Clinical trial results:
International Open-Label Extension of the Phase 3 Study CL-503012 with KIACTA™ in Patients with AA Amyloidosis

Summary

EudraCT number	2013-004150-16
Trial protocol	LT GB PL
Global end of trial date	12 September 2016

Results information

Result version number	v1 (current)
This version publication date	12 November 2017
First version publication date	12 November 2017

Trial information

Trial identification

Sponsor protocol code	CL-503015

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	A.T. Development Switzerland SARL
Sponsor organisation address	Rue Saint-Perre 2 , Lausanne Vaud, Switzerland, 1003
Public contact	Patrick C O'Connor Ph.D, FRCP , Auven Therapeutics, 954 903 0492, Patrick.OConnor@auventx.com
Scientific contact	Patrick C O'Connor Ph.D, FRCP , Auven Therapeutics, 954 903 0492, Patrick.OConnor@auventx.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	19 December 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	12 September 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this open-label extension (OLE) study is to provide access to Kiacta (eprodisate disodium) for those patients who have completed the pivotal, randomized, placebo-controlled Phase 3 Study CL-503012.

Protection of trial subjects:

Institutions, investigators, and contract research organizations, etc., associated with this study have abided by all requirements applicable to the use and disclosure of patients' protected health information (such as the requirements provided for under the Health Insurance Portability and Accountability Act in the United States, the European Union Directive on Data Protection, the Personal Information Protection and Electronic Document Act in Canada and in any other similar regulations or legislation). The study was conducted according to the International Council for Harmonisation harmonised tripartite guideline E6(R1): Good Clinical Practice.

Background therapy:

There is no standard therapy allowed per protocol (this is an orphan medicine).

Evidence for comparator: -

Actual start date of recruitment	17 December 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	Poland: 16
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	Lithuania: 1
Country: Number of subjects enrolled	Russian Federation: 16
Country: Number of subjects enrolled	Peru: 9
Country: Number of subjects enrolled	Ukraine: 4
Country: Number of subjects enrolled	Tunisia: 3
Worldwide total number of subjects	52
EEA total number of subjects	20

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)	40
From 65 to 84 years	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients completing Study CL-503012 who fulfilled the selection criteria were offered the opportunity to participate in Study CL-503015. This study was conducted at 11 study centers in 7 countries.

Pre-assignment

Screening details:

Male or nonpregnant females of at least 18 years of age who completed Study CL-503012 and had undergone all study assessments that could affect the primary endpoint of Study CL-503012.

Period 1

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

Arms

Arm title	Kiacta 400 mg BID, 800 mg BID, or 1200 mg BID

Arm description:

This is an OLE of the Study CL-503012. Therefore, all patients will receive Kiacta 400 mg administered orally as 1 to 3 capsules BID starting at Baseline until EOS.

Arm type	Experimental
Investigational medicinal product name	Kiacta TM
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

This is an OLE of the Study CL-503012. Therefore, all patients will receive Kiacta 400 mg administered orally as 1 to 3 capsules BID starting at Baseline until EOS. The dose regimen will depend on the patient's CrCl as calculated with the Cockcroft-Gault formula. At Baseline, the dose regimen will be based on CrCl of the last Study Cl-503012 visit. At subsequent visits the dose regimen will be adjusted based on CrCl. If the dose regimen requires adjustment during the treatment period due to a change in the CrCl range, the change in renal function will be confirmed, and the Investigator will notify the patient of the new dose regimen.

Number of subjects in period 1	Kiacta 400 mg BID, 800 mg BID, or 1200 mg BID
Started	52
Completed	43
Not completed	9
treatment discontinuation	9

Baseline characteristics

Reporting groups	
Reporting group title	Overall treatment period

Reporting group description: -

Reporting group values	Overall treatment period	Total	
Number of subjects	52	52	
Age categorical Units: Subjects			
Adults (18-64 years)	40	40	
From 65-84 years	12	12	
Gender categorical Units: Subjects			
Female	33	33	
Male	19	19	

End points

End points reporting groups

Reporting group title	Kiacta 400 mg BID, 800 mg BID, or 1200 mg BID

Reporting group description:

This is an OLE of the Study CL-503012. Therefore, all patients will receive Kiacta 400 mg administered orally as 1 to 3 capsules BID starting at Baseline until EOS.

Primary: Collection of data on Kiacta slowing renal function decline

End point title	Collection of data on Kiacta slowing renal function decline[1]

End point description:

All patients were to receive the study drug for a maximum of 12 months unless Kiacta became commercially available in the specific country. Study CL-503015 was terminated prematurely on 21 Jun 2016 after the efficacy analysis of Study CL-503012 showed that Kiacta did not meet the primary efficacy endpoint in slowing renal function decline.

End point type	Primary

End point timeframe:

Patients completing Study CL-503012 and fulfilling selection criteria will be offered the opportunity to participate in this OLE study for a maximum 12 months in those countries where the compassionate use program is not applicable.

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: No statistical analyses were performed. No sample size target was identified. This study planned to include all patients completing Study CL-503012 who fulfilled all selection criteria and who provided their written consent to participate. Data were collected and listings were produced for demography, drug dosage, AEs, clinical laboratory parameters, past and concurrent medical conditions, and concomitant medications. Study CL-503015 was terminated prematurely on 21 Jun 2016.

End point values	Kiacta 400 mg BID, 800 mg BID, or 1200 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: not applicable	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All patients were to receive Kiacta for a maximum of 12 months unless Kiacta became commercially available in the specific country.

Adverse event reporting additional description:

Safety was assessed by the incidence of AEs and SAEs. Adverse events included any clinically significant change or new clinically significant occurrence in laboratory tests, and vital signs when compared with Baseline status.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Kiacta 400 mg BID, 800 mg BID, or 1200 mg BID

Reporting group description:

This is an OLE of the Study CL-503012. Therefore, all patients will receive Kiacta 400 mg administered orally as 1 to 3 capsules BID starting at Baseline until EOS.

Serious adverse events	Kiacta 400 mg BID, 800 mg BID, or 1200 mg BID		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 52 (7.69%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Cardiac disorders			
congestive heart failure			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Heart failure			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Meningeal haemorrhage with severe hypertension			

subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Insufficiency of multiorgan			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Respiratory, thoracic and mediastinal disorders			
infected bronchiectasis			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
pleural effusion worsening			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Kiacta 400 mg BID, 800 mg BID, or 1200 mg BID		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 52 (13.46%)		
Injury, poisoning and procedural complications			
Calcaneal spur			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Fracture of the left humerus			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		
Cardiac disorders			
Mitral insufficiency			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences (all)	1		

Tachicardia subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1		
Blood and lymphatic system disorders Hypertension worsening subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1		
Gastrointestinal disorders Acute diarrhea subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1 1 / 52 (1.92%) 1		
Respiratory, thoracic and mediastinal disorders Infected brochientasis subjects affected / exposed occurrences (all) Pleural effusion subjects affected / exposed occurrences (all)	2 / 52 (3.85%) 3 1 / 52 (1.92%) 1		
Skin and subcutaneous tissue disorders Lichen ruber planus subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1		
Psychiatric disorders Depresion subjects affected / exposed occurrences (all) Sleep disturbances subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1 1 / 52 (1.92%) 1		
Musculoskeletal and connective tissue disorders Restless legs syndrome subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1		
Infections and infestations			

Herpes zoster of right buttock subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1		
Inflammation of skin of left shank subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1		
Common cold subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 1		

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