Clinical trial results:
A Multicentre Phase III Study on the Efficacy, Safety and Pharmacokinetics of LFB-IgSC in Patients with Primary Immunodeficiency (PID) Syndromes.

Summary

EudraCT number	2013-000620-34
Trial protocol	IT HU DE GB
Global end of trial date	14 March 2014

Results information

Result version number	v1 (current)
This version publication date	30 June 2016
First version publication date	18 July 2015

Trial information

Trial identification

Sponsor protocol code	IGSC-1103

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 - BP 40305 - LES ULIS, COUTABOEUF CEDEX, France, 91930
Public contact	Global Clinical Development Leader, LFB Biotechnologies, +33 169825656,
Scientific contact	Global Clinical Development Leader, LFB Biotechnologies, +33 169825656,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001290-PIP01-12
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	17 October 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 March 2014
Global end of trial reached?	Yes
Global end of trial date	14 March 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to assess the efficacy of LFB-IgSC.

Protection of trial subjects:

The following non-inclusion criteria were aimed to avoid or minimise some potentially serious adverse reactions that have been described with immunoglobulins:
• Patients with known anti-IgA antibodies will be excluded. Patients with history of severe allergic reaction to any IVIg, SCIg or an excipient of LFB-IgSC should not be included.
• Patients aged over 70 or with a history of cardiac ischemia, cerebral ischemia, stroke, thrombotic episodes or pulmonary embolism should not be included.
• Patients with renal insufficiency (glomerular filtration rate < 80 ml/min/1.73m2) should not be included.
A Data and Safety Monitoring Board was set-up to evaluate the safety data of the first 3 administrations in the first 5 adult patients and provide recommendations on whether to proceed with the inclusion of the following patients, including the paediatric population subset.

Background therapy:

Not applicable

Evidence for comparator: -

Actual start date of recruitment	30 October 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Hungary: 4
Worldwide total number of subjects	6
EEA total number of subjects	6

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)	5
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Between 24 October 2013 and 5 November 2013, 6 adult patients signed an informed consent form at 3 investigational sites.

Pre-assignment

Screening details:

All the screened patients (i.e. 6 adult patients) have been included and have received the study drug.

Period 1

Period 1 title	Baseline
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Single arm

Arm description: -

Arm type	Experimental
Investigational medicinal product name	LFB-IGSC
Investigational medicinal product code	LFB-IGSC
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

LFB-IgSC is a solution of human normal immunoglobulin for subcutaneous infusion, concentrated at 250 mg/ml.

Number of subjects in period 1	Single arm
Started	6
Completed	6

Period 2

Period 2 title	Treatment period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Single arm

Arm description:

LFB-IgSC was administered once a week, at regular intervals of 7 days ± 1 day.
The administered dose was be equivalent to the dose received by the patients before the study. In other words, the weekly dose of LFB-IgSC was calculated as follows:
• Patients who previously received IVIg infusions every 4 weeks, received a quarter of their IV infusion dose
• Patients who previously received IVIg infusions every 3 weeks, received a third of their IV infusion dose
• Patients who previously received SCIg weekly, received the same dose of LFB-IgSC

Arm type	Experimental
Investigational medicinal product name	LFB-IGSC
Investigational medicinal product code	LFB-IGSC
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

LFB-IgSC is a solution of human normal immunoglobulin for subcutaneous infusion, concentrated at 250 mg/ml.

Number of subjects in period 2	Single arm
Started	6
Completed	0
Not completed	6
Adverse event, non-fatal	2
Study premature termination for safety reason	4

Baseline characteristics

Reporting groups

Reporting group title	Baseline

Reporting group description: -

Reporting group values	Baseline	Total	
Number of subjects	6	6	
Age categorical Units: Subjects			
Adults 18-70 years	6	6	
Age continuous Units: years			
arithmetic mean	46		
full range (min-max)	25 to 69	-	
Gender categorical Units: Subjects			
Female	4	4	
Male	2	2	

Subject analysis sets

Subject analysis set title	Total treated set
Subject analysis set type	Full analysis

Subject analysis set description:
Descriptive analysis

Reporting group values	Total treated set		
Number of subjects	6		
Age categorical Units: Subjects			
Adults 18-70 years	6		
Age continuous Units: years			
arithmetic mean	46		
full range (min-max)	25 to 69		
Gender categorical Units: Subjects			
Female	4		
Male	2		

End points

End points reporting groups

Reporting group title	Single arm
Reporting group description: -	
Reporting group title	Single arm

Reporting group description:

LFB-IgSC was administered once a week, at regular intervals of 7 days ± 1 day.
The administered dose was be equivalent to the dose received by the patients before the study. In other words, the weekly dose of LFB-IgSC was calculated as follows:
• Patients who previously received IVIg infusions every 4 weeks, received a quarter of their IV infusion dose
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• Patients who previously received SCIg weekly, received the same dose of LFB-IgSC

Subject analysis set title	Total treated set
Subject analysis set type	Full analysis

Subject analysis set description:

Descriptive analysis

Primary: number of serious bacterial infections (SBI)

End point title	number of serious bacterial infections (SBI)[1]

End point description:

No SBI was observed during the study. However, this result is of limited value due to the low number of included patients and the short duration of patient follow-up. The 98% confidence interval of the rate of SBI per patient and per year is [0.00 – 2.94].

End point type	Primary

End point timeframe:

from November 2013 to March 2014

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: Descriptive analyses

End point values	Total treated set			
Subject group type	Subject analysis set			
Number of subjects analysed	6			
Units: SBI per patient and per year	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From November 2013 to March 2014

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Single arm

Reporting group description: -

Serious adverse events	Single arm		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 6 (16.67%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
General disorders and administration site conditions			
infusion site reaction	Additional description: Ulcerated skin lesions at the infusion site		
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	2 / 2		
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	6 / 6 (100.00%)		
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	11		
General disorders and administration site conditions			
Infusion site reaction	Additional description: Infusion site reactions were made of one or several signs/symptoms, including swelling, erythema, nodule, pruritus, pain, hematoma, papule, vesicle, ulcer, necrosis, discoloration.		

subjects affected / exposed occurrences (all)	6 / 6 (100.00%) 155		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
14 March 2014	In early March 2014, LFB made the decision to prematurely stop the study due to adverse local reactions. The last visit of the last patient was performed on 14 March 2014.	-

Notes:

Limitations and caveats

None reported