Clinical trial results:
A single arm, open-label, Phase 2 study to assess the efficacy and safety of lucitanib given orally as a single agent to patients with advanced/metastatic lung cancer and FGF-, VEGF-, or PDGF-related genetic alterations

Summary

EudraCT number	2013-003874-29
Trial protocol	IT DE ES
Global end of trial date	26 July 2016

Results information

Result version number	v1 (current)
This version publication date	12 May 2019
First version publication date	12 May 2019

Trial information

Trial identification

Sponsor protocol code	E-3810-II-02

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02109016
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Clovis Oncology UK Ltd
Sponsor organisation address	Sheraton House, Castle Park, Cambridge, United Kingdom, CB3 0AX
Public contact	Dr Lindsey Rolfe, Clovis Oncology UK Ltd, +44 1223 370037, info@clovisoncology.com
Scientific contact	Dr Lindsey Rolfe, Clovis Oncology UK Ltd, +44 1223 370037, info@clovisoncology.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	26 July 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 July 2016
Global end of trial reached?	Yes
Global end of trial date	26 July 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the objective response rate (ORR) of lucitanib in patients with advanced/metastatic lung cancer and fibroblast growth factor (FGF)-, vascular endothelial growth factor (VEGF)-, or platelet-derived growth factor (PDGF)-related genetic alterations

Protection of trial subjects:

A data monitoring committee (DMC) consisting of 2 of the clinical trial investigators and sponsor personnel met every 3-6 months during the study to review the efficacy and safety data, and provide recommendations regarding study continuation/discontinuation and protocol modifications.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 March 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: 4
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	Italy: 8
Worldwide total number of subjects	18
EEA total number of subjects	14

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)	11
From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 18 patients enrolled at 10 study centers from the US, Germany, Italy, Spain, and France; all 18 patients received at least one dose of lucitanib.

Pre-assignment

Screening details:

Eligible patients were ≥ 18 years of age with advanced/metastatic SCLC or NSCLC that had FGF, VEGF, or PDGF genetic alterations based on local or central testing, and had failed at least 1 prior treatment line.

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	Lucitanib 10mg or 15mg QD

Arm description:

Starting dose of 10 or 15mg lucitanib depending on protocol version in force at the time of enrollment. Taken orally once daily (continuous 28 day treatment cycle). Patients were to continue treatment as long as, according to the investigator, continuation was in their best interest (ie, they appeared to be receiving clinical benefit), and unless there was occurrence of unacceptable toxicity, progressive disease (PD), or withdrawal of consent.

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

Dosage and administration details:

Starting dose of 10mg or 15mg. Taken orally once daily (continuous 28 day treatment cycle). Patients were to take lucitanib at approximately the same time each day under fasting conditions (ie, at least 2 hours prior to and 2 hours after a meal), and to swallow lucitanib with a glass of water.

Number of subjects in period 1	Lucitanib 10mg or 15mg QD
Started	18
Completed	0
Not completed	18
Consent withdrawn by subject	1
Disease progression	10
Adverse event, non-fatal	4
Death	3

Baseline characteristics

Reporting groups	
Reporting group title	Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	18	18	
Age categorical Units: Subjects			
Adults (18-64 years)	11	11	
From 65-84 years	7	7	
Gender categorical Units: Subjects			
Female	5	5	
Male	13	13	
Race Units: Subjects			
Black or African American	3	3	
White	4	4	
Missing	11	11	
Ethnicity Units: Subjects			
Not Hispanic or Latino	8	8	
Unknown	8	8	
Missing	2	2	
Number of prior anticancer therapies Units: Number			
median	3		
full range (min-max)	2 to 7	-	

End points

End points reporting groups

Reporting group title	Lucitanib 10mg or 15mg QD

Reporting group description:

Starting dose of 10 or 15mg lucitanib depending on protocol version in force at the time of enrollment. Taken orally once daily (continuous 28 day treatment cycle). Patients were to continue treatment as long as, according to the investigator, continuation was in their best interest (ie, they appeared to be receiving clinical benefit), and unless there was occurrence of unacceptable toxicity, progressive disease (PD), or withdrawal of consent.

Primary: Objective Response Rate (CR or PR) according to RECIST v 1.1 as determined by investigator

End point title	Objective Response Rate (CR or PR) according to RECIST v 1.1 as determined by investigator[1]

End point description:

Proportion of patients with a best overall confirmed response of partial response (PR) or complete response (CR) recorded from the start of the treatment until disease progression or recurrence.

End point type	Primary

End point timeframe:

Cycle 1 Day 1 to End of Treatment

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: Because of the early termination of the study, efficacy analyses were limited. Post-baseline tumor assessments were available for 13 of the 18 patients at the time of study discontinuation. Only one of 13 patients (7.7%) had a best response of confirmed PR. The duration of response for this patient was 113 days.

End point values	Lucitanib 10mg or 15mg QD			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: percentage of patients	8			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response according to RECIST v1.1

End point title	Duration of Response according to RECIST v1.1

End point description:

Duration of response in patients with confirmed response by investigator. Because of the early termination of the study, efficacy analyses were limited. Post-baseline tumor assessments were available for 13 of the 18 patients at the time of study discontinuation. Only one of 13 patients (7.7%) had a best response of confirmed PR. The duration of response for this patient was 113 days.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 to End of Treatment

End point values	Lucitanib 10mg or 15mg QD			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Median number of days	113			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from the date of first dose of study drug and until 28 days after last dose of study drug.

Adverse event reporting additional description:

If a subject experiences the same preferred term (system organ class) multiple times, then the subject will be counted only once for that preferred term (system organ class).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Lucitanib 10mg or 15mg QD

Reporting group description:

Starting dose of 10 or 15mg depending on protocol version in force at the time of enrollment. Taken orally once daily (continuous 28 day treatment cycle). Patients were to continue treatment as long as, according to the investigator, continuation was in their best interest (ie, they appeared to be receiving clinical benefit), and unless there was occurrence of unacceptable toxicity, progressive disease (PD), or withdrawal of consent.

Serious adverse events	Lucitanib 10mg or 15mg QD		
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 18 (66.67%)		
number of deaths (all causes)	4		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	3 / 18 (16.67%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 3		
Pericardial effusion malignant			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypertension			

subjects affected / exposed	2 / 18 (11.11%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Hypotension			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Performance status decreased			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Anal fistula			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haemoptysis			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumothorax			

subjects affected / exposed	1 / 18 (5.56%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory distress				
subjects affected / exposed	1 / 18 (5.56%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Renal failure acute				
subjects affected / exposed	1 / 18 (5.56%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Empyema				
subjects affected / exposed	1 / 18 (5.56%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	1 / 18 (5.56%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Prostate infection				
subjects affected / exposed	1 / 18 (5.56%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Septic shock				
subjects affected / exposed	1 / 18 (5.56%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Tuberculosis				
subjects affected / exposed	1 / 18 (5.56%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

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

Non-serious adverse events	Lucitanib 10mg or 15mg QD		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 18 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	3 / 18 (16.67%)		
occurrences (all)	3		
Metastases to central nervous system			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Pericardial effusion malignant			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Vascular disorders			
Hypertension			
subjects affected / exposed	14 / 18 (77.78%)		
occurrences (all)	79		
Hypotension			
subjects affected / exposed	3 / 18 (16.67%)		
occurrences (all)	3		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	4 / 18 (22.22%)		
occurrences (all)	5		
Chest pain			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	6 / 18 (33.33%)		
occurrences (all)	13		
General physical health deterioration			
subjects affected / exposed	3 / 18 (16.67%)		
occurrences (all)	4		

Oedema peripheral			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	2		
Performance status decreased			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	2		
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Cough			
subjects affected / exposed	4 / 18 (22.22%)		
occurrences (all)	5		
Dysphonia			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Dyspnoea			
subjects affected / exposed	3 / 18 (16.67%)		
occurrences (all)	4		
Epistaxis			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	2		
Haemoptysis			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	2		
Increased bronchial secretion			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Pleuritic pain			

subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	2		
Pneumothorax			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Respiratory distress			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Respiratory failure			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Psychiatric disorders			
Distractibility			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Investigations			
Blood bilirubin increased			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	2		
Blood magnesium decreased			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Blood pressure increased			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Blood thyroid stimulating hormone increased			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Ejection fraction decreased			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	2		
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Thyroxine free decreased			

subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Transaminases increased			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	5		
Weight decreased			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Procedural pain			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Nervous system disorders			
Aphasia			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Dizziness			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	3 / 18 (16.67%)		
occurrences (all)	3		
Hyperreflexia			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Sciatica			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Eye disorders			
Visual acuity reduced			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Gastrointestinal disorders			

Abdominal pain				
subjects affected / exposed	2 / 18 (11.11%)			
occurrences (all)	3			
Anal fistula				
subjects affected / exposed	1 / 18 (5.56%)			
occurrences (all)	2			
Ascites				
subjects affected / exposed	1 / 18 (5.56%)			
occurrences (all)	1			
Colitis				
subjects affected / exposed	1 / 18 (5.56%)			
occurrences (all)	1			
Constipation				
subjects affected / exposed	3 / 18 (16.67%)			
occurrences (all)	3			
Diarrhoea				
subjects affected / exposed	5 / 18 (27.78%)			
occurrences (all)	7			
Dysphagia				
subjects affected / exposed	1 / 18 (5.56%)			
occurrences (all)	1			
Gastrointestinal pain				
subjects affected / exposed	1 / 18 (5.56%)			
occurrences (all)	1			
Nausea				
subjects affected / exposed	3 / 18 (16.67%)			
occurrences (all)	3			
Rectal haemorrhage				
subjects affected / exposed	1 / 18 (5.56%)			
occurrences (all)	1			
Stomatitis				
subjects affected / exposed	2 / 18 (11.11%)			
occurrences (all)	2			
Vomiting				
subjects affected / exposed	3 / 18 (16.67%)			
occurrences (all)	4			

Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Hyperbilirubinaemia			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Nail toxicity			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Haematuria			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Pollakiuria			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Proteinuria			
subjects affected / exposed	5 / 18 (27.78%)		
occurrences (all)	13		
Renal failure			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Renal failure acute			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Strangury			

subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Urinary retention			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	5		
Back pain			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	2		
Fistula			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Muscle spasms			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	2		
Musculoskeletal chest pain			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Musculoskeletal pain			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	2		
Pain in extremity			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Infections and infestations			
Empyema			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Infection			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Lung infection			

subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Pneumonia			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Prostate infection			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	2		
Septic shock			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Tuberculosis			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	6 / 18 (33.33%)		
occurrences (all)	7		
Dehydration			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	3		
Hypercalcaemia			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Hyperglycaemia			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Hypoalbuminaemia			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		

Hypocalcaemia subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1		
Hypokalaemia subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1		
Hypomagnesaemia subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 April 2015	Expanded the patient population to include SCLC and NSCLC with adenomatous, squamous, and large cell histologies, as well as FGF, VEGF, or PDGF genetic alterations.
23 July 2015	Reduced the starting dose of lucitanib from 15 mg QD to 10 mg QD.
27 January 2016	Provided new guidance for the monitoring, lucitanib treatment interruption, and reporting of Posterior Reversible Encephalopathy Syndrome (PRES).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
24 December 2015	Enrollment was closed early on 24 December 2015 because of poor accrual and changing development priorities. All patients currently in screening as of 24 December 2015 were permitted to complete screening activities and enroll on study (if eligible) to receive lucitanib treatment. The last patient was enrolled on 4 January 2016.	-

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Analyses pertaining to secondary objectives (CBR, PFS, OS, kinetics of tumor size change, and PK) and the exploratory objectives were not performed because of early termination of the study.

Notes: