Clinical trial results:
Double-Blind Placebo-Controlled Randomized Phase 2 Study of IPH2102 as Maintenance Treatment in Elderly patients with Acute Myeloid Leukemia (AML) in First Complete Remission

Summary

EudraCT number	2012-001594-93
Trial protocol	FR
Global end of trial date	17 November 2016

Results information

Result version number	v1 (current)
This version publication date	06 January 2018
First version publication date	06 January 2018

Trial information

Trial identification

Sponsor protocol code	IPH2102-201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01687387
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Innate Pharma
Sponsor organisation address	117 avenue de Luminy, Marseille, France, 13009
Public contact	Medical Director, Innate Pharma, 33 (0)430 30 30 30, info@innate-pharma.fr
Scientific contact	Medical Director, Innate Pharma, 33 (0)430 30 30 30, info@innate-pharma.fr

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	20 December 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 November 2016
Global end of trial reached?	Yes
Global end of trial date	17 November 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of IPH2102 administered in patients with AML in first complete remission

Protection of trial subjects:

Information providing the common features of the research were given to patients themselves.
Restraints and risks were explained, as well as the right to refuse or discontinue their participation in the study at any stage, without further affecting the relationship with the investigator and/or their future care.
An independent Data and Safety Monitoring Board reviewed the safety data every 6 months.
This study was performed in accordance with the principles stated in the Declaration of Helsinki adopted by the World Medical Association and in accordance with the International Conference of Harmonization (ICH) guidelines on Good Clinical Practice (GCP) (CPMP/ICH/135/95).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 October 2012
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: 152
Worldwide total number of subjects	152
EEA total number of subjects	152

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)	39

From 65 to 84 years	113
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

169 patients were screened and 152 patients were randomized and treated in France

Pre-assignment

Screening details:

Primary or secondary Acute Myeloid Leukemia in first CR/CRi, following induction chemotherapy and 1 or 2 consolidation cycles. Randomization was to take place within 6 months after the start of induction chemotherapy.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Lirilumab 0.1 mg/kg Q12weeks

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Lirilumab
Investigational medicinal product code	IPH2102
Other name	
Pharmaceutical forms	Solution for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1 hour infusion

Arm title	Lirilumab 1 mg/kg Q4weeks

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Lirilumab
Investigational medicinal product code	IPH2102
Other name	
Pharmaceutical forms	Solution for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1 hour infusion

Arm title	Placebo

Arm description: -

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

Dosage and administration details:

normal saline 1 hour infusion

Number of subjects in period 1	Lirilumab 0.1 mg/kg Q12weeks	Lirilumab 1 mg/kg Q4weeks	Placebo
Started	50	51	51
Completed	12	10	13
Not completed	38	41	38
Relapse	27	37	32
Consent withdrawn by subject	1	-	-
Adverse event, non-fatal	8	3	5
Investigator decision	1	-	1
Sponsor decision	1	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	152	152	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	39	39	
From 65-84 years	113	113	
85 years and over	0	0	
Age continuous Units: years			
median	70		
full range (min-max)	60 to 80	-	
Gender categorical Units: Subjects			
Female	61	61	
Male	91	91	

End points

End points reporting groups

Reporting group title	Lirilumab 0.1 mg/kg Q12weeks
Reporting group description: -	
Reporting group title	Lirilumab 1 mg/kg Q4weeks
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Primary: Leukemia Free Survival

End point title	Leukemia Free Survival

End point description:

Following DSMB decision to stop further treatment in 1 mg/kg Q4W arm, the final primary efficacy analysis consisted of a simple comparison of the remaining active arm with the placebo. So, a one-sided significance level of 0.025 was used for the comparison of the remaining active arm vs. the placebo arm. Moreover, for exploratory purpose, the comparison between the stopped active arm and the placebo will was performed using the same one-sided stratified log-rank test.

End point type	Primary

End point timeframe:

The primary endpoint is Leukemia-Free Survival (LFS) defined as the time from the date of randomization until the occurrence of a relapse, as determined by the IRC, or death from any cause

End point values	Lirilumab 0.1 mg/kg Q12weeks	Lirilumab 1 mg/kg Q4weeks	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	51	51	
Units: months				
median (confidence interval 95%)	17.6 (11.2 to 25)	6.7 (2.9 to 14.8)	13.9 (7.9 to 27.9)	

Statistical analyses

Statistical analysis title	Lirilumab 0.1 mg/kg vs placebo
Comparison groups	Lirilumab 0.1 mg/kg Q12weeks v Placebo
Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.025
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.98

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.61
upper limit	1.56
Variability estimate	Standard deviation

Statistical analysis title	Lirilumab 1 mg/kg vs Placebo
Comparison groups	Lirilumab 1 mg/kg Q4weeks v Placebo
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.025
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.88
upper limit	2.28
Variability estimate	Standard deviation

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs and SAEs were collected throughout the study from the time of patient signing the consent form until 28 days after the last administration, or until the patient's last study visit

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Lirilumab 0.1 mg/kg Q12weeks
Reporting group description: -	
Reporting group title	Lirilumab 1 mg/kg Q4weeks
Reporting group description: -	
Reporting group title	Placebo

Reporting group description: -

Serious adverse events	Lirilumab 0.1 mg/kg Q12weeks	Lirilumab 1 mg/kg Q4weeks	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 50 (34.00%)	12 / 51 (23.53%)	11 / 51 (21.57%)
number of deaths (all causes)	26	32	23
number of deaths resulting from adverse events	1	2	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	3 / 50 (6.00%)	0 / 51 (0.00%)	2 / 51 (3.92%)
occurrences causally related to treatment / all	2 / 3	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive lobular breast carcinoma			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung cancer metastatic			
subjects affected / exposed	0 / 50 (0.00%)	1 / 51 (1.96%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphoma			

subjects affected / exposed	1 / 50 (2.00%)	0 / 51 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelodysplastic syndrome			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Myxofibrosarcoma			
subjects affected / exposed	1 / 50 (2.00%)	0 / 51 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Papillary thyroid cancer			
subjects affected / exposed	1 / 50 (2.00%)	0 / 51 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Polycythaemia vera			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal adenocarcinoma			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Respiratory therapy			
subjects affected / exposed	1 / 50 (2.00%)	0 / 51 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 50 (2.00%)	0 / 51 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

General physical health deterioration			
subjects affected / exposed	2 / 50 (4.00%)	0 / 51 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	1 / 50 (2.00%)	0 / 51 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Prostatitis			
subjects affected / exposed	1 / 50 (2.00%)	0 / 51 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 50 (0.00%)	1 / 51 (1.96%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary mass			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Suicide attempt			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Biopsy spleen			
subjects affected / exposed	1 / 50 (2.00%)	0 / 51 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			

Head injury			
subjects affected / exposed	0 / 50 (0.00%)	1 / 51 (1.96%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury corneal			
subjects affected / exposed	0 / 50 (0.00%)	1 / 51 (1.96%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	0 / 50 (0.00%)	1 / 51 (1.96%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Hydrocele			
subjects affected / exposed	0 / 50 (0.00%)	1 / 51 (1.96%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 50 (0.00%)	1 / 51 (1.96%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Encephalopathy			
subjects affected / exposed	1 / 50 (2.00%)	0 / 51 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	1 / 50 (2.00%)	0 / 51 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sciatica			

subjects affected / exposed	1 / 50 (2.00%)	0 / 51 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 50 (0.00%)	1 / 51 (1.96%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	2 / 51 (3.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Chorioretinal disorder			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal wall haematoma			
subjects affected / exposed	1 / 50 (2.00%)	0 / 51 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 50 (0.00%)	1 / 51 (1.96%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Umbilical hernia			
subjects affected / exposed	1 / 50 (2.00%)	1 / 51 (1.96%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			

subjects affected / exposed	0 / 50 (0.00%)	1 / 51 (1.96%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Acute febrile neutrophilic dermatosis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Urinary incontinence			
subjects affected / exposed	1 / 50 (2.00%)	0 / 51 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention			
subjects affected / exposed	1 / 50 (2.00%)	0 / 51 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 50 (0.00%)	1 / 51 (1.96%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 50 (0.00%)	1 / 51 (1.96%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chondrocalcinosis			
subjects affected / exposed	1 / 50 (2.00%)	0 / 51 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myalgia			

subjects affected / exposed	1 / 50 (2.00%)	0 / 51 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 50 (0.00%)	1 / 51 (1.96%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Anal abscess			
subjects affected / exposed	1 / 50 (2.00%)	0 / 51 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 50 (0.00%)	1 / 51 (1.96%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	1 / 50 (2.00%)	0 / 51 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 50 (2.00%)	0 / 51 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 50 (2.00%)	0 / 51 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	1 / 50 (2.00%)	0 / 51 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Sialoadenitis			

subjects affected / exposed	1 / 50 (2.00%)	0 / 51 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal sepsis			
subjects affected / exposed	0 / 50 (0.00%)	1 / 51 (1.96%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 50 (2.00%)	0 / 51 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 50 (0.00%)	1 / 51 (1.96%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Lirilumab 0.1 mg/kg Q12weeks	Lirilumab 1 mg/kg Q4weeks	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	48 / 50 (96.00%)	38 / 51 (74.51%)	43 / 51 (84.31%)
Investigations			
Lipase increased			
subjects affected / exposed	3 / 50 (6.00%)	0 / 51 (0.00%)	0 / 51 (0.00%)
occurrences (all)	3	0	0
Weight increased			
subjects affected / exposed	5 / 50 (10.00%)	1 / 51 (1.96%)	6 / 51 (11.76%)
occurrences (all)	6	1	6
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 50 (10.00%)	2 / 51 (3.92%)	2 / 51 (3.92%)
occurrences (all)	6	2	4
Nervous system disorders			
Headache			

subjects affected / exposed	4 / 50 (8.00%)	8 / 51 (15.69%)	3 / 51 (5.88%)
occurrences (all)	9	9	5
Neuropathy peripheral			
subjects affected / exposed	3 / 50 (6.00%)	2 / 51 (3.92%)	1 / 51 (1.96%)
occurrences (all)	4	2	1
Paraesthesia			
subjects affected / exposed	6 / 50 (12.00%)	0 / 51 (0.00%)	1 / 51 (1.96%)
occurrences (all)	9	0	1
Sciatica			
subjects affected / exposed	3 / 50 (6.00%)	1 / 51 (1.96%)	0 / 51 (0.00%)
occurrences (all)	3	1	0
Anxiety			
subjects affected / exposed	2 / 50 (4.00%)	4 / 51 (7.84%)	3 / 51 (5.88%)
occurrences (all)	2	4	3
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	5 / 50 (10.00%)	3 / 51 (5.88%)	2 / 51 (3.92%)
occurrences (all)	5	3	3
Neutropenia			
subjects affected / exposed	4 / 50 (8.00%)	4 / 51 (7.84%)	5 / 51 (9.80%)
occurrences (all)	5	9	11
Thrombocytopenia			
subjects affected / exposed	7 / 50 (14.00%)	9 / 51 (17.65%)	3 / 51 (5.88%)
occurrences (all)	11	9	4
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	14 / 50 (28.00%)	14 / 51 (27.45%)	14 / 51 (27.45%)
occurrences (all)	19	20	22
Chest pain			
subjects affected / exposed	4 / 50 (8.00%)	1 / 51 (1.96%)	2 / 51 (3.92%)
occurrences (all)	4	1	2
Chills			
subjects affected / exposed	3 / 50 (6.00%)	4 / 51 (7.84%)	1 / 51 (1.96%)
occurrences (all)	4	5	2
Fatigue			

