Clinical trial results:
A trial to compare the injection site pain experience of 0.25 mg semaglutide sc administered by 2 different products

Summary

EudraCT number	2019-002284-10
Trial protocol	NL
Global end of trial date	04 September 2019

Results information

Result version number	v1 (current)
This version publication date	04 September 2020
First version publication date	04 September 2020

Trial information

Trial identification

Sponsor protocol code	INS-4582

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04007107
WHO universal trial number (UTN)	U1111-1233-9590

Notes:

Sponsors

Sponsor organisation name	Novo Nordisk A/S
Sponsor organisation address	Novo Allé, Bagsvaerd, Denmark, 2880
Public contact	Clinical Reporting Anchor and Disclosure (1452), Novo Nordisk A/S, +1 866 8677178, clinicaltrials@novonordisk.com
Scientific contact	Clinical Reporting Anchor and Disclosure (1452), Novo Nordisk A/S, +1 866 8677178, clinicaltrials@novonordisk.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	17 March 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 July 2019
Global end of trial reached?	Yes
Global end of trial date	04 September 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial was to compare, in healthy subjects, the injection site pain experience of a single dose of 0.25 milligrams (mg) semaglutide subcutaneous (sc) given as the DV3396 product to that of the PDS290 product.

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki, adopted by the 18th World Medical Association (WMA) General Assembly, Helsinki, Finland, June 1964, and subsequent amendments and International Council for Harmonisation (ICH) Good Clinical Practice (GCP)(European Medicines Agency (EMA)/Committee for Medicinal Products for Human Use CHMP)/ICH/135/1995), including archiving of essential documents and the EU Clinical Trial Directive (CTD)2001/20/EC.

Background therapy:

Not applicable.

Evidence for comparator:

Not applicable.

Actual start date of recruitment	27 June 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 103
Worldwide total number of subjects	103
EEA total number of subjects	103

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)	89

From 65 to 84 years	14
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The trial was conducted at one site in the Netherlands.

Pre-assignment

Screening details:

Subjects were randomised in a 2x2 scheme evenly to 4 sequences (A,B,C and D) of either DV3396 or PDS290 and side of injection (right/left) on abdomen.

Period 1

Period 1 title	Treatment Period 1 (Day 1)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

Blinding implementation details:

Investigator and subject were blinded to treatment. Qualified, unblinded members of study staff not otherwise involved in the trial procedures were responsible for trial drug administration in order to maintain blinding. To maintain blinding of subjects, a visual blind was in place during dose administration.

Arms

Are arms mutually exclusive?	Yes
Arm title	Sequence A: DV3396 (Right) then PDS290 (Left)

Arm description:

Subjects were to receive a subcutaneous (s.c.) injection of DV3396 product (0.25 milligrams (mg) of semaglutide) on the right side of abdomen (in treatment period 1); followed by an s.c. injection of PDS290 product (0.25 mg of semaglutide) on the left side of abdomen (in treatment period 2). The 2 products were administered on the same day (Day 1) with at least 30 minutes apart from each other.

Arm type	Experimental
Investigational medicinal product name	DV3396
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects were to receive an s.c. injection of DV3396 product (0.25 mg of semaglutide) on right side of abdomen in treatment period 1 on Day 1.

Investigational medicinal product name	PDS290
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects were to receive an s.c. injection of PDS290 product (0.25 mg of semaglutide) on left side of abdomen in treatment period 2 on Day 1.

Arm title	Sequence B: DV3396 (Left) then PDS290 (Right)

Arm description:

Subjects were to receive an s.c. injection of DV3396 product (0.25 mg of semaglutide) on the left side of abdomen (in treatment period 1); followed by an s.c. injection of PDS290 product (0.25 mg of semaglutide) on the right side of abdomen (in treatment period 2). The 2 products were administered on the same day (Day 1) with at least 30 minutes apart from each other.

Arm type	Experimental

Investigational medicinal product name	PDS290
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects were to receive an s.c. injection of PDS290 product (0.25 mg of semaglutide) on right side of abdomen in treatment period 2 on Day 1.

Investigational medicinal product name	DV3396
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects were to receive an s.c. injection of DV3396 product (0.25 mg of semaglutide) on left side of abdomen in treatment period 1 on Day 1.

Arm title	Sequence C: PDS290 (Right) then DV3396 (Left)

Arm description:

Subjects were to receive an s.c. injection of PDS290 product (0.25 mg of semaglutide) on the right side of abdomen (in treatment period 1); followed by an s.c. injection of DV3396 product (0.25 mg of semaglutide) on the left side of abdomen (in treatment period 2). The 2 products were administered on the same day (Day 1) with at least 30 minutes apart from each other.

Arm type	Experimental
Investigational medicinal product name	DV3396
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects were to receive an s.c. injection of DV3396 product (0.25 mg of semaglutide) on left side of abdomen in treatment period 2 on Day 1.

Investigational medicinal product name	PDS290
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects were to receive an s.c. injection of PDS290 product (0.25 mg of semaglutide) on right side of abdomen in treatment period 1 on Day 1.

Arm title	Sequence D: PDS290 (Left) then DV3396 (Right)

Arm description:

Subjects were to receive an s.c. injection of PDS290 product (0.25 mg of semaglutide) on the left side of abdomen (in treatment period 1); followed by an s.c. injection of DV3396 product (0.25 mg of semaglutide) on the right side of abdomen (in treatment period 2). The 2 products were administered on the same day (Day 1) with at least 30 minutes apart from each other.

Arm type	Experimental
Investigational medicinal product name	DV3396
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects were to receive a s.c. injection of DV3396 product (0.25 mg of semaglutide) on right side of abdomen in treatment period 2 on Day 1.

Investigational medicinal product name	PDS290
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects were to receive an s.c. injection of PDS290 product (0.25 mg of semaglutide) on left side of abdomen in treatment period 1 on Day 1.

Number of subjects in period 1	Sequence A: DV3396 (Right) then PDS290 (Left)	Sequence B: DV3396 (Left) then PDS290 (Right)	Sequence C: PDS290 (Right) then DV3396 (Left)
Started	26	26	25
Completed	26	26	25

Number of subjects in period 1	Sequence D: PDS290 (Left) then DV3396 (Right)
Started	26
Completed	26

Period 2

Period 2 title	Treatment Period 2 (Day 1)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Sequence A: DV3396 (Right) then PDS290 (Left)

Arm description:

Subjects were to receive a subcutaneous (s.c.) injection of DV3396 product (0.25 milligrams (mg) of semaglutide) on the right side of abdomen (in treatment period 1); followed by an s.c. injection of PDS290 product (0.25 mg of semaglutide) on the left side of abdomen (in treatment period 2). The 2 products were administered on the same day (Day 1) with at least 30 minutes apart from each other.

Arm type	Experimental
Investigational medicinal product name	DV3396
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects were to receive an s.c. injection of DV3396 product (0.25 mg of semaglutide) on right side of abdomen in treatment period 1 on Day 1.

Investigational medicinal product name	PDS290
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects were to receive an s.c. injection of PDS290 product (0.25 mg of semaglutide) on left side of abdomen in treatment period 2 on Day 1.

Arm title	Sequence B: DV3396 (Left) then PDS290 (Right)

Arm description:

Subjects were to receive an s.c. injection of DV3396 product (0.25 mg of semaglutide) on the left side of abdomen (in treatment period 1); followed by an s.c. injection of PDS290 product (0.25 mg of semaglutide) on the right side of abdomen (in treatment period 2). The 2 products were administered on the same day (Day 1) with at least 30 minutes apart from each other.

Arm type	Experimental
Investigational medicinal product name	DV3396
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects were to receive an s.c. injection of DV3396 product (0.25 mg of semaglutide) on left side of abdomen in treatment period 1 on Day 1.

Investigational medicinal product name	PDS290
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects were to receive an s.c. injection of PDS290 product (0.25 mg of semaglutide) on right side of abdomen in treatment period 2 on Day 1.

Arm title	Sequence C: PDS290 (Right) then DV3396 (Left)

Arm description:

Subjects were to receive an s.c. injection of PDS290 product (0.25 mg of semaglutide) on the right side of abdomen (in treatment period 1); followed by an s.c. injection of DV3396 product (0.25 mg of semaglutide) on the left side of abdomen (in treatment period 2). The 2 products were administered on the same day (Day 1) with at least 30 minutes apart from each other.

Arm type	Experimental
Investigational medicinal product name	PDS290
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects were to receive an s.c. injection of PDS290 product (0.25 mg of semaglutide) on right side of abdomen in treatment period 1 on Day 1.

Investigational medicinal product name	DV3396
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects were to receive an s.c. injection of DV3396 product (0.25 mg of semaglutide) on left side of abdomen in treatment period 2 on Day 1.

Arm title	Sequence D: PDS290 (Left) then DV3396 (Right)

Arm description:

Subjects were to receive an s.c. injection of PDS290 product (0.25 mg of semaglutide) on the left side of abdomen (in treatment period 1); followed by an s.c. injection of DV3396 product (0.25 mg of semaglutide) on the right side of abdomen (in treatment period 2). The 2 products were administered on the same day (Day 1) with at least 30 minutes apart from each other.

Arm type	Experimental
Investigational medicinal product name	PDS290
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects were to receive an s.c. injection of PDS290 product (0.25 mg of semaglutide) on left side of abdomen in treatment period 1 on Day 1.

Investigational medicinal product name	DV3396
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects were to receive a s.c. injection of DV3396 product (0.25 mg of semaglutide) on right side of abdomen in treatment period 2 on Day 1.

Number of subjects in period 2	Sequence A: DV3396 (Right) then PDS290 (Left)	Sequence B: DV3396 (Left) then PDS290 (Right)	Sequence C: PDS290 (Right) then DV3396 (Left)
Started	26	26	25
Completed	26	25	25
Not completed	0	1	0
Withdrawal by Subject	-	1	-

Number of subjects in period 2	Sequence D: PDS290 (Left) then DV3396 (Right)
Started	26
Completed	26
Not completed	0
Withdrawal by Subject	-

Baseline characteristics

Reporting groups	
Reporting group title	Treatment Period 1 (Day 1)
Reporting group description:	
Subjects were to receive 2 s.c. injections of 0.25 mg semaglutide; 1 each of PDS290 product and DV3396 product from any of the sequences A/B/C/D on Day 1. The 2 products were administered at least 30 minutes apart from each other.	

Reporting group values	Treatment Period 1 (Day 1)	Total	
Number of subjects	103	103	
Age Categorical Units: Subjects			
Age Continuous Units: years arithmetic mean standard deviation	 40.9 ± 18.1	 -	
Gender Categorical Units: Subjects			
Female	66	66	
Male	37	37	

End points

End points reporting groups

Reporting group title	Sequence A: DV3396 (Right) then PDS290 (Left)

Reporting group description:

Subjects were to receive a subcutaneous (s.c.) injection of DV3396 product (0.25 milligrams (mg) of semaglutide) on the right side of abdomen (in treatment period 1); followed by an s.c. injection of PDS290 product (0.25 mg of semaglutide) on the left side of abdomen (in treatment period 2). The 2 products were administered on the same day (Day 1) with at least 30 minutes apart from each other.

Reporting group title	Sequence B: DV3396 (Left) then PDS290 (Right)

Reporting group description:

Subjects were to receive an s.c. injection of DV3396 product (0.25 mg of semaglutide) on the left side of abdomen (in treatment period 1); followed by an s.c. injection of PDS290 product (0.25 mg of semaglutide) on the right side of abdomen (in treatment period 2). The 2 products were administered on the same day (Day 1) with at least 30 minutes apart from each other.

Reporting group title	Sequence C: PDS290 (Right) then DV3396 (Left)

Reporting group description:

Subjects were to receive an s.c. injection of PDS290 product (0.25 mg of semaglutide) on the right side of abdomen (in treatment period 1); followed by an s.c. injection of DV3396 product (0.25 mg of semaglutide) on the left side of abdomen (in treatment period 2). The 2 products were administered on the same day (Day 1) with at least 30 minutes apart from each other.

Reporting group title	Sequence D: PDS290 (Left) then DV3396 (Right)

Reporting group description:

Subjects were to receive an s.c. injection of PDS290 product (0.25 mg of semaglutide) on the left side of abdomen (in treatment period 1); followed by an s.c. injection of DV3396 product (0.25 mg of semaglutide) on the right side of abdomen (in treatment period 2). The 2 products were administered on the same day (Day 1) with at least 30 minutes apart from each other.

Reporting group title	Sequence A: DV3396 (Right) then PDS290 (Left)

Reporting group description:

Subjects were to receive a subcutaneous (s.c.) injection of DV3396 product (0.25 milligrams (mg) of semaglutide) on the right side of abdomen (in treatment period 1); followed by an s.c. injection of PDS290 product (0.25 mg of semaglutide) on the left side of abdomen (in treatment period 2). The 2 products were administered on the same day (Day 1) with at least 30 minutes apart from each other.

Reporting group title	Sequence B: DV3396 (Left) then PDS290 (Right)

Reporting group description:

Subjects were to receive an s.c. injection of DV3396 product (0.25 mg of semaglutide) on the left side of abdomen (in treatment period 1); followed by an s.c. injection of PDS290 product (0.25 mg of semaglutide) on the right side of abdomen (in treatment period 2). The 2 products were administered on the same day (Day 1) with at least 30 minutes apart from each other.

Reporting group title	Sequence C: PDS290 (Right) then DV3396 (Left)

Reporting group description:

Subjects were to receive an s.c. injection of PDS290 product (0.25 mg of semaglutide) on the right side of abdomen (in treatment period 1); followed by an s.c. injection of DV3396 product (0.25 mg of semaglutide) on the left side of abdomen (in treatment period 2). The 2 products were administered on the same day (Day 1) with at least 30 minutes apart from each other.

Reporting group title	Sequence D: PDS290 (Left) then DV3396 (Right)

Reporting group description:

Subjects were to receive an s.c. injection of PDS290 product (0.25 mg of semaglutide) on the left side of abdomen (in treatment period 1); followed by an s.c. injection of DV3396 product (0.25 mg of semaglutide) on the right side of abdomen (in treatment period 2). The 2 products were administered on the same day (Day 1) with at least 30 minutes apart from each other.

Subject analysis set title	DV3396
Subject analysis set type	Per protocol

Subject analysis set description:

Subjects were to receive an s.c. injection of DV3396 product (0.25 mg of semaglutide) from any of the sequences A/B/C/D on Day 1.

Subject analysis set title	PDS290
Subject analysis set type	Per protocol

Subject analysis set description:

Subjects were to receive an s.c. injection of PDS290 product (0.25 mg of semaglutide) from any of the sequences A/B/C/D on Day 1.

Primary: Intensity of Injection Site Pain

End point title	Intensity of Injection Site Pain

End point description:

The intensity of pain was measured on a visual analogue scale (VAS). The VAS consists of a horizontal 100 millimetres (mm) line where 0 mm corresponded to no pain and 100 mm corresponded to unbearable pain. After each injection, the participants rated their pain perception at the VAS by marking a vertical line across the 100 mm line. The distance (mm) between the endpoint "no pain" and the vertical line on the VAS was recorded and analysed. The per protocol (PP) set included all subjects who had received both injections of semaglutide and had completed both intensity of injection site pain assessments.

End point type	Primary

End point timeframe:

1 minute after each injection (Day 1)

End point values	DV3396	PDS290		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	102	102		
Units: score on a scale				
arithmetic mean (standard deviation)	35.1 (± 23.1)	4.4 (± 7.5)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The intensity of pain was analysed by a fixed analysis of variance model with VAS score as the dependent variable, and product, injection side (right side, left side), injection number (first injection, second injection), and participant as fixed effects.

Comparison groups	DV3396 v PDS290
Number of subjects included in analysis	204
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	< 0.0001
Method	ANOVA
Parameter estimate	Estimated treatment difference
Point estimate	30.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	26.6
upper limit	34.8

Notes:

[1] - Due to cross-over design of the study, the following "number of subjects included in analysis" is being erroneously displayed as 204. The actual "number of subjects included in analysis" is 102.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 to Day 28.
Results are based on safety analysis set which included all subjects who had received at least 1 injection of semaglutide (included any skin contact with trial product whether the injection was completed or not).

Adverse event reporting additional description:

Treatment emergent AE was defined as an event that had onset date on or after the day of first injection and no later than 28 days after the day of last injection. Trial was crossover and injections were given only 30 minutes apart, so it was not possible to say which product the AE was related to. Hence, AE data are presented for overall study.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22

Reporting groups

Reporting group title	Overall Study

Reporting group description:

Subjects were to receive 2 s.c. injections of 0.25 mg semaglutide; 1 each of PDS290 product and DV3396 product from any of the sequences A/B/C/D on Day 1. The 2 products were administered at least 30 minutes apart from each other.

Serious adverse events	Overall Study		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 103 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Overall Study		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 103 (14.56%)		
Gastrointestinal disorders			
Nausea			
alternative assessment type: Non-systematic			
subjects affected / exposed	15 / 103 (14.56%)		
occurrences (all)	15		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported