



## Clinical trial results:

### Clinical trial - phase II - to test safety and efficacy 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
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##### 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 examination 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
<b>Arm title</b>	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

<b>Arm title</b>	Etravirine 400 mg/day
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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
<b>Arm title</b>	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

<b>Arm title</b>	Etravirine 400 mg/day
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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

<b>Number of subjects in period 2</b>	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
<b>Arm title</b>	Etravirine 200 mg/day

Arm description:

4 months without treatment

Arm type	No intervention
No investigational medicinal product assigned in this arm	

<b>Arm title</b>	Etravirine 400 mg/day
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Arm description:

4 months without treatment

Arm type	No intervention
No investigational medicinal product assigned in this arm	

<b>Number of subjects in period 3</b>	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
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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 <sup>[1]</sup>	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

<b>Statistical analysis title</b>	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
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	17
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### Reporting groups

Reporting group title	Etravirine 200 months 0-2
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Reporting group description:

Etravirine 200 months 0-2

Reporting group title	Etravirine 400 months 0-2
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Reporting group description:

Etravirine 400 months 0-2

Reporting group title	Etravirine 200 months 3-4
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Reporting group description:

Etravirine 200 months 3-4

Reporting group title	Etravirine 400 months 3-4
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Reporting group description:

Etravirine 400 months 3-4

Reporting group title	Etravirine 200 months 5-8
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Reporting group description:

Etravirine 200 months 5-8 follow up without treatment

Reporting group title	Etravirine 400 months 5-8
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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
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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 occurrences (all)	0 / 17 (0.00%) 0	2 / 18 (11.11%) 2	0 / 17 (0.00%) 0
Cardiac disorders Tachycardia subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 2	0 / 18 (0.00%) 0	1 / 17 (5.88%) 1
Nervous system disorders Headache subjects affected / exposed occurrences (all)	6 / 17 (35.29%) 7	10 / 18 (55.56%) 18	1 / 17 (5.88%) 1
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	2 / 18 (11.11%) 3	0 / 17 (0.00%) 0
Oedema peripheral subjects affected / exposed occurrences (all)	Additional description: Feeling of swollen feet		
	0 / 17 (0.00%) 0	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0
Eye disorders Vision blurred subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 18 (0.00%) 0	0 / 17 (0.00%) 0
Gastrointestinal disorders Diarrhea subjects affected / exposed occurrences (all)	3 / 17 (17.65%) 5	4 / 18 (22.22%) 7	0 / 17 (0.00%) 0
Nausea subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	3 / 18 (16.67%) 3	0 / 17 (0.00%) 0
Vomiting subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	1 / 18 (5.56%) 1	0 / 17 (0.00%) 0
Constipation subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 18 (0.00%) 0	0 / 17 (0.00%) 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

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

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

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**Interruptions (globally)**

Were there any global interruptions to the trial? No

**Limitations and caveats**

None reported