltd., +82 2-410-9041, jhkang@hanmi.co.kr |
| Scientific contact | Jahoon Kang, Executive Director of Clinical Research and Development, Hanmi Pharmaceutical Co., Ltd., +82 2-410-9041, jhkang@hanmi.co.kr |

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 | 15 April 2015 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 12 December 2014 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To assess and compare the efficacy of five doses of HM11260C (once weekly subcutaneous injections) over the 12 weeks from baseline in comparison with placebo (once weekly subcutaneous injections) on glycaemic control, as assessed by HbA1c in subjects with T2DM

Protection of trial subjects:

Subjects were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the subject and considering the local culture. During the course of the trial, subjects were provided with individual subject cards indicating the nature of the trial the subject is participating, contact details and any information needed in the event of a medical emergency. Collected personal data and human biological samples were processed in compliance with ICH GCP ensuring that those involved with the conduct of the study abides by the laws governing personal data protection in force in all countries in which it operates.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 30 December 2013 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-----------------------|
| Country: Number of subjects enrolled | Spain: 24 |
| Country: Number of subjects enrolled | Sweden: 9 |
| Country: Number of subjects enrolled | Czech Republic: 13 |
| Country: Number of subjects enrolled | Germany: 20 |
| Country: Number of subjects enrolled | Hungary: 22 |
| Country: Number of subjects enrolled | United States: 163 |
| Country: Number of subjects enrolled | Korea, Republic of: 3 |
| Worldwide total number of subjects | 254 |
| EEA total number of subjects | 88 |

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) | 211 |
| From 65 to 84 years | 43 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Recruitment period from 30-Dec-13 (First patient In) to 14-Jul-14 (Last Patient In)- regions USA, Europe (Czech Republic, Germany, Hungary, Spain and Sweden) and Asia (South Korea)

Pre-assignment

Screening details:

593 subjects were screened for inclusion in this study. Screening period was a 4-week period. The screening visits (Visits 1A and 1B) took place between study days -28 and -5. Eligible subjects who met all of the inclusion criteria and none of the exclusion criteria returned to the clinic on Day 1 for baseline , randomisation, and study drug use.

Period 1

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

Blinding implementation details:

HM11260C and placebo for HM11260C were provided in identically matched pre-filled syringe and packaged identically. Liraglutide was provided in open label.

Arms

| | |
|------------------------------|-------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | HM11260C (0.3 mg) |

Arm description:

subcutaneous (sc) HM11260C 0.3 mg once a week (QW) for 12 weeks

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | Long-acting CA Exendin-4-HMC001 conjugate |
| Investigational medicinal product code | HM11260C |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

0.4 ml of HM11260C was self administered by subcutaneous injection in the morning within 60 minutes before the meal using pre-filled syringe.

| | |
|------------------|-----------------|
| Arm title | HM11260C (1 mg) |
|------------------|-----------------|

Arm description:

subcutaneous (sc) HM11260C 1 mg once a week (QW) for 12 weeks

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | Long-acting CA Exendin-4-HMC001 conjugate |
| Investigational medicinal product code | HM11260C |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

0.4 ml of HM11260C was self administered by subcutaneous injection in the morning within 60 minutes before the meal using pre-filled syringe.

| | |
|------------------|-----------------|
| Arm title | HM11260C (2 mg) |
|------------------|-----------------|

Arm description:

subcutaneous (sc) HM11260C 2 mg once a week (QW) for 12 weeks

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | Long-acting CA Exendin-4-HMC001 conjugate |
| Investigational medicinal product code | HM11260C |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

0.4 ml of HM11260C was self administered by subcutaneous injection in the morning within 60 minutes before the meal using pre-filled syringe.

| | |
|------------------|-----------------|
| Arm title | HM11260C (3 mg) |
|------------------|-----------------|

Arm description:

subcutaneous (sc) HM11260C 3 mg once a week (QW) for 12 weeks

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | Long-acting CA Exendin-4-HMC001 conjugate |
| Investigational medicinal product code | HM11260C |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

0.4 ml of HM11260C was self administered by subcutaneous injection in the morning within 60 minutes before the meal using pre-filled syringe.

| | |
|------------------|-----------------|
| Arm title | HM11260C (4 mg) |
|------------------|-----------------|

Arm description:

subcutaneous (sc) HM11260C 4 mg once a week (QW) for 12 weeks

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | Long-acting CA Exendin-4-HMC001 conjugate |
| Investigational medicinal product code | HM11260C |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

0.4 ml of HM11260C was self administered by subcutaneous injection in the morning within 60 minutes before the meal using pre-filled syringe

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

Arm description:

subcutaneous (sc) Placebo identical to HM11260C once a week (QW) for 12 weeks

| | |
|--|------------------|
| 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:

0.4 ml of Placebo was self administered by subcutaneous injection in the morning within 60 minutes before the meal using pre-filled syringe.

| | |
|------------------|-------------|
| Arm title | Liraglutide |
|------------------|-------------|

Arm description:

open label, daily injection, with titration as per label

| | |
|----------|-------------------|
| Arm type | Active comparator |
|----------|-------------------|

| | |
|--|------------------|
| Investigational medicinal product name | Liraglutide |
| Investigational medicinal product code | |
| Other name | Victoza® |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

Formulation and Administration: Liraglutide will be dispensed in a prefilled, multidose pen that delivers 0.6 mg, 1.2 mg, or 1.8 mg. It will be administered subcutaneously in the abdomen, thigh or upper arm in accordance with the Victoza package insert. Frequency: Liraglutide was administered daily at doses of 0.6 mg on Days 1 to 7, 1.2 mg on Days 8 to 14 and 1.8 mg on Days 15 to 84. It is a forced titration.

| Number of subjects in period 1^[1] | HM11260C (0.3 mg) | HM11260C (1 mg) | HM11260C (2 mg) |
|---|-------------------|-----------------|-----------------|
| Started | 37 | 37 | 33 |
| Completed | 33 | 34 | 27 |
| Not completed | 4 | 3 | 6 |
| Adverse event, non-fatal | - | - | 2 |
| Prohibited treatment | - | - | - |
| Other | 1 | - | - |
| Lost to follow-up | 2 | 2 | 2 |
| Withdrawal by subject | 1 | 1 | 2 |
| Protocol deviation | - | - | - |
| Noncompliance | - | - | - |

| Number of subjects in period 1^[1] | HM11260C (3 mg) | HM11260C (4 mg) | Placebo |
|---|-----------------|-----------------|---------|
| Started | 36 | 36 | 37 |
| Completed | 29 | 27 | 33 |
| Not completed | 7 | 9 | 4 |
| Adverse event, non-fatal | 3 | 1 | - |
| Prohibited treatment | - | 1 | - |
| Other | - | - | - |
| Lost to follow-up | 1 | 1 | 3 |
| Withdrawal by subject | 2 | 4 | 1 |
| Protocol deviation | 1 | 1 | - |
| Noncompliance | - | 1 | - |

| Number of subjects in period 1^[1] | Liraglutide |
|---|-------------|
| Started | 36 |
| Completed | 28 |
| Not completed | 8 |
| Adverse event, non-fatal | 4 |

| | |
|-----------------------|---|
| Prohibited treatment | - |
| Other | - |
| Lost to follow-up | 1 |
| Withdrawal by subject | 3 |
| Protocol deviation | - |
| Noncompliance | - |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: A total of 254 subjects were randomised in the study. Of these, 181 subjects were randomised to HM11260C, 37 to placebo and 36 to liraglutide. 252 subjects received study drug (HM11260C, placebo or liraglutide) and were included in the Safety Set.

Baseline characteristics

Reporting groups

| | |
|------------------------------|---|
| Reporting group title | HM11260C (0.3 mg) |
| Reporting group description: | subcutaneous (sc) HM11260C 0.3 mg once a week (QW) for 12 weeks |
| Reporting group title | HM11260C (1 mg) |
| Reporting group description: | subcutaneous (sc) HM11260C 1 mg once a week (QW) for 12 weeks |
| Reporting group title | HM11260C (2 mg) |
| Reporting group description: | subcutaneous (sc) HM11260C 2 mg once a week (QW) for 12 weeks |
| Reporting group title | HM11260C (3 mg) |
| Reporting group description: | subcutaneous (sc) HM11260C 3 mg once a week (QW) for 12 weeks |
| Reporting group title | HM11260C (4 mg) |
| Reporting group description: | subcutaneous (sc) HM11260C 4 mg once a week (QW) for 12 weeks |
| Reporting group title | Placebo |
| Reporting group description: | subcutaneous (sc) Placebo identical to HM11260C once a week (QW) for 12 weeks |
| Reporting group title | Liraglutide |
| Reporting group description: | open label, daily injection, with titration as per label |

| Reporting group values | HM11260C (0.3 mg) | HM11260C (1 mg) | HM11260C (2 mg) |
|------------------------|-------------------|-----------------|-----------------|
| Number of subjects | 37 | 37 | 33 |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|---|---------|--------|---------|
| Age continuous | | | |
| Collection method or subject population | | | |
| Units: years | | | |
| arithmetic mean | 56.2 | 55.1 | 55.8 |
| standard deviation | ± 10.89 | ± 8.81 | ± 10.19 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 13 | 18 | 15 |
| Male | 24 | 19 | 18 |

| Reporting group values | HM11260C (3 mg) | HM11260C (4 mg) | Placebo |
|------------------------|-----------------|-----------------|---------|
| Number of subjects | 36 | 36 | 37 |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|---|--------|--------|--------|
| Age continuous | | | |
| Collection method or subject population | | | |
| Units: years | | | |
| arithmetic mean | 54.1 | 56.3 | 55.4 |
| standard deviation | ± 9.89 | ± 9.67 | ± 9.29 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 13 | 18 | 21 |
| Male | 23 | 18 | 16 |

| | | | |
|-------------------------------|-------------|-------|--|
| Reporting group values | Liraglutide | Total | |
| Number of subjects | 36 | 252 | |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|---|---------|-----|--|
| Age continuous | | | |
| Collection method or subject population | | | |
| Units: years | | | |
| arithmetic mean | 53.9 | | |
| standard deviation | ± 10.77 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 20 | 118 | |
| Male | 16 | 134 | |

End points

End points reporting groups

| | |
|---|-------------------|
| Reporting group title | HM11260C (0.3 mg) |
| Reporting group description: subcutaneous (sc) HM11260C 0.3 mg once a week (QW) for 12 weeks | |
| Reporting group title | HM11260C (1 mg) |
| Reporting group description: subcutaneous (sc) HM11260C 1 mg once a week (QW) for 12 weeks | |
| Reporting group title | HM11260C (2 mg) |
| Reporting group description: subcutaneous (sc) HM11260C 2 mg once a week (QW) for 12 weeks | |
| Reporting group title | HM11260C (3 mg) |
| Reporting group description: subcutaneous (sc) HM11260C 3 mg once a week (QW) for 12 weeks | |
| Reporting group title | HM11260C (4 mg) |
| Reporting group description: subcutaneous (sc) HM11260C 4 mg once a week (QW) for 12 weeks | |
| Reporting group title | Placebo |
| Reporting group description: subcutaneous (sc) Placebo identical to HM11260C once a week (QW) for 12 weeks | |
| Reporting group title | Liraglutide |
| Reporting group description: open label, daily injection, with titration as per label | |

Primary: Change from Baseline in HbA1c

| | |
|--|-------------------------------|
| End point title | Change from Baseline in HbA1c |
| End point description: Least squares (LS) means and standard errors at Week 13 were obtained from a mixed effect model with repeated measures (MMRM). | |
| End point type | Primary |
| End point timeframe: Week 13 | |

| End point values | HM11260C (0.3 mg) | HM11260C (1 mg) | HM11260C (2 mg) | HM11260C (3 mg) |
|-------------------------------------|-------------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 37 | 37 | 33 | 36 |
| Units: Percentage of Hemoglobin | | | | |
| least squares mean (standard error) | -0.56 (± 0.114) | -0.95 (± 0.111) | -1.19 (± 0.121) | -1.41 (± 0.119) |

| End point values | HM11260C (4 mg) | Placebo | Liraglutide | |
|-------------------------------------|----------------------|---------------------|---------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 36 | 37 | 36 | |
| Units: Percentage of Hemoglobin | | | | |
| least squares mean (standard error) | -1.61 (\pm 0.118) | -0.4 (\pm 0.111) | -1.38 (\pm 0.12) | |

Statistical analyses

| Statistical analysis title | Change from baseline in HbA1c for 0.3mg vs placebo |
|---|--|
| Statistical analysis description: | |
| Full Analysis Set | |
| Comparison groups | HM11260C (0.3 mg) v Placebo |
| Number of subjects included in analysis | 74 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[1] |
| P-value | = 0.3029 |
| Method | Mixed Model Repeated Measures |
| Parameter estimate | LS Mean Difference |
| Point estimate | -0.16 |
| Confidence interval | |
| level | 95.1 % |
| sides | 2-sided |
| lower limit | -0.47 |
| upper limit | 0.15 |
| Variability estimate | Standard error of the mean |

Notes:

[1] - The threshold for significance is a p-value ≤ 0.049 . No adjustments were made for multiple comparisons of each treatment group to placebo.

| Statistical analysis title | Change from baseline in HbA1c for 1 mg vs placebo |
|---|---|
| Statistical analysis description: | |
| Full Analysis Set | |
| Comparison groups | HM11260C (1 mg) v Placebo |
| Number of subjects included in analysis | 74 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[2] |
| P-value | = 0.0005 |
| Method | Mixed Model Repeated Measures |
| Parameter estimate | LS Mean Difference |
| Point estimate | -0.55 |
| Confidence interval | |
| level | 95.1 % |
| sides | 2-sided |
| lower limit | -0.86 |
| upper limit | -0.24 |

| | |
|----------------------|----------------------------|
| Variability estimate | Standard error of the mean |
|----------------------|----------------------------|

Notes:

[2] - The threshold for significance is a p-value ≤ 0.049 . No adjustments were made for multiple comparisons of each treatment group to placebo.

| | |
|-----------------------------------|--|
| Statistical analysis title | Change from baseline in HbA1c for 2 mg vs. placebo |
|-----------------------------------|--|

Statistical analysis description:

Full Analysis Set

| | |
|---|-------------------------------|
| Comparison groups | HM11260C (2 mg) v Placebo |
| Number of subjects included in analysis | 70 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[3] |
| P-value | < 0.0001 |
| Method | Mixed Model Repeated Measures |
| Parameter estimate | LS Mean Difference |
| Point estimate | -0.79 |
| Confidence interval | |
| level | 95.1 % |
| sides | 2-sided |
| lower limit | -1.11 |
| upper limit | -0.47 |
| Variability estimate | Standard error of the mean |

Notes:

[3] - The threshold for significance is a p-value ≤ 0.049 . No adjustments were made for multiple comparisons of each treatment group to placebo.

| | |
|-----------------------------------|--|
| Statistical analysis title | Change from baseline in HbA1c for 3 mg vs. placebo |
|-----------------------------------|--|

Statistical analysis description:

Full Analysis Set

| | |
|---|-------------------------------|
| Comparison groups | HM11260C (3 mg) v Placebo |
| Number of subjects included in analysis | 73 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[4] |
| P-value | < 0.0001 |
| Method | Mixed Model Repeated Measures |
| Parameter estimate | LS Mean Difference |
| Point estimate | -1.01 |
| Confidence interval | |
| level | 95.1 % |
| sides | 2-sided |
| lower limit | -1.33 |
| upper limit | -0.69 |
| Variability estimate | Standard error of the mean |

Notes:

[4] - The threshold for significance is a p-value ≤ 0.049 . No adjustments were made for multiple comparisons of each treatment group to placebo.

| | |
|-----------------------------------|--|
| Statistical analysis title | Change from baseline in HbA1c for 4 mg vs. placebo |
|-----------------------------------|--|

Statistical analysis description:

Full Analysis Set

| | |
|-------------------|---------------------------|
| Comparison groups | HM11260C (4 mg) v Placebo |
|-------------------|---------------------------|

| | |
|---|-------------------------------|
| Number of subjects included in analysis | 73 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[5] |
| P-value | < 0.0001 |
| Method | Mixed Model Repeated Measures |
| Parameter estimate | LS Mean Difference |
| Point estimate | -1.21 |
| Confidence interval | |
| level | 95.1 % |
| sides | 2-sided |
| lower limit | -1.53 |
| upper limit | -0.89 |
| Variability estimate | Standard error of the mean |

Notes:

[5] - The threshold for significance is a p-value ≤ 0.049 . No adjustments were made for multiple comparisons of each treatment group to placebo.

Secondary: Subjects who had a HbA1c level of < 7%

| | |
|------------------------|--|
| End point title | Subjects who had a HbA1c level of < 7% |
| End point description: | Percentage of subjects with HbA1c < 7% by visit, treatment group, and metformin. |
| End point type | Secondary |
| End point timeframe: | |
| Week 13 | |

| End point values | HM11260C (0.3 mg) | HM11260C (1 mg) | HM11260C (2 mg) | HM11260C (3 mg) |
|-------------------------------|-------------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 37 | 37 | 33 | 36 |
| Units: Percentage of Subjects | | | | |
| number (not applicable) | 32.4 | 64.9 | 60.6 | 72.2 |

| End point values | HM11260C (4 mg) | Placebo | Liraglutide | |
|-------------------------------|-----------------|-----------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 36 | 37 | 36 | |
| Units: Percentage of Subjects | | | | |
| number (not applicable) | 69.4 | 24.3 | 61.1 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Fasting Plasma Glucose

| | |
|-----------------|--|
| End point title | Change from Baseline in Fasting Plasma Glucose |
|-----------------|--|

End point description:

Least squares (LS) means and standard errors at Week 13 were obtained from a mixed effect model with repeated measures (MMRM).

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

End point timeframe:

Week 13

| End point values | HM11260C (0.3 mg) | HM11260C (1 mg) | HM11260C (2 mg) | HM11260C (3 mg) |
|-------------------------------------|-------------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 37 | 37 | 33 | 36 |
| Units: mmol/L | | | | |
| least squares mean (standard error) | -0.61 (± 0.293) | -1.35 (± 0.28) | -1.31 (± 0.304) | -2.25 (± 0.303) |

| End point values | HM11260C (4 mg) | Placebo | Liraglutide | |
|-------------------------------------|-----------------|-----------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 36 | 37 | 36 | |
| Units: mmol/L | | | | |
| least squares mean (standard error) | -2.5 (± 0.3) | -0.55 (± 0.281) | -1.51 (± 0.304) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in body weight

| | |
|-----------------|-------------------------------------|
| End point title | Change from baseline in body weight |
|-----------------|-------------------------------------|

End point description:

Least squares (LS) means and standard errors at Week 13 were obtained from a mixed effect model with repeated measures (MMRM).

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

End point timeframe:

Week 13

| End point values | HM11260C (0.3 mg) | HM11260C (1 mg) | HM11260C (2 mg) | HM11260C (3 mg) |
|-------------------------------------|-------------------|------------------|------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 37 | 37 | 33 | 36 |
| Units: kg | | | | |
| least squares mean (standard error) | -1.209 (± 0.526) | -2.014 (± 0.508) | -1.522 (± 0.553) | -2.732 (± 0.55) |

| End point values | HM11260C (4 mg) | Placebo | Liraglutide | |
|-------------------------------------|-----------------------|----------------------|-----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 36 | 37 | 36 | |
| Units: kg | | | | |
| least squares mean (standard error) | -3.309 (\pm 0.543) | -1.29 (\pm 0.511) | -3.212 (\pm 0.558) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in 7-Point Glucose Profile (Mean Daily Blood Glucose)

| | |
|--|--|
| End point title | Change from Baseline in 7-Point Glucose Profile (Mean Daily Blood Glucose) |
| End point description: Least squares (LS) means and standard errors at Week 13 were obtained from a mixed effect model with repeated measures (MMRM). | |
| End point type | Secondary |
| End point timeframe: Week 13 | |

| End point values | HM11260C (0.3 mg) | HM11260C (1 mg) | HM11260C (2 mg) | HM11260C (3 mg) |
|-------------------------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 37 | 37 | 33 | 36 |
| Units: mmol/L | | | | |
| least squares mean (standard error) | -0.637 (\pm 0.274) | -1.519 (\pm 0.257) | -2.008 (\pm 0.295) | -2.348 (\pm 0.288) |

| End point values | HM11260C (4 mg) | Placebo | Liraglutide | |
|-------------------------------------|-----------------------|-----------------------|-----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 36 | 37 | 36 | |
| Units: mmol/L | | | | |
| least squares mean (standard error) | -2.628 (\pm 0.295) | -0.582 (\pm 0.267) | -2.107 (\pm 0.286) | |

Statistical analyses

Secondary: Change from Baseline in Other diabetes-related parameters (fasting insulin)

| | |
|-----------------|---|
| End point title | Change from Baseline in Other diabetes-related parameters (fasting insulin) |
|-----------------|---|

End point description:

Least squares (LS) means and standard errors at Week 13 were obtained from a mixed effect model with repeated measures (MMRM).

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

End point timeframe:

Week 13

| End point values | HM11260C (0.3 mg) | HM11260C (1 mg) | HM11260C (2 mg) | HM11260C (3 mg) |
|-------------------------------------|-------------------|-----------------|------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 37 | 37 | 33 | 36 |
| Units: pmol/L | | | | |
| least squares mean (standard error) | 10.72 (± 21.534) | 3.07 (± 21.014) | 25.37 (± 22.428) | 2.66 (± 22.626) |

| End point values | HM11260C (4 mg) | Placebo | Liraglutide | |
|-------------------------------------|------------------|-----------------|------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 36 | 37 | 36 | |
| Units: pmol/L | | | | |
| least squares mean (standard error) | 13.32 (± 23.704) | 4.33 (± 21.384) | 60.23 (± 22.333) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Other diabetes-related parameters (C-Peptide)

| | |
|-----------------|---|
| End point title | Change from Baseline in Other diabetes-related parameters (C-Peptide) |
|-----------------|---|

End point description:

Least squares (LS) means and standard errors at Week 13 were obtained from a mixed effect model with repeated measures (MMRM).

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

End point timeframe:

Week 13

| End point values | HM11260C (0.3 mg) | HM11260C (1 mg) | HM11260C (2 mg) | HM11260C (3 mg) |
|-------------------------------------|----------------------|-----------------------|----------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 37 | 37 | 33 | 36 |
| Units: nmol/L | | | | |
| least squares mean (standard error) | 0.013 (\pm 0.034) | -0.046 (\pm 0.032) | 0.009 (\pm 0.035) | 0.027 (\pm 0.035) |

| End point values | HM11260C (4 mg) | Placebo | Liraglutide | |
|-------------------------------------|----------------------|----------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 36 | 37 | 36 | |
| Units: nmol/L | | | | |
| least squares mean (standard error) | 0.008 (\pm 0.036) | 0.027 (\pm 0.033) | 0.043 (\pm 0.035) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Other diabetes-related parameters (Glycated Albumin)

| | |
|-----------------|--|
| End point title | Change from Baseline in Other diabetes-related parameters (Glycated Albumin) |
|-----------------|--|

End point description:

Least squares (LS) means and standard errors at Week 13 were obtained from a mixed effect model with repeated measures (MMRM).

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

End point timeframe:

Week 13

| End point values | HM11260C (0.3 mg) | HM11260C (1 mg) | HM11260C (2 mg) | HM11260C (3 mg) |
|-------------------------------------|----------------------|---------------------|----------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 37 | 37 | 33 | 36 |
| Units: percent | | | | |
| least squares mean (standard error) | -0.13 (\pm 0.043) | -0.29 (\pm 0.04) | -0.35 (\pm 0.044) | -0.42 (\pm 0.043) |

| End point values | HM11260C (4 mg) | Placebo | Liraglutide | |
|-----------------------------|-----------------|-----------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 36 | 37 | 36 | |
| Units: percent | | | | |

| | | | | |
|-------------------------------------|----------------------|----------------------|----------------------|--|
| least squares mean (standard error) | -0.45 (\pm 0.044) | -0.13 (\pm 0.041) | -0.36 (\pm 0.044) | |
|-------------------------------------|----------------------|----------------------|----------------------|--|

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Serum Lipid Profile (Parameters LDL-C, HDL-C, TG)

| | |
|--|---|
| End point title | Change from Baseline in Serum Lipid Profile (Parameters LDL-C, HDL-C, TG) |
| End point description: Least squares (LS) means and standard errors at Week 13 were obtained from a mixed effect model with repeated measures (MMRM). | |
| End point type | Secondary |
| End point timeframe: Week 13 | |

| End point values | HM11260C (0.3 mg) | HM11260C (1 mg) | HM11260C (2 mg) | HM11260C (3 mg) |
|-------------------------------------|-----------------------|----------------------|-----------------------|-----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 37 | 37 | 33 | 36 |
| Units: mmol/L | | | | |
| least squares mean (standard error) | | | | |
| Parameter LDL-C | -0.09 (\pm 0.091) | 0.11 (\pm 0.089) | -0.09 (\pm 0.094) | -0.06 (\pm 0.096) |
| Parameter HDL-C | 0 (\pm 0.027) | 0.05 (\pm 0.026) | 0.02 (\pm 0.028) | -0.02 (\pm 0.028) |
| Parameter TG | -0.016 (\pm 0.137) | -0.27 (\pm 0.135) | -0.305 (\pm 0.143) | -0.414 (\pm 0.146) |

| End point values | HM11260C (4 mg) | Placebo | Liraglutide | |
|-------------------------------------|-----------------------|-----------------------|-----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 36 | 37 | 36 | |
| Units: mmol/L | | | | |
| least squares mean (standard error) | | | | |
| Parameter LDL-C | -0.22 (\pm 0.095) | 0.09 (\pm 0.088) | -0.16 (\pm 0.096) | |
| Parameter HDL-C | -0.01 (\pm 0.028) | 0.02 (\pm 0.026) | 0.01 (\pm 0.029) | |
| Parameter TG | -0.592 (\pm 0.145) | -0.093 (\pm 0.133) | -0.154 (\pm 0.145) | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs were collected beginning at screening and continuing through the final patient visit. SAEs, regardless of suspected causality, were recorded until at least 30 days after the subject had stopped study participation.

Adverse event reporting additional description:

Reported AEs were TEAEs that had a start date on or after the first dose of IP or, if the start date was before the date of the first dose of IP, increased in severity on or after the date of the first dose of IP. Treatment-emergent SAEs and TEAEs were reported for the Safety Set, consisting of all participants who received any study drug.

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

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 16.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|------------------|
| Reporting group title | HM11260C (0.3mg) |
|-----------------------|------------------|

Reporting group description:

Subjects received HM11260C 0.3mg every 7 days as a subcutaneous injection in the abdomen via a pre-filled syringe.

| | |
|-----------------------|----------------|
| Reporting group title | HM11260C (1mg) |
|-----------------------|----------------|

Reporting group description:

Subjects received HM11260C 1mg every 7 days as a subcutaneous injection in the abdomen via a pre-filled syringe.

| | |
|-----------------------|----------------|
| Reporting group title | HM11260C (2mg) |
|-----------------------|----------------|

Reporting group description:

Subjects received HM11260C 2mg every 7 days as a subcutaneous injection in the abdomen via a pre-filled syringe.

| | |
|-----------------------|----------------|
| Reporting group title | HM11260C (3mg) |
|-----------------------|----------------|

Reporting group description:

Subjects received HM11260C 3mg every 7 days as a subcutaneous injection in the abdomen via a pre-filled syringe.

| | |
|-----------------------|----------------|
| Reporting group title | HM11260C (4mg) |
|-----------------------|----------------|

Reporting group description:

Subjects received HM11260C 4mg every 7 days as a subcutaneous injection in the abdomen via a pre-filled syringe.

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Subjects received matching placebo every 7 days as a subcutaneous injection in the abdomen via a pre-filled syringe.

| | |
|-----------------------|-------------|
| Reporting group title | Liraglutide |
|-----------------------|-------------|

Reporting group description:

Subjects received liraglutide daily according to the package label via pre-filled, multi-dose pen.

| Serious adverse events | HM11260C (0.3mg) | HM11260C (1mg) | HM11260C (2mg) |
|---|------------------|----------------|----------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 37 (0.00%) | 1 / 33 (3.03%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from | 0 | 0 | 0 |

| | | | |
|--|----------------|----------------|----------------|
| adverse events | | | |
| General disorders and administration site conditions | | | |
| Device failure | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 37 (0.00%) | 0 / 33 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Allergy to arthropod sting | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 37 (0.00%) | 1 / 33 (3.03%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 0 / 37 (0.00%) | 0 / 33 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | HM11260C (3mg) | HM11260C (4mg) | Placebo |
|--|----------------|----------------|----------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | 0 / 36 (0.00%) | 0 / 37 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Device failure | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | 0 / 36 (0.00%) | 0 / 37 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Allergy to arthropod sting | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 36 (0.00%) | 0 / 37 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Pneumonia | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 36 (2.78%) | 0 / 36 (0.00%) | 0 / 37 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|--|----------------|--|--|
| Serious adverse events | Liraglutide | | |
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| General disorders and administration site conditions | | | |
| Device failure | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Immune system disorders | | | |
| Allergy to arthropod sting | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 5 %

| | | | |
|---|------------------|------------------|------------------|
| Non-serious adverse events | HM11260C (0.3mg) | HM11260C (1mg) | HM11260C (2mg) |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 19 / 37 (51.35%) | 26 / 37 (70.27%) | 25 / 33 (75.76%) |
| Investigations | | | |
| Lipase increased | | | |
| subjects affected / exposed | 0 / 37 (0.00%) | 5 / 37 (13.51%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 5 | 2 |
| Nervous system disorders | | | |

| | | | |
|---|----------------------|----------------------|-----------------------|
| Headache subjects affected / exposed occurrences (all) | 2 / 37 (5.41%) 2 | 4 / 37 (10.81%) 4 | 3 / 33 (9.09%) 5 |
| Dizziness subjects affected / exposed occurrences (all) | 1 / 37 (2.70%) 1 | 2 / 37 (5.41%) 2 | 1 / 33 (3.03%) 1 |
| General disorders and administration site conditions | | | |
| Injection site bruising subjects affected / exposed occurrences (all) | 2 / 37 (5.41%) 7 | 1 / 37 (2.70%) 1 | 2 / 33 (6.06%) 2 |
| Injection site pain subjects affected / exposed occurrences (all) | 2 / 37 (5.41%) 3 | 2 / 37 (5.41%) 3 | 1 / 33 (3.03%) 1 |
| Oedema peripheral subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 0 / 37 (0.00%) 0 | 0 / 33 (0.00%) 0 |
| Pyrexia subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 2 / 37 (5.41%) 2 | 1 / 33 (3.03%) 1 |
| Gastrointestinal disorders | | | |
| Nausea subjects affected / exposed occurrences (all) | 4 / 37 (10.81%) 5 | 3 / 37 (8.11%) 4 | 9 / 33 (27.27%) 10 |
| Diarrhoea subjects affected / exposed occurrences (all) | 5 / 37 (13.51%) 5 | 1 / 37 (2.70%) 1 | 3 / 33 (9.09%) 3 |
| Vomiting subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 1 / 37 (2.70%) 2 | 4 / 33 (12.12%) 4 |
| Abdominal pain upper subjects affected / exposed occurrences (all) | 1 / 37 (2.70%) 1 | 2 / 37 (5.41%) 2 | 0 / 33 (0.00%) 0 |
| Constipation subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 0 / 37 (0.00%) 0 | 0 / 33 (0.00%) 0 |
| Abdominal discomfort | | | |

| | | | |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 0 / 37 (0.00%) 0 | 0 / 33 (0.00%) 0 |
| Dyspepsia subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 1 / 37 (2.70%) 1 | 0 / 33 (0.00%) 0 |
| Abdominal distension subjects affected / exposed occurrences (all) | 1 / 37 (2.70%) 1 | 0 / 37 (0.00%) 0 | 0 / 33 (0.00%) 0 |
| Eructation subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 0 / 37 (0.00%) 0 | 0 / 33 (0.00%) 0 |
| Gastritis subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 0 / 37 (0.00%) 0 | 0 / 33 (0.00%) 0 |
| Hepatobiliary disorders Hepatomegaly subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 0 / 37 (0.00%) 0 | 0 / 33 (0.00%) 0 |
| Skin and subcutaneous tissue disorders Hyperhidrosis subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 0 / 37 (0.00%) 0 | 0 / 33 (0.00%) 0 |
| Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) | 3 / 37 (8.11%) 3 | 2 / 37 (5.41%) 2 | 1 / 33 (3.03%) 1 |
| Urinary tract infection subjects affected / exposed occurrences (all) | 2 / 37 (5.41%) 2 | 2 / 37 (5.41%) 2 | 0 / 33 (0.00%) 0 |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 1 / 37 (2.70%) 1 | 0 / 37 (0.00%) 0 | 0 / 33 (0.00%) 0 |
| Sinusitis subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 2 / 37 (5.41%) 2 | 0 / 33 (0.00%) 0 |
| Metabolism and nutrition disorders | | | |

| | | | |
|---|---------------------|---------------------|---------------------|
| Decreased appetite subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 0 / 37 (0.00%) 0 | 0 / 33 (0.00%) 0 |
| Hypercholesterolaemia subjects affected / exposed occurrences (all) | 0 / 37 (0.00%) 0 | 0 / 37 (0.00%) 0 | 0 / 33 (0.00%) 0 |

| Non-serious adverse events | HM11260C (3mg) | HM11260C (4mg) | Placebo |
|--|---|--|--|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 24 / 36 (66.67%) | 24 / 36 (66.67%) | 23 / 37 (62.16%) |
| Investigations Lipase increased subjects affected / exposed occurrences (all) | 4 / 36 (11.11%) 4 | 1 / 36 (2.78%) 1 | 1 / 37 (2.70%) 1 |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all) | 3 / 36 (8.33%) 3 0 / 36 (0.00%) 0 | 4 / 36 (11.11%) 5 2 / 36 (5.56%) 3 | 5 / 37 (13.51%) 6 0 / 37 (0.00%) 0 |
| General disorders and administration site conditions Injection site bruising subjects affected / exposed occurrences (all) Injection site pain subjects affected / exposed occurrences (all) Oedema peripheral subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all) | 4 / 36 (11.11%) 6 0 / 36 (0.00%) 0 2 / 36 (5.56%) 2 0 / 36 (0.00%) 0 | 0 / 36 (0.00%) 0 0 / 36 (0.00%) 0 0 / 36 (0.00%) 0 0 / 36 (0.00%) 0 | 3 / 37 (8.11%) 4 1 / 37 (2.70%) 1 0 / 37 (0.00%) 0 0 / 37 (0.00%) 0 |
| Gastrointestinal disorders Nausea | | | |

| | | | |
|--|-----------------|------------------|-----------------|
| subjects affected / exposed | 8 / 36 (22.22%) | 12 / 36 (33.33%) | 6 / 37 (16.22%) |
| occurrences (all) | 10 | 23 | 6 |
| Diarrhoea | | | |
| subjects affected / exposed | 4 / 36 (11.11%) | 2 / 36 (5.56%) | 2 / 37 (5.41%) |
| occurrences (all) | 5 | 7 | 2 |
| Vomiting | | | |
| subjects affected / exposed | 4 / 36 (11.11%) | 8 / 36 (22.22%) | 0 / 37 (0.00%) |
| occurrences (all) | 5 | 14 | 0 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | 2 / 36 (5.56%) | 0 / 37 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Constipation | | | |
| subjects affected / exposed | 5 / 36 (13.89%) | 0 / 36 (0.00%) | 0 / 37 (0.00%) |
| occurrences (all) | 5 | 0 | 0 |
| Abdominal discomfort | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | 2 / 36 (5.56%) | 0 / 37 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| Dyspepsia | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | 2 / 36 (5.56%) | 0 / 37 (0.00%) |
| occurrences (all) | 3 | 2 | 0 |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 36 (0.00%) | 0 / 37 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eructation | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | 0 / 36 (0.00%) | 0 / 37 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gastritis | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | 0 / 36 (0.00%) | 0 / 37 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hepatobiliary disorders | | | |
| Hepatomegaly | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 36 (0.00%) | 2 / 37 (5.41%) |
| occurrences (all) | 0 | 0 | 2 |
| Skin and subcutaneous tissue disorders | | | |
| Hyperhidrosis | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | 2 / 36 (5.56%) 2 | 0 / 37 (0.00%) 0 |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | 1 / 36 (2.78%) | 1 / 37 (2.70%) |
| occurrences (all) | 1 | 1 | 1 |
| Urinary tract infection | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | 1 / 36 (2.78%) | 0 / 37 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | 1 / 36 (2.78%) | 0 / 37 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | 0 / 36 (0.00%) | 0 / 37 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | 2 / 36 (5.56%) | 0 / 37 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Hypercholesterolaemia | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 2 / 36 (5.56%) | 0 / 37 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |

| Non-serious adverse events | Liraglutide | | |
|---|------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 29 / 36 (80.56%) | | |
| Investigations | | | |
| Lipase increased | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | |
| occurrences (all) | 2 | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 3 / 36 (8.33%) | | |
| occurrences (all) | 3 | | |
| Dizziness | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 2 | | |

| | | | |
|--|------------------|--|--|
| General disorders and administration site conditions | | | |
| Injection site bruising | | | |
| subjects affected / exposed | 7 / 36 (19.44%) | | |
| occurrences (all) | 14 | | |
| Injection site pain | | | |
| subjects affected / exposed | 3 / 36 (8.33%) | | |
| occurrences (all) | 6 | | |
| Oedema peripheral | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastrointestinal disorders | | | |
| Nausea | | | |
| subjects affected / exposed | 12 / 36 (33.33%) | | |
| occurrences (all) | 15 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 5 / 36 (13.89%) | | |
| occurrences (all) | 6 | | |
| Vomiting | | | |
| subjects affected / exposed | 4 / 36 (11.11%) | | |
| occurrences (all) | 4 | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Constipation | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | | |
| occurrences (all) | 0 | | |
| Abdominal distension | | | |

| | | | |
|--|---|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Eructation</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Gastritis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>2 / 36 (5.56%)</p> <p>2</p> <p>2 / 36 (5.56%)</p> <p>2</p> <p>2 / 36 (5.56%)</p> <p>2</p> | | |
| <p>Hepatobiliary disorders</p> <p>Hepatomegaly</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 36 (0.00%)</p> <p>0</p> | | |
| <p>Skin and subcutaneous tissue disorders</p> <p>Hyperhidrosis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 36 (0.00%)</p> <p>0</p> | | |
| <p>Infections and infestations</p> <p>Nasopharyngitis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Urinary tract infection</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Upper respiratory tract infection</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Sinusitis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 36 (0.00%)</p> <p>0</p> <p>0 / 36 (0.00%)</p> <p>0</p> <p>0 / 36 (0.00%)</p> <p>0</p> <p>0 / 36 (0.00%)</p> <p>0</p> | | |
| <p>Metabolism and nutrition disorders</p> <p>Decreased appetite</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Hypercholesterolaemia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>3 / 36 (8.33%)</p> <p>3</p> <p>0 / 36 (0.00%)</p> <p>0</p> | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|---|
| 25 September 2013 | Version 1.1 Global protocol amendment of protocol Version 01 to clarify about PK assessment, IWRS, and drug accountability procedures and so on. |
| 10 April 2014 | Version 2.0 Global protocol amendment (excluding Germany) developed from and replacing protocol Version 1.1: the amendment was issued primarily to update the contraception inclusion criterion and modify other criteria. |
| 29 May 2014 | Version 3.0 Global protocol amendment (excluding Germany) of protocol Version 2.0: the amendment was issued further to the decision when to conduct the interim analysis. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Per Global Protocol AM#3, v.4.0, 17-Dec-14 Glucagon assay performed as part of the "other-diabetes-related parameters" was not sensitive enough and did not provide results within the normal range for glucagon. It was removed as an efficacy assessment

Notes: