Clinical trial results:
A comparative, double-blind, randomised, multicentre efficacy and safety study of ClairYg® versus Tégéline® in maintenance treatment of Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP)

Summary

EudraCT number	2012-001996-34
Trial protocol	FR
Global end of trial date	08 June 2015

Results information

Result version number	v1 (current)
This version publication date	13 July 2016
First version publication date	13 July 2016

Trial information

Trial identification

Sponsor protocol code	IGNG-0904

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	Short name: ECLIPSE

Notes:

Sponsors

Sponsor organisation name	LFB biotechnologies
Sponsor organisation address	3, avenue des tropiques - BP 40305, COURTABOEUF, France, 91958
Public contact	Global Clinical Development Leader, LFB BIOTECHNOLOGIES, 0033 169825656,
Scientific contact	Global Clinical Development Leader, LFB BIOTECHNOLOGIES, 0033 169825656,

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	15 April 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 June 2015
Global end of trial reached?	Yes
Global end of trial date	08 June 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary objective:
The primary objective is to assess the efficacy of ClairYg® in controlling the neurological status of patients with CIDP.

Protection of trial subjects:

None

Background therapy:

None

Evidence for comparator:

Tegeline was the only intravenous immunoglobulin that had the indication "CIDP" when the study was started.

Actual start date of recruitment	23 November 2012
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	France: 40
Worldwide total number of subjects	40
EEA total number of subjects	40

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)	24

From 65 to 84 years	16
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruited in France

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	45[1]
Number of subjects completed	40

Pre-assignment subject non-completion reasons

Reason: Number of subjects	screening failure: 5

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: It was planned to screen 44 patients in order to have 40 randomised and assessable patients.
It has been necessary to screen 45 patients in order to have 40 randomised patients.

Period 1

Period 1 title	Before 1st administration of study drug
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

The hospital pharmacist was not blind and randomised the patient via an Interactive Voice Respose System (IVRS).

Arms

Are arms mutually exclusive?	Yes
Arm title	Clairyg arm

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Clairyg
Investigational medicinal product code	IGNG
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients were already under intravenous immunoglobulin when they were recruited.
- The allowed range of doses per course was 0.4 to 2 g/kg
- The allowed range of course frequency was every 2 to 9 weeks (during 6 months).

During the study, the dose and course frequency was maintained at the same level as before the randomisation.

The study drug was administered intravenously, with an infusion pump.

Arm title	Tégéline arm

Arm description: -

Arm type	Active comparator

Investigational medicinal product name	Tegeline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients were already under intravenous immunoglobulin when they were recruited.
- The allowed range of doses per course was 0.4 to 2 g/kg
- The allowed range of course frequency was every 2 to 9 weeks (during 6 months).

During the study, the dose and course frequency was maintained at the same level as before the randomisation.

The study drug was administered intravenously, with an infusion pump.

Number of subjects in period 1	Clairyg arm	Tégéline arm
Started	20	20
Completed	20	20

Period 2

Period 2 title	Treatment period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Data analyst, Carer, Assessor, Subject

Blinding implementation details:

The hospital pharmacist was not blind and prepared the product to be administered in blind containers, ready for the administration to the patient.

Arms

Are arms mutually exclusive?	Yes
Arm title	Clairyg arm

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Clairyg
Investigational medicinal product code	IGNG
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients were already under intravenous immunoglobulin when they were recruited.
- The allowed range of doses per course was 0.4 to 2 g/kg
- The allowed range of course frequency was every 2 to 9 weeks (during 6 months).

During the study, the dose and course frequency was maintained at the same level as before the randomisation.

The study drug was administered intravenously, with an infusion pump.

Arm title	Tégéline arm
Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	Tegeline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients were already under intravenous immunoglobulin when they were recruited.
- The allowed range of doses per course was 0.4 to 2 g/kg
- The allowed range of course frequency was every 2 to 9 weeks (during 6 months).

During the study, the dose and course frequency was maintained at the same level as before the randomisation.

The study drug was administered intravenously, with an infusion pump.

Number of subjects in period 2	Clairyg arm	Tégéline arm
Started	20	20
Completed	18	19
Not completed	2	1
Consent withdrawn by subject	-	1
Exclusion criterion	2	-

Baseline characteristics

Reporting groups

Reporting group title	Before 1st administration of study drug

Reporting group description: -

Reporting group values	Before 1st administration of study drug	Total	
Number of subjects	40	40	
Age categorical Units: Subjects			
Adults (18-85 years)	40	40	
Age continuous Units: years			
median	63.5		
full range (min-max)	24 to 84	-	
Gender categorical Units: Subjects			
Male	28	28	
Female	12	12	

Subject analysis sets

Subject analysis set title	FAS Clairyg arm
Subject analysis set type	Full analysis

Subject analysis set description:

All patients who received at least 1 administration of study drug and with at least one post baseline assessment of the primary efficacy endpoint

Subject analysis set title	FAS Tégéline arm
Subject analysis set type	Full analysis

Subject analysis set description:

All patients who received at least one administration of study drug and with at least one post-baseline assessment of the primary efficacy endpoint

Subject analysis set title	PPS Clairyg arm
Subject analysis set type	Per protocol

Subject analysis set description:

All patients in the FAS without any major protocol deviation

Subject analysis set title	PPS Tégéline arm
Subject analysis set type	Per protocol

Subject analysis set description:

All patients in the FAS without any major protocol deviation

Subject analysis set title	Total treated set Clairyg arm
Subject analysis set type	Safety analysis

Subject analysis set description:

All patients who received at least one administration of IMP

Subject analysis set title	Total treated set Tegeline arm
Subject analysis set type	Safety analysis

Subject analysis set description:

All patients who received at least one administration of study drug

Reporting group values	FAS Clairyg arm	FAS Tégéline arm	PPS Clairyg arm
Number of subjects	19	20	18
Age categorical Units: Subjects			
Adults (18-85 years)	19	20	18
Age continuous Units: years median full range (min-max)			
Gender categorical Units: Subjects			
Male Female			

Reporting group values	PPS Tégéline arm	Total treated set Clairyg arm	Total treated set Tegeline arm
Number of subjects	19	20	20
Age categorical Units: Subjects			
Adults (18-85 years)	19	20	20
Age continuous Units: years median full range (min-max)		 63.5 24 to 74	 63 43 to 84
Gender categorical Units: Subjects			
Male Female		13 7	15 5

End points

End points reporting groups

Reporting group title	Clairyg arm
Reporting group description: -	
Reporting group title	Tégéline arm
Reporting group description: -	
Reporting group title	Clairyg arm
Reporting group description: -	
Reporting group title	Tégéline arm
Reporting group description: -	
Subject analysis set title	FAS Clairyg arm
Subject analysis set type	Full analysis
Subject analysis set description:	
All patients who received at least 1 administration of study drug and with at least one post baseline assessment of the primary efficacy endpoint	
Subject analysis set title	FAS Tégéline arm
Subject analysis set type	Full analysis
Subject analysis set description:	
All patients who received at least one administration of study drug and with at least one post-baseline assessment of the primary efficacy endpoint	
Subject analysis set title	PPS Clairyg arm
Subject analysis set type	Per protocol
Subject analysis set description:	
All patients in the FAS without any major protocol deviation	
Subject analysis set title	PPS Tégéline arm
Subject analysis set type	Per protocol
Subject analysis set description:	
All patients in the FAS without any major protocol deviation	
Subject analysis set title	Total treated set Clairyg arm
Subject analysis set type	Safety analysis
Subject analysis set description:	
All patients who received at least one administration of IMP	
Subject analysis set title	Total treated set Tegeline arm
Subject analysis set type	Safety analysis
Subject analysis set description:	
All patients who received at least one administration of study drug	

Primary: number of patients without relapse

End point title	number of patients without relapse[1]
End point description:	
End point type	Primary
End point timeframe:	
number of patients without relapse in Clairyg arm and in Tégéline arm.	

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: A purely descriptive comparison between Clairyg and Tegeline was choosen with a sample size of 40 evaluable patients choosen empirically. Tegeline and Clairyg primary efficacy endpoint was compared descriptively using an exact Fisher test with a two-sided 5% significance level.

End point values	FAS Clairyg arm	FAS Tégéline arm	PPS Clairyg arm	PPS Tégéline arm
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19	20	18	19
Units: number of no relapse	18	18	17	17

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The investigators were instructed to record in the CRF all AEs that occurred after the patient signed the consent form. They reported a total of 162 treatment-emergent AEs that occurred in 26 patients (65%).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15.0

Reporting groups

Reporting group title	Clairyg arm
Reporting group description: -	
Reporting group title	Tégéline arm

Reporting group description: -

Serious adverse events	Clairyg arm	Tégéline arm	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)	2 / 20 (10.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Cardiac disorders			
Hypertensive crisis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Superinfection	Additional description: Superinfection of chronic obstructive pulmonary disease		
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 4 %

Non-serious adverse events	Clairyg arm	Tégéline arm	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 20 (55.00%)	15 / 20 (75.00%)	

Nervous system disorders Headache subjects affected / exposed occurrences (all)	 3 / 20 (15.00%) 18	 12 / 20 (60.00%) 46	
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all)	 1 / 20 (5.00%) 3	 2 / 20 (10.00%) 4	
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	 0 / 20 (0.00%) 0	 4 / 20 (20.00%) 7	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 May 2013	Amendement was issued with the main objective of reinforcing the safety monitoring of patients, following communications from health authorities related to thromboembolic events and haemolysis risks with IVIg infusions. Noteworthy, no individual case safety report with thromboembolic event or haemolysis was received by LFB Biotechnologies in any of the clinical trials conducted with ClairYg. The amendment added new exclusion criteria for patients at risk and new biological tests to more closely monitor these risks.
24 April 2014	The primary efficacy endpoint was modified because it was found to be not adapted to maintenance treatment with the minimal efficient dose. New primary efficacy endpoint: Proportion of patients with no relapse throughout the 6-month follow-up i.e. whose adjusted INCAT disability score: - remains at the same baseline level or improves or - increases by one point without reinforcement in CIDP treatment schedule

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported