Clinical trial results:
SERENDEM study: MD1003 in patients suffering from demyelinating neuropathies, an open label pilot study

Summary

EudraCT number	2015-001150-15
Trial protocol	FR
Global end of trial date	18 March 2019

Results information

Result version number	v1 (current)
This version publication date	15 August 2020
First version publication date	15 August 2020

Trial information

Trial identification

Sponsor protocol code	"MD1003CT2015-01-SERENDEM

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	MEDDAY SA
Sponsor organisation address	24 rue de la Pépinière, Paris, France,
Public contact	Frédéric Sedel, MEDDAY PHARMACEUTICALS, frederic.sedel@medday-pharma.com
Scientific contact	Frédéric Sedel, MEDDAY PHARMACEUTICALS, frederic.sedel@medday-pharma.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	13 December 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 March 2019
Global end of trial reached?	Yes
Global end of trial date	18 March 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective is to detect a signal of efficacy of high dose biotin in demyelinating polyneuropathies

Protection of trial subjects:

This protocol complied with the principal laid down by the 18th World Medical Assembly (Helsinki, 1964 an following amendments) and all applicable amendments laid down by the World Medical Assemblies, as well as the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. The trial complied with the laws and regulations of the country in which the study was performed, and any applicable guidelines.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 December 2016
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	France: 15
Worldwide total number of subjects	15
EEA total number of subjects	15

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)	10
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment	
Recruitment details: -	
Pre-assignment	
Screening details: -	
Pre-assignment period milestones	
Number of subjects started	15
Number of subjects completed	15

Period 1	
Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded
Arms	
Arm title	Single arm
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	MD1003
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

MD1003 capsules consisting of 100 mg biotin and excipients (lactose, magnesium stearate, croscarmellose sodium, silica) taken orally three times a day (one in the morning, one at noon, and one in the evening)

Number of subjects in period 1	Single arm
Started	15
Completed	14
Not completed	1
Adverse event, non-fatal	1

Baseline characteristics

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	15	15	
Age categorical Units: Subjects			
Age continuous Units: years			
median	62.1		
full range (min-max)	30.8 to 83.5	-	
Gender categorical Units: Subjects			
Female	8	8	
Male	7	7	

Subject analysis sets

Subject analysis set title	FAS
Subject analysis set type	Full analysis

Subject analysis set description:

All patients who received at least one dose of study medication and with at least one assessment at baseline and during the study will be included in Full Analysis Set.

Reporting group values	FAS		
Number of subjects	15		
Age categorical Units: Subjects			
Age continuous Units: years			
median	62.1		
full range (min-max)	30.8 to 83.5		
Gender categorical Units: Subjects			
Female	8		
Male	7		

End points

End points reporting groups

Reporting group title	Single arm
Reporting group description: -	
Subject analysis set title	FAS
Subject analysis set type	Full analysis

Subject analysis set description:

All patients who received at least one dose of study medication and with at least one assessment at baseline and during the study will be included in Full Analysis Set.

Primary: Number of patients with at least 10% improvement for at least 2 out of the 4 criteria of demyelination, in at least 3 out of 8 nerves

End point title	Number of patients with at least 10% improvement for at least 2 out of the 4 criteria of demyelination, in at least 3 out of 8 nerves[1]

End point description:

End point type	Primary

End point timeframe:

Baseline to end of study (week 48)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The primary endpoint, for the primary analysis, was summarized as the number and percentage of patients with a clinical significant relative change (at least 10%) for at least two out of the four criteria in at least three nerves out of the eight investigated by disease group and overall on the FAS population.

End point values	Single arm	FAS		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	15	15		
Units: none	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: ONLS absolute change

End point title	ONLS absolute change

End point description:

End point type	Secondary

End point timeframe:

From baseline to week 48

End point values	Single arm	FAS		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	15	15		
Units: none				
arithmetic mean (full range (min-max))	-0.5 (-3 to 2)	-0.5 (-3 to 2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Timed 10-meter walk test absolute change

End point title	Timed 10-meter walk test absolute change

End point description:

End point type	Secondary

End point timeframe:

From baseline to week 48

End point values	Single arm	FAS		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	15	15		
Units: none				
arithmetic mean (full range (min-max))	-0.6 (-2 to 2)	-0.6 (-2 to 2)		

Statistical analyses

No statistical analyses for this end point

Secondary: MRC total score absolute change

End point title	MRC total score absolute change

End point description:

End point type	Secondary

End point timeframe:

From baseline to Week 48

End point values	Single arm	FAS		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	15	15		
Units: none				
arithmetic mean (full range (min-max))	4.5 (-8 to 27)	4.5 (-8 to 27)		

Statistical analyses

No statistical analyses for this end point

Secondary: INCAT sensory sum score absolute change

End point title	INCAT sensory sum score absolute change

End point description:

End point type	Secondary

End point timeframe:

From baseline to week 48

End point values	Single arm	FAS		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	15	15		
Units: none				
arithmetic mean (full range (min-max))	-2.2 (-8 to 4)	-2.2 (-8 to 4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Distance 6-min walk test absolute change

End point title	Distance 6-min walk test absolute change

End point description:

End point type	Secondary

End point timeframe:

From baseline to week 48

End point values	Single arm	FAS		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	15	15		
Units: none				
arithmetic mean (full range (min-max))	61.1 (-15 to 151)	61.1 (-15 to 151)		

Statistical analyses

No statistical analyses for this end point

Secondary: Posturography: speed absolute change in spontaneous speed condition

End point title	Posturography: speed absolute change in spontaneous speed condition

End point description:

End point type	Secondary

End point timeframe:

From baseline to week 48

End point values	Single arm	FAS		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	13	13		
Units: none				
arithmetic mean (full range (min-max))	0.111 (-0.2 to 0.45)	0.111 (-0.2 to 0.45)		

Statistical analyses

No statistical analyses for this end point

Secondary: Excitability testing: strengh-duration time constant absolute change

End point title	Excitability testing: strengh-duration time constant absolute change

End point description:

End point type	Secondary

End point timeframe:

From baseline to week 48

End point values	Single arm	FAS		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	15	15		
Units: none				
arithmetic mean (full range (min-max))	0.068 (-0.11 to 0.28)	0.068 (-0.11 to 0.28)		

Statistical analyses

No statistical analyses for this end point

Secondary: Excitability testing: rheobase absolute change

End point title	Excitability testing: rheobase absolute change

End point description:

End point type	Secondary

End point timeframe:

From baseline to week 48

End point values	Single arm	FAS		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	15	15		
Units: none				
arithmetic mean (full range (min-max))	-5.905 (-18.29 to 0.67)	-5.905 (-18.29 to 0.67)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Screening to 30 days after last study drug intake	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.0
Reporting groups	
Reporting group title	Overall - safety set

Reporting group description: -

Serious adverse events	Overall - safety set		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 15 (13.33%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Clear cell renal cell carcinoma			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Autoimmune encephalopathy			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

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

Non-serious adverse events	Overall - safety set		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 15 (93.33%)		
Investigations			
Laboratory test interference			

subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Haemoglobin decreased			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Burn oesophageal			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Foot fracture			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Surgical and medical procedures			
Breast reconstruction			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Nervous system disorders			
Insomnia			
subjects affected / exposed	3 / 15 (20.00%)		
occurrences (all)	3		
BALANCE DISORDER			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Memory impairment			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
MUSCLE CONTRACTIONS INVOLUNTARY			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		

Neuralgia subjects affected / exposed occurrences (all) Restless legs syndrome subjects affected / exposed occurrences (all) Sciatica subjects affected / exposed occurrences (all)	 1 / 15 (6.67%) 2 1 / 15 (6.67%) 1 1 / 15 (6.67%) 1		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) Oedema peripheral subjects affected / exposed occurrences (all)	 3 / 15 (20.00%) 3 1 / 15 (6.67%) 1		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Gastric disorder subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	 1 / 15 (6.67%) 1 1 / 15 (6.67%) 1 1 / 15 (6.67%) 1 1 / 15 (6.67%) 1		
Respiratory, thoracic and mediastinal disorders Sleep apnoea syndrome subjects affected / exposed occurrences (all)	 1 / 15 (6.67%) 1		
Skin and subcutaneous tissue disorders Pruritus			

subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Alopecia			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Rash papular			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 15 (20.00%)		
occurrences (all)	4		
Muscle spasms			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Musculoskeletal stiffness			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 February 2017	Protocol was amended to allow for the inclusion of patients with CMT1b in addition to patients with CMT1a.

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.

None

Notes: