Clinical trial results:
A Phase IIa, open label, single-site, 48 week randomised controlled trial evaluating the safety and efficacy of Exenatide once-weekly in the treatment of patients with Multiple System Atrophy

Summary

EudraCT number	2020-000122-26
Trial protocol	GB
Global end of trial date	31 July 2024

Results information

Result version number	v1 (current)
This version publication date	19 June 2025
First version publication date	19 June 2025

Trial information

Trial identification

Sponsor protocol code	125591

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04431713
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University College London (UCL)
Sponsor organisation address	250 Euston Road, London, United Kingdom, NW1 2PG
Public contact	Catherine Maidens, University College London (UCL), ctimps@ucl.ac.uk
Scientific contact	Catherine Maidens, University College London (UCL), ctimps@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	22 March 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 March 2024
Global end of trial reached?	Yes
Global end of trial date	31 July 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This is an open label, randomised trial to collect pilot data from which to estimate the effectiveness of Exenatide in modifying disease progression of patients with Multiple System Atrophy. The primary endpoint will be the difference in total Unified Multiple System Atrophy Rating Scale (UMSARS-I) score (Parts I and II) at 48 weeks comparing exenatide to best medically treated patients.

The Unified MSA rating scale is globally recognised as the best available scale to objectively rate the severity of MSA. Part 1 (Historical review of symptom severity) and Part 2 (motor examination) have been previously used many times as an outcome measure in trials of MSA. Part 3 captures additional autonomic symptoms eg dizziness from low blood pressure, while Part 4 captures overall disability from the disease.

Protection of trial subjects:

NA

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 September 2020
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: 50
Worldwide total number of subjects	50
EEA total number of subjects	0

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)	30
From 65 to 84 years	20
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patient were recruited from specialist outpatient clinics for MSA at UCLH, referrals from movement disorder specialists across the UK and self-referral to the trial team via email.

Pre-assignment

Screening details:

Between 23 September 2020 and 06 May 2022, 53 participants were screened for eligibility. Fifty participants were randomly assigned to either exenatide or to act as contemporaneous controls. Reasons for screening failures included low BMI, significant cognitive impairment and previous exposure to IMP.

Period 1

Period 1 title	Baseline
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Open-label.

Arms

Are arms mutually exclusive?	Yes
Arm title	Exenatide

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Exenatide
Investigational medicinal product code	
Other name	Bydureon, BCise
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

2mg once weekly for 48-weeks.

Arm title	Standard of Care

Arm description: -

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Exenatide	Standard of Care
Started	25	25
Completed	25	25

Period 2	
Period 2 title	Overall Trial
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded
Blinding implementation details: Open-label.	

Arms	
Are arms mutually exclusive?	Yes
Arm title	Exenatide
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Exenatide
Investigational medicinal product code	
Other name	Bydureon, BCise
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use
Dosage and administration details: 2mg once weekly for 48-weeks.	
Arm title	Standard of Care
Arm description: -	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 2	Exenatide	Standard of Care
Started	25	25
Completed	21	23
Not completed	4	2
Death unrelated to IMP	2	2
Lost to follow-up	2	-

Baseline characteristics

Reporting groups	
Reporting group title	Exenatide
Reporting group description: -	
Reporting group title	Standard of Care
Reporting group description: -	

Reporting group values	Exenatide	Standard of Care	Total
Number of subjects	25	25	50
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	63.3	62.4	
standard deviation	± 8.4	± 7.3	-
Gender categorical Units: Subjects			
Female	13	13	26
Male	12	12	24
MSA Sub-type Units: Subjects			
MSA-P	14	14	28
MSA-C	11	11	22

End points

End points reporting groups

Reporting group title	Exenatide
Reporting group description: -	
Reporting group title	Standard of Care
Reporting group description: -	
Reporting group title	Exenatide
Reporting group description: -	
Reporting group title	Standard of Care
Reporting group description: -	

Primary: UMSARS Parts I and II Combined

End point title	UMSARS Parts I and II Combined
End point description:	
The primary endpoint is the total Unified Multiple System Atrophy Rating Scale (UMSARS) score (Parts I and II). Higher scores indicate worse disease severity.	
End point type	Primary
End point timeframe:	
48-weeks	

End point values	Exenatide	Standard of Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	24		
Units: Score				
arithmetic mean (confidence interval 95%)	6.1 (3.0 to 9.3)	13.3 (9.2 to 17.3)		

Statistical analyses

Statistical analysis title	Intention-to-treat Population
Statistical analysis description:	
Compared exenatide participants to best medically treated participants using a two-level mixed model that included the total UMSARS scores from four time-points (12 weeks, 24 weeks, 36 weeks and 48 weeks) with interaction terms between the intervention and time-point indicator variables to enable estimation of the effect of intervention at 48 weeks. This model also adjusted for baseline UMSARS score and MSA subtype using fixed effects.	
Comparison groups	Exenatide v Standard of Care

Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Mixed models analysis

Secondary: Loss of Independent Ambulation

End point title	Loss of Independent Ambulation

End point description:

Proportion of patients with loss of independent ambulation, defined by a score of 4 in UMSARS-I Item 7 (walking).

End point type	Secondary

End point timeframe:

48-weeks

End point values	Exenatide	Standard of Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	25		
Units: Number of Participants	2	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Multiple System Atrophy Quality of Life (MSA-QoL) Scale

End point title	Multiple System Atrophy Quality of Life (MSA-QoL) Scale

End point description:

Higher scores indicate worse quality of life.

End point type	Secondary

End point timeframe:

48-weeks

End point values	Exenatide	Standard of Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	23		
Units: Score				
arithmetic mean (standard deviation)				
Motor Subscore	53.1 (± 19.8)	53.7 (± 23.7)		
Non-motor Subscore	37.4 (± 17.8)	39.3 (± 15.4)		
Emotional/Social Functioning Subscore	33.3 (± 22.8)	43.1 (± 23.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Falls

End point title	Number of Falls
End point description: Number of falls at 48-weeks.	
End point type	Secondary
End point timeframe: 48-weeks	

End point values	Exenatide	Standard of Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	23		
Units: Number of Events				
arithmetic mean (standard deviation)	1.7 (± 2.9)	3.0 (± 6.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Milestones on UMSARS Part 1 (Speech, Swallow and Falling)

End point title	Milestones on UMSARS Part 1 (Speech, Swallow and Falling)
End point description: The proportion of patients reaching a score of ≥ 3 on UMSARS item 1 (speech), item 2 (swallowing) and item 8 (falling).	
End point type	Secondary
End point timeframe: 48-weeks	

End point values	Exenatide	Standard of Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	23		
Units: Number of Participants				
UMSARS Part 1 Item 1 (Speech)	3	7		
UMSARS Part 1 Item 2 (Swallowing)	2	8		
UMSARS Part 1 Item 8 (Falling)	3	6		

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Global Impression (CGI) Scale

End point title	Clinical Global Impression (CGI) Scale

End point description:

End point type	Secondary

End point timeframe:

48-weeks.

End point values	Exenatide	Standard of Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	23		
Units: Score				
arithmetic mean (standard deviation)	3.1 (± 1.0)	2.4 (± 0.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Montreal Cognitive Assessment (MoCA)

End point title	Montreal Cognitive Assessment (MoCA)

End point description:

Lower scores indicate cognitive decline, and a score of 26 or more reflects normal cognition.

End point type	Secondary

End point timeframe:

48-weeks.

End point values	Exenatide	Standard of Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	23		
Units: Score				
arithmetic mean (standard deviation)	26.0 (± 2.7)	27.2 (± 2.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: UMSARS Part IV

End point title	UMSARS Part IV
End point description: Higher scores indicate worse disability.	
End point type	Secondary
End point timeframe: 48-weeks.	

End point values	Exenatide	Standard of Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	23		
Units: Score				
arithmetic mean (standard deviation)	2.8 (± 1.1)	3.0 (± 0.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Beck Depression Inventory II (BDI-II)

End point title	Beck Depression Inventory II (BDI-II)
End point description: Measures depression status, with worse scores indicating more severe depression.	
End point type	Secondary
End point timeframe: 48-weeks.	

End point values	Exenatide	Standard of Care		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	23		
Units: Score				
arithmetic mean (standard deviation)	14.3 (± 8.8)	15.2 (± 8.0)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Baseline to week 52 (12 weeks after study drug was discontinued).	
Assessment type	Systematic

Dictionary used	
Dictionary name	CTCAE
Dictionary version	5.0

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	10 / 25 (40.00%)	10 / 25 (40.00%)	
number of deaths (all causes)	2	2	
number of deaths resulting from adverse events	0	0	
Vascular disorders			
Vascular Disorders			
subjects affected / exposed	0 / 25 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Myocardial Infarction			
subjects affected / exposed	0 / 25 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Surgical and medical procedures			
Possible Detachment of Percutaneous Endoscopic Gastrostomy Tube			
subjects affected / exposed	0 / 25 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Dysphagia			

subjects affected / exposed	0 / 25 (0.00%)	4 / 25 (16.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	2 / 25 (8.00%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Falls			
subjects affected / exposed	2 / 25 (8.00%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Worsening of MSA			
subjects affected / exposed	2 / 25 (8.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 25 (4.00%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhea			
subjects affected / exposed	1 / 25 (4.00%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Serum Amylase Increased			
subjects affected / exposed	2 / 25 (8.00%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Aspiration			
subjects affected / exposed	2 / 25 (8.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Respiratory Failure			
subjects affected / exposed	1 / 25 (4.00%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 25 (4.00%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	1 / 25 (4.00%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Urinary Retention			
subjects affected / exposed	1 / 25 (4.00%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Lung Infection			
subjects affected / exposed	1 / 25 (4.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 25 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 25 (0.00%)	3 / 25 (12.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper Respiratory Infection			

subjects affected / exposed	3 / 25 (12.00%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary Tract Infections			
subjects affected / exposed	3 / 25 (12.00%)	2 / 25 (8.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyponatremia			
subjects affected / exposed	0 / 25 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	0 / 25 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Exenatide	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	25 / 25 (100.00%)	24 / 25 (96.00%)	
Nervous system disorders			
Gait Disturbance			
subjects affected / exposed	17 / 25 (68.00%)	17 / 25 (68.00%)	
occurrences (all)	19	19	
General disorders and administration site conditions			
Fatigue and Pain			
subjects affected / exposed	6 / 25 (24.00%)	6 / 25 (24.00%)	
occurrences (all)	8	6	
Other, Miscellaneous			
subjects affected / exposed	21 / 25 (84.00%)	22 / 25 (88.00%)	
occurrences (all)	64	52	
Gastrointestinal disorders			

Nausea, Bloating, Constipation subjects affected / exposed occurrences (all)	14 / 25 (56.00%) 36	12 / 25 (48.00%) 17	
Hepatobiliary disorders Serum Amylase increase subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1	1 / 25 (4.00%) 1	
Skin and subcutaneous tissue disorders Skin Disorders e.g., Nodules, Rashes subjects affected / exposed occurrences (all)	12 / 25 (48.00%) 14	4 / 25 (16.00%) 5	
Infections and infestations Infections e.g., UTI, Chest subjects affected / exposed occurrences (all)	16 / 25 (64.00%) 38	14 / 25 (56.00%) 16	
Metabolism and nutrition disorders Weight Loss, Anorexia subjects affected / exposed occurrences (all)	11 / 25 (44.00%) 14	4 / 25 (16.00%) 4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 October 2020	Amendment 1 - Non-substantial updates.
05 March 2021	Amendment 2 - Update to protocol.
15 September 2021	Amendment 3 - Update to protocol.
09 December 2021	Amendment 4 - Update to PIS and ICF.
03 August 2022	Amendment 5 - Update to protocol.
15 September 2022	Amendment 6 - Update to PIS and ICF.
28 June 2023	Amendment 7 - SmPc update
19 June 2024	Amendment 8 - Update to protocol (exploratory analysis).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Open label trial design.

Notes: