# Clinical trial results:
# International, multicentre, efficacy and safety study of I10E in the maintenance treatment of patients with Chronic Inflammatory Demyelinating Polyradiculoneuropathy: Extension of PRISM study I10E-1302.

## Summary

| | |
|---|---|
| EudraCT number | 2013-005558-31 |
| Trial protocol | GB ES IT FR DE |
| Global end of trial date | 28 July 2017 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 14 October 2020 |
| First version publication date | 14 October 2020 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | I10E-1306 |

**Additional study identifiers**

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

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | LFB Biotechnologies |
| Sponsor organisation address | 3 Avenue des Tropiques, COURTABOEUF, France, 91930 |
| Public contact | Global Clinical Development Leader, LFB BIOTECHNOLOGIES, +33 169 82 70 10, |
| Scientific contact | Global Clinical Development Leader, LFB BIOTECHNOLOGIES, +33 169 82 70 10, |

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 | 18 August 2020 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 28 July 2017 |
| Global end of trial reached? | Yes |
| Global end of trial date | 28 July 2017 |
| Was the trial ended prematurely? | Yes |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective is to assess the efficacy of I10E administered at a reduced maintenance dose in sustaining CIDP response after an initial 6-month treatment in PRISM study.

Protection of trial subjects:

This study was conducted in compliance with good clinical practice (GCP) as described in the International Conference on Harmonisation (ICH) document "Guidance for Industry-E6 Good Clinical Practice: Consolidated Guidance" dated April 1996. These practices were consistent with the principles stated in the Declaration of Helsinki (October 2013 revised version). All other applicable regulations were followed.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 09 November 2015 |
| 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 | Poland: 3 |
| Country: Number of subjects enrolled | Spain: 2 |
| Country: Number of subjects enrolled | United Kingdom: 1 |
| Country: Number of subjects enrolled | France: 2 |
| Country: Number of subjects enrolled | Italy: 4 |
| Country: Number of subjects enrolled | Tunisia: 6 |
| Country: Number of subjects enrolled | Turkey: 1 |
| Worldwide total number of subjects | 19 |
| 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 | 0 |

| | |
|---|---|
| months) | |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 15 |
| From 65 to 84 years | 4 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Between 09 November 2015 and 23 June 2017, 20 subjects from 14 sites signed an informed consent.

### Pre-assignment

Screening details: -

### Pre-assignment period milestones

| | |
|---|---|
| Number of subjects started | 20[1] |
| Number of subjects completed | 19 |

### Pre-assignment subject non-completion reasons

| | |
|---|---|
| Reason: Number of subjects | screening failure: 1 |

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: 20 subjects signed an informed consent but only 19 subjects enrolled (1 screening failure).

### Period 1

| | |
|---|---|
| Period 1 title | Treatment period (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Non-randomised - controlled |
| Blinding used | Not blinded |

### Arms

| | |
|---|---|
| **Arm title** | Single arm |

Arm description:

Participation in the study was proposed to all subjects who completed and responded to treatment in PRISM study, satisfying in eligibility criteria and were willing to continue I10E at a reduced maintenance dose.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | IQYMUNE |
| Investigational medicinal product code | I10E |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Each subject was expected to receive 16 doses of I10E (study drug) at 0.5 g/kg over 1 to 2 days, every 3 weeks.
Study drug was administered intravenously, with an infusion pump (B-Braun Infusomat Space).

| **Number of subjects in period 1** | Single arm |
|---|---|
| Started | 19 |
| Completed | 5 |
| Not completed | 14 |
| Consent withdrawn by subject | 1 |
| Physician decision | 1 |

| | |
|---|---|
| early termination of the study by the sponsor | 8 |
| Lack of efficacy | 4 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Treatment period |

Reporting group description: -

| Reporting group values | Treatment period | Total | |
|---|---|---|---|
| Number of subjects | 19 | 19 | |
| Age categorical<br>Units: Subjects | | | |
| Adults (18-79 years) | 19 | 19 | |
| Age continuous<br>Units: years<br>median<br>full range (min-max) | <br><br>50.0<br>24 to 79 | <br><br><br>- | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 7 | 7 | |
| Male | 12 | 12 | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Single arm |

Reporting group description:

Participation in the study was proposed to all subjects who completed and responded to treatment in PRISM study, satisfying in eligibility criteria and were willing to continue I10E at a reduced maintenance dose.

| | |
|---|---|
| Subject analysis set title | Total Treated set |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

All subjects who received at least one infusion of I10E.

### Primary: Responder rate

| | |
|---|---|
| End point title | Responder rate[1] |

End point description:

The responder rate at EOS visit based on the adjusted INCAT disability score was not analysed since the study was early terminated.
Responders were defined as subjects with either:
No change or decrease in the adjusted INCAT disability score and without any change in CIDP treatment between baseline and EOS visit.
OR
An increase by 1 point in the adjusted INCAT disability score without requirement of any change in CIDP treatment between baseline and EOS visit.

| | |
|---|---|
| End point type | Primary |

End point timeframe:

During treatment period the adjusted INCAT disability score was evaluated at week 0 (baseline), week 3, week 6, week 9, week 12, week 15, week 18, week 21, week 24, week 27, week 30, week 33, week 36, week 39, week 42, week 45, week 48 (End-of-Study).

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: The responder rate at EOS visit based on the adjusted INCAT disability score was not analysed since the study was early terminated.

| End point values | Single arm | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 0[2] | | | |
| Units: Subjects | | | | |

Notes:

[2] - study stopped prematurely

### Statistical analyses

No statistical analyses for this end point

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: Throughout the study. | |
| Assessment type | Non-systematic |
| **Dictionary used** | |
| Dictionary name | MedDRA |
| Dictionary version | 17.1 |
| **Reporting groups** | |
| Reporting group title | Single arm |
| Reporting group description: Participation in the study was proposed to all subjects who completed and responded to treatment in PRISM study, satisfying in eligibility criteria and were willing to continue I10E at a reduced maintenance dose. | |

| Serious adverse events | Single arm | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Renal and urinary disorders | | | |
| Urinary retention | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 5 %

| Non-serious adverse events | Single arm | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 12 / 19 (63.16%) | | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | | |
| occurrences (all) | 1 | | |
| Hypotension | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | | |
| occurrences (all) | 1 | | |

| | | | |
|---|---|---|---|
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 2 / 19 (10.53%) | | |
| occurrences (all) | 2 | | |
| Chills | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | | |
| occurrences (all) | 1 | | |
| Injection site erythema | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | | |
| occurrences (all) | 1 | | |
| Injection site oedema | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | | |
| occurrences (all) | 1 | | |
| Pain | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | | |
| occurrences (all) | 1 | | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | | |
| occurrences (all) | 2 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Nasal congestion | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | | |
| occurrences (all) | 4 | | |
| Psychiatric disorders | | | |
| Conversion disorder | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | | |
| occurrences (all) | 1 | | |
| Insomnia | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | | |
| occurrences (all) | 1 | | |
| Investigations | | | |
| Blood pressure increased | | | |
| subjects affected / exposed | 2 / 19 (10.53%) | | |
| occurrences (all) | 2 | | |
| Blood lactate dehydrogenase increased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 19 (5.26%) | | |
| occurrences (all) | 1 | | |
| Injury, poisoning and procedural complications | | | |
| Ligament sprain | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | | |
| occurrences (all) | 1 | | |
| Post-traumatic pain | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | | |
| occurrences (all) | 1 | | |
| Cardiac disorders | | | |
| Palpitations | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | | |
| occurrences (all) | 1 | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 3 / 19 (15.79%) | | |
| occurrences (all) | 5 | | |
| Migraine | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | | |
| occurrences (all) | 2 | | |
| Neuralgia | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | | |
| occurrences (all) | 1 | | |
| Sciatica | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | | |
| occurrences (all) | 1 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | | |
| occurrences (all) | 1 | | |
| Ear and labyrinth disorders | | | |
| Tinnitus | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | | |
| occurrences (all) | 1 | | |
| Gastrointestinal disorders | | | |

| | | | |
|---|---|---|---|
| Abdominal pain<br>subjects affected / exposed<br>occurrences (all) | 1 / 19 (5.26%)<br>1 | | |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all) | 1 / 19 (5.26%)<br>1 | | |
| Duodenal ulcer<br>subjects affected / exposed<br>occurrences (all) | 1 / 19 (5.26%)<br>1 | | |
| Gastritis<br>subjects affected / exposed<br>occurrences (all) | 1 / 19 (5.26%)<br>1 | | |
| Hiatus hernia<br>subjects affected / exposed<br>occurrences (all) | 1 / 19 (5.26%)<br>1 | | |
| Vomiting<br>subjects affected / exposed<br>occurrences (all) | 1 / 19 (5.26%)<br>1 | | |
| Skin and subcutaneous tissue disorders | | | |
| Dry skin<br>subjects affected / exposed<br>occurrences (all) | 1 / 19 (5.26%)<br>1 | | |
| Eczema nummular<br>subjects affected / exposed<br>occurrences (all) | 1 / 19 (5.26%)<br>1 | | |
| Erythema<br>subjects affected / exposed<br>occurrences (all) | 1 / 19 (5.26%)<br>3 | | |
| Rash pruritic<br>subjects affected / exposed<br>occurrences (all) | 1 / 19 (5.26%)<br>1 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Pain in extremity<br>subjects affected / exposed<br>occurrences (all) | 3 / 19 (15.79%)<br>3 | | |
| Arthralgia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 19 (10.53%) | | |
| occurrences (all) | 3 | | |
| Back pain | | | |
| subjects affected / exposed | 2 / 19 (10.53%) | | |
| occurrences (all) | 2 | | |
| Neck pain | | | |
| subjects affected / exposed | 2 / 19 (10.53%) | | |
| occurrences (all) | 2 | | |
| Muscle spasms | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | | |
| occurrences (all) | 1 | | |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | | |
| occurrences (all) | 1 | | |
| Tendonitis | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | | |
| occurrences (all) | 1 | | |
| Infections and infestations | | | |
| Conjunctivitis | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | | |
| occurrences (all) | 1 | | |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | | |
| occurrences (all) | 1 | | |
| Infected bite | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | | |
| occurrences (all) | 1 | | |
| Influenza | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | | |
| occurrences (all) | 2 | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | | |
| occurrences (all) | 2 | | |
| Tooth abscess | | | |
| subjects affected / exposed | 1 / 19 (5.26%) | | |
| occurrences (all) | 1 | | |

| | | | |
|---|---|---|---|
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 1 / 19 (5.26%)<br>1 | | |
| Urinary tract infection<br>subjects affected / exposed<br>occurrences (all) | 1 / 19 (5.26%)<br>2 | | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 06 January 2016 | Modification of some exclusion criteria - Removal of routine free bilirubin testing - Additional renal safety follow-up - Description of the patient population - Rules for follow-up of adverse events - Timing of safety monitoring (vital signs) - Update of IMP storage conditions.<br>This amendment led to the protocol version 4.0 dated 06 January 2016. |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date | Interruption | Restart date |
|---|---|---|
| 04 July 2017 | This study was prematurely stopped because 4 subjects relapsed among 14 enrolled and treated subjects at the time of the early assessment of study results. An increase by ≥2 points in adjusted INCAT disability score compared to baseline was observed after administration of 2, 3, 6 or 7 courses of I10E at 0.5 g/kg every 3 weeks.<br>LFB BIOTECHNOLOGIES judged that it was not acceptable to continue the study due to the magnitude of nonresponders at this lower dose corresponding to 50% decrease compared to the standard maintenance dose of 1.0 g/kg (every 3 weeks +/- 7 days) used in PRISM study. Subjects prematurely withdrawn from the study were to be managed at the discretion of the investigators. | - |

Notes:

## Limitations and caveats

None reported