Clinical trial results:
Safety and Efficacy of yIFN treatment in Friedreich ataxia

Summary

EudraCT number	2015-002432-40
Trial protocol	IT
Global end of trial date	17 July 2018

Results information

Result version number	v1 (current)
This version publication date	08 June 2022
First version publication date	08 June 2022
Summary attachment (see zip file)	PMID 30237783 (fnins-14-00872.pdf) PMID 31930551 (Vavla_et_al-2020-Movement_Disorders(2).pdf)

Trial information

Trial identification

Sponsor protocol code	042/15

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03888664
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Associazione La Nostra Famiglia
Sponsor organisation address	via don Luigi Monza 20, Bosisio Parini, Italy, 23842
Public contact	Clinical trials unit, Associazione La Nostra Famiglia, +39 031877919, trialsclinici@lanostrafamiglia.it
Scientific contact	Clinical trials unit, Associazione La Nostra Famiglia, +39 031877919, trialsclinici@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	17 July 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 July 2018
Global end of trial reached?	Yes
Global end of trial date	17 July 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To test the safety of treatment with gamma interferon in Friedreich's Ataxia patients, administered for 6 months at the initial dose of 100 micrograms three times per week (first 2 weeks of treatment) and at the final dose of 200 micrograms three times per week (for the remaining 22 weeks of treatment).

Protection of trial subjects:

Presence among trial documentation of a patient report form for any adverse event experienced. Phone check made by investigators 15 days after start of treatment. Presence of a dedicated phone number for safety issues available 24/7.

Background therapy:

None.

Evidence for comparator:

Single-arm trial - no comparator.

Actual start date of recruitment	11 January 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	Italy: 12
Worldwide total number of subjects	12
EEA total number of subjects	12

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)	7
Adults (18-64 years)	4
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Screening was performed on patients referring to the clinical center for their routine treatment of FRDA. 22 patients were potentially eligible for participation. Of these, 13 patients were screened for inclusion. Of these, 12 patients were enrolled, 1 patient was excluded.
Reason for exclusion: severe hypovisus occurred before study start.

Period 1

Period 1 title	Pre-treatment
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

Single-arm trial

Arms

Arm title	No treatment - baseline

Arm description:

Baseline evaluation without treatment

Arm type	Experimental
Investigational medicinal product name	Imukin
Investigational medicinal product code	L03AB03
Other name	interferon gamma-1b
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Baseline evanluation period without drug treatment

Number of subjects in period 1	No treatment - baseline
Started	12
Completed	12

Period 2

Period 2 title	100 micrograms thrice a week dose
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details: Single-arm trial	

Arms

Arm title	Gamma interferon 100 micrograms
Arm description: 2 weeks with gamma interferon 100 micrograms thrice a week	
Arm type	Experimental
Investigational medicinal product name	Imukin
Investigational medicinal product code	L03AB03
Other name	interferon gamma-1b
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details: 100 micrograms subcutaneous injection, three times per week, during the first 2 weeks of use	

Number of subjects in period 2	Gamma interferon 100 micrograms
Started	12
Completed	12

Period 3

Period 3 title	200 micrograms thrice a week dose
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded
Blinding implementation details: Single-arm trial	

Arms

Arm title	Gamma interferon 200 micrograms
Arm description: 22 weeks with gamma interferon 200 micrograms thrice a week	
Arm type	Experimental
Investigational medicinal product name	Imukin
Investigational medicinal product code	L03AB03
Other name	interferon gamma-1b
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details: 200 micrograms subcutaneous injection, three times per week, during the following 22 weeks of use	

Number of subjects in period 3	Gamma interferon 200 micrograms
Started	12
Completed	11
Not completed	1
Adverse event, non-fatal	1

Period 4	
Period 4 title	Follow-up without treatment
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded
Blinding implementation details: Single-arm trial	

Arms	
Arm title	No treatment - Follow up
Arm description: No treatment for the following 24 weeks	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 4	No treatment - Follow up
Started	11
Completed	11

Baseline characteristics

Reporting groups

Reporting group title	Pre-treatment

Reporting group description: -

Reporting group values	Pre-treatment	Total	
Number of subjects	12	12	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous			
Age in years of the enrolled subjects			
Units: years			
arithmetic mean	17.33		
standard deviation	± 4.54	-	
Gender categorical			
Biological sex for all enrolled subjects			
Units: Subjects			
Female	5	5	
Male	7	7	

End points

End points reporting groups

Reporting group title	No treatment - baseline
Reporting group description: Baseline evaluation without treatment	
Reporting group title	Gamma interferon 100 micrograms
Reporting group description: 2 weeks with gamma interferon 100 micrograms thrice a week	
Reporting group title	Gamma interferon 200 micrograms
Reporting group description: 22 weeks with gamma interferon 200 micrograms thrice a week	
Reporting group title	No treatment - Follow up
Reporting group description: No treatment for the following 24 weeks	

Primary: Number of adverse drug reactions

End point title	Number of adverse drug reactions
End point description: Sum of the number of AE reported by treated patients each day at different time points along the study: baseline before treatment; during the first 2 weeks of treatment at 100 micrograms; during the following 22 weeks of treatment at 200 micrograms; during the following 24 weeks of follow-up without treatment	
End point type	Primary
End point timeframe: Baseline; week 2; week 24; week 48	

End point values	Gamma interferon 100 micrograms	Gamma interferon 200 micrograms	No treatment - Follow up	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12[1]	12[2]	11[3]	
Units: 382				
number (not applicable)				
Fever	1	38	0	
Headache	7	110	0	
Shivers	0	49	0	
Fatigue	6	44	0	
Pain at injection site	2	19	0	
Flu-like symptoms	0	19	0	
Nasal congestion	0	5	0	
Myalgia	1	0	0	
Abdominal pain	0	3	0	
Diarrhea	1	0	0	
Nausea	1	4	0	
Vomiting	0	8	0	
Appetite decreased	2	31	0	

Nosebleed	0	5	0	
Bruising at injection site	0	4	0	
Dyschromia at injection site	0	12	0	
Depression	0	10	0	

Notes:

[1] - All enrolled subjects

[2] - All enrolled subjects

[3] - All enrolled subjects

Statistical analyses

Statistical analysis title	Chi-squared of adverse events

Statistical analysis description:

Chi-squared analysis of adverse events numbers collected across study periods 2 and 3. Periods 1 and 4 were not analyzed because no adverse events occurred.

Comparison groups	Gamma interferon 100 micrograms v Gamma interferon 200 micrograms
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	equivalence[4]
P-value	< 0.0001 [5]
Method	Chi-squared

Notes:

[4] - Null hypothesis: no difference in the number of AE during treatment with 100 or 200 micrograms

[5] - the number of AE is different during treatment with 100 or 200 micrograms

Adverse events

Adverse events information

Timeframe for reporting adverse events:

2 weeks after treatment start (100 micrograms thrice a week)
3 months after treatment start (100 micrograms thrice a week for 2 weeks then 200 micrograms thrice a week)
6 months after treatment start (as above)
12 months after treatment start (as above

Adverse event reporting additional description:

Adverse events reporting was solicited by the administration of a pre-defined form and through phone interviews.
Moreover, patients were instructed to contact a dedicated phone number available 24/7 in case of any adverse event.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17

Reporting groups

Reporting group title	All patients

Reporting group description:

All enrolled patients

Serious adverse events	All patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 12 (16.67%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Headache	Additional description: Persistent headache, occurred 24h after the adminsitration of Imukin 100 micrograms and resolved with the administration of paracetamol 1g. Event occurred again with every Imukin dose until treatment discontinuation.		
subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	6 / 6		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Vomiting	Additional description: Persistent vomiting, occurred 24h after the administration of Imukin 100 micrograms and resolved with the administration of paracetamol 1g. Event occurred again with every Imukin dose until treatment discontinuation.		
subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	6 / 6		
deaths causally related to treatment / all	0 / 0		
Abdominal pain	Additional description: Persistent abdominal pain, occurred 24h after the administration of Imukin 100 micrograms and resolved with the administration of paracetamol 1g. Event occurred again with every Imukin dose until treatment discontinuation.		

subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	6 / 6		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Myalgia intercostal	Additional description: Episode of intense coughing, followed by intense chest pain which, upon medical examination, was diagnosed as "basal right thoracic pain of presumed muscular parietal nature"		
subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	6 / 6		
deaths causally related to treatment / all	0 / 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	12 / 12 (100.00%)		
Vascular disorders			
Epistaxis	Additional description: Epistaxis		
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	5		
Nervous system disorders			
Headache	Additional description: Headache		
subjects affected / exposed	10 / 12 (83.33%)		
occurrences (all)	117		
General disorders and administration site conditions			
Hyperpyrexia	Additional description: Fever, increased body temperature		
subjects affected / exposed	7 / 12 (58.33%)		
occurrences (all)	39		
Chills	Additional description: Chills		
subjects affected / exposed	5 / 12 (41.67%)		
occurrences (all)	49		
Fatigue	Additional description: Sensation of fatigue		
subjects affected / exposed	9 / 12 (75.00%)		
occurrences (all)	50		
Injection site pain	Additional description: Pain at the injection site		

subjects affected / exposed	5 / 12 (41.67%)		
occurrences (all)	21		
Influenza like illness	Additional description: Flu like illness		
subjects affected / exposed	4 / 12 (33.33%)		
occurrences (all)	19		
Injection site bruising	Additional description: Bruising at injection site		
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	4		
Injection site discolouration	Additional description: Skin dyschromia at injection site		
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	12		
Gastrointestinal disorders			
Abdominal pain	Additional description: Abdominal pain		
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	3		
Diarrhoea	Additional description: Diarrhea		
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Nausea	Additional description: Nausea		
subjects affected / exposed	3 / 12 (25.00%)		
occurrences (all)	5		
Vomiting	Additional description: Vomiting		
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	8		
Respiratory, thoracic and mediastinal disorders			
Nasal congestion	Additional description: Nasal congestion		
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	5		
Psychiatric disorders			
Depression	Additional description: Depressive symptoms		
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	10		
Musculoskeletal and connective tissue disorders			
Myalgia	Additional description: Muscle pain, myalgia		
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		

Metabolism and nutrition disorders			
Decreased appetite	Additional description: Reduced appetite		
subjects affected / exposed	4 / 12 (33.33%)		
occurrences (all)	33		

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

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/31930551

http://www.ncbi.nlm.nih.gov/pubmed/33162876