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
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Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	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 standard deviation	 56.2 ± 10.89	 55.1 ± 8.81	 55.8 ± 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 (± 0.118)	-0.4 (± 0.111)	-1.38 (± 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 (± 0.543)	-1.29 (± 0.511)	-3.212 (± 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 (± 0.274)	-1.519 (± 0.257)	-2.008 (± 0.295)	-2.348 (± 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 (± 0.295)	-0.582 (± 0.267)	-2.107 (± 0.286)	

Statistical analyses

No statistical analyses for this end point

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 (± 0.034)	-0.046 (± 0.032)	0.009 (± 0.035)	0.027 (± 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 (± 0.036)	0.027 (± 0.033)	0.043 (± 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 (± 0.043)	-0.29 (± 0.04)	-0.35 (± 0.044)	-0.42 (± 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 (± 0.044)	-0.13 (± 0.041)	-0.36 (± 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 (± 0.091)	0.11 (± 0.089)	-0.09 (± 0.094)	-0.06 (± 0.096)
Parameter HDL-C	0 (± 0.027)	0.05 (± 0.026)	0.02 (± 0.028)	-0.02 (± 0.028)
Parameter TG	-0.016 (± 0.137)	-0.27 (± 0.135)	-0.305 (± 0.143)	-0.414 (± 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 (± 0.095)	0.09 (± 0.088)	-0.16 (± 0.096)	
Parameter HDL-C	-0.01 (± 0.028)	0.02 (± 0.026)	0.01 (± 0.029)	
Parameter TG	-0.592 (± 0.145)	-0.093 (± 0.133)	-0.154 (± 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	2 / 37 (5.41%)	4 / 37 (10.81%)	3 / 33 (9.09%)
occurrences (all)	2	4	5
Dizziness			
subjects affected / exposed	1 / 37 (2.70%)	2 / 37 (5.41%)	1 / 33 (3.03%)
occurrences (all)	1	2	1
General disorders and administration site conditions			
Injection site bruising			
subjects affected / exposed	2 / 37 (5.41%)	1 / 37 (2.70%)	2 / 33 (6.06%)
occurrences (all)	7	1	2
Injection site pain			
subjects affected / exposed	2 / 37 (5.41%)	2 / 37 (5.41%)	1 / 33 (3.03%)
occurrences (all)	3	3	1
Oedema peripheral			
subjects affected / exposed	0 / 37 (0.00%)	0 / 37 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 37 (0.00%)	2 / 37 (5.41%)	1 / 33 (3.03%)
occurrences (all)	0	2	1
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	4 / 37 (10.81%)	3 / 37 (8.11%)	9 / 33 (27.27%)
occurrences (all)	5	4	10
Diarrhoea			
subjects affected / exposed	5 / 37 (13.51%)	1 / 37 (2.70%)	3 / 33 (9.09%)
occurrences (all)	5	1	3
Vomiting			
subjects affected / exposed	0 / 37 (0.00%)	1 / 37 (2.70%)	4 / 33 (12.12%)
occurrences (all)	0	2	4
Abdominal pain upper			
subjects affected / exposed	1 / 37 (2.70%)	2 / 37 (5.41%)	0 / 33 (0.00%)
occurrences (all)	1	2	0
Constipation			
subjects affected / exposed	0 / 37 (0.00%)	0 / 37 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Abdominal discomfort			

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

Decreased appetite			
subjects affected / exposed	0 / 37 (0.00%)	0 / 37 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 37 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	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	4 / 36 (11.11%)	1 / 36 (2.78%)	1 / 37 (2.70%)
occurrences (all)	4	1	1
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 36 (8.33%)	4 / 36 (11.11%)	5 / 37 (13.51%)
occurrences (all)	3	5	6
Dizziness			
subjects affected / exposed	0 / 36 (0.00%)	2 / 36 (5.56%)	0 / 37 (0.00%)
occurrences (all)	0	3	0
General disorders and administration site conditions			
Injection site bruising			
subjects affected / exposed	4 / 36 (11.11%)	0 / 36 (0.00%)	3 / 37 (8.11%)
occurrences (all)	6	0	4
Injection site pain			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	0	1
Oedema peripheral			
subjects affected / exposed	2 / 36 (5.56%)	0 / 36 (0.00%)	0 / 37 (0.00%)
occurrences (all)	2	0	0
Pyrexia			
subjects affected / exposed	0 / 36 (0.00%)	0 / 36 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0	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	0 / 36 (0.00%)	2 / 36 (5.56%)	0 / 37 (0.00%)
occurrences (all)	0	2	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			

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

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: