Clinical trial results:
Open-label, Phase 2 Study of Single-agent Erlotinib for Patients with Pediatric Ependymoma Previously Treated with Oral Etoposide in Protocol OSI-774-205

Summary

EudraCT number	2010-023478-38
Trial protocol	GB
Global end of trial date	13 September 2012

Results information

Result version number	v1 (current)
This version publication date	22 February 2016
First version publication date	12 June 2015

Trial information

Trial identification

Sponsor protocol code	OSI-774-206

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01247922
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	OSI Pharmaceuticals LLC
Sponsor organisation address	1 Astellas Way, Northbrook, IL, United States, 60062
Public contact	Clinical Trial Disclosure, Astellas Pharma Global Development, Inc., Astellas.resultsdisclosure@astellas.com
Scientific contact	Clinical Trial Disclosure, Astellas Pharma Global Development, Inc., 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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	13 September 2012
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 September 2012
Global end of trial reached?	Yes
Global end of trial date	13 September 2012
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 safety profile of single-agent erlotinib in patients with recurrent or refractory pediatric ependymoma who were previously treated with oral etoposide in Protocol OSI-774-205.

Protection of trial subjects:

This clinical study was written, conducted and reported in accordance with the protocol, ICH 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	23 May 2011
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	United Kingdom: 1
Country: Number of subjects enrolled	Canada: 3
Worldwide total number of subjects	4
EEA total number of subjects	1

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)	2

Adolescents (12-17 years)	2
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants recruited for this OSI-774-206 study were participants with pediatric ependymoma previously treated with oral etoposide in Study OSI-774-205 who progressed while on study or discontinued due to unacceptable toxicity.

Pre-assignment

Screening details:

Participants who consented to enter this OSI-774-206 study and fulfilled all the eligibility criteria (no more than 14 days prior to registration) were enrolled in this study no more than 21 days from the last dose of oral etoposide in Study OSI-774-205.

Period 1

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

Arms

Arm title	Erlotinib

Arm description:

Participants who received erlotinib in a continuous oral dose of 85 mg/m^2 per day until dose modification, interruption or study discontinuation occurred.

The number of participants who completed the study has been defined to be the participants who discontinued treatment due to disease progression.

Arm type	Experimental
Investigational medicinal product name	Erlotinib
Investigational medicinal product code	OSI-774
Other name	Tarceva®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received a continuous oral dose of 85 mg/m^2 per day (taken at approximately the same time of day, 1 hour before or 2 hours after meals) until dose modification, interruption or study discontinuation occurred. Erlotinib was either swallowed whole or crushed and mixed with 1 heaping teaspoon of applesauce immediately before administration to the participant. Doses of erlotinib were to be reduced and/or delayed for toxicities at any time during the study. Erlotinib was provided as tablets containing erlotinib hydrochloride equivalent to 150, 100 and 25 mg of erlotinib.

Number of subjects in period 1	Erlotinib
Started	4
Completed	4

Baseline characteristics

Reporting groups

Reporting group title	Erlotinib

Reporting group description:

Participants who received erlotinib in a continuous oral dose of 85 mg/m^2 per day until dose modification, interruption or study discontinuation occurred.

The number of participants who completed the study has been defined to be the participants who discontinued treatment due to disease progression.

Reporting group values	Erlotinib	Total	
Number of subjects	4	4	
Age categorical Units: Subjects			
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	2	2	
Adolescents (12-17 years)	2	2	
Adults (18-64 years)	0	0	
Gender categorical Units: Subjects			
Female	1	1	
Male	3	3	

End points

End points reporting groups

Reporting group title	Erlotinib

Reporting group description:

Participants who received erlotinib in a continuous oral dose of 85 mg/m^2 per day until dose modification, interruption or study discontinuation occurred.

The number of participants who completed the study has been defined to be the participants who discontinued treatment due to disease progression.

Primary: Safety assessed through evaluation of physical examinations, vital signs, clinical laboratory tests, and adverse events (AEs)

End point title	Safety assessed through evaluation of physical examinations, vital signs, clinical laboratory tests, and adverse events (AEs)[1]

End point description:

Safety is monitored through AEs, which includes abnormal or clinically significant vital sign assessments, laboratory test, physical examination findings associated with signs and/or symptoms requiring withdrawal, dose modification or medical intervention. A treatment-emergent adverse event (TEAE) was defined as an adverse event observed after starting administration of the study drug. An AE was considered serious (SAE) if it resulted in death, a life-threatening situation, inpatient hospitalization or prolongation of an existing hospitalization, persistent or significant disability/incapacity, congenital anomaly/birth defect in the offspring of a patient who received study drug or other important medical events.
The analysis population is the Safety Analysis Set (SAF) consisted of all enrolled patients who received at least 1 dose of study drug.

End point type	Primary

End point timeframe:

From first dose of study drug to 30 days after last dose of study drug

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: This study was designed to assess the safety profile of single-agent erlotinib in patients with recurrent or refractory pediatric ependymoma who were previously treated with oral etoposide in Protocol OSI-774-205. No formal statistical analysis was performed due to sample size (n=4).

End point values	Erlotinib			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: participants				
Any TEAE	4			
With at least 1 SAE	2			
With at least 1 treatment-related SAE	0			
Discontinued study due to treatment-related AEs	0			
Died on treatment or within 30 days	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Best overall response

End point title	Best overall response

End point description:

Best overall response was derived from an integrated clinical assessment by the study investigator as per institutional standards. This included radiographic assessments deemed appropriate by the investigator in the normal care of the patient. A determination of best overall response at the end of study treatment (complete response, partial response, minor response or stable disease) was only made if (1) any disease-related neurologic symptoms were stable or improving over the interval of the radiographic assessment and (2) corticosteroid dosing for the control of tumor-related signs/symptoms was stable or decreasing. The analysis population is SAF.

End point type	Secondary

End point timeframe:

End of treatment (mean treatment duration was 170.5 days)

End point values	Erlotinib			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: participants				
Complete response	0			
Partial response	0			
Minor response	0			
Stable disease	2			
Disease progression	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Median treatment duration

End point title	Median treatment duration

End point description:

End point type	Secondary

End point timeframe:

From first dose of study drug up to last dose of study drug

End point values	Erlotinib			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: days	91			

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 to 30 days after last dose of study drug

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13.0

Reporting groups

Reporting group title	Erlotinib

Reporting group description: -

Serious adverse events	Erlotinib		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 4 (50.00%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events			
Nervous system disorders			
Convulsion			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neuropathy peripheral			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
VIIth nerve paralysis			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Brain death			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

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

Non-serious adverse events	Erlotinib		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)		
Investigations			
Blood bilirubin increased			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Weight decreased			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Weight increased			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	2		
Vascular disorders			
Peripheral coldness			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	2		
Nervous system disorders			
Dysarthria			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	3 / 4 (75.00%)		
occurrences (all)	3		
Partial seizures			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 4 (75.00%)		
occurrences (all)	5		

Pain			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Eye disorders			
Vision blurred			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	2		
Abdominal pain upper			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Dyspepsia			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 4 (50.00%)		
occurrences (all)	2		
Dysphonia			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		

Epistaxis			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Oropharyngeal pain			
subjects affected / exposed	2 / 4 (50.00%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Ingrowing nail			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Rash maculo-papular			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	2		
Skin striae			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Muscular weakness			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Posture abnormal			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		

Pneumonia subjects affected / exposed occurrences (all) Rash pustular subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1 1 / 4 (25.00%) 2		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	2 / 4 (50.00%) 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

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

The protocol-specified futility criteria were met at the second interim analysis dated 15 Aug 2012 for OSI-774-205. Per the DMC recommendation and FDA's agreement, the enrollment of patients in that study and Study OSI-774-206 was permanently closed.

Notes: