Clinical trial results:
A randomized, double-blind, placebo-controlled phase IIB study evaluating the efficacy of mesdopetam on daily on-time without troublesome dyskinesia in patients with Parkinson's disease

Summary

EudraCT number	2020-002010-41
Trial protocol	FR IT
Global end of trial date	30 January 2023

Results information

Result version number	v1 (current)
This version publication date	31 January 2024
First version publication date	31 January 2024
Summary attachment (see zip file)	Poster_Study results (IRLAB Phase IIb mesdopetam MDS congress Aug 2023.pdf)

Trial information

Trial identification

Sponsor protocol code	IRL790C005

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04435431
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Integrative Research Laboratories Sweden AB (IRLAB)
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Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	25 August 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 December 2022
Global end of trial reached?	Yes
Global end of trial date	30 January 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

•To evaluate the effectiveness of adjunctive treatment with mesdopetam dosed at 2.5 mg, 5 mg or 7.5 mg b.i.d. (permitting a single 2.5 mg dose reduction to a minimum dose of 2.5 mg, up to Day 28) compared to placebo in patients with PD exhibiting troublesome ON-phase dyskinesia.

Protection of trial subjects:

This study was conducted in compliance with the International Conference on Harmonization Good Clinical Practice (ICH GCP) Guideline for good clinical practice E6(R2) and with the ethical principles originating in the Declaration of Helsinki. Written informed consent was obtained from all study subjects before any study related procedures were performed.

Background therapy:

Patients included in the study had to be on a stable regimen of antiparkinson medications for at least 30 days prior to first home diary completion, which must include a levodopa preparation administered 3-8 times/day (excluding nighttime levodopa) and willing to continue the same doses and regimens during study participation. Rescue medications such as Madopar dispersable and Apomorphine injections were allowed if prescribed PRN prior to study entry.

Evidence for comparator:

-

Actual start date of recruitment	29 October 2020
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	Poland: 62
Country: Number of subjects enrolled	France: 20
Country: Number of subjects enrolled	Italy: 15
Country: Number of subjects enrolled	Serbia: 15
Country: Number of subjects enrolled	Israel: 7
Country: Number of subjects enrolled	United States: 36
Worldwide total number of subjects	155
EEA total number of subjects	97

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)	65
From 65 to 84 years	90
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The recruitment period was 22.5 months (29 Oct 2020 - 12 Sep 2022). 156 subjects were randomized to mesdopetam 2.5 mg (40 subj), 5.0 mg (38 subj) or 7.5 mg (39 subj) or to placebo (39 subj). 125 subjects completed the study: 2.5 mg (32 subj), 5.0 mg (31 subj), 7.5 mg (29 subj), placebo (33 subj).

Pre-assignment

Screening details:

The screening period was up to 8 weeks before start of Investigational Medicinal Product (IMP) administration. At the screening visit consenting patients were screened for eligibility according to study specific inclusion/exclusion criteria. 192 subjects were screened of which 156 were randomized.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Data analyst, Carer, Subject, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Mesdopetam 2.5 mg

Arm description:

Mesdopetam (IRL790) 2.5 mg hard capsule. Oral administration b.i.d.

Arm type	Experimental
Investigational medicinal product name	Mesdopetam
Investigational medicinal product code	IRL790
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

IMP was given twice daily (b.i.d.) during 84 consecutive days. The starting dose was 5 mg b.i.d. (mesdopetam or placebo) during the dose run-in period (one week) and thereafter mesdopetam 2.5 mg, 5 mg or 7.5 mg or placebo b.i.d as randomized. If a patient experienced increased parkinsonism and/or consistent increase in motor OFF time, during the treatment period from Visit 2 up to Visit 3 (i.e. Day 9 – Day 28 ±4 days), the dosing could be reduced by 2,5 mg b.i.d. A dose reduction was allowed at only one occasion, where after the dosing should be kept stable until the EOT visit (Day 84).
The capsules were swallowed together with 200 mL of water in the morning and in the afternoon approximately 8 hours apart on each administration day.
Formulation details: 2.5 mg free base equivalent: White hard Hydroxypropyl Methylcellulose (HPMC) capsule, coni snap size 3, colour white containing mesdopetam x ½ L-tartrate.

Arm title	Mesdopetam 5 mg

Arm description:

Mesdopetam (IRL790) 5 mg hard capsule. Oral administration b.i.d.

Arm type	Experimental
Investigational medicinal product name	Mesdopetam
Investigational medicinal product code	IRL790
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

IMP was given twice daily (b.i.d.) during 84 consecutive days. The starting dose was 5 mg b.i.d. (mesdopetam or placebo) during the dose run-in period (one week) and thereafter mesdopetam 2.5 mg, 5 mg or 7.5 mg or placebo b.i.d as randomized. If a patient experienced increased parkinsonism and/or

consistent increase in motor OFF time, during the treatment period from Visit 2 up to Visit 3 (i.e. Day 9 – Day 28 ±4 days), the dosing could be reduced by 2,5 mg b.i.d. A dose reduction was allowed at only one occasion, where after the dosing should be kept stable until the EOT visit (Day 84).
The capsules were swallowed together with 200 mL of water in the morning and in the afternoon approximately 8 hours apart on each administration day.
Formulation details: 5 mg free base equivalent: White hard Hydroxypropyl Methylcellulose (HPMC) capsule, coni snap size 3, colour white containing mesdopetam x ½ L-tartrate.

Arm title	Mesdopetam 7.5 mg

Arm description:

Mesdopetam (IRL790) 7.5 mg hard capsule. Oral administration b.i.d.

Arm type	Experimental
Investigational medicinal product name	Mesdopetam
Investigational medicinal product code	IRL790
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Other use

Dosage and administration details:

IMP was given twice daily (b.i.d.) during 84 consecutive days. The starting dose was 5 mg b.i.d. (mesdopetam or placebo) during the dose run-in period (one week) and thereafter mesdopetam 2.5 mg, 5 mg or 7.5 mg or placebo b.i.d as randomized. If a patient experienced increased parkinsonism and/or consistent increase in motor OFF time, during the treatment period from Visit 2 up to Visit 3 (i.e. Day 9 – Day 28 ±4 days), the dosing could be reduced by 2,5 mg b.i.d. A dose reduction was allowed at only one occasion, where after the dosing should be kept stable until the EOT visit (Day 84).
The capsules were swallowed together with 200 mL of water in the morning and in the afternoon approximately 8 hours apart on each administration day.
Formulation details: 7.5 mg free base equivalent: White hard Hydroxypropyl Methylcellulose (HPMC) capsule, coni snap size 3, colour white containing mesdopetam x ½ L-tartrate.

Arm title	Placebo

Arm description:

Placebo comparator. Matching placebo hard capsule. Oral administration b.i.d.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

IMP was given twice daily (b.i.d.) during 84 consecutive days. The starting dose was 5 mg b.i.d. (mesdopetam or placebo) during the dose run-in period (one week) and thereafter mesdopetam 2.5 mg, 5 mg or 7.5 mg or placebo b.i.d as randomized. If a patient experienced increased parkinsonism and/or consistent increase in motor OFF time, during the treatment period from Visit 2 up to Visit 3 (i.e. Day 9 – Day 28 ±4 days), the dosing could be reduced by 2,5 mg b.i.d. A dose reduction was allowed at only one occasion, where after the dosing should be kept stable until the EOT visit (Day 84). The capsules were swallowed together with 200 mL of water in the morning and in the afternoon approximately 8 hours apart on each administration day.
Formulation details: White hard HPMC capsule, coni snap size 3, colour white containing starch. Capsules are identical in appearance to active IMP.

Number of subjects in period 1	Mesdopetam 2.5 mg	Mesdopetam 5 mg	Mesdopetam 7.5 mg
Started	40	38	38
Completed	32	31	29
Not completed	8	7	9
Adverse event, serious fatal	1	-	1

Physician decision	1	-	-
Consent withdrawn by subject	1	4	3
Adverse event, non-fatal	4	3	2
Non-compliance with study drug	-	-	2
Protocol deviation	1	-	1

Number of subjects in period 1	Placebo
Started	39
Completed	33
Not completed	6
Adverse event, serious fatal	-
Physician decision	-
Consent withdrawn by subject	2
Adverse event, non-fatal	4
Non-compliance with study drug	-
Protocol deviation	-

Baseline characteristics

Reporting groups	
Reporting group title	Mesdopetam 2.5 mg
Reporting group description:	
Mesdopetam (IRL790) 2.5 mg hard capsule. Oral administration b.i.d.	
Reporting group title	Mesdopetam 5 mg
Reporting group description:	
Mesdopetam (IRL790) 5 mg hard capsule. Oral administration b.i.d.	
Reporting group title	Mesdopetam 7.5 mg
Reporting group description:	
Mesdopetam (IRL790) 7.5 mg hard capsule. Oral administration b.i.d.	
Reporting group title	Placebo
Reporting group description:	
Placebo comparator. Matching placebo hard capsule. Oral administration b.i.d.	

