Clinical trial results:
A safety open-label study of Gevokizumab in the treatment of patients with chronic non-infectious Uveitis disease, an eXtension study. The EYEGUARD-X study.

Summary

EudraCT number	2013-004973-29
Trial protocol	DE GB IT PT ES AT GR
Global end of trial date	02 November 2015

Results information

Result version number	v1 (current)
This version publication date	18 September 2016
First version publication date	18 September 2016

Trial information

Trial identification

Sponsor protocol code	CL3-78989-019

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02375685
WHO universal trial number (UTN)	U1111-1151-7937

Notes:

Sponsors

Sponsor organisation name	Institut de Recherches Internationales Servier
Sponsor organisation address	50 rue Carnot, Suresnes, France,
Public contact	Clinical Studies Department, Institut de Recherches Internationales Servier, +33 155 72 43 66, clinicaltrials@servier.com
Scientific contact	Clinical Studies Department, Institut de Recherches Internationales Servier, +33 155 72 43 66, clinicaltrials@servier.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	02 November 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 November 2015
Global end of trial reached?	Yes
Global end of trial date	02 November 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The objective of this study is to evaluate long-term safety of gevokizumab in patient with chronic non-infectious uveitis who previously well tolerated the study drug and may benefit from longterm treatment with gevokizumab

Protection of trial subjects:

This study was conducted in accordance with Good Clinical Practice standards, ethical principles stated in the Declaration of Helsinki and applicable regulatory requirements. After the subject has ended his/her participation in the trial, the investigator provided appropriate medication and/or arranged access to appropriate care for the patient.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 August 2014
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	Portugal: 1
Country: Number of subjects enrolled	Spain: 10
Country: Number of subjects enrolled	Austria: 4
Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	Germany: 6
Country: Number of subjects enrolled	Greece: 3
Country: Number of subjects enrolled	Italy: 4
Country: Number of subjects enrolled	Australia: 3
Country: Number of subjects enrolled	Korea, Republic of: 18
Country: Number of subjects enrolled	Taiwan: 15
Country: Number of subjects enrolled	Tunisia: 2
Country: Number of subjects enrolled	Turkey: 8
Worldwide total number of subjects	77
EEA total number of subjects	31

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)	76
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

To be eligible, all subjects were to have chronic non-infectious uveitis disease, and to have completed the study CL3-78989-002 (EYEGUARD™-B), or X052130/CL3-78989-005 (EYEGUARD™-A) or X052131/CL3-78989-006 (EYEGUARD™-C), or were receiving a gevokizumab treatment as compassionate use.

Pre-assignment period milestones

Number of subjects started	77
Number of subjects completed	

Period 1

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

Arms

Arm title	Gevokizumab 60 mg
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Gevokizumab
Investigational medicinal product code	S78989
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

planned: one dose of gevokizumab 60 mg every 4 weeks from Week 0 up to Week 92

Number of subjects in period 1	Gevokizumab 60 mg
Started	77
Completed	0
Not completed	77
non-medical reason	5
Adverse event, non-fatal	1
study discontinuation	71

Baseline characteristics

Reporting groups	
Reporting group title	treatment period

Reporting group description: -

Reporting group values	treatment period	Total	
Number of subjects	77	77	
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)	76	76	
From 65-84 years	1	1	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	40.7		
standard deviation	± 12.9	-	
Gender categorical Units: Subjects			
Female	38	38	
Male	39	39	

End points

End points reporting groups

Reporting group title	Gevokizumab 60 mg
Reporting group description: -	
Subject analysis set title	safety set
Subject analysis set type	Safety analysis
Subject analysis set description:	
All patients having taken at least one dose of IMP.	

Primary: Number of patients with at least one adverse event

End point title	Number of patients with at least one adverse event[1]
End point description:	
End point type	Primary
End point timeframe:	
Throughout 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 was planned for this endpoint

End point values	Gevokizumab 60 mg	safety set		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	77	77		
Units: number of patients	42	42		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All adverse events reported during the study (from W0 to the last visit) were taken into account.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Gevokizumab 60 mg

Reporting group description: -

Serious adverse events	Gevokizumab 60 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 77 (14.29%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Investigations			
Intraocular pressure increased			
subjects affected / exposed	1 / 77 (1.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Mycobacterium tuberculosis complex test positive			
subjects affected / exposed	1 / 77 (1.30%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Weight decreased			
subjects affected / exposed	1 / 77 (1.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Behcet's syndrome			
subjects affected / exposed	2 / 77 (2.60%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Pregnancy, puerperium and perinatal conditions			
Pregnancy			
subjects affected / exposed	1 / 77 (1.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 77 (1.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Cataract			
subjects affected / exposed	1 / 77 (1.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Retinal haemorrhage			
subjects affected / exposed	1 / 77 (1.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Retinal infiltrates			
subjects affected / exposed	1 / 77 (1.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Retinal neovascularisation			
subjects affected / exposed	1 / 77 (1.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vitreous detachment			
subjects affected / exposed	1 / 77 (1.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vitreous haemorrhage			

subjects affected / exposed	2 / 77 (2.60%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 77 (1.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Umbilical hernia			
subjects affected / exposed	1 / 77 (1.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 77 (1.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Insomnia			
subjects affected / exposed	1 / 77 (1.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 77 (1.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 77 (1.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Orchitis			

subjects affected / exposed	1 / 77 (1.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tuberculosis			
subjects affected / exposed	1 / 77 (1.30%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Metabolic acidosis			
subjects affected / exposed	1 / 77 (1.30%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 2.5 %

Non-serious adverse events	Gevokizumab 60 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	39 / 77 (50.65%)		
Investigations			
Intraocular pressure increased			
subjects affected / exposed	3 / 77 (3.90%)		
occurrences (all)	4		
Mycobacterium tuberculosis complex test positive			
subjects affected / exposed	3 / 77 (3.90%)		
occurrences (all)	3		
Vascular disorders			
Behcet's syndrome			
subjects affected / exposed	3 / 77 (3.90%)		
occurrences (all)	4		
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 77 (3.90%)		
occurrences (all)	3		
General disorders and administration site conditions			

Influenza like illness subjects affected / exposed occurrences (all)	3 / 77 (3.90%) 3		
Eye disorders Cataract subjects affected / exposed occurrences (all) Vitreal cells subjects affected / exposed occurrences (all) Uveitis subjects affected / exposed occurrences (all) Ocular hypertension subjects affected / exposed occurrences (all) Macular oedema subjects affected / exposed occurrences (all)	 2 / 77 (2.60%) 2 2 / 77 (2.60%) 2 7 / 77 (9.09%) 11 2 / 77 (2.60%) 3 5 / 77 (6.49%) 9		
Gastrointestinal disorders Aphthous stomatitis subjects affected / exposed occurrences (all)	 2 / 77 (2.60%) 2		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	 2 / 77 (2.60%) 3		
Infections and infestations Gastroenteritis subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Hordeolum	 2 / 77 (2.60%) 2 4 / 77 (5.19%) 7		

subjects affected / exposed occurrences (all)	2 / 77 (2.60%) 2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 July 2014	-- Update one of the inclusion criteria regarding the timelines between last study drug administration and inclusion in this study. - -Add instructions in case of indeterminate result of interferon-gamma release assay (IGRA). - -Update the study completion date, which depended on the end of CL3-78989-002 core study (event-driven trial).
27 November 2014	The requirement of the last IGRA re-test result before the first study drug administration for patients coming from compassionate use or for patients having received their last study drug administration more than 6 weeks before the inclusion visit.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
21 September 2015	Sponsor's decision unrelated to safety	-

Notes:

Limitations and caveats

None reported