Clinical trial results:
A Phase II Open-label Rollover Study for Subjects that have Participated in a Linsitinib Trial

Summary

EudraCT number	2013-004076-34
Trial protocol	CZ PL GB
Global end of trial date	21 December 2016

Results information

Result version number	v1 (current)
This version publication date	27 December 2017
First version publication date	27 December 2017

Trial information

Trial identification

Sponsor protocol code	7487-CL-0209

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02057380
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Astellas Pharma Global Development (APGD) US
Sponsor organisation address	1 Astellas Way, Northbrook, United States, 60062
Public contact	Clinical Trial Disclosure, Astellas Pharma Global Development (APGD) US, astellas.resultsdisclosure@astellas.com
Scientific contact	Clinical Trial Disclosure, Astellas Pharma Global Development (APGD) US, astellas.resultsdisclosure@astellas.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	21 December 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 December 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial was to provide access to continued treatment for participants who took part in other linsitinib Astellas sponsored trials and for whom the investigator feels the participants may benefit from continued treatment.

Protection of trial subjects:

This clinical study was written, conducted and reported in accordance with the protocol, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice (GCP) Guidelines, and applicable local regulations, including the European Directive 2001/20/EC, on the protection of human rights, and with the ethical principles that have their origin in the Declaration of Helsinki. Astellas ensures that the use and disclosure of protected health information (PHI) obtained during a research study complies with the federal, national and/or regional legislation related to the privacy and protection of personal information.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 April 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	United States: 5
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Brazil: 1
Country: Number of subjects enrolled	Czech Republic: 1
Country: Number of subjects enrolled	Poland: 2
Country: Number of subjects enrolled	Singapore: 1
Country: Number of subjects enrolled	Thailand: 1
Worldwide total number of subjects	13
EEA total number of subjects	5

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)	6
From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was a phase 2, open-label, rollover study for adult participants with advanced solid tumors who previously participated in the completed linsitinib studies conducted across 42 centers.

Pre-assignment

Screening details:

Participants continued with the regimen and study drug dose they received during the previous linsitinib study, including linsitinib alone or in combination with other approved cancer treatments such as erlotinib or paclitaxel, or erlotinib alone. During the study, one participant was incorrectly identified as coming from Arm C instead of Arm B.

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	Arm A: Linsitinib 150 mg BID

Arm description:

Participants received 150 mg of linsitinib orally twice a day (BID).

Arm type	Experimental
Investigational medicinal product name	Linsitinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received linsitinib orally twice a day with food and up to 200 ml of water at approximately the same time each day. Two doses of linsitinib were received 12 hours apart.

Arm title	Arm C: Erlotinib 150 mg QD

Arm description:

Participants received 150 mg of erlotinib orally once a day (QD).

Arm type	Experimental
Investigational medicinal product name	Erlotinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received erlotinib orally at least one hour before or two hours after food with up to 200 ml of water.

Arm title	Arm D: Linsitinib 150 mg BID + Paclitaxel

Arm description:

Participants received 150 mg of linsitinib orally twice a day (BID) with weekly paclitaxel as an IV infusion.

Arm type	Experimental

Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received paclitaxel as an IV infusion according to institution practice and product package insert.

Investigational medicinal product name	Linsitinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received linsitinib orally twice a day with food and up to 200 ml of water at approximately the same time each day. Two doses of linsitinib were received 12 hours apart.

Arm title	Arm H: Linsitinib 150 mg BID

Arm description:

Participants received 150 mg of linsitinib orally twice a day (BID) for 28 days each cycle.

Arm type	Experimental
Investigational medicinal product name	Linsitinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received linsitinib orally twice a day with food and up to 200 ml of water at approximately the same time each day. Two doses of linsitinib were received 12 hours apart.

Number of subjects in period 1	Arm A: Linsitinib 150 mg BID	Arm C: Erlotinib 150 mg QD	Arm D: Linsitinib 150 mg BID + Paclitaxel
Started	2	8	2
Completed	0	4	2
Not completed	2	4	0
Treatment Discontinued due to Disease Progression	2	4	-

Number of subjects in period 1	Arm H: Linsitinib 150 mg BID
Started	1
Completed	0
Not completed	1
Treatment Discontinued due to Disease Progression	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall Study
Reporting group description: Overall Study	

Reporting group values	Overall Study	Total	
Number of subjects	13	13	
Age categorical Units: Subjects			
47-78 years	13	13	
Gender categorical Units:			
Male	2	2	
Female	11	11	
Ethnicity and Race Units: Subjects			
White	7	7	
Hispanic or Latino	1	1	
Asian	2	2	
Race Not Collected	3	3	

End points

End points reporting groups

Reporting group title	Arm A: Linsitinib 150 mg BID
Reporting group description:	
Participants received 150 mg of linsitinib orally twice a day (BID).	
Reporting group title	Arm C: Erlotinib 150 mg QD
Reporting group description:	
Participants received 150 mg of erlotinib orally once a day (QD).	
Reporting group title	Arm D: Linsitinib 150 mg BID + Paclitaxel
Reporting group description:	
Participants received 150 mg of linsitinib orally twice a day (BID) with weekly paclitaxel as an IV infusion.	
Reporting group title	Arm H: Linsitinib 150 mg BID
Reporting group description:	
Participants received 150 mg of linsitinib orally twice a day (BID) for 28 days each cycle.	

Primary: Number of Participants with Adverse Events

End point title	Number of Participants with Adverse Events[1]

End point description:

Safety was assessed by evaluation of treatment-emergent adverse events (TEAEs), clinical laboratory variables, vital signs, physical examination and the 12 lead electrocardiogram (ECG). A TEAE was defined as an adverse event (AE) with an onset date on or after the administration of study drug or any ongoing AE that worsened in severity up to 30 days after administration of the last dose of study drug. One participant was incorrectly identified in the listings as coming from Arm C instead of Arm B based on interactive response technology (IRT) data used to assign treatment arms. Treatment in Arm B consisted of 150 mg linsitinib twice a day plus 150 mg of erlotinib once a day. Analysis population was safety analysis set (SAF) and it consisted of all participants who received at least 1 dose of study drug.

End point type	Primary

End point timeframe:

From first dose of study drug until 30 days after last dose; maximum duration of treatment was 925 days

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: Statistical analysis was not completed for this endpoint.

End point values	Arm A: Linsitinib 150 mg BID	Arm C: Erlotinib 150 mg QD	Arm D: Linsitinib 150 mg BID + Paclitaxel	Arm H: Linsitinib 150 mg BID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	8	2	1
Units: Participants				
Any AE	2	8	2	1
Any TEAE	2	6	1	1
Deaths	0	0	0	0
Serious TEAEs	1	3	1	1
TEAEs Leading to Discontinuation	0	0	1	0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From first dose of study drug until 30 days after last dose; maximum duration of treatment was 925 days	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups	
Reporting group title	Arm A: Linsitinib 150 mg BID
Reporting group description:	
Participants received 150 mg of linsitinib orally twice a day (BID).	
Reporting group title	Arm C: Erlotinib 150 mg QD
Reporting group description:	
Participants received 150 mg of erlotinib orally once a day (QD).	
Reporting group title	Arm D: Linsitinib 150 mg BID + Paclitaxel
Reporting group description:	
Participants received 150 mg of linsitinib orally twice a day (BID) with weekly paclitaxel as an IV infusion.	
Reporting group title	Arm H: Linsitinib 150 mg BID
Reporting group description:	
Participants received 150 mg of linsitinib orally twice a day (BID) for 28 days each cycle.	

Serious adverse events	Arm A: Linsitinib 150 mg BID	Arm C: Erlotinib 150 mg QD	Arm D: Linsitinib 150 mg BID + Paclitaxel
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 2 (50.00%)	3 / 8 (37.50%)	1 / 2 (50.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	1 / 2 (50.00%)	0 / 8 (0.00%)	0 / 2 (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
Nervous system disorders			
Transient ischaemic attack			
subjects affected / exposed	0 / 2 (0.00%)	1 / 8 (12.50%)	0 / 2 (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
Gastrointestinal disorders			

Ileus			
subjects affected / exposed	0 / 2 (0.00%)	0 / 8 (0.00%)	1 / 2 (50.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 2 (0.00%)	0 / 8 (0.00%)	1 / 2 (50.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 2 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 8 (12.50%)	0 / 2 (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
Viral infection			
subjects affected / exposed	0 / 2 (0.00%)	1 / 8 (12.50%)	0 / 2 (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

Serious adverse events	Arm H: Linsitinib 150 mg BID		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Transient ischaemic attack			

subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Ileus			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 1 (100.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Viral infection			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Arm A: Linsitinib 150 mg BID	Arm C: Erlotinib 150 mg QD	Arm D: Linsitinib 150 mg BID + Paclitaxel
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 2 (100.00%)	6 / 8 (75.00%)	1 / 2 (50.00%)
Vascular disorders			

Hypertension			
subjects affected / exposed	0 / 2 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 2 (50.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Influenza like illness			
subjects affected / exposed	0 / 2 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Oedema peripheral			
subjects affected / exposed	0 / 2 (0.00%)	2 / 8 (25.00%)	0 / 2 (0.00%)
occurrences (all)	0	2	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 2 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Nasal congestion			
subjects affected / exposed	0 / 2 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	2	0
Throat irritation			
subjects affected / exposed	0 / 2 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Wheezing			
subjects affected / exposed	0 / 2 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Investigations			
Intraocular pressure increased			
subjects affected / exposed	1 / 2 (50.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Red blood cells urine positive			
subjects affected / exposed	1 / 2 (50.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Vitamin D decreased			
subjects affected / exposed	1 / 2 (50.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0

White blood cells urine positive			
subjects affected / exposed	1 / 2 (50.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 2 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Wrist fracture			
subjects affected / exposed	0 / 2 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Amnesia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Aphasia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Dizziness			
subjects affected / exposed	0 / 2 (0.00%)	2 / 8 (25.00%)	0 / 2 (0.00%)
occurrences (all)	0	2	0
Headache			
subjects affected / exposed	0 / 2 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Deafness transitory			
subjects affected / exposed	1 / 2 (50.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Ear pain			
subjects affected / exposed	0 / 2 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 2 (50.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Duodenogastric reflux			

subjects affected / exposed	0 / 2 (0.00%)	0 / 8 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	1
Gastritis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 8 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	1
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 2 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Hiatus hernia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 8 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	1
Loose tooth			
subjects affected / exposed	1 / 2 (50.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Nausea			
subjects affected / exposed	0 / 2 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	0 / 2 (0.00%)	0 / 8 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Dermatitis allergic			
subjects affected / exposed	0 / 2 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	2	0
Drug eruption			
subjects affected / exposed	0 / 2 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	4	0
Dry skin			
subjects affected / exposed	1 / 2 (50.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	1	1	0
Haemorrhage subcutaneous			
subjects affected / exposed	0 / 2 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	1	0

Hyperhidrosis			
subjects affected / exposed	1 / 2 (50.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Nail ridging			
subjects affected / exposed	0 / 2 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Bilirubinuria			
subjects affected / exposed	0 / 2 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Haematuria			
subjects affected / exposed	0 / 2 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Proteinuria			
subjects affected / exposed	0 / 2 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 2 (50.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Muscle spasms			
subjects affected / exposed	1 / 2 (50.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 2 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Nail infection			
subjects affected / exposed	0 / 2 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	1	0

Nasopharyngitis			
subjects affected / exposed	1 / 2 (50.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Paronychia			
subjects affected / exposed	0 / 2 (0.00%)	2 / 8 (25.00%)	0 / 2 (0.00%)
occurrences (all)	0	2	0
Sinusitis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Subcutaneous abscess			
subjects affected / exposed	1 / 2 (50.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 2 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Food intolerance			
subjects affected / exposed	1 / 2 (50.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Vitamin D deficiency			
subjects affected / exposed	1 / 2 (50.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Arm H: Linsitinib 150 mg BID		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Influenza like illness			

subjects affected / exposed occurrences (all) Oedema peripheral subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0 0 / 1 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all) Nasal congestion subjects affected / exposed occurrences (all) Throat irritation subjects affected / exposed occurrences (all) Wheezing subjects affected / exposed occurrences (all)	 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0		
Investigations Intraocular pressure increased subjects affected / exposed occurrences (all) Red blood cells urine positive subjects affected / exposed occurrences (all) Vitamin D decreased subjects affected / exposed occurrences (all) White blood cells urine positive subjects affected / exposed occurrences (all)	 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0 0 / 1 (0.00%) 0		
Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all) Wrist fracture	 0 / 1 (0.00%) 0 		

subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Amnesia			
subjects affected / exposed	1 / 1 (100.00%)		
occurrences (all)	1		
Aphasia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Dizziness			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Deafness transitory			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Ear pain			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Duodenogastric reflux			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Gastritis			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Hiatus hernia			

subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Loose tooth			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	1 / 1 (100.00%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Dermatitis allergic			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Drug eruption			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Dry skin			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Haemorrhage subcutaneous			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Hyperhidrosis			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Nail ridging			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Bilirubinuria			

subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Haematuria			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Proteinuria			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Muscle spasms			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Musculoskeletal pain			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	1 / 1 (100.00%)		
occurrences (all)	2		
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Nail infection			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Paronychia			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Sinusitis			

subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Subcutaneous abscess			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Food intolerance			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		
Vitamin D deficiency			
subjects affected / exposed	0 / 1 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 July 2015	There was 1 substantial amendment to the protocol that expanded eligibility criteria, lengthened the planned study period and the duration of participants treatment and clarified local requirements for adverse events (AEs).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported