Clinical trial results:
AN OPEN-LABEL PROOF OF CONCEPT PHASE IIA TRIAL OF ALXN1007 FOR THE TREATMENT OF NON-CRITERIA MANIFESTATIONS OF ANTIPHOSPHOLIPID SYNDROME

Summary

EudraCT number	2013-003588-73
Trial protocol	GB IT ES
Global end of trial date	20 June 2016

Results information

Result version number	v1 (current)
This version publication date	02 July 2017
First version publication date	02 July 2017

Trial information

Trial identification

Sponsor protocol code	ALXN1007-APS-201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02128269
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Alexion Pharmaceuticals Inc.
Sponsor organisation address	100 College Street, New Haven, United States, 06510
Public contact	European Clinical Trial Information, Alexion Europe SAS, +33 153643848, clinicaltrials.eu@alxn.com
Scientific contact	European Clinical Trial Information, Alexion Europe SAS, +33 153643848, clinicaltrials.eu@alxn.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	14 April 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 June 2016
Global end of trial reached?	Yes
Global end of trial date	20 June 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Safety and tolerability of intravenous (IV) ALXN1007 in persistently antiphospholipid (aPL) positive patients with at least 1 of the following non-criteria manifestations of antiphospholipid syndrome (APS): aPL nephropathy, skin ulcers, and/or thrombocytopenia.

Protection of trial subjects:

All patients must be vaccinated against N. meningitidis if not already vaccinated within the time period of active coverage specified by the vaccine manufacturer.
Patients must be vaccinated at least 14 days prior to receiving the first dose of ALXN1007, or
Patients must be vaccinated and receive treatment with appropriate antibiotics until 14 days after the vaccination.

Background therapy:

Patients may continue on their APS medications, but every effort should be made to keep the patients' concomitant medications stable through the Week 24 visit.

Evidence for comparator: -

Actual start date of recruitment	01 December 2013
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: 2
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	Japan: 2
Country: Number of subjects enrolled	United States: 4
Worldwide total number of subjects	9
EEA total number of subjects	3

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)	7
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Screening discontinued early due to slow patient enrollment

Pre-assignment

Screening details:

22 total patients screened

Period 1

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

Arms

Arm title	ALXN1007

Arm description:

ALXN1007: 10 mg/kg IV q 2 weeks x 12 doses

Arm type	Experimental
Investigational medicinal product name	ALXN1007
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

ALXN1007: 10 mg/kg IV q 2 weeks x 12 doses

Number of subjects in period 1	ALXN1007
Started	9
Completed	7
Not completed	2
Physician decision	1
Adverse event, non-fatal	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall Trial

Reporting group description:

All patients (included those who discontinued prematurely) were followed for 12 weeks after last infusion

Reporting group values	Overall Trial	Total	
Number of subjects	9	9	
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)	7	7	
From 65-84 years	2	2	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	3	3	
Male	6	6	

End points

End points reporting groups

Reporting group title	ALXN1007
Reporting group description:	
ALXN1007: 10 mg/kg IV q 2 weeks x 12 doses	

Primary: Safety and Tolerability

End point title	Safety and Tolerability[1]
End point description:	
Measured by Percentage of Patients Reporting Adverse Events	
End point type	Primary
End point timeframe:	
24 Weeks	

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 comparative analysis was done. Only percentage of patients experiencing adverse events was reported based on all patients with at least one dose of ALXN1007. Adverse events are summarized for 24 week treatment period and 12 week follow up period combined.

End point values	ALXN1007			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: Patient numbers	8			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Treatment Period (24 weeks) and Follow-up Period (12 weeks)	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups	
Reporting group title	ALXN1007
Reporting group description: ALXN1007: 10 mg/kg IV q 2 weeks x 12 doses	

Serious adverse events	ALXN1007		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 9 (22.22%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Lumbar vertebral fracture			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Wrist fracture			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Abortion missed			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholestasis			

subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Liver Cytolysis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Lumbar spinal stenosis			
subjects affected / exposed	1 / 9 (11.11%)		
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 %

Non-serious adverse events	ALXN1007		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 9 (88.89%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Vascular disorders			
Varicose vein			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Nervous system disorders			
Carpal tunnel syndrome			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Dizziness			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Hypoaesthesia			

subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Restless legs syndrome			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Antiphospholipid syndrome			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Thrombocytopenia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	2		
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Pain			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Enterocolitis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		

Haemorrhoids subjects affected / exposed occurrences (all) Hypoaesthesia oral subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Colitis subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1 1 / 9 (11.11%) 1 2 / 9 (22.22%) 2 1 / 9 (11.11%) 2		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Epistaxis subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1 1 / 9 (11.11%) 1		
Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Infections and infestations Bronchitis subjects affected / exposed occurrences (all) Cystitis subjects affected / exposed occurrences (all) Gastroenteritis	2 / 9 (22.22%) 2 1 / 9 (11.11%) 1		

subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Labyrinthitis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Oral herpes			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Paronychia			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Pharyngitis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Sinusitis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Staphylococcal infection			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Tracheitis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	2		
Upper respiratory tract infection			
subjects affected / exposed	4 / 9 (44.44%)		
occurrences (all)	8		
Urethritis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 November 2013	Amendment included changes to laboratory safety assessments, acceptable birth control methods, antibody testing, study drug storage conditions, and the adverse event severity assessment grading scale.
24 January 2014	The Amendment revised the required use of contraception to 6 months after receiving the last dose of study drug for both female and male patients.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
31 August 2015	Screening for the study was stopped due to slow patient recruitment. Initially enrolled patients completed the study.	-

Notes:

Limitations and caveats

None reported