Clinical trial results:
An international, multicentre, efficacy and safety study of I10E in initial and maintenance treatment of patients with Chronic Inflammatory Demyelinating Polyradiculoneuropathy.

Summary

EudraCT number	2013-005557-73
Trial protocol	GB ES IT FR DE
Global end of trial date	29 September 2017

Results information

Result version number	v1 (current)
This version publication date	15 January 2020
First version publication date	15 January 2020

Trial information

Trial identification

Sponsor protocol code	I10E-1302

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 1 69 82 70 10,
Scientific contact	Global Clinical Development Leader , LFB BIOTECHNOLOGIES, +33 1 69 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 December 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 September 2017
Global end of trial reached?	Yes
Global end of trial date	29 September 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to assess the efficacy of I10E in improving the disability of patients with CIDP.

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	24 February 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	Tunisia: 8
Country: Number of subjects enrolled	Turkey: 3
Country: Number of subjects enrolled	Poland: 8
Country: Number of subjects enrolled	Spain: 6
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Italy: 16
Worldwide total number of subjects	44
EEA total number of subjects	33

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)	32
From 65 to 84 years	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Between 24 Feb 2015 and 22 Mar 2017, 59 subjects from 23 sites signed an informed consent.

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	59[1]
Number of subjects completed	43

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Consent withdrawn by subject: 1
Reason: Number of subjects	Screening failure: 15

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: 59 subjects signed an informed consent in the pre-assigment period.
Among them, 18 subjects were considered as a screening failure including 3 subjects re-screened and finally enrolled.
Of 44 enrolled subjects, one subject was discontinued (consent withdrawn by subject) from the study before the first administration of study drug.

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:

This study included patients never previously treated with IgG and patients already treated with IgG but in clinical relapse following IgG therapy discontinuation.

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:

I10E (study drug) was administered at 2 g/kg over 2 to 5 days for the first course, then at 1 g/kg over 1 to 2 days for 7 additional courses at 3-week intervals.
Study drug was administered intravenously, with an infusion pump (B-Braun Infusomat Space).

Number of subjects in period 1[2]	Single arm
Started	43
Completed	37
Not completed	6
Consent withdrawn by subject	1
Adverse event, non-fatal	2
Lack of efficacy	2
Protocol deviation	1

Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Of 44 enrolled subjects, one patient was discontinued (consent withdrawn by subject) from the study before the first administration of study drug.

Baseline characteristics

Reporting groups

Reporting group title	Treatment period

Reporting group description: -

Reporting group values	Treatment period	Total	
Number of subjects	43	43	
Age categorical Units: Subjects			
18 years and more	43	43	
Age continuous Units: years median full range (min-max)	 50.0 21 to 79	 -	
Gender categorical Units: Subjects			
Female	19	19	
Male	24	24	

Subject analysis sets

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

Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis

Subject analysis set description:

All TTS patients having an available assessment of the primary efficacy criteria.

Reporting group values	Total Treated Set	Full Analysis Set	
Number of subjects	43	42	
Age categorical Units: Subjects			
18 years and more	43	42	
Age continuous Units: years median full range (min-max)	 50.0 21 to 79	 50.0 21 to 79	
Gender categorical Units: Subjects			
Female	19	18	
Male	24	24	

End points

End points reporting groups

Reporting group title	Single arm

Reporting group description:

This study included patients never previously treated with IgG and patients already treated with IgG but in clinical relapse following IgG therapy discontinuation.

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

Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis

Subject analysis set description:

All TTS patients having an available assessment of the primary efficacy criteria.

Primary: Responder Rate

End point title	Responder Rate[1]

End point description:

The primary efficacy endpoint was the responder rate at End of Study (EoS). Responders were defined as patients with a decrease ≥1 point in the adjusted INCAT disability score compared to baseline.
If a patient was treated with a not-allowed treatment during the study period, then all adjusted INCAT disability score measured after the intake of these not-allowed treatments were censored.
If the score at EoS visit was missing, then the Last Observation Carried Forward (LOCF) approach was applied to replace this missing value.

End point type	Primary

End point timeframe:

During treatment period the adjusted INCAT disability score was evaluated at week 3, week 6, week 9, week 12, week 15, week 18, week 21, week 24 (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: For this single-arm study, the response rate was tested against the historical response rate of 33.3% with a 1-sided Clopper-Pearson exact test at the nominal level of significance of 2.5% on the Full Analysis Set. The null and alternative hypotheses were as follows:
H0: pI10E <= 33.3%
H1: pI10E > 33.3%
The estimate of the response rate was 76.2% (Exact 2-sided 95% Clopper-Pearson CI[60.5%;87.9%]).
The p-value of the 1-sided Clopper-Pearson exact test was < 0.0001.

End point values	Full Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	42			
Units: Subjects	32			

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	Total treated Set

Reporting group description: -

Serious adverse events	Total treated Set		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 43 (16.28%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Investigations			
Fibrin D dimer increased			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colorectal adenocarcinoma			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Synovial rupture			

subjects affected / exposed	1 / 43 (2.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Transient ischaemic attack			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Pancreatitis acute			
subjects affected / exposed	1 / 43 (2.33%)		
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	Total treated Set		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	39 / 43 (90.70%)		
Nervous system disorders			

Headache			
subjects affected / exposed	20 / 43 (46.51%)		
occurrences (all)	79		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	8 / 43 (18.60%)		
occurrences (all)	11		
Asthenia			
subjects affected / exposed	4 / 43 (9.30%)		
occurrences (all)	4		
Chills			
subjects affected / exposed	3 / 43 (6.98%)		
occurrences (all)	10		
Malaise			
subjects affected / exposed	3 / 43 (6.98%)		
occurrences (all)	5		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 43 (6.98%)		
occurrences (all)	3		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	3 / 43 (6.98%)		
occurrences (all)	5		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	5 / 43 (11.63%)		
occurrences (all)	6		
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	3 / 43 (6.98%)		
occurrences (all)	3		
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	3 / 43 (6.98%)		
occurrences (all)	4		
Rash			

subjects affected / exposed occurrences (all)	3 / 43 (6.98%) 3		
Musculoskeletal and connective tissue disorders Myalgia subjects affected / exposed occurrences (all) Arthralgia subjects affected / exposed occurrences (all)	 5 / 43 (11.63%) 5 4 / 43 (9.30%) 6		
Infections and infestations Influenza subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	 8 / 43 (18.60%) 10 5 / 43 (11.63%) 5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 March 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 This Amendment led to protocol version 5.0 dated 06 January 2016

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported