Clinical trial results:
Phase II Study of ADI-PEG 20 in Patients with Relapsed Sensitive or Refractory Small Cell Lung Cancer

Summary

EudraCT number	2009-017885-22
Trial protocol	BE DE GB
Global end of trial date	15 July 2013

Results information

Result version number	v1 (current)
This version publication date	29 March 2020
First version publication date	29 March 2020

Trial information

Trial identification

Sponsor protocol code	LUD2009-007

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01266018
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Ludwig Institute for Cancer Research
Sponsor organisation address	666 3rd Ave, New York, United States, 10017-4011
Public contact	Clinical Trial Information, Ludwig Institute for Cancer Research, 001 2124501515, clintrialinformation@licr.org
Scientific contact	Clinical Trial Information, Ludwig Institute for Cancer Research, 001 2124501515, clintrialinformation@licr.org

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 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 June 2013
Global end of trial reached?	Yes
Global end of trial date	15 July 2013
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to assess the clinical efficacy of ADI-PEG 20, via the primary endpoint of tumor response by RECIST, in subjects with relapsed sensitive or refractory Small Cell Lung Cancer (SCLC).

Protection of trial subjects:

The study was conducted in full conformity with the current revision of the Declaration of Helsinki, International Conference on Harmonisation (ICH) Guidelines and applicable local laws and regulations, with the understanding that local laws and regulations took precedence over respective sections in the Declaration of Helsinki and/or the ICH Guidelines. Before study drug could be shipped and subjects could be entered into the study, the Institutional Review Board (IRB) or its equivalent must have approved the protocol and informed consent form in writing.
The investigator was to obtain witnessed written informed consent from each subject or the subject's legally authorized representative after adequate explanation of the aims, methods, anticipated benefits, and potential hazards of the study and before any study procedures were performed. Subjects were only to be identified by their initials, date of birth, and subject number on the case report forms (CRFs) or other documents submitted to the Sponsor.

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	04 January 2012
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 Kingdom: 3
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	United States: 11
Country: Number of subjects enrolled	Taiwan: 6
Worldwide total number of subjects	22
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)	14
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was a 2-arm, open-label, phase 2 study of pegylated arginine deiminase (ADI-PEG) 20 in subjects with relapsed sensitive or refractory small cell lung cancer (SCLC). ADI-PEG 20 was administered intramuscularly (IM) at a fixed dose of 320 IU/m^2 once weekly for a 4-week cycle.

Pre-assignment

Screening details:

22 subjects were enrolled in the study and were treated.

Period 1

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

Blinding implementation details:

none

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1 Sensitive Disease

Arm description:

Cohort 1 comprised subjects with "sensitive" disease, defined as subjects who were treated with 1 previous line of chemotherapy and maintained an appropriate response for 90 days or more. Subjects received 4 administrations of ADI-PEG 20 (320 IU/m^2) followed by 1 week of follow-up in each treatment cycle.

Arm type	Experimental
Investigational medicinal product name	ADI-PEG 20
Investigational medicinal product code	
Other name	Arginine deiminase pegylated
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

ADI-PEG 20 was administered intramuscularly (IM) at a fixed dose of 320 IU/m^2 (36.8 mg/m^2) once weekly for 4 weeks followed by a 1-week follow-up (1 cycle).

Arm title	Cohort 2 Refractory Disease

Arm description:

Cohort 2 comprised subjects with “refractory” disease, defined as subjects who either (a) were treated with 1 previous line of chemotherapy and either had no response or progressed < 90 days after completing treatment or (b) required third-line therapy, i.e., had completed 2 previous lines of chemotherapy, regardless of response. Subjects
received 4 administrations of ADI-PEG 20 (320 IU/m^2) followed by 1 week of follow-up in each treatment cycle.

Arm type	Experimental
Investigational medicinal product name	ADI-PEG 20
Investigational medicinal product code	
Other name	Arginine deiminase pegylated
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

ADI-PEG 20 was administered intramuscularly (IM) at a fixed dose of 320 IU/m^2 (36.8 mg/m^2) once weekly for 4 weeks followed by a 1-week follow-up (1 cycle).

Number of subjects in period 1	Cohort 1 Sensitive Disease	Cohort 2 Refractory Disease
Started	9	13
Completed	8	13
Not completed	1	0
Physician decision	1	-

Baseline characteristics

Reporting groups	
Reporting group title	overall study

Reporting group description: -

Reporting group values	overall study	Total	
Number of subjects	22	22	
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)	14	14	
From 65-84 years	8	8	
85 years and over	0	0	
Age continuous			
Age at baseline			
Units: years			
arithmetic mean	63.4		
standard deviation	± 9.4	-	
Gender categorical Units: Subjects			
Female	8	8	
Male	14	14	

End points

End points reporting groups

Reporting group title	Cohort 1 Sensitive Disease

Reporting group description:

Cohort 1 comprised subjects with "sensitive" disease, defined as subjects who were treated with 1 previous line of chemotherapy and maintained an appropriate response for 90 days or more. Subjects received 4 administrations of ADI-PEG 20 (320 IU/m^2) followed by 1 week of follow-up in each treatment cycle.

Reporting group title	Cohort 2 Refractory Disease

Reporting group description:

Cohort 2 comprised subjects with “refractory” disease, defined as subjects who either (a) were treated with 1 previous line of chemotherapy and either had no response or progressed < 90 days after completing treatment or (b) required third-line therapy, i.e., had completed 2 previous lines of chemotherapy, regardless of response. Subjects
received 4 administrations of ADI-PEG 20 (320 IU/m^2) followed by 1 week of follow-up in each treatment cycle.

Primary: Best overall response

End point title	Best overall response[1]

End point description:

Tumor responses were evaluated using any appropriate imaging type and were categorized according to Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1. Per RECIST for target lesions and assessed by MRI:

Complete Response (CR): Disappearance of all target lesions [no evidence of disease]; Partial Response (PR): ≥ 30% decrease in the sum of the longest diameter of target lesions; Progressive Disease (PD): ≥ 20% increase in the sum of the longest diameter of target lesions; Stable Disease (SD): small changes that do not meet above criteria.

End point type	Primary

End point timeframe:

Every 4 to 8 weeks for up to 16 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: Because no subject in the refractory disease cohort had a response, the study was terminated early and declared negative.

End point values	Cohort 1 Sensitive Disease	Cohort 2 Refractory Disease		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8[2]	12[3]		
Units: number of subjects				
stable disease	2	2		
progressive disease	6	10		

Notes:

[2] - includes all subjects who were evaluable for tumor response

[3] - Includes all subjects who were evaluable for tumor response

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All adverse events (AEs) occurring between the signing of informed consent and the off-study date were documented, regardless of the causal relationship to study drug. AEs occurring after the first dose of study drug were considered treatment emergent.

Adverse event reporting additional description:

Analysis of treatment-emergent adverse events (TEAEs) reported from clinical laboratory tests, physical examinations, and vital signs.
AE documentation included onset/resolution dates, severity using NCI CTCAE (v4.0), seriousness, study drug action taken, treatment, and outcome.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13.1

Reporting groups

Reporting group title	All Subjects (Safety Analysis Set)

Reporting group description:

Includes all subjects in Cohort 1 (n = 9) and Cohort 2 (n = 13) who received at least 1 dose of study drug.

Serious adverse events	All Subjects (Safety Analysis Set)		
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 22 (45.45%)		
number of deaths (all causes)	3		
number of deaths resulting from adverse events	3		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Nervous system disorders			
Hypoaesthesia			

subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Paraesthesia			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Somnolence			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Leukopenia			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Lymphopenia			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	3 / 22 (13.64%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	All Subjects (Safety Analysis Set)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 22 (95.45%)		
Investigations			
White blood cell count decreased			
subjects affected / exposed	4 / 22 (18.18%)		
occurrences (all)	5		
Platelet count decreased			
subjects affected / exposed	3 / 22 (13.64%)		
occurrences (all)	3		
Blood creatinine increased			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Haemoglobin decreased			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Cardiac disorders			
Tachycardia			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Headache			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	4		
General disorders and administration site conditions			

Fatigue subjects affected / exposed occurrences (all)	10 / 22 (45.45%) 12		
Asthenia subjects affected / exposed occurrences (all)	4 / 22 (18.18%) 5		
Chest discomfort subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 2		
Gastrointestinal disorders			
Constipation subjects affected / exposed occurrences (all)	4 / 22 (18.18%) 4		
Nausea subjects affected / exposed occurrences (all)	4 / 22 (18.18%) 5		
Vomiting subjects affected / exposed occurrences (all)	4 / 22 (18.18%) 4		
Diarrhoea subjects affected / exposed occurrences (all)	3 / 22 (13.64%) 3		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 3		
Cough subjects affected / exposed occurrences (all)	4 / 22 (18.18%) 5		
Wheezing subjects affected / exposed occurrences (all)	3 / 22 (13.64%) 3		
Productive cough subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 3		
Skin and subcutaneous tissue disorders			

Pruritus subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 2		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 2		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) Muscular weakness subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 2 2 / 22 (9.09%) 2 2 / 22 (9.09%) 2		
Infections and infestations Lower respiratory tract infection subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 2		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all) Dehydration subjects affected / exposed occurrences (all) Hyperglycaemia subjects affected / exposed occurrences (all)	7 / 22 (31.82%) 8 2 / 22 (9.09%) 2 2 / 22 (9.09%) 2		

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