subjects affected / exposed	2 / 50 (4.00%)	5 / 51 (9.80%)	3 / 51 (5.88%)
occurrences (all)	2	5	4
Influenza like illness			
subjects affected / exposed	4 / 50 (8.00%)	2 / 51 (3.92%)	5 / 51 (9.80%)
occurrences (all)	5	2	9
Oedema peripheral			
subjects affected / exposed	2 / 50 (4.00%)	1 / 51 (1.96%)	3 / 51 (5.88%)
occurrences (all)	2	1	3
Pyrexia			
subjects affected / exposed	3 / 50 (6.00%)	6 / 51 (11.76%)	5 / 51 (9.80%)
occurrences (all)	3	6	5
Eye disorders			
Conjunctivitis			
subjects affected / exposed	0 / 50 (0.00%)	3 / 51 (5.88%)	2 / 51 (3.92%)
occurrences (all)	0	3	2
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 50 (6.00%)	3 / 51 (5.88%)	2 / 51 (3.92%)
occurrences (all)	4	3	4
Abdominal pain upper			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	3 / 51 (5.88%)
occurrences (all)	0	0	3
Constipation			
subjects affected / exposed	5 / 50 (10.00%)	2 / 51 (3.92%)	3 / 51 (5.88%)
occurrences (all)	5	4	3
Diarrhoea			
subjects affected / exposed	6 / 50 (12.00%)	7 / 51 (13.73%)	2 / 51 (3.92%)
occurrences (all)	6	8	2
Haemorrhoids			
subjects affected / exposed	1 / 50 (2.00%)	0 / 51 (0.00%)	4 / 51 (7.84%)
occurrences (all)	1	0	4
Nausea			
subjects affected / exposed	6 / 50 (12.00%)	2 / 51 (3.92%)	3 / 51 (5.88%)
occurrences (all)	6	3	3
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	2 / 50 (4.00%)	2 / 51 (3.92%)	3 / 51 (5.88%)
occurrences (all)	2	2	5
Dyspnoea			
subjects affected / exposed	1 / 50 (2.00%)	4 / 51 (7.84%)	1 / 51 (1.96%)
occurrences (all)	1	4	1
Rhinorrhoea			
subjects affected / exposed	2 / 50 (4.00%)	0 / 51 (0.00%)	3 / 51 (5.88%)
occurrences (all)	2	0	3
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	3 / 50 (6.00%)	3 / 51 (5.88%)	3 / 51 (5.88%)
occurrences (all)	3	3	3
Pruritus			
subjects affected / exposed	10 / 50 (20.00%)	8 / 51 (15.69%)	7 / 51 (13.73%)
occurrences (all)	11	9	12
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	6 / 50 (12.00%)	3 / 51 (5.88%)	5 / 51 (9.80%)
occurrences (all)	6	3	5
Arthritis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 51 (0.00%)	3 / 51 (5.88%)
occurrences (all)	0	0	3
Back pain			
subjects affected / exposed	6 / 50 (12.00%)	3 / 51 (5.88%)	7 / 51 (13.73%)
occurrences (all)	7	3	8
Muscle spasms			
subjects affected / exposed	2 / 50 (4.00%)	0 / 51 (0.00%)	3 / 51 (5.88%)
occurrences (all)	3	0	3
Musculoskeletal pain			
subjects affected / exposed	4 / 50 (8.00%)	1 / 51 (1.96%)	2 / 51 (3.92%)
occurrences (all)	4	1	2
Myalgia			
subjects affected / exposed	2 / 50 (4.00%)	0 / 51 (0.00%)	4 / 51 (7.84%)
occurrences (all)	2	0	4
Neck pain			

subjects affected / exposed	0 / 50 (0.00%)	1 / 51 (1.96%)	5 / 51 (9.80%)
occurrences (all)	0	1	6
Osteoarthritis			
subjects affected / exposed	1 / 50 (2.00%)	2 / 51 (3.92%)	6 / 51 (11.76%)
occurrences (all)	1	2	6
Infections and infestations			
Bronchitis			
subjects affected / exposed	17 / 50 (34.00%)	6 / 51 (11.76%)	14 / 51 (27.45%)
occurrences (all)	20	9	15
Gastroenteritis			
subjects affected / exposed	4 / 50 (8.00%)	1 / 51 (1.96%)	3 / 51 (5.88%)
occurrences (all)	5	1	4
Nasopharyngitis			
subjects affected / exposed	6 / 50 (12.00%)	2 / 51 (3.92%)	6 / 51 (11.76%)
occurrences (all)	6	2	7
Oral herpes			
subjects affected / exposed	2 / 50 (4.00%)	0 / 51 (0.00%)	3 / 51 (5.88%)
occurrences (all)	2	0	3
Pharyngitis			
subjects affected / exposed	3 / 50 (6.00%)	0 / 51 (0.00%)	1 / 51 (1.96%)
occurrences (all)	3	0	1
Rhinitis			
subjects affected / exposed	3 / 50 (6.00%)	0 / 51 (0.00%)	2 / 51 (3.92%)
occurrences (all)	3	0	2
Urinary tract infection			
subjects affected / exposed	2 / 50 (4.00%)	2 / 51 (3.92%)	5 / 51 (9.80%)
occurrences (all)	8	4	7

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 September 2013	Addition of a biological ancillary study for volunteer patients

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Following DSMB meeting recommendation to stop further treatment for ongoing patients in lirilumab 1 mg/kg, the primary efficacy analysis was performed on the placebo and 0.1 mg/kg arms, with the alpha error decreased to 2.5% and the power to 55%.

Notes: