



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 Response 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 full range (min-max) | 63.5 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 | | 13 | 15 |
| Female | | 7 | 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 chosen with a sample size of 40 evaluable patients chosen 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