Clinical trial results:
Clinical trial - phase II - to test safety and efficay of Etravirine's treatment in Friedreich Ataxia's patients

Summary

EudraCT number	2019-002618-38
Trial protocol	IT
Global end of trial date	17 January 2023

Results information

Result version number	v1 (current)
This version publication date	20 June 2024
First version publication date	20 June 2024

Trial information

Trial identification

Sponsor protocol code	721

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04273165
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Associazione La Nostra Famiglia
Sponsor organisation address	Via Don Luigi Monza, 1, Ponte Lambro, Italy, 22037
Public contact	Segreteria Scientifica, Associazione La Nostra Famiglia, +39 031877330, medea@lanostrafamiglia.it
Scientific contact	Segreteria Scientifica, Associazione La Nostra Famiglia, +39 031877330, medea@lanostrafamiglia.it

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	28 May 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 January 2023
Global end of trial reached?	Yes
Global end of trial date	17 January 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Test the safety of ETR treatment in patients with FRDA (two groups of patients treated with 2 different doses: 200 mg / day and 400 mg / day). The goal is to monitor all EAs that will occur during 4 months of treatment with ETR compared to EAs recorded during 4 months of observation before and 4 months after treatment.

Protection of trial subjects:

Presence among trial documentation of a patient report form for any adverse event experienced. Presence of a dedicated phone number for safety issues available 24/7. Physical exmination during visits, including vital signs, whole body skin inspection, blood testing, urine testing.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 September 2020
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Scientific research
Long term follow-up duration	4 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Italy: 35
Worldwide total number of subjects	35
EEA total number of subjects	35

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)	1
Adolescents (12-17 years)	4
Adults (18-64 years)	30

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment was promoted by advertising the study through patients' associations and among patients currently followed at the clinical site. Recruitment was done at the clinical site.

Pre-assignment

Screening details:

38 patients were screened for inclusion. Of these, 35 were enrolled and 3 excluded. Of the excluded, 2 were not capable of completing the exercise test, 1 withdrew consent immediately after the screening visit.

Period 1

Period 1 title	Etravirine treatment months 0 to 2
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

No blinding was done

Arms

Are arms mutually exclusive?	Yes
Arm title	Etravirine 200 mg/day

Arm description:

2 months treatment with etravirine 200 mg/day

Arm type	Experimental
Investigational medicinal product name	Intelence
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Intelence tablets strength 200mg ; 1 tablet per day in the morning, for 2 months

Arm title	Etravirine 400 mg/day

Arm description:

2 months treatment with etravirine 400 mg/day

Arm type	Experimental
Investigational medicinal product name	Intelence
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Intelence tablets strength 200mg ; 2 tablets per day in the morning, for 2 months

Number of subjects in period 1	Etravirine 200 mg/day	Etravirine 400 mg/day
Started	17	18
Completed	17	17
Not completed	0	1
Adverse event, non-fatal	-	1

Period 2	
Period 2 title	Continuation of etravirine months 3 to 4
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms	
Are arms mutually exclusive?	Yes
Arm title	Etravirine 200 mg/day

Arm description:

2 months treatment with etravirine 200 mg/day

Arm type	Experimental
Investigational medicinal product name	Intelence
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Intelence tablets strength 200mg ; 1 tablet per day in the morning, for 2 months

Arm title	Etravirine 400 mg/day

Arm description:

2 months treatment with etravirine 400 mg/day

Arm type	Experimental
Investigational medicinal product name	Intelence
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Intelence tablets strength 200mg ; 2 tablets per day in the morning, for 2 months

Number of subjects in period 2	Etravirine 200 mg/day	Etravirine 400 mg/day
Started	17	17
Completed	17	17

Period 3	
Period 3 title	Follow-up without treatment mo. 5 to 8
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded
Arms	
Are arms mutually exclusive?	Yes
Arm title	Etravirine 200 mg/day
Arm description: 4 months without treatment	
Arm type	No intervention
No investigational medicinal product assigned in this arm	
Arm title	Etravirine 400 mg/day
Arm description: 4 months without treatment	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 3	Etravirine 200 mg/day	Etravirine 400 mg/day
Started	17	17
Completed	17	17

Baseline characteristics

Reporting groups

Reporting group title	Etravirine treatment months 0 to 2

Reporting group description: -

Reporting group values	Etravirine treatment months 0 to 2	Total	
Number of subjects	35	35	
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)	1	1	
Adolescents (12-17 years)	4	4	
Adults (18-64 years)	30	30	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	11.83		
standard deviation	± 5.7	-	
Gender categorical Units: Subjects			
Female	19	19	
Male	16	16	

End points

End points reporting groups	
Reporting group title	Etravirine 200 mg/day
Reporting group description: 2 months treatment with etravirine 200 mg/day	
Reporting group title	Etravirine 400 mg/day
Reporting group description: 2 months treatment with etravirine 400 mg/day	
Reporting group title	Etravirine 200 mg/day
Reporting group description: 2 months treatment with etravirine 200 mg/day	
Reporting group title	Etravirine 400 mg/day
Reporting group description: 2 months treatment with etravirine 400 mg/day	
Reporting group title	Etravirine 200 mg/day
Reporting group description: 4 months without treatment	
Reporting group title	Etravirine 400 mg/day
Reporting group description: 4 months without treatment	

Primary: Number of adverse drug reactions	
End point title	Number of adverse drug reactions
End point description: see adverse events	
End point type	Primary
End point timeframe: 2 months treatment 4 months treatment 4 months treatment then 4 months no treatment	

End point values	Etravirine 200 mg/day	Etravirine 400 mg/day	Etravirine 200 mg/day	Etravirine 400 mg/day
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	17[1]	17	17
Units: number	17	18	17	17

Notes:

[1] - 1 drop out due to non severe ADR

End point values	Etravirine 200 mg/day	Etravirine 400 mg/day		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	17		
Units: number	17	17		

Statistical analyses

Statistical analysis title	Chi-squared of adverse events
Comparison groups	Etravirine 200 mg/day v Etravirine 400 mg/day v Etravirine 200 mg/day v Etravirine 400 mg/day v Etravirine 200 mg/day v Etravirine 400 mg/day
Number of subjects included in analysis	102
Analysis specification	Post-hoc
Analysis type	superiority
P-value	< 0.05
Method	Chi-squared
Parameter estimate	no estimation

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Period 1: Etravirine treatment months 0 to 2 Period 2: Continuation of etravirine months 3 to 4 Period 3: Follow-up without treatment months 5 to 8	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17

Reporting groups	
Reporting group title	Etravirine 200 months 0-2
Reporting group description: Etravirine 200 months 0-2	
Reporting group title	Etravirine 400 months 0-2
Reporting group description: Etravirine 400 months 0-2	
Reporting group title	Etravirine 200 months 3-4
Reporting group description: Etravirine 200 months 3-4	
Reporting group title	Etravirine 400 months 3-4
Reporting group description: Etravirine 400 months 3-4	
Reporting group title	Etravirine 200 months 5-8
Reporting group description: Etravirine 200 months 5-8 follow up without treatment	
Reporting group title	Etravirine 400 months 5-8
Reporting group description: Etravirine 200 months 5-8 follow up without treatment	

Serious adverse events	Etravirine 200 months 0-2	Etravirine 400 months 0-2	Etravirine 200 months 3-4
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 17 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Cardiac disorders			
Tachycardia	Additional description: Supraventricular tachycardic arrhythmia		
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 17 (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

Serious adverse events	Etravirine 400 months 3-4	Etravirine 200 months 5-8	Etravirine 400 months 5-8

Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Cardiac disorders			
Tachycardia	Additional description: Supraventricular tachycardic arrhythmia		
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (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

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

Non-serious adverse events	Etravirine 200 months 0-2	Etravirine 400 months 0-2	Etravirine 200 months 3-4
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 17 (100.00%)	18 / 18 (100.00%)	2 / 17 (11.76%)
Investigations			
Blood cholesterol increased			
subjects affected / exposed	2 / 17 (11.76%)	2 / 18 (11.11%)	2 / 17 (11.76%)
occurrences (all)	2	2	2
Blood triglycerides increased			
subjects affected / exposed	3 / 17 (17.65%)	0 / 18 (0.00%)	2 / 17 (11.76%)
occurrences (all)	3	0	3
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Alanine aminotransferase increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Amylase increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Leukopenia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			

Hypotension			
subjects affected / exposed	0 / 17 (0.00%)	2 / 18 (11.11%)	0 / 17 (0.00%)
occurrences (all)	0	2	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	1 / 17 (5.88%)
occurrences (all)	2	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 17 (35.29%)	10 / 18 (55.56%)	1 / 17 (5.88%)
occurrences (all)	7	18	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 17 (5.88%)	2 / 18 (11.11%)	0 / 17 (0.00%)
occurrences (all)	1	3	0
Oedema peripheral	Additional description: Feeling of swollen feet		
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Vision blurred			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Diarrhea			
subjects affected / exposed	3 / 17 (17.65%)	4 / 18 (22.22%)	0 / 17 (0.00%)
occurrences (all)	5	7	0
Nausea			
subjects affected / exposed	1 / 17 (5.88%)	3 / 18 (16.67%)	0 / 17 (0.00%)
occurrences (all)	1	3	0
Vomiting			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			

Rash			
subjects affected / exposed	2 / 17 (11.76%)	2 / 18 (11.11%)	0 / 17 (0.00%)
occurrences (all)	2	2	0
Hyperhidrosis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Urinary incontinence			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	3	0	0
Psychiatric disorders			
Anger			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Muscle spasms			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Etravirine 400 months 3-4	Etravirine 200 months 5-8	Etravirine 400 months 5-8
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 17 (29.41%)	0 / 17 (0.00%)	11 / 17 (64.71%)
Investigations			
Blood cholesterol increased			
subjects affected / exposed	2 / 17 (11.76%)	0 / 17 (0.00%)	1 / 17 (5.88%)
occurrences (all)	2	1	1
Blood triglycerides increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Amylase increased			

subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Leukopenia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 17 (11.76%)	0 / 17 (0.00%)	2 / 17 (11.76%)
occurrences (all)	3	0	4
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	2 / 17 (11.76%)
occurrences (all)	0	0	2
Oedema peripheral	Additional description: Feeling of swollen feet		
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Diarrhea			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	3 / 17 (17.65%)
occurrences (all)	1	0	3
Nausea			
subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	2 / 17 (11.76%)
occurrences (all)	2	0	5
Vomiting			

subjects affected / exposed	1 / 17 (5.88%)	0 / 17 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	4
Constipation			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Hyperhidrosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Urinary incontinence			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anger			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	2
Musculoskeletal and connective tissue disorders			
Muscle spasms			
subjects affected / exposed	0 / 17 (0.00%)	0 / 17 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 March 2022	Extended recruitment and overall trial duration

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported