



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
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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
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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
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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
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Reporting group description: -

Reporting group values	Treatment period	Total	
Number of subjects	19	19	
Age categorical			
Units: Subjects			
Adults (18-79 years)	19	19	
Age continuous			
Units: years			
median	50.0		
full range (min-max)	24 to 79	-	
Gender categorical			
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
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.1
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Reporting groups

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

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