Reporting group values	Mesdopetam 2.5 mg	Mesdopetam 5 mg	Mesdopetam 7.5 mg
Number of subjects	40	38	38
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	17	15	17
From 65-84 years	23	23	21
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	65.0	64.9	65.0
standard deviation	± 9.3	± 9.6	± 10.2
Gender categorical Units: Subjects			
Female	14	17	17
Male	26	21	21
Ethnicity Units: Subjects			
Hispanic or Latino	2	2	5
Not Hispanic or Latino	38	36	33
Race Units: Subjects			
White	40	35	36
Black or African American		1	2
Asian		1	
Unknown		1	

Height at Screening			
Units: cm			
arithmetic mean	167.8	167.0	167.8
standard deviation	± 7.6	± 8.8	± 8.5
Weight at Screening			
Units: kg			
arithmetic mean	76.9	73.1	73.1
standard deviation	± 15.0	± 14.8	± 13.7
BMI at Screening			
Units: kg/m2			
arithmetic mean	27.1	26.1	26.0
standard deviation	± 4.3	± 4.6	± 5.0

Reporting group values	Placebo	Total	
Number of subjects	39	155	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	16	65	
From 65-84 years	23	90	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	64.5		
standard deviation	± 8.5	-	
Gender categorical			
Units: Subjects			
Female	25	73	
Male	14	82	
Ethnicity			
Units: Subjects			
Hispanic or Latino	6	15	
Not Hispanic or Latino	33	140	
Race			
Units: Subjects			
White	39	150	
Black or African American		3	
Asian		1	
Unknown		1	
Height at Screening			
Units: cm			
arithmetic mean	165.7		
standard deviation	± 9.3	-	
Weight at Screening			
Units: kg			

arithmetic mean	70.3		
standard deviation	± 17.3	-	
BMI at Screening			
Units: kg/m2			
arithmetic mean	25.6		
standard deviation	± 6.1	-	

Subject analysis sets

Subject analysis set title	Safety Analysis Set
Subject analysis set type	Full analysis

Subject analysis set description:

The Safety Analysis Set (SAS) includes all randomized patients who received at least 1 dose of IMP.

Reporting group values	Safety Analysis Set		
Number of subjects	155		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	65		
From 65-84 years	90		
85 years and over	0		
Age continuous			
Units: years			
arithmetic mean	64.9		
standard deviation	± 9.3		
Gender categorical			
Units: Subjects			
Female	73		
Male	82		
Ethnicity			
Units: Subjects			
Hispanic or Latino	15		
Not Hispanic or Latino	140		
Race			
Units: Subjects			
White	150		
Black or African American	3		
Asian	1		
Unknown	1		
Height at Screening			
Units: cm			
arithmetic mean	167.1		
standard deviation	± 8.5		

Weight at Screening Units: kg arithmetic mean standard deviation	 73.4 ± 15.3		
BMI at Screening Units: kg/m2 arithmetic mean standard deviation	 26.2 ± 5.0		

End points

End points reporting groups

Reporting group title	Mesdopetam 2.5 mg
Reporting group description:	
Mesdopetam (IRL790) 2.5 mg hard capsule. Oral administration b.i.d.	
Reporting group title	Mesdopetam 5 mg
Reporting group description:	
Mesdopetam (IRL790) 5 mg hard capsule. Oral administration b.i.d.	
Reporting group title	Mesdopetam 7.5 mg
Reporting group description:	
Mesdopetam (IRL790) 7.5 mg hard capsule. Oral administration b.i.d.	
Reporting group title	Placebo
Reporting group description:	
Placebo comparator. Matching placebo hard capsule. Oral administration b.i.d.	
Subject analysis set title	Safety Analysis Set
Subject analysis set type	Full analysis
Subject analysis set description:	
The Safety Analysis Set (SAS) includes all randomized patients who received at least 1 dose of IMP.	

Primary: Change in average daily hours of ON-time without troublesome dyskinesia with mesdopetam compared to placebo as assessed with 24-hour patient home diaries from baseline to end of treatment (EOT) (Visit 5, Week 12).

End point title	Change in average daily hours of ON-time without troublesome dyskinesia with mesdopetam compared to placebo as assessed with 24-hour patient home diaries from baseline to end of treatment (EOT) (Visit 5, Week 12).
End point description:	
Patients recorded their 24-hours motor function in 30-minute intervals, beginning at midnight. For each 30-minute interval the patient rated the state he or she had been in for the past 30 minutes; OFF, ON (without troublesome dyskinesia), ON with troublesome dyskinesia or Asleep. Improvement in total daily hours of ON-time without troublesome dyskinesia is defined as an increase in the daily hours spent in this motor state.	
End point type	Primary
End point timeframe:	
The change from baseline to end of treatment (EOT) (Visit 5, Week 12).	

End point values	Mesdopetam 2.5 mg	Mesdopetam 5 mg	Mesdopetam 7.5 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	35[1]	35[2]	33[3]	37[4]
Units: Total daily hours	1211	1737	2233	1985

Notes:

[1] - Full Analysis Set

[2] - Full Analysis Set

[3] - Full Analysis Set

[4] - Full Analysis Set

Statistical analyses

Statistical analysis title	Primary endpoint

Statistical analysis description:

Change in average daily hours of ON-time without troublesome dyskinesia with mesdopetam compared to placebo as assessed with 24-hour patient home diaries from baseline to end of treatment (EOT) (Visit 5, Week 12).

Comparison groups	Mesdopetam 7.5 mg v Placebo
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.73
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.248
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.163
upper limit	1.659
Variability estimate	Standard error of the mean

Secondary: Change from Baseline with mesdopetam compared to placebo in ON-phase dyskinesia assessed with the sum score of the modified UDysRS (parts 1, 3 and 4)

End point title	Change from Baseline with mesdopetam compared to placebo in ON-phase dyskinesia assessed with the sum score of the modified UDysRS (parts 1, 3 and 4)

End point description:

End point type	Secondary

End point timeframe:

The change from baseline to end of treatment (EOT) (Visit 5, Week 12).

End point values	Mesdopetam 2.5 mg	Mesdopetam 5 mg	Mesdopetam 7.5 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	35	35	33	37
Units: Sum score	115	93	120	58

Statistical analyses

Statistical analysis title	UDysRS
Comparison groups	Placebo v Mesdopetam 7.5 mg

Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.026
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-6.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.6
upper limit	-0.8
Variability estimate	Standard error of the mean

Secondary: Change from Baseline with mesdopetam compared to placebo in average daily OFF-time.

End point title	Change from Baseline with mesdopetam compared to placebo in average daily OFF-time.

End point description:

Patients recorded their 24-hours motor function in 30-minute intervals, beginning at midnight. For each 30-minute interval the patient rated the state he or she had been in for the past 30 minutes; OFF, ON (without troublesome dyskinesia), ON with troublesome dyskinesia or Asleep.

End point type	Secondary

End point timeframe:

The change from baseline to end of treatment (EOT) (Visit 5, Week 12).

End point values	Mesdopetam 2.5 mg	Mesdopetam 5 mg	Mesdopetam 7.5 mg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	35	35	33	37
Units: Total daily hours	29	324	768	69

Statistical analyses

Statistical analysis title	OFF time
Comparison groups	Mesdopetam 7.5 mg v Placebo
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.165
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	0.3
Variability estimate	Standard error of the mean

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Collection of AEs started after the patient signed the ICF (Screening visit) and continued until the last follow-up assessment (End of Study visit/Early Withdrawal visit).	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups	
Reporting group title	Mesdopetam 2.5 mg
Reporting group description:	
Mesdopetam (IRL790) 2.5 mg hard capsule. Oral administration b.i.d.	
Reporting group title	Mesdopetam 5 mg
Reporting group description:	
Mesdopetam (IRL790) 5 mg hard capsule. Oral administration b.i.d.	
Reporting group title	Mesdopetam 7.5 mg
Reporting group description:	
Mesdopetam (IRL790) hard capsule 7.5 mg. Oral administration b.i.d.	
Reporting group title	Placebo
Reporting group description:	
Placebo comparator. Matching placebo hard capsule. Oral administration b.i.d.	

Serious adverse events	Mesdopetam 2.5 mg	Mesdopetam 5 mg	Mesdopetam 7.5 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 40 (2.50%)	1 / 38 (2.63%)	2 / 38 (5.26%)
number of deaths (all causes)	1	0	1
number of deaths resulting from adverse events	1	0	1
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 40 (0.00%)	1 / 38 (2.63%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical vertebral fracture			
subjects affected / exposed	0 / 40 (0.00%)	0 / 38 (0.00%)	0 / 38 (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
Vascular disorders			
Hypertensive emergency			

subjects affected / exposed	0 / 40 (0.00%)	0 / 38 (0.00%)	0 / 38 (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			
Arrhythmia			
subjects affected / exposed	1 / 40 (2.50%)	0 / 38 (0.00%)	0 / 38 (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 / 40 (2.50%)	0 / 38 (0.00%)	0 / 38 (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
Myocardial infarction			
subjects affected / exposed	1 / 40 (2.50%)	0 / 38 (0.00%)	0 / 38 (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
Acute myocardial infarction			
subjects affected / exposed	0 / 40 (0.00%)	0 / 38 (0.00%)	0 / 38 (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			
Parkinsonism			
subjects affected / exposed	0 / 40 (0.00%)	1 / 38 (2.63%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Sudden death			
subjects affected / exposed	0 / 40 (0.00%)	0 / 38 (0.00%)	1 / 38 (2.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	0 / 40 (0.00%)	0 / 38 (0.00%)	0 / 38 (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
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 40 (2.50%)	0 / 38 (0.00%)	0 / 38 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 40 (2.50%)	0 / 38 (0.00%)	0 / 38 (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
COVID-19			
subjects affected / exposed	0 / 40 (0.00%)	0 / 38 (0.00%)	1 / 38 (2.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 38 (0.00%)	1 / 38 (2.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypocalcaemia			
subjects affected / exposed	1 / 40 (2.50%)	0 / 38 (0.00%)	0 / 38 (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
Hypokalaemia			
subjects affected / exposed	1 / 40 (2.50%)	0 / 38 (0.00%)	0 / 38 (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	3 / 39 (7.69%)		
number of deaths (all causes)	0		

number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 39 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cervical vertebral fracture			
subjects affected / exposed	1 / 39 (2.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypertensive emergency			
subjects affected / exposed	1 / 39 (2.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	0 / 39 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac failure			
subjects affected / exposed	0 / 39 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			
subjects affected / exposed	0 / 39 (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 / 39 (2.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Parkinsonism			

subjects affected / exposed	0 / 39 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Sudden death			
subjects affected / exposed	0 / 39 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 39 (2.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 39 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 39 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
COVID-19			
subjects affected / exposed	0 / 39 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urosepsis			
subjects affected / exposed	0 / 39 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypocalcaemia			

subjects affected / exposed	0 / 39 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	0 / 39 (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	Mesdopetam 2.5 mg	Mesdopetam 5 mg	Mesdopetam 7.5 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 40 (22.50%)	8 / 38 (21.05%)	6 / 38 (15.79%)
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	2 / 40 (5.00%)	1 / 38 (2.63%)	2 / 38 (5.26%)
occurrences (all)	5	1	2
Nervous system disorders			
Parkinsonism			
subjects affected / exposed	1 / 40 (2.50%)	2 / 38 (5.26%)	1 / 38 (2.63%)
occurrences (all)	2	2	2
Dyskinesia			
subjects affected / exposed	4 / 40 (10.00%)	1 / 38 (2.63%)	1 / 38 (2.63%)
occurrences (all)	4	1	1
Musculoskeletal and connective tissue disorders			
Mobility decreased			
subjects affected / exposed	2 / 40 (5.00%)	4 / 38 (10.53%)	2 / 38 (5.26%)
occurrences (all)	3	5	5

Non-serious adverse events	Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 39 (23.08%)		
Injury, poisoning and procedural complications			
Fall			

subjects affected / exposed occurrences (all)	2 / 39 (5.13%) 2		
Nervous system disorders Parkinsonism subjects affected / exposed occurrences (all) Dyskinesia subjects affected / exposed occurrences (all)	 4 / 39 (10.26%) 4 3 / 39 (7.69%) 4		
Musculoskeletal and connective tissue disorders Mobility decreased subjects affected / exposed occurrences (all)	 0 / 39 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 March 2021	- Added U-hCG test at visit 3 and visit 4. - Clarifying details added to exclusion criterion 11. - Added definition of woman of childbearing potential and/or postmenopausal woman according to CTFG Guideline Recommendations related to contraception and pregnancy testing in clinical trials, Version 1.1, dated 21/09/2020. - Addition of safety parameters (vital signs, haematology/clinical chemistry incl prolactin, dipstick urinalysis and ECG) at Visit 1 (Baseline) if 29 days or more between the Screening visit and Visit 1 (Baseline). - Clarification that the three 24-hour home diaries can be completed during three consecutive days or any combination of days during the week prior V1, V3, V4 and V5. - Correction of Stage 2 Hoehn and Yahr description. - Revision of approximate number of sites participating in the study (increased from 28 to 35).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported