Clinical trial results:
A 20-week, double blind, randomized, placebo controlled, parallel group trial to assess the safety and efficacy of HM11260C on body weight in obese subjects without diabetes

Summary

EudraCT number	2013-004251-21
Trial protocol	DE HU NL
Global end of trial date	17 February 2015

Results information

Result version number	v1 (current)
This version publication date	06 November 2016
First version publication date	06 November 2016

Trial information

Trial identification

Sponsor protocol code	HM-EXC-205

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02075281
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	25 August 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 February 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the effect of HM11260C, in combination with a hypocaloric diet, on body weight over the 20 weeks from baseline in obese subjects.

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	09 April 2014
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	Korea, Republic of: 24
Country: Number of subjects enrolled	United States: 216
Country: Number of subjects enrolled	Netherlands: 13
Country: Number of subjects enrolled	Germany: 41
Country: Number of subjects enrolled	Hungary: 3
Worldwide total number of subjects	297
EEA total number of subjects	57

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)	297
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment period from 09Apr2014 (First patient screened)/23Apr2014 (First patient randomized) to 25Jul2014 (Last Patient screened)/19Aug2014 (Last Patient randomized). Regions: USA, Europe (Germany, Hungary, Netherlands) and Asia (South Korea)

Pre-assignment

Screening details:

Study design: 4 weeks screening period, then 2 weeks titration period, 18 weeks treatment period and 6 weeks follow-up period. 509 subjects screened.

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 prefilled syringe and packaged identically.

Arms

Are arms mutually exclusive?	Yes
Arm title	HM11260C (4 mg QW)

Arm description:

subcutaneous (sc) HM11260C 4 mg once a week (QW) for 20 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:

0.8 ml of HM11260C (5.0 mg/ml concentration) was self administered by subcutaneous injection in the morning before the meal using prefilled syringe.

Arm title	HM11260C (6 mg QW)

Arm description:

subcutaneous (sc) HM11260C 6 mg once a week (QW) for 20 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:

0.8 ml of HM11260C (7.5 mg/ml concentration) was self administered by subcutaneous injection in the morning before the meal using prefilled syringe.

Arm title	HM11260C (6 mg Q2W)

Arm description:

subcutaneous (sc) HM11260C 4 mg was administered on day 1, then 6 mg was administered on day 8, and then 6 mg once every two weeks (Q2W) for 18 weeks, with placebo administered once every 2 weeks between HM11260C doses

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:

0.8 ml of HM11260C (7.5 mg/ml concentration) was self administered by subcutaneous injection in the morning before the meal using prefilled syringe.

Arm title	HM11260C (8 mg Q2W)

Arm description:

subcutaneous (sc) HM11260C 4 mg was administered on day 1, then 8 mg was administered on day 8, then 8 mg once every two weeks (Q2W) for 18 weeks, with placebo administered once every 2 weeks between HM11260C doses

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:

0.8 ml of HM11260C (10.0 mg/ml concentration) was self administered by subcutaneous injection in the morning before the meal using prefilled syringe.

Arm title	Placebo

Arm description:

subcutaneous (sc) Placebo identical to HM11260C once a week (QW) for 20 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:

0.8 ml of Placebo was self administered by subcutaneous injection in the morning before the meal using prefilled syringe.

Number of subjects in period 1[1]	HM11260C (4 mg QW)	HM11260C (6 mg QW)	HM11260C (6 mg Q2W)
Started	59	59	59
Completed	44	43	41
Not completed	15	16	18
Lost to follow-up	2	1	2
Adverse event, non-fatal	3	11	7
Other	4	-	1
Prohibited Treatment	1	-	1
Clinically Significant Lab Abnormalities	-	-	1

Withdrawal by subject	5	4	4
Noncompliance	-	-	2
Protocol deviation	-	-	-

Number of subjects in period 1[1]	HM11260C (8 mg Q2W)	Placebo
Started	58	60
Completed	40	48
Not completed	18	12
Lost to follow-up	-	2
Adverse event, non-fatal	11	3
Other	-	1
Prohibited Treatment	-	-
Clinically Significant Lab Abnormalities	1	-
Withdrawal by subject	6	4
Noncompliance	-	1
Protocol deviation	-	1

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 297 subjects were enrolled and randomized into the study. A total of 295 subjects received study drug (HM11260C or placebo) and were included in the Safety Set.

Baseline characteristics

Reporting groups	
Reporting group title	HM11260C (4 mg QW)
Reporting group description:	
subcutaneous (sc) HM11260C 4 mg once a week (QW) for 20 weeks	
Reporting group title	HM11260C (6 mg QW)
Reporting group description:	
subcutaneous (sc) HM11260C 6 mg once a week (QW) for 20 weeks	
Reporting group title	HM11260C (6 mg Q2W)
Reporting group description:	
subcutaneous (sc) HM11260C 4 mg was administered on day 1, then 6 mg was administered on day 8, and then 6 mg once every two weeks (Q2W) for 18 weeks, with placebo administered once every 2 weeks between HM11260C doses	
Reporting group title	HM11260C (8 mg Q2W)
Reporting group description:	
subcutaneous (sc) HM11260C 4 mg was administered on day 1, then 8 mg was administered on day 8, then 8 mg once every two weeks (Q2W) for 18 weeks, with placebo administered once every 2 weeks between HM11260C doses	

Reporting group title	Placebo
Reporting group description:	
subcutaneous (sc) Placebo identical to HM11260C once a week (QW) for 20 weeks	

Reporting group values	HM11260C (4 mg QW)	HM11260C (6 mg QW)	HM11260C (6 mg Q2W)
Number of subjects	59	59	59
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	42.9	43	43.3
standard deviation	± 12.14	± 13.02	± 12.45
Gender categorical			
Units: Subjects			
Female	41	46	43
Male	18	13	16

Reporting group values	HM11260C (8 mg Q2W)	Placebo	Total
Number of subjects	58	60	295
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	43.9	43.7	
standard deviation	± 9.16	± 11.84	-

Gender categorical Units: Subjects			
Female	51	44	225
Male	7	16	70

End points

End points reporting groups

Reporting group title	HM11260C (4 mg QW)
Reporting group description:	
subcutaneous (sc) HM11260C 4 mg once a week (QW) for 20 weeks	
Reporting group title	HM11260C (6 mg QW)
Reporting group description:	
subcutaneous (sc) HM11260C 6 mg once a week (QW) for 20 weeks	
Reporting group title	HM11260C (6 mg Q2W)
Reporting group description:	
subcutaneous (sc) HM11260C 4 mg was administered on day 1, then 6 mg was administered on day 8, and then 6 mg once every two weeks (Q2W) for 18 weeks, with placebo administered once every 2 weeks between HM11260C doses	
Reporting group title	HM11260C (8 mg Q2W)
Reporting group description:	
subcutaneous (sc) HM11260C 4 mg was administered on day 1, then 8 mg was administered on day 8, then 8 mg once every two weeks (Q2W) for 18 weeks, with placebo administered once every 2 weeks between HM11260C doses	

Reporting group title	Placebo
Reporting group description:	
subcutaneous (sc) Placebo identical to HM11260C once a week (QW) for 20 weeks	

Primary: Change from Baseline in Body Weight for HM11260C

End point title	Change from Baseline in Body Weight for HM11260C
End point description:	
Least squares (LS) means and standard errors at Week 21 were obtained from a mixed effect model with repeated measures (MMRM). Full Analysis Set (FAS) population: all participants who received study drug and had at least 1 efficacy or safety assessment recorded after dosing.	
End point type	Primary
End point timeframe:	
Week 21	

End point values	HM11260C (4 mg QW)	HM11260C (6 mg QW)	HM11260C (6 mg Q2W)	HM11260C (8 mg Q2W)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	49	59	59	58
Units: kg				
least squares mean (standard error)	-6.63 (± 0.621)	-7.32 (± 0.627)	-6.4 (± 0.626)	-7.06 (± 0.635)

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	60			

Units: kg				
least squares mean (standard error)	-0.13 (± 0.605)			

Statistical analyses

Statistical analysis title	Change in Body Weight for 4 mg QW vs placebo
Comparison groups	HM11260C (4 mg QW) v Placebo
Number of subjects included in analysis	109
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	< 0.0001
Method	Mixed Model Repeated Measures
Parameter estimate	LS Mean Difference
Point estimate	-6.5
Confidence interval	
level	95.1 %
sides	2-sided
lower limit	-8.22
upper limit	-4.79
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 in Body Weight for 6 mg QW vs placebo

Statistical analysis description:

Superiority for HM11260C 6 mg QW vs placebo, the threshold for significance is a p-value <=0.049. No adjustments were made for multiple comparisons of each treatment group to placebo.

Comparison groups	HM11260C (6 mg QW) v Placebo
Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	< 0.0001
Method	Mixed Model Repeated Measures
Parameter estimate	LS Mean Difference
Point estimate	-7.2
Confidence interval	
level	95.1 %
sides	2-sided
lower limit	-8.92
upper limit	-5.47
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 in Body Weight for 6 mg Q2W vs placebo
Comparison groups	HM11260C (6 mg Q2W) v Placebo

Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	< 0.0001
Method	Mixed Model Repeated Measures
Parameter estimate	LS Mean Difference
Point estimate	-6.28
Confidence interval	
level	95.1 %
sides	2-sided
lower limit	-8
upper limit	-4.56
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 in Body Weight for 8 mg Q2W vs placebo
Comparison groups	HM11260C (8 mg Q2W) v Placebo
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	superiority[4]
Method	Mixed Model Repeated Measures
Parameter estimate	LS Mean Difference
Point estimate	-6.93
Confidence interval	
level	95.1 %
sides	2-sided
lower limit	-8.67
upper limit	-5.2
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.

Secondary: Change from Baseline in Glucose Metabolism Parameters (Fasting Plasma Glucose)

End point title	Change from Baseline in Glucose Metabolism Parameters (Fasting Plasma Glucose)

End point description:

Least squares (LS) means and standard errors at Week 21 were obtained from a mixed effect model with repeated measures (MMRM). FAS population.

End point type	Secondary

End point timeframe:

Week 21

End point values	HM11260C (4 mg QW)	HM11260C (6 mg QW)	HM11260C (6 mg Q2W)	HM11260C (8 mg Q2W)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	59	59	59	58
Units: mmol/L				
least squares mean (standard error)	-0.311 (± 0.0836)	-0.428 (± 0.0854)	-0.497 (± 0.088)	-0.515 (± 0.0882)

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: mmol/L				
least squares mean (standard error)	0.056 (± 0.081)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Glucose Metabolism Parameters (HbA1c)

End point title	Change from Baseline in Glucose Metabolism Parameters (HbA1c)

End point description:

Least squares (LS) means and standard errors at Week 21 were obtained from a mixed effect model with repeated measures (MMRM). FAS population.

End point type	Secondary

End point timeframe:

Week 21

End point values	HM11260C (4 mg QW)	HM11260C (6 mg QW)	HM11260C (6 mg Q2W)	HM11260C (8 mg Q2W)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	59	59	59	58
Units: Percentage				
least squares mean (standard error)	-0.24 (± 0.029)	-0.29 (± 0.03)	-0.29 (± 0.03)	-0.3 (± 0.03)

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: Percentage				
least squares mean (standard error)	0.05 (± 0.027)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Glucose Metabolism Parameters (Fasting Insulin)

End point title	Change from Baseline in Glucose Metabolism Parameters (Fasting Insulin)

End point description:

Least squares (LS) means and standard errors at Week 21 were obtained from a mixed effect model with repeated measures (MMRM). FAS population.

End point type	Secondary

End point timeframe:

Week 21

End point values	HM11260C (4 mg QW)	HM11260C (6 mg QW)	HM11260C (6 mg Q2W)	HM11260C (8 mg Q2W)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	59	59	59	58
Units: pmol/L				
least squares mean (standard error)	-0.24 (± 13.137)	-21.7 (± 13.341)	1.79 (± 13.598)	-12.19 (± 13.563)

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: pmol/L				
least squares mean (standard error)	18.33 (± 12.763)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Glucose Metabolism Parameters (C-Peptide)

End point title	Change from Baseline in Glucose Metabolism Parameters (C-Peptide)

End point description:

Least squares (LS) means and standard errors at Week 21 were obtained from a mixed effect model

with repeated measures (MMRM). FAS population.

End point type	Secondary

End point timeframe:

Week 21

End point values	HM11260C (4 mg QW)	HM11260C (6 mg QW)	HM11260C (6 mg Q2W)	HM11260C (8 mg Q2W)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	59	59	59	58
Units: nmol/L				
least squares mean (standard error)	-0.011 (± 0.0213)	-0.049 (± 0.0216)	0.016 (± 0.022)	0.002 (± 0.0219)

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: nmol/L				
least squares mean (standard error)	-0.014 (± 0.0207)			

Statistical analyses

No statistical analyses for this end point

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

End point title	Change from Baseline in Serum Lipid Profile Parameters (Total Cholesterol, LDL-C)

End point description:

Least squares (LS) means and standard errors at Week 21 were obtained from a mixed effect model with repeated measures (MMRM). FAS population.

End point type	Secondary

End point timeframe:

Week 21

End point values	HM11260C (4 mg QW)	HM11260C (6 mg QW)	HM11260C (6 mg Q2W)	HM11260C (8 mg Q2W)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	59	59	59	58
Units: mmol/L				
least squares mean (standard error)				
Total Cholesterol	-0.23 (± 0.082)	-0.32 (± 0.083)	-0.27 (± 0.084)	-0.23 (± 0.086)

LDL-C	0 (± 0.075)	-0.1 (± 0.077)	0.01 (± 0.078)	0 (± 0.079)

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: mmol/L				
least squares mean (standard error)				
Total Cholesterol LDL-C	0.11 (± 0.079) 0.26 (± 0.073)			

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 45 days after the subject had received last dose of study drug.

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 (4mg QW)

Reporting group description:

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

Reporting group title	HM11260C (6mg QW)

Reporting group description:

Subjects received HM11260C 6mg as a weekly subcutaneous injection in the abdomen via a pre-filled syringe.

Reporting group title	HM11260C (6mg Q2W)

Reporting group description:

Subjects received a weekly subcutaneous injection in the abdomen via a pre-filled syringe. HM11260C 4mg was administered on Day 1, HM11260C 6mg was administered on Day 8, and thereafter HM11260C 6 mg was administered every 14 days, with placebo between HM11260C doses.

Reporting group title	HM11260C (8mg Q2W)

Reporting group description:

Subjects received a weekly subcutaneous injection in the abdomen via a pre-filled syringe. HM11260C 4mg was administered on Day 1, HM11260C 8mg was administered on Day 8, and thereafter HM11260C 8 mg was administered every 14 days, with placebo between HM11260C doses.

Reporting group title	Placebo

Reporting group description:

Subjects received placebo as a weekly subcutaneous injection in the abdomen via a pre-filled syringe.

Serious adverse events	HM11260C (4mg QW)	HM11260C (6mg QW)	HM11260C (6mg Q2W)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 59 (1.69%)	3 / 59 (5.08%)	0 / 59 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			

subjects affected / exposed	1 / 59 (1.69%)	0 / 59 (0.00%)	0 / 59 (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
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 59 (0.00%)	1 / 59 (1.69%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 59 (0.00%)	1 / 59 (1.69%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 59 (0.00%)	1 / 59 (1.69%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 59 (0.00%)	0 / 59 (0.00%)	0 / 59 (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
Cholelithiasis			
subjects affected / exposed	0 / 59 (0.00%)	0 / 59 (0.00%)	0 / 59 (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
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	0 / 59 (0.00%)	1 / 59 (1.69%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Erysipelas			

subjects affected / exposed	0 / 59 (0.00%)	1 / 59 (1.69%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 59 (0.00%)	0 / 59 (0.00%)	0 / 59 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 59 (0.00%)	1 / 59 (1.69%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	HM11260C (8mg Q2W)	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 58 (3.45%)	0 / 60 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			
subjects affected / exposed	0 / 58 (0.00%)	0 / 60 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 58 (0.00%)	0 / 60 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 58 (0.00%)	0 / 60 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			

subjects affected / exposed	0 / 58 (0.00%)	0 / 60 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 58 (1.72%)	0 / 60 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	1 / 58 (1.72%)	0 / 60 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	0 / 58 (0.00%)	0 / 60 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Erysipelas			
subjects affected / exposed	0 / 58 (0.00%)	0 / 60 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	1 / 58 (1.72%)	0 / 60 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 58 (0.00%)	0 / 60 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	HM11260C (4mg QW)	HM11260C (6mg QW)	HM11260C (6mg Q2W)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	51 / 59 (86.44%)	54 / 59 (91.53%)	51 / 59 (86.44%)
Investigations			
Lipase increased			
subjects affected / exposed	4 / 59 (6.78%)	1 / 59 (1.69%)	1 / 59 (1.69%)
occurrences (all)	4	1	1
Heart rate increased			
subjects affected / exposed	0 / 59 (0.00%)	3 / 59 (5.08%)	1 / 59 (1.69%)
occurrences (all)	0	3	1
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 59 (0.00%)	0 / 59 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	11 / 59 (18.64%)	15 / 59 (25.42%)	8 / 59 (13.56%)
occurrences (all)	16	19	18
Dizziness			
subjects affected / exposed	8 / 59 (13.56%)	3 / 59 (5.08%)	7 / 59 (11.86%)
occurrences (all)	14	3	8
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	9 / 59 (15.25%)	3 / 59 (5.08%)	5 / 59 (8.47%)
occurrences (all)	10	3	6
Injection site pain			
subjects affected / exposed	6 / 59 (10.17%)	5 / 59 (8.47%)	3 / 59 (5.08%)
occurrences (all)	30	11	3
Injection site erythema			
subjects affected / exposed	5 / 59 (8.47%)	2 / 59 (3.39%)	1 / 59 (1.69%)
occurrences (all)	17	4	1
Injection site bruising			
subjects affected / exposed	3 / 59 (5.08%)	1 / 59 (1.69%)	1 / 59 (1.69%)
occurrences (all)	3	2	1
Pyrexia			

subjects affected / exposed	0 / 59 (0.00%)	0 / 59 (0.00%)	2 / 59 (3.39%)
occurrences (all)	0	0	2
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	14 / 59 (23.73%)	12 / 59 (20.34%)	15 / 59 (25.42%)
occurrences (all)	20	17	34
Dyspepsia			
subjects affected / exposed	12 / 59 (20.34%)	16 / 59 (27.12%)	9 / 59 (15.25%)
occurrences (all)	47	25	13
Constipation			
subjects affected / exposed	10 / 59 (16.95%)	12 / 59 (20.34%)	9 / 59 (15.25%)
occurrences (all)	17	15	17
Abdominal pain upper			
subjects affected / exposed	3 / 59 (5.08%)	6 / 59 (10.17%)	5 / 59 (8.47%)
occurrences (all)	6	6	8
Abdominal distension			
subjects affected / exposed	4 / 59 (6.78%)	5 / 59 (8.47%)	2 / 59 (3.39%)
occurrences (all)	4	7	2
Flatulence			
subjects affected / exposed	3 / 59 (5.08%)	3 / 59 (5.08%)	3 / 59 (5.08%)
occurrences (all)	3	4	3
Eructation			
subjects affected / exposed	1 / 59 (1.69%)	5 / 59 (8.47%)	2 / 59 (3.39%)
occurrences (all)	1	5	4
Abdominal discomfort			
subjects affected / exposed	2 / 59 (3.39%)	2 / 59 (3.39%)	3 / 59 (5.08%)
occurrences (all)	2	2	4
Gastrooesophageal reflux disease			
subjects affected / exposed	3 / 59 (5.08%)	2 / 59 (3.39%)	0 / 59 (0.00%)
occurrences (all)	4	2	0
Dry mouth			
subjects affected / exposed	0 / 59 (0.00%)	1 / 59 (1.69%)	3 / 59 (5.08%)
occurrences (all)	0	1	3
Abdominal pain lower			
subjects affected / exposed	0 / 59 (0.00%)	0 / 59 (0.00%)	2 / 59 (3.39%)
occurrences (all)	0	0	2

Nausea			
subjects affected / exposed	32 / 59 (54.24%)	34 / 59 (57.63%)	28 / 59 (47.46%)
occurrences (all)	88	74	70
Vomiting			
subjects affected / exposed	13 / 59 (22.03%)	12 / 59 (20.34%)	10 / 59 (16.95%)
occurrences (all)	18	36	16
Abdominal pain			
subjects affected / exposed	3 / 59 (5.08%)	10 / 59 (16.95%)	2 / 59 (3.39%)
occurrences (all)	3	15	3
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 59 (3.39%)	1 / 59 (1.69%)	4 / 59 (6.78%)
occurrences (all)	2	1	4
Oropharyngeal pain			
subjects affected / exposed	1 / 59 (1.69%)	0 / 59 (0.00%)	1 / 59 (1.69%)
occurrences (all)	1	0	1
Nasal congestion			
subjects affected / exposed	0 / 59 (0.00%)	0 / 59 (0.00%)	0 / 59 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	3 / 59 (5.08%)	4 / 59 (6.78%)	0 / 59 (0.00%)
occurrences (all)	3	5	0
Myalgia			
subjects affected / exposed	0 / 59 (0.00%)	1 / 59 (1.69%)	1 / 59 (1.69%)
occurrences (all)	0	1	2
Joint crepitation			
subjects affected / exposed	0 / 59 (0.00%)	1 / 59 (1.69%)	1 / 59 (1.69%)
occurrences (all)	0	1	1
Arthralgia			
subjects affected / exposed	0 / 59 (0.00%)	1 / 59 (1.69%)	0 / 59 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	7 / 59 (11.86%)	4 / 59 (6.78%)	5 / 59 (8.47%)
occurrences (all)	8	5	6

Nasopharyngitis			
subjects affected / exposed	5 / 59 (8.47%)	4 / 59 (6.78%)	1 / 59 (1.69%)
occurrences (all)	6	4	1

Non-serious adverse events	HM11260C (8mg Q2W)	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	51 / 58 (87.93%)	48 / 60 (80.00%)	
Investigations			
Lipase increased			
subjects affected / exposed	3 / 58 (5.17%)	2 / 60 (3.33%)	
occurrences (all)	3	2	
Heart rate increased			
subjects affected / exposed	1 / 58 (1.72%)	1 / 60 (1.67%)	
occurrences (all)	1	1	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 58 (1.72%)	3 / 60 (5.00%)	
occurrences (all)	2	3	
Nervous system disorders			
Headache			
subjects affected / exposed	15 / 58 (25.86%)	10 / 60 (16.67%)	
occurrences (all)	24	16	
Dizziness			
subjects affected / exposed	7 / 58 (12.07%)	5 / 60 (8.33%)	
occurrences (all)	11	6	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	8 / 58 (13.79%)	7 / 60 (11.67%)	
occurrences (all)	8	7	
Injection site pain			
subjects affected / exposed	4 / 58 (6.90%)	5 / 60 (8.33%)	
occurrences (all)	6	5	
Injection site erythema			
subjects affected / exposed	2 / 58 (3.45%)	1 / 60 (1.67%)	
occurrences (all)	2	1	
Injection site bruising			

subjects affected / exposed	1 / 58 (1.72%)	3 / 60 (5.00%)	
occurrences (all)	1	4	
Pyrexia			
subjects affected / exposed	0 / 58 (0.00%)	3 / 60 (5.00%)	
occurrences (all)	0	3	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	16 / 58 (27.59%)	12 / 60 (20.00%)	
occurrences (all)	36	23	
Dyspepsia			
subjects affected / exposed	15 / 58 (25.86%)	2 / 60 (3.33%)	
occurrences (all)	20	2	
Constipation			
subjects affected / exposed	12 / 58 (20.69%)	5 / 60 (8.33%)	
occurrences (all)	19	5	
Abdominal pain upper			
subjects affected / exposed	9 / 58 (15.52%)	3 / 60 (5.00%)	
occurrences (all)	17	9	
Abdominal distension			
subjects affected / exposed	8 / 58 (13.79%)	1 / 60 (1.67%)	
occurrences (all)	9	1	
Flatulence			
subjects affected / exposed	6 / 58 (10.34%)	1 / 60 (1.67%)	
occurrences (all)	6	4	
Eructation			
subjects affected / exposed	5 / 58 (8.62%)	0 / 60 (0.00%)	
occurrences (all)	8	0	
Abdominal discomfort			
subjects affected / exposed	3 / 58 (5.17%)	1 / 60 (1.67%)	
occurrences (all)	3	1	
Gastrooesophageal reflux disease			
subjects affected / exposed	3 / 58 (5.17%)	2 / 60 (3.33%)	
occurrences (all)	4	3	
Dry mouth			
subjects affected / exposed	3 / 58 (5.17%)	2 / 60 (3.33%)	
occurrences (all)	3	2	

Abdominal pain lower			
subjects affected / exposed	3 / 58 (5.17%)	3 / 60 (5.00%)	
occurrences (all)	3	3	
Nausea			
subjects affected / exposed	36 / 58 (62.07%)	11 / 60 (18.33%)	
occurrences (all)	117	14	
Vomiting			
subjects affected / exposed	19 / 58 (32.76%)	4 / 60 (6.67%)	
occurrences (all)	28	4	
Abdominal pain			
subjects affected / exposed	8 / 58 (13.79%)	2 / 60 (3.33%)	
occurrences (all)	15	2	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 58 (1.72%)	2 / 60 (3.33%)	
occurrences (all)	1	2	
Oropharyngeal pain			
subjects affected / exposed	2 / 58 (3.45%)	5 / 60 (8.33%)	
occurrences (all)	2	5	
Nasal congestion			
subjects affected / exposed	0 / 58 (0.00%)	3 / 60 (5.00%)	
occurrences (all)	0	3	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	5 / 58 (8.62%)	4 / 60 (6.67%)	
occurrences (all)	7	4	
Myalgia			
subjects affected / exposed	1 / 58 (1.72%)	3 / 60 (5.00%)	
occurrences (all)	1	3	
Joint crepitation			
subjects affected / exposed	0 / 58 (0.00%)	3 / 60 (5.00%)	
occurrences (all)	0	4	
Arthralgia			
subjects affected / exposed	1 / 58 (1.72%)	3 / 60 (5.00%)	
occurrences (all)	1	3	
Infections and infestations			

Upper respiratory tract infection subjects affected / exposed occurrences (all)	5 / 58 (8.62%) 6	5 / 60 (8.33%) 7	
Nasopharyngitis subjects affected / exposed occurrences (all)	3 / 58 (5.17%) 3	8 / 60 (13.33%) 9	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 December 2013	Version 2 The protocol amendment was undertaken primarily for modifying inclusion and exclusion criteria and other sections.
25 April 2014	Version 3 The protocol amendment was undertaken primarily for updating the contraception inclusion criterion for females of child-bearing potential and males and exclusion criterion.
10 December 2014	Version 4 This amendment was due to glucagon assay. Glucagon assessments and analyses were removed from the study as the glucagon assay performed during the study up to that time was not sensitive enough and did not give results within the normal range for glucagon.

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 amendment #3, 10-Dec-2014 glucagon secondary objective and assessment were both removed as the assay was not sensitive enough and did not give results within the normal range for glucagon.

Notes: