Clinical trial results:
An Open-Label, Randomized, Parallel Group Study Assessing the Immunogenicity and Safety of Sarilumab Administered as Monotherapy in Patients With Active Rheumatoid Arthritis

Summary

EudraCT number	2013-002790-22
Trial protocol	HU CZ EE
Global end of trial date	26 May 2015

Results information

Result version number	v1 (current)
This version publication date	09 June 2016
First version publication date	09 June 2016

Trial information

Trial identification

Sponsor protocol code	EFC13752

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02121210
WHO universal trial number (UTN)	U1111-1143-4344

Notes:

Sponsors

Sponsor organisation name	Sanofi aventis recherche & développement
Sponsor organisation address	1 avenue Pierre Brossolette, Chilly-Mazarin, France, 91380
Public contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com

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	01 June 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 May 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the immunogenicity of sarilumab administered as monotherapy from baseline to Week 24.

Protection of trial subjects:

Subjects were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the subject and considering the local culture. During the course of the trial, subjects were provided with individual subject cards indicating the nature of the trial the subject is participating, contact details and any information needed in the event of a medical emergency.
Collected personal data and human biological samples were processed in compliance with the Sanofi-Aventis Group Personal Data Protection Charter ensuring that the Group abides by the laws governing personal data protection in force in all countries in which it operates.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 June 2014
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	Poland: 17
Country: Number of subjects enrolled	Czech Republic: 14
Country: Number of subjects enrolled	Estonia: 13
Country: Number of subjects enrolled	Hungary: 18
Country: Number of subjects enrolled	Chile: 8
Country: Number of subjects enrolled	Russian Federation: 24
Country: Number of subjects enrolled	United States: 38
Worldwide total number of subjects	132
EEA total number of subjects	62

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)	105
From 65 to 84 years	27
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 27 centres in 7 countries. A total of 201 subjects were screened between 03 June 2014 and 20 October 2014.

Pre-assignment

Screening details:

Of 201 subjects, 69 subjects were screen failures due to exclusion criteria met and inclusion criteria not met. 132 subjects were randomized in 1:1 ratio to either sarilumab 150 mg every two weeks (q2w) or sarilumab 200 mg q2w.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Sarilumab 150 mg q2w

Arm description:

Sarilumab 150 mg q2w for 24 weeks.

Arm type	Experimental
Investigational medicinal product name	Sarilumab
Investigational medicinal product code	SAR153191 (REGN88)
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injection in the abdomen, thigh or upper arm.

Arm title	Sarilumab 200 mg q2w

Arm description:

Sarilumab 200 mg q2w for 24 weeks.

Arm type	Experimental
Investigational medicinal product name	Sarilumab
Investigational medicinal product code	SAR153191 (REGN88)
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injection in the abdomen, thigh or upper arm.

Number of subjects in period 1	Sarilumab 150 mg q2w	Sarilumab 200 mg q2w
Started	65	67
Completed	58	58
Not completed	7	9
Other than specified above	-	2
Adverse Event	5	7
Lack of efficacy	2	-

Baseline characteristics

Reporting groups	
Reporting group title	Sarilumab 150 mg q2w
Reporting group description: Sarilumab 150 mg q2w for 24 weeks.	
Reporting group title	Sarilumab 200 mg q2w
Reporting group description: Sarilumab 200 mg q2w for 24 weeks.	

Reporting group values	Sarilumab 150 mg q2w	Sarilumab 200 mg q2w	Total
Number of subjects	65	67	132
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	51.1	53.6	
standard deviation	± 12.7	± 14.1	-
Gender categorical Units: Subjects			
Female	49	57	106
Male	16	10	26

End points

End points reporting groups

Reporting group title	Sarilumab 150 mg q2w
Reporting group description: Sarilumab 150 mg q2w for 24 weeks.	
Reporting group title	Sarilumab 200 mg q2w
Reporting group description: Sarilumab 200 mg q2w for 24 weeks.	

Primary: Percentage of Subjects With Incidence of Antidrug Antibodies (ADA)

End point title	Percentage of Subjects With Incidence of Antidrug Antibodies (ADA)[1]

End point description:

ADA to sarilumab and anti-sarilumab neutralizing antibodies in serum samples were determined using a validated electrochemiluminescence immunoassay method. Percentage of subjects with positive ADA during treatment emergent adverse event (TEAE) period (time from first dose of investigational medicinal product [IMP] to last dose of IMP + 60 days) was determined. Persistent ADA Response: treatment-emergent ADA detected at 2 or more consecutive sampling time points during the TEAE period, where the first and last ADA positive samples were separated by a period of at least 16 weeks or if the last measured sample was positive. ADA samples were collected prior to IMP administration at Week 0 (baseline), Week 2, 4, 12, 24 and 30. Analysis was performed on immunogenicity population included all randomized subjects who received at least one dose of sarilumab with at least one post-dose, evaluable ADA sample.

End point type	Primary

End point timeframe:

From Baseline to Week 30 [End of study (EOS)]

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: Only descriptive statistics are provided for this endpoint.

End point values	Sarilumab 150 mg q2w	Sarilumab 200 mg q2w		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	66		
Units: Percentage of subjects				
number (not applicable)				
Overall positive	24.6	18.2		
Persistent positive	12.3	6.1		
Persistent neutralizing positive	10.8	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Sarilumab Concentration

End point title	Serum Sarilumab Concentration

End point description:

Trough concentration (Ctrough). Analysis was performed on pharmacokinetics (PK) population consisted of all randomized population actually received at least one or partial dose of IMP, with at least one post-dose, non-missing serum sarilumab concentration. Number of subjects analyzed=subjects with serum sarilumab concentration assessment at specified time-points.

End point type	Secondary

End point timeframe:

Pre-dose at Week 0 (Baseline), 2, 4, 12, 16, 20, 24 and 30

End point values	Sarilumab 150 mg q2w	Sarilumab 200 mg q2w		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	52		
Units: ng/mL				
arithmetic mean (standard deviation)	7350 (± 8030)	17200 (± 15900)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All adverse events (AEs) were collected from signature of the informed consent form up to the final visit (Week 30) regardless of seriousness or relationship to investigational product.

Adverse event reporting additional description:

Reported adverse events are treatment emergent adverse events that is AEs that developed/worsened during the time from the first dose of IMP to last dose of IMP + 60 days.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Sarilumab 150 mg q2w

Reporting group description:

Sarilumab 150 mg q2w for 24 weeks.

Reporting group title	Sarilumab 200 mg q2w

Reporting group description:

Sarilumab 200 mg q2w for 24 weeks.

Serious adverse events	Sarilumab 150 mg q2w	Sarilumab 200 mg q2w	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 65 (1.54%)	2 / 67 (2.99%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Laceration			
subjects affected / exposed	0 / 65 (0.00%)	1 / 67 (1.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 65 (0.00%)	1 / 67 (1.49%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Osteoarthritis			

subjects affected / exposed	1 / 65 (1.54%)	0 / 67 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Sarilumab 150 mg q2w	Sarilumab 200 mg q2w	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 65 (24.62%)	23 / 67 (34.33%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 65 (0.00%)	4 / 67 (5.97%)	
occurrences (all)	0	4	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	8 / 65 (12.31%)	11 / 67 (16.42%)	
occurrences (all)	12	19	
General disorders and administration site conditions			
Injection Site Erythema			
subjects affected / exposed	5 / 65 (7.69%)	2 / 67 (2.99%)	
occurrences (all)	6	3	
Infections and infestations			
Upper Respiratory Tract Infection			
subjects affected / exposed	3 / 65 (4.62%)	4 / 67 (5.97%)	
occurrences (all)	5	4	
Urinary Tract Infection			
subjects affected / exposed	2 / 65 (3.08%)	4 / 67 (5.97%)	
occurrences (all)	2	4	

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? No

Limitations and caveats

None reported