Clinical trial results:
LONG-TERM SAFETY AND EFFICACY STUDY OF IGNG, A NEW LIQUID PREPARATION OF HUMAN NORMAL IMMUNOGLOBULIN FOR INTRAVENOUS USE, ADMINISTERED IN CURRENT PRACTICE TO PRIMARY IMMUNODEFICIENT PATIENTS

Summary

EudraCT number	2007-001410-17
Trial protocol	FR
Global end of trial date	28 January 2011

Results information

Result version number	v1 (current)
This version publication date	30 June 2016
First version publication date	04 October 2014

Trial information

Trial identification

Sponsor protocol code	IGNG-0629

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, COURTABOEUF, France, 91958
Public contact	Anne HUFSCHMITT, LFB Biotechnologies, 33 169827014,
Scientific contact	Anne HUFSCHMITT, LFB Biotechnologies, 33 169827014,

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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	20 June 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 January 2011
Global end of trial reached?	Yes
Global end of trial date	28 January 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to assess the clinical and biological safety of IGNG by considering adverse events in patients treated for their primary immunodeficiency as per current practice over at least a 2-year-period.

Protection of trial subjects:

Patients will be followed in this study in conditions corresponding to the current practice of the investigational centres, which are familiar in treating patients with human normal immunoglobulins for PID. Patients will benefit from IGNG administered in the same conditions and by the same medical staff as in current practice. Consequently, the study does not contain additional risk.

Background therapy:

Not applicable

Evidence for comparator:

No comparator.

Actual start date of recruitment	13 June 2007
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	31 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 23
Worldwide total number of subjects	23
EEA total number of subjects	23

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)	6
Adults (18-64 years)	17
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Between 13 June 2007 and 17 June 2008, 23 patients (17 adults and 6 adolescents) were included in 10 French investigational sites.

Pre-assignment

Screening details:

Patients who met all the inclusion criteria and none of the exclusion criteria were included in this clinical trial after their informed consent was signed. In females of childbearing potential, a negative pregnancy test had to be obtained before inclusion.

Period 1

Period 1 title	Inclusion visit or visit 0
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	IGNG (ClairYg)

Arm description:

All patients

Arm type	Experimental
Investigational medicinal product name	ClairYg
Investigational medicinal product code	IGNG
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

The treatment dose and schedule were set by investigators, based on their common clinical practice, but between 0.2 and 0.8 g/kg every 3 or 4 weeks.

Number of subjects in period 1	IGNG (ClairYg)
Started	23
Completed	23

Period 2

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

Arms

Arm title	IGNG (Clairyg)

Arm description:

All the patients received the experimental product.

Arm type	Experimental
Investigational medicinal product name	Clairyg
Investigational medicinal product code	IGNG
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

The doses recommended in the protocol could vary depending on the patient and were between 0.2 and 0.8 g/kg administered every 3 or 4 weeks.

Number of subjects in period 2	IGNG (Clairyg)
Started	23
Completed	16
Not completed	7
Consent withdrawn by subject	5
Adverse event, non-fatal	2

Period 3

Period 3 title	End of study visit
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	IGNG (ClairYg)

Arm description:

All patients in the same arm

Arm type	Experimental
Investigational medicinal product name	ClairYg
Investigational medicinal product code	IGNG
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

The doses recommended in the protocol could vary depending on the patient and were between 0.2 and 0.8 g/kg administered every 3 or 4 weeks.

Number of subjects in period 3	IGNG (ClairYg)
Started	16
Completed	16

Baseline characteristics

Reporting groups

Reporting group title	Inclusion visit or visit 0

Reporting group description: -

Reporting group values	Inclusion visit or visit 0	Total	
Number of subjects	23	23	
Age categorical			
2 different subject categories: adolescents and adults			
Units: Subjects			
Adolescents (12-17 years)	6	6	
Adults (18-64 years)	17	17	
Age continuous			
We do not understand what is required here.			
Units: years			
arithmetic mean	34.4		
standard deviation	± 16.2	-	
Gender categorical			
Units: Subjects			
Female	11	11	
Male	12	12	

Subject analysis sets

Subject analysis set title	Total Treated Set (TTS)
Subject analysis set type	Full analysis

Subject analysis set description:

Tthe Total Treated Set (TTS) includes all patients who received at least one infusion of the investigational drug.
All of the analyses were performed on this population.

Reporting group values	Total Treated Set (TTS)		
Number of subjects	23		
Age categorical			
2 different subject categories: adolescents and adults			
Units: Subjects			
Adolescents (12-17 years)	6		
Adults (18-64 years)	17		
Age continuous			
We do not understand what is required here.			
Units: years			
arithmetic mean	34.4		
standard deviation	± 16.2		
Gender categorical			
Units: Subjects			
Female	11		
Male	12		

End points

End points reporting groups

Reporting group title	IGNG (ClairYg)
Reporting group description:	
All patients	
Reporting group title	IGNG (Clairyg)
Reporting group description:	
All the patients received the experimental product.	
Reporting group title	IGNG (ClairYg)
Reporting group description:	
All patients in the same arm	
Subject analysis set title	Total Treated Set (TTS)
Subject analysis set type	Full analysis
Subject analysis set description:	
Tthe Total Treated Set (TTS) includes all patients who received at least one infusion of the investigational drug. All of the analyses were performed on this population.	

Primary: number of adverse events

End point title	number of adverse events[1]
End point description:	
All adverse events, disregarding if they are related to study drug or not.	
End point type	Primary
End point timeframe:	
troughout the 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: descriptive analysis

End point values	IGNG (Clairyg)	Total Treated Set (TTS)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	23	23		
Units: number	333	333		

Statistical analyses

No statistical analyses for this end point

Secondary: Annual rate of serious bacterial infection

End point title	Annual rate of serious bacterial infection
End point description:	

End point type	Secondary
End point timeframe:	
throughout the study	

End point values	IGNG (Clairyg)	Total Treated Set (TTS)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	23[2]	23		
Units: annual rate				
arithmetic mean (confidence interval 98%)	0.05 (0.01 to 0.17)	0.05 (0.01 to 0.17)		

Notes:

[2] - Annual rate is calculated using the exact Poisson test

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

overall the study

Adverse event reporting additional description:

For non-serious adverse events only most common adverse events (occurence > 5) are reporting here.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	9.1

Reporting groups

Reporting group title	All patients

Reporting group description: -

Serious adverse events	All patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 23 (47.83%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
probable lymph node infection with atypical mycobacterium			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Splenomegaly	Additional description: aggravated		
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Anaphylactic shock	Additional description: Related (Probable)		

subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Superinfection of the eardrum			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Cataract	Additional description: aggravation of cataract		
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Inguinal hernia			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal pain			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis	Additional description: Severe		
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Mastoiditis			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Atelectasis			

subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Chronic respiratory disease	Additional description: chronic respiratory insufficiency		
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory distress			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary hypertension			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 1		
Asthma			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia pneumococcal			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Superinfection	Additional description: bronchial superinfection		
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchiectasis			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cirrhosis	Additional description: Decompensated cirrhosis		

subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Liver disorder			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatitis chronic active			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Pyelonephritis			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
kidney failure			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal failure chronic	Additional description: Related (Dubious)		
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal failure acute			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue			

disorders			
retractile capsulitis of the shoulder			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Sinusitis	Additional description: acute		
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
left purulent lynphadenitis			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Implant site infection			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Superinfection of the molluscum			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0.45 %

Non-serious adverse events	All patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 23 (100.00%)		
Vascular disorders			
Epistaxis			
subjects affected / exposed	5 / 23 (21.74%)		
occurrences (all)	13		
General disorders and administration site conditions			
Asthenia			

subjects affected / exposed	6 / 23 (26.09%)		
occurrences (all)	12		
Hyperthermia			
subjects affected / exposed	4 / 23 (17.39%)		
occurrences (all)	5		
Pain at the administration site			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	8		
Pain			
subjects affected / exposed	3 / 23 (13.04%)		
occurrences (all)	16		
Headache			
subjects affected / exposed	3 / 23 (13.04%)		
occurrences (all)	10		
Pruritus			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	7		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	5 / 23 (21.74%)		
occurrences (all)	8		
uper abdominal pain			
subjects affected / exposed	5 / 23 (21.74%)		
occurrences (all)	5		
Diarrhoea	Additional description: non infectious		
subjects affected / exposed	5 / 23 (21.74%)		
occurrences (all)	9		
Gastrointestinal disorder			
subjects affected / exposed	3 / 23 (13.04%)		
occurrences (all)	5		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	7		
Musculoskeletal and connective tissue disorders			

Joint pain subjects affected / exposed occurrences (all)	4 / 23 (17.39%) 15		
Back pain subjects affected / exposed occurrences (all)	7 / 23 (30.43%) 10		
Pain in the extremities subjects affected / exposed occurrences (all)	5 / 23 (21.74%) 13		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 October 2007	The Sponsor's name is changed from LFB SA to LFB Biotechnologies.
08 February 2008	This amendment has been mainly put forward in order to open paediatric Investigational centres. It also includes an additional adult Investigational centre to increase the number of adult patients. Consequently, the recruitment period, which ought to end on 31st of December 2007, will be extended to 30th June 2008. Therefore, the recruitment period will last 1 year instead of 6 months initially scheduled.
12 February 2009	In the initial protocol, the study duration for each patient was 2 years. This amendment extends the study until the product is marketed. An additional consent form will be signed by the patients if they want to continue the study until the product is marketed. Patient's assurance will be extended accordingly.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported