Clinical trial results:
A 56-week, Multicenter, Double-blind, Placebo-controlled, Randomized Study to Evaluate the Efficacy and Safety of Efpeglenatide Once Weekly in Patients with Type 2 Diabetes Mellitus Inadequately Controlled with Diet and Exercise

Summary

EudraCT number	2016-001857-42
Trial protocol	GB DE PL
Global end of trial date	07 September 2020

Results information

Result version number	v1 (current)
This version publication date	04 August 2021
First version publication date	04 August 2021

Trial information

Trial identification

Sponsor protocol code	EFC14822

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03353350
WHO universal trial number (UTN)	U1111-1182-1806

Notes:

Sponsors

Sponsor organisation name	Hanmi Pharmaceuticals Co., Ltd.
Sponsor organisation address	14 Wiryeseong daero, Songpa gu, Seoul, Korea, Republic of, 05545
Public contact	Clinical Director's Office, Hanmi Pharmaceutical Co., Ltd., 82 24100473, sujin.jung@hanmi.co.kr
Scientific contact	Clinical Director's Office, Hanmi Pharmaceutical Co., Ltd., 82 24100469, jdchoi@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	07 March 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 January 2020
Global end of trial reached?	Yes
Global end of trial date	07 September 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the superiority of once weekly injection of efpeglenatide 2, 4, or 6 mg in comparison to placebo in HbA1c change from baseline to Week 30 in participants with T2DM inadequately controlled with diet and exercise.

Protection of trial subjects:

The study was conducted in accordance with consensus ethics principles derived from international ethics guidelines, including the Declaration of Helsinki, and the ICH guidelines for GCP, all applicable laws, rules, and regulations. Informed consent was obtained prior to the conduct of any study related procedures. The participant ICF was modified according to local regulations and requirements.
An IDMC reviewed and analyzed unblinded safety data throughout the study, as well as safety data from the other ongoing clinical studies conducted with efpeglenatide (a single IDMC for the whole efpeglenatide program). Several subject´s visits and on-site monitoring activities were impacted by the COVID-19 pandemic in all countries. Starting in March 2020, a Business Continuity Plan was implemented to closely monitor the situation and to be able to identify risks, better assess the impact and set up contingency plans as needed. The patient treatment and safety were not impacted. There were no patients with COVID-19 infection.

Background therapy: -

Evidence for comparator:

No comparator

Actual start date of recruitment	05 December 2017
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	2 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 49
Country: Number of subjects enrolled	United Kingdom: 70
Country: Number of subjects enrolled	Germany: 7
Country: Number of subjects enrolled	Ukraine: 58
Country: Number of subjects enrolled	United States: 222
Worldwide total number of subjects	406
EEA total number of subjects	56

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)	271
From 65 to 84 years	134
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Subjects who met all of the inclusion criteria and none of the exclusion criteria were enrolled into the study and were randomly assigned into 1 of 3 dose levels of efpeglenatide (2, 4, or 6 mg) or to placebo. Participants aged ≥18 years with T2DM, treated with diet and exercise, and with HbA1c between 7.0% and 10.0% (inclusive) were eligible.

Pre-assignment

Screening details:

Up to 3-week Screening Period (Week -3/-1, Visit 1-2). A total of 900 participants were screened, 406 participants with T2DM inadequately controlled with diet/exercise were randomly assigned to efpeglenatide or to matching placebo. 494 (54.9%) participants were screen failures.

Period 1

Period 1 title	30-week Core Treatment Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer

Blinding implementation details:

During the double-blind treatment period, which included titration (baseline-Day 1, weeks 1-3 (visit 3-4), investigators and participants were blinded to the allocation of active or placebo treatment arms. Efpeglenatide and matching placebo formulation : 500 µL of a sterile, nonpyrogenic, clear, colorless solution in a 1 mL disposable PFS, SC injection once weekly on the same day of the week.

Arms

Are arms mutually exclusive?	Yes
Arm title	Efpeglenatide 2mg

Arm description:

Through the the double-blind treatment period, participants were randomly assigned to Efpeglenatide 2 mg from Week 4 (Visit 5) until Week 30.

Arm type	Experimental
Investigational medicinal product name	Efpeglenatide 2 mg
Investigational medicinal product code	
Other name	SAR439977, HM11260C
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

The IMP included efpeglenatide 2 mg for Subcutaneous (SC) injection during the 56 weeks of treatment.

Arm title	Efpeglenatide 4 mg

Arm description:

Through the the double-blind treatment period, participants were randomly assigned to Efpeglenatide 4 mg from Week 4 (Visit 5) until Week 30.

Arm type	Experimental
Investigational medicinal product name	Efpeglenatide 4 mg
Investigational medicinal product code	
Other name	SAR439977, HM11260C
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

The IMP included efpeglenatide 4 mg for Subcutaneous (SC) injection during the 56 weeks of treatment.

Arm title	Efpeglenatide 6 mg

Arm description:

Through the the double-blind treatment period, participants were randomly assigned to Efpeglenatide 6 mg from Week 4 (Visit 5) until Week 30.

Arm type	Experimental
Investigational medicinal product name	Efpeglenatide 6 mg
Investigational medicinal product code	
Other name	SAR439977, HM11260C
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

The IMP included efpeglenatide 6 mg for Subcutaneous (SC) injection during the 56 weeks of treatment.

Arm title	Placebo

Arm description:

Through the the double-blind treatment period, participants were randomly assigned to Placebo from Week 4 (Visit 5) until Week 30.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	SAR439977, HM11260C
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Matching placebo (sterile, nonpyrogenic, clear, colorless solution in a 1 mL disposable PFS) for Subcutaneous (SC) injection during the 56 weeks of treatment.

Number of subjects in period 1	Efpeglenatide 2mg	Efpeglenatide 4 mg	Efpeglenatide 6 mg
Started	100	101	103
Completed	81	77	81
Not completed	19	24	22
Consent withdrawn by subject	12	19	19
Adverse event, non-fatal	4	2	3
Other	2	2	-
Protocol deviation	1	1	-

Number of subjects in period 1	Placebo
Started	102
Completed	80
Not completed	22
Consent withdrawn by subject	19
Adverse event, non-fatal	-
Other	2
Protocol deviation	1

Period 2

Period 2 title	26-week Treatment Extension Period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer

Blinding implementation details:

During the double-blind treatment period, which included titration (baseline-Day 1, weeks 1-3 (visit 3-4), investigators and participants were blinded to the allocation of active or placebo treatment arms. Efpeglenatide and matching placebo formulation : 500 µL of a sterile, nonpyrogenic, clear, colorless solution in a 1 mL disposable PFS, SC injection once weekly on the same day of the week.

Arms

Are arms mutually exclusive?	Yes
Arm title	Efpeglenatide 2mg

Arm description:

From Week 4 (Visit 5) through the rest of the double-blind treatment period, participants remained on the randomly assigned Efpeglenatide 2 mg until the EOT at Week 56 (Visit 14).

Arm type	Experimental
Investigational medicinal product name	Efpeglenatide 2 mg
Investigational medicinal product code	
Other name	SAR439977, HM11260C
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

The IMP included efpeglenatide 2 mg for Subcutaneous (SC) injection during the 56 weeks of treatment.

Arm title	Efpeglenatide 4 mg

Arm description:

From Week 4 (Visit 5) through the rest of the double-blind treatment period, participants remained on the randomly assigned Efpeglenatide 4 mg until the EOT at Week 56 (Visit 14).

Arm type	Experimental
Investigational medicinal product name	Efpeglenatide 4 mg
Investigational medicinal product code	
Other name	SAR439977, HM11260C
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

The IMP included efpeglenatide 4 mg for Subcutaneous (SC) injection during the 56 weeks of treatment.

Arm title	Efpeglenatide 6 mg

Arm description:

From Week 4 (Visit 5) through the rest of the double-blind treatment period, participants remained on the randomly assigned Efpeglenatide 6 mg until the EOT at Week 56 (Visit 14).

Arm type	Experimental
Investigational medicinal product name	Efpeglenatide 6 mg
Investigational medicinal product code	
Other name	SAR439977, HM11260C
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

The IMP included efpeglenatide 6 mg for Subcutaneous (SC) injection during the 56 weeks of treatment.

Arm title	Placebo

Arm description:

From Week 4 (Visit 5) through the rest of the double-blind treatment period, participants remained on the randomly assigned Placebo until the EOT at Week 56 (Visit 14).

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	SAR439977, HM11260C
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Matching placebo (sterile, nonpyrogenic, clear, colorless solution in a 1 mL disposable PFS) for Subcutaneous (SC) injection during the 56 weeks of treatment.

Number of subjects in period 2	Efpeglenatide 2mg	Efpeglenatide 4 mg	Efpeglenatide 6 mg
Started	81	77	81
Completed	78	73	67
Not completed	3	4	14
Consent withdrawn by subject	3	3	12
Adverse event, non-fatal	-	-	1
Other	-	1	1
Protocol deviation	-	-	-

Number of subjects in period 2	Placebo
Started	80
Completed	75
Not completed	5
Consent withdrawn by subject	2
Adverse event, non-fatal	1
Other	-
Protocol deviation	2

Baseline characteristics

Reporting groups	
Reporting group title	Efpeglenatide 2mg
Reporting group description:	
Through the the double-blind treatment period, participants were randomly assigned to Efpeglenatide 2 mg from Week 4 (Visit 5) until Week 30.	
Reporting group title	Efpeglenatide 4 mg
Reporting group description:	
Through the the double-blind treatment period, participants were randomly assigned to Efpeglenatide 4 mg from Week 4 (Visit 5) until Week 30.	
Reporting group title	Efpeglenatide 6 mg
Reporting group description:	
Through the the double-blind treatment period, participants were randomly assigned to Efpeglenatide 6 mg from Week 4 (Visit 5) until Week 30.	
Reporting group title	Placebo
Reporting group description:	
Through the the double-blind treatment period, participants were randomly assigned to Placebo from Week 4 (Visit 5) until Week 30.	

Reporting group values	Efpeglenatide 2mg	Efpeglenatide 4 mg	Efpeglenatide 6 mg
Number of subjects	100	101	103
Age categorical Units: Subjects			
Adults (18-64 years)	67	74	65
From 65-84 years	33	27	38
85 years and over	0	0	0
Age continuous Units: years			
median	59	55	61
full range (min-max)	33 to 79	27 to 82	32 to 80
Gender categorical Units: Subjects			
Female	45	49	42
Male	55	52	61

Reporting group values	Placebo	Total	
Number of subjects	102	406	
Age categorical Units: Subjects			
Adults (18-64 years)	65	271	
From 65-84 years	36	134	
85 years and over	1	1	
Age continuous Units: years			
median	59		
full range (min-max)	30 to 86	-	
Gender categorical Units: Subjects			
Female	51	187	

Male	51	219	

Subject analysis sets

Subject analysis set title	Randomized population
Subject analysis set type	Full analysis

Subject analysis set description:

The randomized population included any participant who had been allocated to a randomized treatment by IRT regardless of whether the treatment kit was used and with a signed informed consent.

Subject analysis set title	Efficacy population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The Efficacy (ITT) population was defined as all randomized participants, irrespective of compliance with the study protocol and procedures analyzed, according to the treatment group allocated by randomization.

Subject analysis set title	Safety population
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety population was defined as randomized population who actually received at least 1 dose or part of a dose of the IMP, analyzed according to the treatment actually received.

Reporting group values	Randomized population	Efficacy population	Safety population
Number of subjects	406	406	406
Age categorical Units: Subjects			
Adults (18-64 years)	271	271	271
From 65-84 years	134	134	134
85 years and over	1	1	1
Age continuous Units: years			
median	59	59	59
full range (min-max)	27 to 86	27 to 86	27 to 86
Gender categorical Units: Subjects			
Female	187	187	187
Male	219	219	219

End points

End points reporting groups

Reporting group title	Efpeglenatide 2mg
Reporting group description:	
Through the the double-blind treatment period, participants were randomly assigned to Efpeglenatide 2 mg from Week 4 (Visit 5) until Week 30.	
Reporting group title	Efpeglenatide 4 mg
Reporting group description:	
Through the the double-blind treatment period, participants were randomly assigned to Efpeglenatide 4 mg from Week 4 (Visit 5) until Week 30.	
Reporting group title	Efpeglenatide 6 mg
Reporting group description:	
Through the the double-blind treatment period, participants were randomly assigned to Efpeglenatide 6 mg from Week 4 (Visit 5) until Week 30.	
Reporting group title	Placebo
Reporting group description:	
Through the the double-blind treatment period, participants were randomly assigned to Placebo from Week 4 (Visit 5) until Week 30.	
Reporting group title	Efpeglenatide 2mg
Reporting group description:	
From Week 4 (Visit 5) through the rest of the double-blind treatment period, participants remained on the randomly assigned Efpeglenatide 2 mg until the EOT at Week 56 (Visit 14).	
Reporting group title	Efpeglenatide 4 mg
Reporting group description:	
From Week 4 (Visit 5) through the rest of the double-blind treatment period, participants remained on the randomly assigned Efpeglenatide 4 mg until the EOT at Week 56 (Visit 14).	
Reporting group title	Efpeglenatide 6 mg
Reporting group description:	
From Week 4 (Visit 5) through the rest of the double-blind treatment period, participants remained on the randomly assigned Efpeglenatide 6 mg until the EOT at Week 56 (Visit 14).	
Reporting group title	Placebo
Reporting group description:	
From Week 4 (Visit 5) through the rest of the double-blind treatment period, participants remained on the randomly assigned Placebo until the EOT at Week 56 (Visit 14).	
Subject analysis set title	Randomized population
Subject analysis set type	Full analysis
Subject analysis set description:	
The randomized population included any participant who had been allocated to a randomized treatment by IRT regardless of whether the treatment kit was used and with a signed informed consent.	
Subject analysis set title	Efficacy population
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
The Efficacy (ITT) population was defined as all randomized participants, irrespective of compliance with the study protocol and procedures analyzed, according to the treatment group allocated by randomization.	
Subject analysis set title	Safety population
Subject analysis set type	Safety analysis
Subject analysis set description:	
The safety population was defined as randomized population who actually received at least 1 dose or part of a dose of the IMP, analyzed according to the treatment actually received.	

Primary: Analysis of HbA1c (%) change from Baseline to Week 30	
End point title	Analysis of HbA1c (%) change from Baseline to Week 30

End point description:

The 3 efpeglenatide doses were tested in the order of 6 mg, 4 mg, and 2 mg for superiority to placebo. The primary objective of the study was met as demonstrated by the statistical superiority of efpeglenatide over placebo in all 3 dose groups.

End point type	Primary

End point timeframe:

From Baseline to Week 30

End point values	Efpeglenatide 2mg	Efpeglenatide 4 mg	Efpeglenatide 6 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	100	101	103	102
Units: percent				
arithmetic mean (standard deviation)				
Baseline	8.08 (± 0.86)	8.09 (± 0.93)	8.05 (± 0.95)	7.97 (± 0.89)
Week 30	6.88 (± 1.03)	6.61 (± 0.80)	6.44 (± 0.67)	7.50 (± 1.03)
Change from Baseline to Week 30	-1.14 (± 0.96)	-1.48 (± 1.01)	-1.59 (± 1.04)	-0.46 (± 1.16)

Statistical analyses

Statistical analysis title	Statistical Analysis Plan - 2 mg vs Placebo

Statistical analysis description:

The primary efficacy endpoint (change from baseline to Week 30 in HbA1c) was analyzed using an ANCOVA model with missing values imputed based upon retrieved dropouts in 2 separate parts. Descriptive statistics were based on observed data.

Comparison groups	Efpeglenatide 2mg v Placebo
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.0054
Method	ANCOVA
Parameter estimate	LS Mean (SE)
Point estimate	-0.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.86
upper limit	-0.15
Variability estimate	Standard error of the mean
Dispersion value	0.18

Notes:

[1] - LS mean changes from baseline in HbA1c:
-1.06% in the efpeglenatide 2 mg

The LS mean differences were statistically significant for each efpeglenatide dose group versus placebo:
-0.51% (95% CI: -0.86% to -0.15%; p=0.0054) in the efpeglenatide 2 mg

Statistical analysis title	Statistical Analysis Plan - 4 mg vs Placebo

Statistical analysis description:

The primary efficacy endpoint (change from baseline to Week 30 in HbA1c) was analyzed using an ANCOVA model with missing values imputed based upon retrieved dropouts in 2 separate parts. Descriptive statistics were based on observed data.

Comparison groups	Efpeglenatide 4 mg v Placebo
Number of subjects included in analysis	203
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Mean (SE)
Point estimate	-0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.17
upper limit	-0.49
Variability estimate	Standard error of the mean
Dispersion value	0.17

Notes:

[2] - LS mean changes from baseline in HbA1c:
-1.39% in the efpeglenatide 4 mg group

The LS mean differences were statistically significant for each efpeglenatide dose group versus placebo:
-0.83% (95% CI: -1.17% to -0.49%; p<0.0001) in the efpeglenatide 4 mg

Statistical analysis title	Statistical Analysis Plan - 6 mg vs Placebo

Statistical analysis description:

The primary efficacy endpoint (change from baseline to Week 30 in HbA1c) was analyzed using an ANCOVA model with missing values imputed based upon retrieved dropouts in 2 separate parts. Descriptive statistics were based on observed data.

Comparison groups	Placebo v Efpeglenatide 6 mg
Number of subjects included in analysis	205
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Mean (SE)
Point estimate	-1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.35
upper limit	-0.72
Variability estimate	Standard error of the mean
Dispersion value	0.16

Notes:

[3] - LS mean changes from baseline in HbA1c:
-1.59% in the efpeglenatide 6 mg

The LS mean differences were statistically significant for each efpeglenatide dose group versus placebo:
-1.04% (95% CI: -1.35% to -0.72%; p<0.0001) in the efpeglenatide 6 mg

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment emergent adverse events (TEAEs) have been measured during Whole On-treatment Period. It is defined as the time from the first injection of the IMP up to 30 days (7 days for hypoglycemia) after the last injection of the IMP.

Adverse event reporting additional description:

Efpeglenatide was generally well-tolerated with an acceptable safety profile in line with other GLP-1 RA class in general.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Efpeglenatide 2 mg

Reporting group description:

From Week 4 (Visit 5) through the rest of the double-blind treatment period, participants remained on the randomly assigned Efpeglenatide 2 mg until the EOT at Week 56 (Visit 14).

Reporting group title	Efpeglenatide 4 mg

Reporting group description:

From Week 4 (Visit 5) through the rest of the double-blind treatment period, participants remained on the randomly assigned Efpeglenatide 4 mg until the EOT at Week 56 (Visit 14).

Reporting group title	Efpeglenatide 6 mg

Reporting group description:

From Week 4 (Visit 5) through the rest of the double-blind treatment period, participants remained on the randomly assigned Efpeglenatide 6 mg until the EOT at Week 56 (Visit 14).

Reporting group title	Placebo

Reporting group description:

From Week 4 (Visit 5) through the rest of the double-blind treatment period, participants remained on the randomly assigned Placebo until the EOT at Week 56 (Visit 14).

Serious adverse events	Efpeglenatide 2 mg	Efpeglenatide 4 mg	Efpeglenatide 6 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 102 (10.78%)	6 / 103 (5.83%)	6 / 99 (6.06%)
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)			
Breast cancer metastatic			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	1 / 99 (1.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngeal cancer			

subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	1 / 99 (1.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Benign ovarian tumour			
subjects affected / exposed	1 / 102 (0.98%)	0 / 103 (0.00%)	0 / 99 (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
Malignant melanoma			
subjects affected / exposed	1 / 102 (0.98%)	0 / 103 (0.00%)	0 / 99 (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
Neuroendocrine carcinoma			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	0 / 99 (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
Prostate cancer			
subjects affected / exposed	0 / 102 (0.00%)	1 / 103 (0.97%)	0 / 99 (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
Injury, poisoning and procedural complications			
Foreign body in respiratory tract			
subjects affected / exposed	1 / 102 (0.98%)	0 / 103 (0.00%)	0 / 99 (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
Heat stroke			
subjects affected / exposed	0 / 102 (0.00%)	1 / 103 (0.97%)	0 / 99 (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
Pneumoconiosis			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	0 / 99 (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
Cardiac disorders			

Ventricular tachycardia			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	1 / 99 (1.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	0 / 99 (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
Angina unstable			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	0 / 99 (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
Atrial fibrillation			
subjects affected / exposed	1 / 102 (0.98%)	0 / 103 (0.00%)	0 / 99 (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
Cardiac failure			
subjects affected / exposed	1 / 102 (0.98%)	0 / 103 (0.00%)	0 / 99 (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
Cardiac failure congestive			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	0 / 99 (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
Coronary artery disease			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	0 / 99 (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
Coronary artery stenosis			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	0 / 99 (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
Myocardial infarction			

subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	0 / 99 (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
Nervous system disorders			
Vertebral artery stenosis			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	1 / 99 (1.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral artery stenosis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 103 (0.97%)	0 / 99 (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
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 102 (0.98%)	0 / 103 (0.00%)	0 / 99 (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
Non-cardiac chest pain			
subjects affected / exposed	0 / 102 (0.00%)	1 / 103 (0.97%)	0 / 99 (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
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 102 (0.98%)	0 / 103 (0.00%)	0 / 99 (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
Colitis			
subjects affected / exposed	1 / 102 (0.98%)	0 / 103 (0.00%)	0 / 99 (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
Reproductive system and breast disorders			
Benign prostatic hyperplasia			

subjects affected / exposed	1 / 102 (0.98%)	0 / 103 (0.00%)	0 / 99 (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
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 102 (0.98%)	0 / 103 (0.00%)	0 / 99 (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
Panic attack			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	0 / 99 (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
Stress			
subjects affected / exposed	0 / 102 (0.00%)	1 / 103 (0.97%)	0 / 99 (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
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	1 / 102 (0.98%)	0 / 103 (0.00%)	0 / 99 (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
Ureterolithiasis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 103 (0.97%)	0 / 99 (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
Infections and infestations			
Cystitis			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	1 / 99 (1.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epiglottitis			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	1 / 99 (1.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastroenteritis			
subjects affected / exposed	1 / 102 (0.98%)	0 / 103 (0.00%)	0 / 99 (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
Meningitis viral			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	0 / 99 (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
Pneumonia			
subjects affected / exposed	0 / 102 (0.00%)	1 / 103 (0.97%)	0 / 99 (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
Pyelonephritis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 103 (0.97%)	0 / 99 (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
Sepsis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 103 (0.97%)	0 / 99 (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
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	1 / 102 (0.98%)	0 / 103 (0.00%)	0 / 99 (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	Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 102 (8.82%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer metastatic			

subjects affected / exposed	0 / 102 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Laryngeal cancer			
subjects affected / exposed	0 / 102 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Benign ovarian tumour			
subjects affected / exposed	0 / 102 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Malignant melanoma			
subjects affected / exposed	0 / 102 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neuroendocrine carcinoma			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Prostate cancer			
subjects affected / exposed	0 / 102 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Foreign body in respiratory tract			
subjects affected / exposed	0 / 102 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Heat stroke			
subjects affected / exposed	0 / 102 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumoconiosis			

subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Ventricular tachycardia				
subjects affected / exposed	0 / 102 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute myocardial infarction				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Angina unstable				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Atrial fibrillation				
subjects affected / exposed	0 / 102 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure				
subjects affected / exposed	0 / 102 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure congestive				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Coronary artery disease				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Coronary artery stenosis				

subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	1 / 102 (0.98%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Vertebral artery stenosis				
subjects affected / exposed	0 / 102 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebral artery stenosis				
subjects affected / exposed	0 / 102 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Chest pain				
subjects affected / exposed	0 / 102 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Non-cardiac chest pain				
subjects affected / exposed	0 / 102 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal pain				
subjects affected / exposed	0 / 102 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colitis				
subjects affected / exposed	0 / 102 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 102 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 102 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Panic attack			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Stress			
subjects affected / exposed	0 / 102 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	0 / 102 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ureterolithiasis			
subjects affected / exposed	0 / 102 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Cystitis			
subjects affected / exposed	0 / 102 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Epiglottitis			

subjects affected / exposed	0 / 102 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	0 / 102 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Meningitis viral			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	0 / 102 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis			
subjects affected / exposed	0 / 102 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	0 / 102 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 102 (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	Efpeglenatide 2 mg	Efpeglenatide 4 mg	Efpeglenatide 6 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	80 / 102 (78.43%)	79 / 103 (76.70%)	83 / 99 (83.84%)
Investigations			
Lipase increased			
subjects affected / exposed	8 / 102 (7.84%)	5 / 103 (4.85%)	5 / 99 (5.05%)
occurrences (all)	8	5	5
Weight decreased			
subjects affected / exposed	2 / 102 (1.96%)	2 / 103 (1.94%)	5 / 99 (5.05%)
occurrences (all)	2	2	5
Vascular disorders			
Hypertension			
subjects affected / exposed	8 / 102 (7.84%)	3 / 103 (2.91%)	6 / 99 (6.06%)
occurrences (all)	8	3	6
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 102 (5.88%)	10 / 103 (9.71%)	15 / 99 (15.15%)
occurrences (all)	6	10	15
Dizziness			
subjects affected / exposed	2 / 102 (1.96%)	10 / 103 (9.71%)	6 / 99 (6.06%)
occurrences (all)	2	10	6
General disorders and administration site conditions			
Injection site pain			
subjects affected / exposed	9 / 102 (8.82%)	11 / 103 (10.68%)	11 / 99 (11.11%)
occurrences (all)	9	11	11
Fatigue			
subjects affected / exposed	3 / 102 (2.94%)	4 / 103 (3.88%)	5 / 99 (5.05%)
occurrences (all)	3	4	5
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	9 / 102 (8.82%)	17 / 103 (16.50%)	25 / 99 (25.25%)
occurrences (all)	9	17	25
Constipation			
subjects affected / exposed	9 / 102 (8.82%)	14 / 103 (13.59%)	16 / 99 (16.16%)
occurrences (all)	9	14	16
Gastrooesophageal reflux disease			

subjects affected / exposed	7 / 102 (6.86%)	6 / 103 (5.83%)	4 / 99 (4.04%)
occurrences (all)	7	6	4
Dyspepsia			
subjects affected / exposed	5 / 102 (4.90%)	7 / 103 (6.80%)	12 / 99 (12.12%)
occurrences (all)	5	7	12
Abdominal distension			
subjects affected / exposed	4 / 102 (3.92%)	5 / 103 (4.85%)	8 / 99 (8.08%)
occurrences (all)	4	5	8
Flatulence			
subjects affected / exposed	0 / 102 (0.00%)	2 / 103 (1.94%)	7 / 99 (7.07%)
occurrences (all)	0	2	7
Abdominal pain upper			
subjects affected / exposed	6 / 102 (5.88%)	2 / 103 (1.94%)	2 / 99 (2.02%)
occurrences (all)	6	2	2
Nausea			
subjects affected / exposed	6 / 102 (5.88%)	15 / 103 (14.56%)	22 / 99 (22.22%)
occurrences (all)	6	15	22
Vomiting			
subjects affected / exposed	3 / 102 (2.94%)	8 / 103 (7.77%)	9 / 99 (9.09%)
occurrences (all)	3	8	9
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 102 (0.98%)	2 / 103 (1.94%)	5 / 99 (5.05%)
occurrences (all)	1	2	5
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 102 (3.92%)	1 / 103 (0.97%)	1 / 99 (1.01%)
occurrences (all)	4	1	1
Back pain			
subjects affected / exposed	1 / 102 (0.98%)	4 / 103 (3.88%)	5 / 99 (5.05%)
occurrences (all)	1	4	5
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	10 / 102 (9.80%)	7 / 103 (6.80%)	11 / 99 (11.11%)
occurrences (all)	10	7	1
Sinusitis			

subjects affected / exposed	0 / 102 (0.00%)	1 / 103 (0.97%)	2 / 99 (2.02%)
occurrences (all)	0	1	2
Upper respiratory tract infection			
subjects affected / exposed	3 / 102 (2.94%)	5 / 103 (4.85%)	6 / 99 (6.06%)
occurrences (all)	3	5	6
Viral upper respiratory tract infection			
subjects affected / exposed	6 / 102 (5.88%)	5 / 103 (4.85%)	6 / 99 (6.06%)
occurrences (all)	6	5	6
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 102 (1.96%)	11 / 103 (10.68%)	8 / 99 (8.08%)
occurrences (all)	2	11	8

Non-serious adverse events	Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	79 / 102 (77.45%)		
Investigations			
Lipase increased			
subjects affected / exposed	2 / 102 (1.96%)		
occurrences (all)	2		
Weight decreased			
subjects affected / exposed	0 / 102 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Hypertension			
subjects affected / exposed	4 / 102 (3.92%)		
occurrences (all)	4		
Nervous system disorders			
Headache			
subjects affected / exposed	7 / 102 (6.86%)		
occurrences (all)	7		
Dizziness			
subjects affected / exposed	6 / 102 (5.88%)		
occurrences (all)	6		
General disorders and administration site conditions			
Injection site pain			

subjects affected / exposed	6 / 102 (5.88%)		
occurrences (all)	6		
Fatigue			
subjects affected / exposed	3 / 102 (2.94%)		
occurrences (all)	3		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	9 / 102 (8.82%)		
occurrences (all)	9		
Constipation			
subjects affected / exposed	6 / 102 (5.88%)		
occurrences (all)	6		
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 102 (0.00%)		
occurrences (all)	0		
Dyspepsia			
subjects affected / exposed	2 / 102 (1.96%)		
occurrences (all)	2		
Abdominal distension			
subjects affected / exposed	2 / 102 (1.96%)		
occurrences (all)	2		
Flatulence			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences (all)	1		
Abdominal pain upper			
subjects affected / exposed	2 / 102 (1.96%)		
occurrences (all)	2		
Nausea			
subjects affected / exposed	2 / 102 (1.96%)		
occurrences (all)	2		
Vomiting			
subjects affected / exposed	0 / 102 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			

Cough subjects affected / exposed occurrences (all)	3 / 102 (2.94%) 3		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all)	 7 / 102 (6.86%) 7 3 / 102 (2.94%) 3		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Sinusitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all) Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	 8 / 102 (7.84%) 8 6 / 102 (5.88%) 6 7 / 102 (6.86%) 7 7 / 102 (6.86%) 7		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	 2 / 102 (1.96%) 2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 January 2018	• Updates to the following sections were made: statistical analysis and methods of unblinding. • Other sections added to the protocol, to update text with new available information, to align the procedures with those in other studies within the program and/or for better clarity: - Schedule of activities, exploratory endpoints and dosing instructions (for PK predose); - Benefit/Risk assessment; - Exclusion criteria; - Antidrug antibody measurements; - Committee Structure. • Inconsistencies, typographical, and spelling checks were also run throughout the document and corrected.
27 March 2018	The protocol was updated to clarify the contraception requirements for WOCBP.
07 June 2018	• The protocol was updated to add the rationale for the selected efpeglenatide doses and to add an appendix subsection related to acute kidney failure as a consequence of severe GI events and dehydration. Monthly home urine pregnancy tests were added. • In addition, sponsor used this opportunity to edit other sections of the protocol, to update text with new available information (including statistical analysis update), to align the procedures with those in other studies within the program and/or for better clarity. • Inconsistencies, typographical, and spelling errors throughout the document were also corrected.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported