Clinical trial results:
Pharmacodynamic Studies of a Histone Deacetylase Inhibitor in FRDA

Summary

EudraCT number	2011-002744-27
Trial protocol	GB
Global end of trial date	30 June 2015

Results information

Result version number	v1 (current)
This version publication date	15 October 2022
First version publication date	15 October 2022

Trial information

Trial identification

Sponsor protocol code	CR01849

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Imperial College London
Sponsor organisation address	Hammersmith Campus, Hammersmith Hospital, Du Dane Road, , London, United Kingdom, W12 0NN
Public contact	Festenstein, Imperial College London, r.festenstein@imperial.ac.uk
Scientific contact	Festenstein, Imperial College London, r.festenstein@imperial.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	30 June 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 June 2015
Global end of trial reached?	Yes
Global end of trial date	30 June 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary aim is to determine whether Nicotinamide is effective at upregulating the Frataxin (FXN) gene in patients with Friedreich's ataxia (FRDA) where this gene is abnormally 'switched off'.

Protection of trial subjects:

N/A

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 August 2011
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	United Kingdom: 10
Worldwide total number of subjects	10
EEA total number of subjects	10

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	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants must have a molecular genetic diagnosis of FRDA, consisting of a GAA-repeat expansion on both alleles of the FXN gene.
Exclusion Criteria for the interventional study:
Participants with significant clinical dysphagia.
Participants taking Sodium Valproate or any other known histone deacetylase inhibitor.

Period 1

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

Arms

Arm title	Nicotinamide
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Nicotinamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Dose escalation study up to 0.5g to 8g

Number of subjects in period 1	Nicotinamide
Started	10
Completed	10

Baseline characteristics

Reporting groups	
Reporting group title	Overall study

Reporting group description: -

Reporting group values	Overall study	Total	
Number of subjects	10	10	
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)	10	10	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	6	6	
Male	4	4	

End points

End points reporting groups

Reporting group title	Nicotinamide

Reporting group description: -

Primary: Significant upregulation of Frataxin in patients

End point title	Significant upregulation of Frataxin in patients[1]

End point description:

End point type	Primary

End point timeframe:

Daily administration up to 9 weeks

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: Bayesian statistical analysis see Libri et al 2014 Lancet.

End point values	Nicotinamide			
Subject group type	Reporting group			
Number of subjects analysed	10[2]			
Units: 1.8				
arithmetic mean (confidence interval 95%)	1.8 (1.5 to 2.2)			

Notes:

[2] - The mean is a fold-increase

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 1 year	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	1.0
Reporting groups	
Reporting group title	Nicotinamide

Reporting group description: -

Serious adverse events	Nicotinamide		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 10 (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	Nicotinamide		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 10 (100.00%)		
Hepatobiliary disorders			
Nausea			
subjects affected / exposed	10 / 10 (100.00%)		
occurrences (all)	10		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 April 2014	Essentially the trial was an adapative design and each step was implemented as a substantial ammendment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/24794816