



Clinical trial results:

A phase 2a study to explore treatment with Sodium Valproate in adults with McArdle Disease (Glycogen Storage Disorder Type V, GSDV)

Summary

EudraCT number	2014-001637-88
Trial protocol	DK
Global end of trial date	10 December 2018

Results information

Result version number	v1 (current)
This version publication date	26 March 2021
First version publication date	26 March 2021
Summary attachment (see zip file)	Journal article (019 Scalco m.fl. - 2020 - Results of an open label feasibility study of sodium valproate in people with McArdle Disease.pdf) Results file (Eudra-CT skabelon_MGS_CV.docx)

Trial information

Trial identification

Sponsor protocol code	2014-650
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03112889
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	John Vissing
Sponsor organisation address	Blegdamsvej 9, Copenhagen, Denmark, 2100
Public contact	Neuromuscular research unit, Neuromuscular research unit, Rigshospitalet, 0045 35456135,
Scientific contact	Neuromuscular research unit, Neuromuscular research unit, Rigshospitalet, 0045 35456135,

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	10 December 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 December 2018
Global end of trial reached?	Yes
Global end of trial date	10 December 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Investigate whether sodium valproate can improve muscle functioning in subjects with McArdle Disease (Glycogen storage disease type V)

Protection of trial subjects:

Measures to protect patients included avoidance of pre-treatment muscle biopsy if the patient had previously had one performed. Regular trial monitoring was done on the part of the sponsor. Rapid notification of SAE. All subjects were given emergency contact details of the CI and investigators and regular telephone contact with the subjects was maintained during the trial between study visits.

Background therapy:

No specific background therapy apart from study-drug

Evidence for comparator: -

Actual start date of recruitment	01 March 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	Denmark: 8
Worldwide total number of subjects	8
EEA total number of subjects	8

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)	6
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

10 subjects were contacted to take part in this clinical trial. All patients were attending a highly specialized service for neuromuscular disorders including McArdle disease at Rigshospitalet, Copenhagen, Denmark. Recruitment started in October 2015 and last subject was recruited in June 2016.

Pre-assignment

Screening details:

8 patients were screened, 0 were not eligible.

6 subjects completed the study, 4 male and 2 females. Mean age of included subjects was 45 years (range 21-66, SD 18).

Period 1

Period 1 title	Overall period (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Not applicable (open-label study)

Arms

Arm title	Overall study arm
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Arm description:

Open-label study of one study arm.

Arm type	Experimental
Investigational medicinal product name	Sodium Valproate
Investigational medicinal product code	VPA
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Modified release VPA was prescribed at a treatment dose of 20 mg/kg/day. The dose was rounded up or down to the nearest value dependent on weight.

VPA dose was titrated over 4 weeks from a starting dose of 5 ml/kg/day to the treatment dose of 20mg/kg/day in order to minimise side effects.

At the end of the study VPA was titrated down over 4 weeks.

Number of subjects in period 1	Overall study arm
Started	8
Completed	6
Not completed	2
Adverse event, non-fatal	1
Lost to follow-up	1

Baseline characteristics

Reporting groups

Reporting group title	Overall period
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Reporting group description: -

Reporting group values	Overall period	Total	
Number of subjects	8	8	
Age categorical			
All patients included in this open-label study			
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)	6	6	
From 65-84 years	2	2	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	45		
standard deviation	± 18	-	
Gender categorical			
All patients included in this open-label study			
Units: Subjects			
Female	2	2	
Male	6	6	

End points

End points reporting groups

Reporting group title	Overall study arm
Reporting group description:	
Open-label study of one study arm.	

Primary: Peak oxygen uptake (VO₂peak)

End point title	Peak oxygen uptake (VO ₂ peak) ^[1]
End point description:	
Subjects performed exercise on a bike ergometer. Oxygen consumption was assessed by a face mask attached to a cardiopulmonary exercise training gas exchange analyser (Cosmed, Milan, Italy). An incremental exercise test was performed during the screening visit (20 watts baseline workload, with 5W increments every 2 minutes) to determine peak oxygen uptake (VO ₂ peak). Heart rate was monitored during exercise by using a 3-lead cardiac monitor and rating of perceived exertion (RPE) were recorded every minute. Maximal workload was the highest attained workload at end of exercise (if held for at least 60 seconds).	
End point type	Primary
End point timeframe:	
Change from baseline to post 28 weeks treatment.	

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: No statistical analyses for this end-point. Trial is a descriptive open-label feasibility trial. The aim of the trial is to provide information on whether a larger-scale trial is possible and if so data from this trial will be used to estimate parameters for making a well-informed power-calculation in a future randomized clinical trial.

End point values	Overall study arm			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Millilitres of oxygen per minute				
arithmetic mean (standard deviation)	0 (± 3)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AE documented at week 16 and 28. SAE reported within 24 hours.

Adverse event reporting additional description:

AE were assessed as either not IMP-related, possibly IMP-related or probably IMP-related

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.0
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Reporting groups

Reporting group title	All patients
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Reporting group description:

All included patients, since this was an open label trial.

Serious adverse events	All patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	All patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 8 (100.00%)		
Nervous system disorders			
Tremor	Additional description: Tremor of hands		
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
Cognitive disorder	Additional description: Problems remembering		
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
General disorders and administration site conditions			
Fatigue	Additional description: General tiredness		

subjects affected / exposed	5 / 8 (62.50%)		
occurrences (all)	6		
Dry mouth			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Eye disorders			
Eye symptom	Additional description: Twitching eye-muscles		
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Gastrointestinal disorders			
Diarrhoea	Additional description: Upset stomach		
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Pain	Additional description: Pain in muscles or joints		
subjects affected / exposed	4 / 8 (50.00%)		
occurrences (all)	5		
Arthritis	Additional description: None		
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Inflammation	Additional description: Ankle inflammation		
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
fracture	Additional description: High energy foot fracture		

subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Infections and infestations			
Viral infection	Additional description: Common cold		
subjects affected / exposed occurrences (all)	3 / 8 (37.50%) 3		
Gum infections	Additional description: None		
subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Urinary tract infection			
subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Erysipelas			
subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

This study was a small open-label study, statistical analysis was descriptive in scope.

Notes:

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/32811700>