EU Clinical Trials Register

Clinical trial results:
A randomised, double blind, placebo controlled, single centre, 60 week trial of Exenatide once weekly for the treatment of moderate severity Parkinson's disease.

Summary

EudraCT number	2013-003363-64
Trial protocol	GB
Global end of trial date	12 May 2016

Results information

Result version number	v1 (current)
This version publication date	22 March 2018
First version publication date	22 March 2018

Trial information

Trial identification

Sponsor protocol code	13/0384

Additional study identifiers

ISRCTN number	ISRCTN75891427
ClinicalTrials.gov id (NCT number)	NCT01971242
WHO universal trial number (UTN)	-
Other trial identifiers	FoxTrialFinder: Exenatide-pd

Notes:

Sponsors

Sponsor organisation name	Comprehensive Clinical Trials Unit at UCL
Sponsor organisation address	Institute of Clinical Trials and Methodology, 90 High Holborn , London, United Kingdom, WC1V 6LJ
Public contact	CCTU Enquiry Desk, Comprehensive Clinical Trials Unit at UCL, CCTU-enquiries@ucl.ac.uk
Scientific contact	CCTU Enquiry Desk, Comprehensive Clinical Trials Unit at UCL, CCTU-enquiries@ucl.ac.uk

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	27 October 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 April 2016
Global end of trial reached?	Yes
Global end of trial date	12 May 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To generate further data to explore whether 48 weeks exposure to Exenatide has an advantage over placebo based on a standard validated assessment of Parkinson's disease severity (the MDS UPDRS part 3 motor subscale). This was measured during the "practically defined OFF medication state" i.e. after patients had withheld their conventional PD medication overnight. The hypothesis was that Exenatide would be associated with reduced MDS UPDRS part 3 scores at the study end.

Protection of trial subjects:

The trial was conducted in compliance with the approved protocol, UCL CCTU Standard Operating Procedures, the Declaration of Helsinki (2008), the principles of Good Clinical Practice (GCP) as laid down by the Commission Directive 2005/28/EC with implementation in national legislation in the UK by Statutory Instrument 2004/1031 and subsequent amendments, the UK Data Protection Act, the EU Tissue and Cells Directives 2004/23/EC, 2006 17/EC and 2006/86/EC, and the National Health Service (NHS) Research Governance Framework for Health and Social Care (RGF).

Protocol pre-defined reasons for a temporary halt of trial medication were in place in the event of participants experiencing abdominal pain consistent with a clinical diagnosis of pancreatitis or excessive/undesirable weight loss (>10% of body weight during a 12 week interval).

Protocol pre-defined reasons for discontinuation of trial medication were in place in the event of participants experiencing any of the following: diagnosis of acute pancreatitis; an elevation in serum Amylase (>50% above baseline); developing clinical suspicion of thyroid malignancy; accelerated disease progression (defined as greater than 50% (and absolute value of 20 points) decline in MDS UPDRS part 3 motor sub-score from baseline in both the ON medication and the practically defined OFF medication states).

Broader protocol pre-defined reasons for discontinuation of trial medication: unacceptable treatment toxicity or adverse event; inter-current illness that prevented further treatment; any change in the participant's condition that in the clinician's opinion justifies the discontinuation of treatment. All participants could choose to discontinue trial treatment at any time, without giving a reason, without penalty or loss of benefits to which they would otherwise be entitled.

Investigation and treatment of adverse events were as per NHS standard of care.

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	15 April 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 62

Worldwide total number of subjects	62
EEA total number of subjects	62

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)	41
From 65 to 84 years	21
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients with moderate Parkinson's disease were randomly assigned (1:1) to receive subcutaneous injections of exenatide 2 mg or placebo once weekly for
48 weeks in addition to their regular medication, followed by a 12-week washout period. The trial was done at the Leonard Wolfson Experimental Neuroscience Centre (London, UK).

Pre-assignment

Screening details:

Inclusion: Patients aged 25–75 years, idiopathic Parkinson's disease as measured by Queen Square Brain Bank criteria, on dopaminergic treatment with wearing-off effects, judged able to administer the trial drug, and at Hoehn and Yahr stage 2·5 or less when on treatment. Exclusion: concurrent dementia (MATTIS DRS<120), BMI<18.5 and diabetes.

Pre-assignment period milestones

Number of subjects started	68[1]
Number of subjects completed	62

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Physician decision: 1
Reason: Number of subjects	Consent withdrawn by subject: 3
Reason: Number of subjects	Protocol deviation: 2

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The number of subjects reported in the pre-assignment period are the numbers who were screened for the trial but not randomised into the trial. The worldwide number enrolled is the number of patients who were eligible, consented and randomised into the trial.

Period 1

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

Blinding implementation details:

The trial statistician generated and uploaded unique three-digit identifiers for every active and placebo drug kit to the randomisation service to allow allocation of masked study drug kits (sufficient for 12 weeks) at randomisation and follow-up visits by assessing clinicians. The randomisation service then provided the relevant kit numbers that were to be dispensed to the patient from the hospital pharmacy.

Arms

Are arms mutually exclusive?	Yes
Arm title	Exenatide

Arm description:

Exenatide extended release 2mg subcutaneous injection (Bydureon) once weekly for 48 weeks.

Arm type	Experimental
Investigational medicinal product name	Exenatide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Each dose of Exenatide extended release is supplied as a vial containing the Exenatide powder and an inactive ingredient called polylactide-co-glycolide and sucrose. This is supplied together with diluent (sterile water containing carboxymethylcellulose sodium, polysorbate 20, sodium phosphate monobasic monohydrate, sodium phosphate dibasic heptahydrate and sodium chloride) to allow reconstitution of the powder in solution for subcutaneous administration by the patient on a weekly basis. 2mg once weekly for 48 weeks.

Arm title	Placebo

Arm description:

Each dose of Placebo - Exenatide extended release is supplied as a vial containing a powder together with diluent to allow reconstitution of solution for subcutaneous administration by the patient on a weekly basis.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Each dose of Placebo- Exenatide extended release is supplied as a vial containing a powder together with diluent to allow reconstitution of solution for subcutaneous administration by the patient on a weekly basis. Once weekly for 48 weeks.

Number of subjects in period 1	Exenatide	Placebo
Started	32	30
Completed	31	29
Not completed	1	1
Consent withdrawn by subject	-	1
Adverse event, non-fatal	1	-

Baseline characteristics

Reporting groups

Reporting group title	Exenatide
Reporting group description:	
Exenatide extended release 2mg subcutaneous injection (Bydureon) once weekly for 48 weeks.	
Reporting group title	Placebo
Reporting group description:	
Each dose of Placebo - Exenatide extended release is supplied as a vial containing a powder together with diluent to allow reconstitution of solution for subcutaneous administration by the patient on a weekly basis.	

Reporting group values	Exenatide	Placebo	Total
Number of subjects	32	30	62
Age categorical			
Units: Subjects			
Adults (18-64 years)	18	23	41
From 65-84 years	14	7	21
Age continuous			
Units: years			
arithmetic mean	61.9	58.3	
standard deviation	± 8.2	± 8.3	-
Gender categorical			
Units: Subjects			
Female	9	7	16
Male	23	23	46
Hoehn & Yahr			
Units: Subjects			
Stage 1.0 - 2.0	30	30	60
Stage 2.5	2	0	2
Age at Diagnosis			
Units: Years			
arithmetic mean	56.2	52.5	
standard deviation	± 7.9	± 7.8	-
Duration of diagnosis at baseline			
Units: Years			
arithmetic mean	6.3	6.5	
standard deviation	± 3.3	± 3.4	-
Levodoa equivalent dose			
Units: mg			
arithmetic mean	760	816.8	
standard deviation	± 268.4	± 203.4	-
MDS UPDRS part 3 Off medication			
Units: unit(s)			
arithmetic mean	32.8	27.1	
standard deviation	± 9.7	± 10.3	-
MDS UPDRS Part 1 On medication			
Units: unit(s)			
arithmetic mean	9.8	9.2	

standard deviation	± 4.8	± 3.8	-
MDS UPDRS part 2 On medication Units: unit(s)			
arithmetic mean	12.5	10.7	
standard deviation	± 6.7	± 5.3	-
MDS UPDRS part 3 On medication Units: unit(s)			
arithmetic mean	19.4	14.4	
standard deviation	± 8.4	± 8.2	-
MDS UPDRS part 4 On medication Units: unit(s)			
arithmetic mean	4.7	5.3	
standard deviation	± 3.1	± 3.0	-
MATTIS Dementia Rating scale Units: unit(s)			
arithmetic mean	138.0	139.8	
standard deviation	± 5.0	± 3.7	-

End points

End points reporting groups

Reporting group title	Exenatide
Reporting group description:	
Exenatide extended release 2mg subcutaneous injection (Bydureon) once weekly for 48 weeks.	
Reporting group title	Placebo
Reporting group description:	
Each dose of Placebo - Exenatide extended release is supplied as a vial containing a powder together with diluent to allow reconstitution of solution for subcutaneous administration by the patient on a weekly basis.	

Primary: Change from baseline in MDS UPDRS part 3 Off medication at 60 weeks

End point title	Change from baseline in MDS UPDRS part 3 Off medication at 60 weeks
End point description:	
The primary endpoint measure for this trial is the MDS UPDRS (part 3) motor sub-score in the practically defined OFF medication state at 60 weeks.	
End point type	Primary
End point timeframe:	
At 60 weeks from randomisation	

End point values	Exenatide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	28		
Units: units				
arithmetic mean (standard deviation)	31.9 (± 12.0)	29.2 (± 12.0)		

Statistical analyses

Statistical analysis title	Primary outcome analysis
Statistical analysis description:	
We used an analysis of covariance (ANCOVA) model to estimate the difference in MDS UPDRS part 3 subscore between treatments (Exenatide - placebo) at 60 weeks together with a two-sided 95% confidence interval, adjusting for the Hoehn and Yahr score and baseline MDS UPDRS scores which were included as covariates.	
Comparison groups	Exenatide v Placebo
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0318
Method	ANCOVA
Parameter estimate	Slope
Point estimate	-3.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.7
upper limit	-0.3

Secondary: Change from baseline in MDS UPDRS part 3 Off medication at 48 weeks

End point title	Change from baseline in MDS UPDRS part 3 Off medication at 48 weeks

End point description:

Movement Disorder Society Unified Parkinson's Disease Rating Scale part 3 Motor Examination subsection score.

End point type	Secondary

End point timeframe:

At 48 weeks post randomisation

End point values	Exenatide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	29		
Units: units				
arithmetic mean (standard deviation)	30.2 (± 11.1)	28.8 (± 10.8)		

Statistical analyses

Statistical analysis title	Secondary outcome analysis

Statistical analysis description:

For secondary outcomes, the differences between the two groups were summarised using estimates and confidence intervals, using the ANCOVA approach.

Comparison groups	Exenatide v Placebo
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0026
Method	ANCOVA
Parameter estimate	Slope
Point estimate	-4.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.1
upper limit	-1.6

Secondary: Change from baseline in MDS UPDRS part 1 On medication at 60 weeks

End point title	Change from baseline in MDS UPDRS part 1 On medication at 60 weeks

End point description:

Movement Disorder Society Unified Parkinson's Disease Rating Scale part 1 non-Motor Experiences of Daily Living subsection score.

End point type	Secondary

End point timeframe:

At 60 weeks post randomisation.

End point values	Exenatide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	28		
Units: Units				
arithmetic mean (standard deviation)	9.3 (± 4.0)	10.1 (± 5.3)		

Statistical analyses

Statistical analysis title	Secondary outcome analysis

Statistical analysis description:

For secondary outcomes, the differences between the two groups were summarised using estimates and confidence intervals, using the ANCOVA approach. Outcome measures in the ON medication state were additionally adjusted for change from baseline in LED to account for the possible confounding effect of increased Parkinson's medication during the trial.

Comparison groups	Exenatide v Placebo
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.22
Method	ANCOVA
Parameter estimate	Slope
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.2
upper limit	0.8

Secondary: Change from baseline in MDS UPDRS part 1 On medication at 48 weeks

End point title	Change from baseline in MDS UPDRS part 1 On medication at 48 weeks

End point description:

Movement Disorder Society Unified Parkinson's Disease Rating Scale part 1 non-Motor Experiences of Daily Living subsection score.

End point type	Secondary

End point values	Exenatide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	29		
Units: Units				
arithmetic mean (standard deviation)	8.8 (± 4.4)	9.7 (± 5.6)		

Statistical analyses

Statistical analysis title	Secondary outcome analysis
Comparison groups	Exenatide v Placebo
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.21
Method	ANCOVA
Parameter estimate	Slope
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.7
upper limit	1.5

Secondary: Change from baseline in MDS UPDRS part 2 On medication at 60 weeks

End point title	Change from baseline in MDS UPDRS part 2 On medication at 60 weeks
End point description:	
Movement Disorder Society Unified Parkinson's Disease Rating Scale part 2 Motor Experiences of Daily Living subsection score.	
End point type	Secondary
End point timeframe:	
At 60 weeks post randomisation.	

End point values	Exenatide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	28		
Units: Units				
arithmetic mean (standard deviation)	11.6 (± 6.6)	11.0 (± 6.7)		

Statistical analyses

Statistical analysis title	Secondary outcome analysis
Comparison groups	Exenatide v Placebo
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.55
Method	ANCOVA
Parameter estimate	Slope
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.7
upper limit	1.5

Secondary: Change from baseline in MDS UPDRS part 2 On medication at 48 weeks

End point title	Change from baseline in MDS UPDRS part 2 On medication at 48 weeks

End point description:

Movement Disorder Society Unified Parkinson's Disease Rating Scale part 2 Motor Experiences of Daily Living subsection score.

End point type	Secondary

End point timeframe:

At 48 weeks post randomisation.

End point values	Exenatide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	29		
Units: Units				
arithmetic mean (standard deviation)	11.7 (± 6.3)	10.8 (± 5.6)		

Statistical analyses

Statistical analysis title	Secondary outcome analysis
Comparison groups	Exenatide v Placebo
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.58
Method	ANCOVA
Parameter estimate	Slope
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.7
upper limit	1.5

Secondary: Change from baseline in MDS UPDRS part 3 On medication at 60 weeks

End point title	Change from baseline in MDS UPDRS part 3 On medication at 60 weeks

End point description:

Movement Disorder Society Unified Parkinson's Disease Rating Scale part 3 Motor Examination subsection score.

End point type	Secondary

End point timeframe:

at 60 weeks post randomisation.

End point values	Exenatide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	28		
Units: unit(s)				
arithmetic mean (standard deviation)	19.9 (± 10.3)	14.5 (± 7.1)		

Statistical analyses

Statistical analysis title	Secondary outcome analysis
Comparison groups	Exenatide v Placebo
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.61
Method	ANCOVA
Parameter estimate	Slope
Point estimate	0.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.1
upper limit	0.9

Secondary: Change from baseline in MDS UPDRS part 3 On medication at 48 weeks

End point title	Change from baseline in MDS UPDRS part 3 On medication at 48 weeks

End point description:

Movement Disorder Society Unified Parkinson's Disease Rating Scale part 3 Motor Examination subsection score.

End point type	Secondary

End point timeframe:

At 48 weeks post randomisation.

End point values	Exenatide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	29		
Units: unit(s)				
arithmetic mean (standard deviation)	20.5 (± 9.5)	15.7 (± 7.1)		

Statistical analyses

Statistical analysis title	Secondary outcome analysis
Comparison groups	Exenatide v Placebo
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.99
Method	ANCOVA
Parameter estimate	Slope
Point estimate	-0.002
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	2.4

Secondary: Change from baseline in MDS UPDRS part 4 On medication at 60 weeks

End point title	Change from baseline in MDS UPDRS part 4 On medication at 60 weeks

End point description:

Movement Disorder Society Unified Parkinson's Disease Rating Scale part 4 Motor Complications subsection score.

End point type	Secondary

End point timeframe:

At 60 weeks post randomisation.

End point values	Exenatide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	28		
Units: unit(s)				
arithmetic mean (standard deviation)	5.2 (± 2.3)	6.1 (± 3.7)		

Statistical analyses

Statistical analysis title	Secondary outcome analysis
Comparison groups	Exenatide v Placebo
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.42
Method	ANCOVA
Parameter estimate	Slope
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.1
upper limit	0.9

Secondary: Change from baseline in MDS UPDRS part 4 On medication at 48 weeks

End point title	Change from baseline in MDS UPDRS part 4 On medication at 48 weeks

End point description:

Movement Disorder Society Unified Parkinson's Disease Rating Scale part 4 Motor Complications subsection score.

End point type	Secondary

End point timeframe:

At 48 weeks post randomisation.

End point values	Exenatide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	29		
Units: unit(s)				
arithmetic mean (standard deviation)	4.9 (± 2.5)	5.6 (± 3.0)		

Statistical analyses

Statistical analysis title	Secondary outcome analysis
Comparison groups	Exenatide v Placebo
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.48
Method	ANCOVA
Parameter estimate	Slope
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	0.9

Secondary: Change from baseline in MATTIS Dementia Rating scale at 60 weeks

End point title	Change from baseline in MATTIS Dementia Rating scale at 60 weeks

End point description:

The Mattis Dementia Rating Scale (DRS-2) assesses a patient's overall level of cognitive functioning with respect to five abilities: Attention, Initiation/Perseveration, Construction, Conceptualization, and Memory using a series of 36 tasks and 32 stimulus cards.

End point type	Secondary

End point timeframe:

At 60 weeks post randomisation.

End point values	Exenatide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	28		
Units: unit(s)				
arithmetic mean (standard deviation)	139.9 (± 3.6)	140.2 (± 4.6)		

Statistical analyses

Statistical analysis title	Secondary outcome analysis
Comparison groups	Exenatide v Placebo
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.33
Method	ANCOVA
Parameter estimate	Slope
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	2.5

Secondary: Change from baseline in MATTIS Dementia rating scale at 48 weeks

End point title	Change from baseline in MATTIS Dementia rating scale at 48 weeks

End point description:

The Mattis Dementia Rating Scale (DRS-2) assesses a patient's overall level of cognitive functioning with respect to five abilities: Attention, Initiation/Perseveration, Construction, Conceptualization, and Memory using a series of 36 tasks and 32 stimulus cards.

End point type	Secondary

End point timeframe:

At 48 weeks post randomisation.

End point values	Exenatide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	29		
Units: unit(s)				
arithmetic mean (standard deviation)	139.7 (± 4.1)	140.2 (± 3.9)		

Statistical analyses

Statistical analysis title	Secondary outcome analysis
Comparison groups	Exenatide v Placebo
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.57
Method	ANCOVA
Parameter estimate	Slope
Point estimate	0.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	1.9

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	1.9

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From randomisation to 60 weeks.

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4

Reporting groups

Reporting group title	Exenatide

Reporting group description: -

Reporting group title	Placebo

Reporting group description: -

Serious adverse events	Exenatide	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 32 (12.50%)	2 / 30 (6.67%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 32 (3.13%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 32 (3.13%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial flutter			
subjects affected / exposed	1 / 32 (3.13%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Collapse			

	Exenatide	Placebo	
subjects affected / exposed	1 / 32 (3.13%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Faecal Impaction			
subjects affected / exposed	0 / 32 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute urinary retention			
subjects affected / exposed	1 / 32 (3.13%)	0 / 30 (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			
Unintentional weight loss			
subjects affected / exposed	0 / 32 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	Exenatide	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 32 (96.88%)	29 / 30 (96.67%)	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	4 / 32 (12.50%)	3 / 30 (10.00%)	
occurrences (all)	5	3	
Nervous system disorders			
Increased time off medication			
subjects affected / exposed	8 / 32 (25.00%)	11 / 30 (36.67%)	
occurrences (all)	8	12	
Sleep disorder			
subjects affected / exposed	3 / 32 (9.38%)	6 / 30 (20.00%)	
occurrences (all)	3	6	
Increased dystonia			

subjects affected / exposed	3 / 32 (9.38%)	5 / 30 (16.67%)	
occurrences (all)	3	5	
Dyskinesia			
subjects affected / exposed	1 / 32 (3.13%)	2 / 30 (6.67%)	
occurrences (all)	2	2	
Freezing			
subjects affected / exposed	1 / 32 (3.13%)	2 / 30 (6.67%)	
occurrences (all)	1	2	
General disorders and administration site conditions			
Pain			
subjects affected / exposed	9 / 32 (28.13%)	6 / 30 (20.00%)	
occurrences (all)	13	11	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	12 / 32 (37.50%)	10 / 30 (33.33%)	
occurrences (all)	12	11	
Nausea			
subjects affected / exposed	16 / 32 (50.00%)	8 / 30 (26.67%)	
occurrences (all)	16	10	
Diarrhoea			
subjects affected / exposed	7 / 32 (21.88%)	4 / 30 (13.33%)	
occurrences (all)	8	6	
Abdominal pain			
subjects affected / exposed	5 / 32 (15.63%)	3 / 30 (10.00%)	
occurrences (all)	5	3	
Loss of appetite			
subjects affected / exposed	3 / 32 (9.38%)	1 / 30 (3.33%)	
occurrences (all)	3	1	
Indigestion			
subjects affected / exposed	0 / 32 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	2	
Bloating			
subjects affected / exposed	2 / 32 (6.25%)	0 / 30 (0.00%)	
occurrences (all)	3	0	
Respiratory, thoracic and mediastinal disorders			

Upper respiratory tract infection		
subjects affected / exposed	3 / 32 (9.38%)	3 / 30 (10.00%)
occurrences (all)	4	3
Skin and subcutaneous tissue disorders		
Injection site reaction		
subjects affected / exposed	25 / 32 (78.13%)	22 / 30 (73.33%)
occurrences (all)	27	26
Renal and urinary disorders		
Lower urinary tract symptoms		
subjects affected / exposed	6 / 32 (18.75%)	6 / 30 (20.00%)
occurrences (all)	6	7
Urinary tract infection		
subjects affected / exposed	0 / 32 (0.00%)	2 / 30 (6.67%)
occurrences (all)	0	3
Psychiatric disorders		
Anxiety		
subjects affected / exposed	2 / 32 (6.25%)	1 / 30 (3.33%)
occurrences (all)	2	1
Musculoskeletal and connective tissue disorders		
Back pain		
subjects affected / exposed	2 / 32 (6.25%)	5 / 30 (16.67%)
occurrences (all)	2	5
Metabolism and nutrition disorders		
Weight loss		
subjects affected / exposed	24 / 32 (75.00%)	18 / 30 (60.00%)
occurrences (all)	24	18
Weight gain		
subjects affected / exposed	7 / 32 (21.88%)	11 / 30 (36.67%)
occurrences (all)	7	11

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 January 2015	Protocol updated to v3.0 to add patients with Type 1 or Type 2 Diabetes mellitus to the exclusion criteria. Other corrections and clarifications throughout.
22 May 2015	Protocol updated to v4.0 with changes in withheld PD medication, participants not being shown an instructional video re lumbar puncture and clarifications throughout.
20 August 2015	Protocol updated to v5.0 with the additional dispensing of a kit to maintain sufficient IMP supply after a high number of vial breakages.
13 November 2015	Protocol updated to v6.0 with the following: excessive weight loss resulting in dose temporarily stopped not discontinued and becoming a notifiable event; exploratory outcomes added; additional blood test at visit seven; clarifications.

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.

The small size of our study meant that, despite randomisation with a block design according to Hoehn and Yahr status, the Exenatide group had higher MDS-UPDRS part 3 scores and lower LED at baseline than the placebo group.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/28781108