Clinical trial results:
A Randomized, Phase 2 Study of Single-agent Erlotinib versus Oral Etoposide in Patients with Recurrent or Refractory Pediatric Ependymoma

Summary

EudraCT number	2009-016836-11
Trial protocol	GB
Global end of trial date	26 November 2012

Results information

Result version number	v1
This version publication date	06 April 2016
First version publication date	22 April 2015

Trial information

Trial identification

Sponsor protocol code	OSI-774-205

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01032070
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	OSI Pharmaceuticals LLC
Sponsor organisation address	1 Astellas Way, Northbrook, United States,
Public contact	Clinical Trial Disclosure, Astellas Pharma Global Devlopment, Inc., Astellas.resultsdisclosure@astellas.com
Scientific contact	Clinical Trial Disclosure, Astellas Pharma Global Devlopment, 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	26 November 2012
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 November 2012
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to determine the objective response rate (ORR) of single-agent erlotinib versus oral etoposide in patients with recurrent paediatric ependymoma.

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 and/or regional legislation related to the privacy and protection of personal information.

The study was designed to consider stopping early at an interim analysis due to lack of efficacy, minimizing additional patient exposure to treatment that is unlikely to provide benefit.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 September 2010
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	12 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	Canada: 8
Country: Number of subjects enrolled	United States: 13
Worldwide total number of subjects	25
EEA total number of subjects	4

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)	12
Adolescents (12-17 years)	8
Adults (18-64 years)	5
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Patients who were candidates for participation in the study were screened for inclusion/exclusion criteria before enrollment in the study. If they have met the criteria, they were randomized into the study.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Erlotinib

Arm description:

Participants who received erlotinib orally at a dose of 85 mg/m^2 per day continuously until either progression, death, patient request or investigator decision to discontinue study drug or intolerable toxicity.

The number of subjects that completed the study has been defined to be the subjects that has discontinued due to disease progression.

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

Dosage and administration details:

Erlotinib was to administered orally at a dose of 85 mg/m^2 per day continuously until either progression, death, patient request or investigator decision to discontinue study drug or intolerable toxicity. Erlotinib was provided as tablets containing erlotinib hydrochloride equivalent to 150, 100 and 25 mg of erlotinib.

Arm title	Etoposide

Arm description:

Participants who received etoposide orally at a dose of 50 mg/m^2 per day for 21 days followed by a 7-day rest period until either progression, death, patient request or investigator decision to discontinue study drug or intolerable toxicity.

The number of subjects that completed the study has been defined to be the subjects that has discontinued due to disease progression.

Arm type	Active comparator
Investigational medicinal product name	Etoposide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

Etoposide 50 mg/m^2 per day was administered orally for 21 days followed by a 7-day rest period until either progression, death, patient request or investigator decision to discontinue study drug or intolerable toxicity.

Number of subjects in period 1	Erlotinib	Etoposide
Started	13	12
Completed	13	8
Not completed	0	4
Medical or ethical reasons	-	2
Withdrawal by Subject	-	2

Baseline characteristics

Reporting groups	
Reporting group title	Erlotinib

Reporting group description:

Participants who received erlotinib orally at a dose of 85 mg/m^2 per day continuously until either progression, death, patient request or investigator decision to discontinue study drug or intolerable toxicity.

The number of subjects that completed the study has been defined to be the subjects that has discontinued due to disease progression.

Reporting group title	Etoposide

Reporting group description:

Participants who received etoposide orally at a dose of 50 mg/m^2 per day for 21 days followed by a 7-day rest period until either progression, death, patient request or investigator decision to discontinue study drug or intolerable toxicity.

The number of subjects that completed the study has been defined to be the subjects that has discontinued due to disease progression.

Reporting group values	Erlotinib	Etoposide	Total
Number of subjects	13	12	25
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	12.8	9.2	
standard deviation	± 5.87	± 4.99	-
Gender categorical Units: Subjects			
Female	3	3	6
Male	10	9	19
Race Units: Subjects			
Asian-Indian Subcontinent	0	1	1
Asian-Southeast Asia	0	1	1
Black	1	1	2
Other	1	0	1
White	11	9	20
Ethnicity Units: Subjects			
Hispanic/Latino	1	2	3
Not Hispanic/Latino	12	10	22
Tumor Type for Initial Disease Diagnosis Units: Subjects			
Anaplastic Ependymoma	6	9	15
Ependymoma	6	3	9
Myxopapillary Ependymoma	1	0	1

Body Surface Area Units: m^2 arithmetic mean standard deviation	 1.51 ± 0.556	 1.17 ± 0.439	 -
Total Number of Disease Recurrences Units: recurrences median full range (min-max)	 3 1 to 9	 2 1 to 3	 -

End points

End points reporting groups

Reporting group title	Erlotinib

Reporting group description:

Participants who received erlotinib orally at a dose of 85 mg/m^2 per day continuously until either progression, death, patient request or investigator decision to discontinue study drug or intolerable toxicity.

The number of subjects that completed the study has been defined to be the subjects that has discontinued due to disease progression.

Reporting group title	Etoposide

Reporting group description:

Participants who received etoposide orally at a dose of 50 mg/m^2 per day for 21 days followed by a 7-day rest period until either progression, death, patient request or investigator decision to discontinue study drug or intolerable toxicity.

The number of subjects that completed the study has been defined to be the subjects that has discontinued due to disease progression.

Primary: Percentage of participants with an Objective Response

End point title	Percentage of participants with an Objective Response

End point description:

Objective response is defined as a best overall response of CR (complete response) or PR (partial response), evaluated using modified International Society of Pediatric Oncology Brain, Tumor Subcommittee for the Reporting of Trials criteria. Response was confirmed at least 28 days after the first assessment where the response criteria were met. Response was assessed by magnetic resonance imaging (MRI) every 8 weeks. CR: Complete disappearance of all enhancing tumor and mass effect; On a stable or decreasing dose of corticosteroids (or receiving only adrenal replacement doses); Stable or improving neurologic examination sustained for ≥ 4 weeks ; If cerebral spinal fluid (CSF) evaluation was positive, it must become negative (confirmed at least 2 times at consecutive samplings).
PR: ≥ 50% reduction in tumor size by bi-dimensional measurement; On a stable or decreasing dose of corticosteroids; Stable or improving neurologic examination sustained for ≥ 4 weeks.

End point type	Primary

End point timeframe:

From randomization until the end of treatment. The median time on treatment was 52 days for erlotinib and 58 days for etoposide.

End point values	Erlotinib	Etoposide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	12		
Units: percentage of participants				
number (confidence interval 95%)	0 (0 to 24.7)	16.7 (2.1 to 48.4)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Erlotinib v Etoposide
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 0.22 [2]
Method	Fisher exact

Notes:

[1] - The study was not powered for this comparison due to small sample size.

[2] - P-value is not adjusted for multiple comparisons.

Secondary: Duration of Response

End point title	Duration of Response[3]

End point description:

Duration of response (complete or partial response [CR/PR]) was defined as the time from the date of the first documented response (CR/PR) to the first documented progression or death due to underlying cancer. If a participant had not progressed or died, the duration of overall response was censored at the date of last adequate disease assessment. Duration of response was only defined for participants whose best overall response was CR or PR. Progression was defined as a worsening of neurologic status that could not be explained by other causes, a > 25% increase in tumor size, the appearance of new lesions or CSF positivity, or increasing doses of corticosteroids required to maintain stable status. Due to the low number of participants, data cannot be calculated and is denoted as "99999" as applicable.

End point type	Secondary

End point timeframe:

From randomization until the end of treatment. The median time on treatment was 52 days for erlotinib and 58 days for etoposide

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Data values are not provided for the erlotinib arm as there were no subjects analyzed (no participants achieved CR or PR), and no data can be calculated for the etoposide arm due to the low number of participants.

End point values	Etoposide			
Subject group type	Reporting group			
Number of subjects analysed	2[4]			
Units: days				
median (confidence interval 95%)	99999 (99999 to 99999)			

Notes:

[4] - These 2 participants experienced a PR and were censored at 174 and 463 days.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with a Minor Response

End point title	Percentage of participants with a Minor Response

End point description:

Best overall response of Minor response (MR), defined as: ≥ 25% to < 50% reduction in tumor size by bi-dimensional measurement; On a stable or decreasing dose of corticosteroids; Stable or improving neurologic examination sustained for ≥ 4 weeks.

End point type	Secondary

End point timeframe:

From randomization until the end of treatment. The median time on treatment was 52 days for erlotinib and 58 days for etoposide.

End point values	Erlotinib	Etoposide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	12		
Units: percentage of participants				
number (confidence interval 95%)	0 (0 to 24.7)	25 (5.5 to 57.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with Disease Control

End point title	Percentage of participants with Disease Control

End point description:

Disease control is a best overall response of CR or PR or MR or SD (stable disease): CR: Complete disappearance of all enhancing tumor and mass effect; On a stable or decreasing dose of corticosteroids (or receiving only adrenal replacement doses); Stable or improving neurologic examination sustained for ≥ 4 weeks; If CSF evaluation was positive, it must become negative (confirmed at least 2 times consecutively). PR: ≥ 50% reduction in tumor size by bi-dimensional measurement; On a stable or decreasing dose of corticosteroids; Stable or improving neurologic examination sustained for ≥ 4 weeks. MR: ≥ 25% to < 50% reduction in tumor size by bi-dimensional measurement; On a stable or decreasing dose of corticosteroids; Stable or improving neurologic examination sustained for ≥ 4 weeks. SD: Neurologic examination is at least stable; Maintenance corticosteroid dose is not increased; MRI meets neither the criteria for minor response nor for progressive disease; Sustained for ≥ 8 weeks.

End point type	Secondary

End point timeframe:

From randomization until the end of treatment. The median time on treatment was 52 days for erlotinib and 58 days for etoposide.

End point values	Erlotinib	Etoposide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	12		
Units: percentage of participants				
number (confidence interval 95%)	15.4 (1.9 to 45.4)	41.7 (15.2 to 72.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival

End point title	Progression Free Survival

End point description:

Defined as the time from randomization to disease progression based on central nervous system (CNS)-specific evaluation criteria as assessed by the investigator or death due to any cause, whichever occurs first. Participants did not progress or die before the data cutoff date for analysis were censored at the date of last disease assessment (including both radiologic assessment and neurologic assessment) where non-progression was documented. If a participant received any further anticancer therapy without prior documentation of disease progression, the participant was censored at the date of last disease assessment before starting new anti-cancer treatment. Participants were also censored at the date of last disease assessment with no documented progression if patients discontinued treatment for undocumented progression, toxicity or other reason before the data cutoff date for analysis. Due to low number of events, upper limit cannot be calculated and is denoted as "99999."

End point type	Secondary

End point timeframe:

From randomization until the end of treatment. The median time on treatment was 52 days for erlotinib and 58 days for etoposide.

End point values	Erlotinib	Etoposide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	12		
Units: days				
median (confidence interval 95%)	52 (29 to 62)	65 (23 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with Prolonged Stable Disease

End point title	Percentage of participants with Prolonged Stable Disease

End point description:

Prolonged stable disease (SD) was defined as SD with a duration of at least 16 weeks. The percentage of participants with prolonged SD was defined as participants who achieved a best overall response of CR or PR or MR or SD, and did not progress within 16 weeks from randomization. Progression was defined as a worsening of neurologic status that could not be explained by other causes, a > 25% increase in tumor size, the appearance of new lesions or CSF positivity, or increasing doses of corticosteroids required to maintain stable status.

End point type	Secondary

End point timeframe:

From randomization until the end of treatment. The median time on treatment was 52 days for erlotinib and 58 days for etoposide.

End point values	Erlotinib	Etoposide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	12		
Units: percentage of participants				
number (confidence interval 95%)	0 (0 to 24.7)	41.7 (15.2 to 72.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Stable Disease

End point title	Duration of Stable Disease

End point description:

Duration of stable disease (SD, defined as participants with an overall best response of complete, partial or minor response or stable disease) was defined as the time from the date of randomization to the first documented progression or death due to underlying cancer. If a participant had not progressed or died, the duration of SD was censored at the date of last adequate disease assessment. Duration of SD was only defined for participants whose best overall response was CR, PR, MR or SD. Progression was defined as a worsening of neurologic status that could not be explained by other causes, a > 25% increase in tumor size, the appearance of new lesions or CSF positivity, or increasing doses of corticosteroids required to maintain stable status.
Due to the low number of events, data cannot be calculated and is denoted as "99999" as applicable.

End point type	Secondary

End point timeframe:

From randomization until the end of treatment. The median time on treatment was 52 days for erlotinib and 58 days for etoposide.

End point values	Erlotinib	Etoposide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	5		
Units: days				
median (confidence interval 95%)	79 (78 to 80)	99999 (117 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival

End point description:

Overall survival was defined as the time from the date of randomization until the documented date of death. Participants who were still alive by the data cutoff date for analysis were censored on the last day the participant was known to be alive.

Due to the low number of events, overall survival cannot be reported in days, instead presented as the number of participants who died.

End point type	Secondary

End point timeframe:

From the randomization up to 12 months after the last dose. Median duration of follow-up was 12.9 months for erlotinib and 14.4 months for etoposide

End point values	Erlotinib	Etoposide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	12		
Units: participants	3	6		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

An AE was defined as any untoward medical occurrence in a study participant and did not necessarily have a causal relationship with the study treatment. Clinically significant vital sign aseessments, findings associated with signs and/or symptoms requiring withdrawal, dose modification or medical intervention were recorded as AEs. An AE was considered serious 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 relationship of each AE to study drug was assessed as either relaed or not related.

End point type	Secondary

End point timeframe:

From the date of first dose of study drug until 30 days after the last dose. The median time on treatment was 52 days for erlotinib and 58 days for etoposide.

End point values	Erlotinib	Etoposide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	12		
Units: participants				
number (not applicable)				
Any adverse event	13	11		
Drug-related adverse event	11	10		
Adverse event leading to death	1	0		
Drug-related adverse event leading to death	0	0		
Serious adverse event	6	5		
Drug-related serious adverse event	0	1		
AE leading to discontinuation	0	0		
Drug-related AE leading to discontinuation	0	0		

AE leading to dose interruption	2	5		
Drug-related AE leading to dose interruption	1	3		
AE leading to dose interruption and reduction	1	2		
Related AE leading to dose interruption/reduction	1	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the curve from time 0 to 24 hours post-dose for erlotinib

End point title	Area under the curve from time 0 to 24 hours post-dose for erlotinib[5]

End point description:

Pharmacokinetic parameters were determined from the serial plasma concentration data obtained for erlotinib. Area under the plasma concentration-time curve from time zero to 24 hours (the dosing interval) measured at the steady state using sparse sampling.

End point type	Secondary

End point timeframe:

Day 14 predose and 0.5 to 1.5 hours, 2 to 3 hours and 4 to 8 hours post-dose

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data values are not provided for the etoposide arm as the pharmacokinetic parameters were only measured for the investigative drug, and not for the comparator, as already pre-determined in the study plan/protocol.

End point values	Erlotinib			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: h*ng/mL				
geometric mean (confidence interval 95%)	26716.7 (20269 to 35215.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum observed plasma concentration of erlotinib (Cmax)

End point title	Maximum observed plasma concentration of erlotinib (Cmax)[6]

End point description:

Pharmacokinetic parameters were determined from the serial plasma concentration data obtained for erlotinib. Maximum observed plasma concentration (Cmax) was measured at steady on Day 14 using sparse sampling.

End point type	Secondary

End point timeframe:

Day 14 predose and 0.5 to 1.5 hours, 2 to 3 hours and 4 to 8 hours post-dose

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data values are not provided for the etoposide arm as the pharmacokinetic parameters were only measured for the investigative drug, and not for the comparator, as already pre-determined in the study plan/protocol.

End point values	Erlotinib			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: ng/mL				
geometric mean (confidence interval 95%)	1969.5 (1627.7 to 2382.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to maximum observed plasma concentration of erlotinib (Tmax)

End point title	Time to maximum observed plasma concentration of erlotinib (Tmax)[7]

End point description:

Pharmacokinetic parameters were determined from the serial plasma concentration data obtained for erlotinib. Time to the maximum observed plasma concentration of erlotinib (Tmax) was measured at steady state on Day 14 using sparse sampling.

End point type	Secondary

End point timeframe:

Day 14 predose and 0.5 to 1.5 hours, 2 to 3 hours and 4 to 8 hours post-dose

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data values are not provided for the etoposide arm as the pharmacokinetic parameters were only measured for the investigative drug, and not for the comparator, as already pre-determined in the study plan/protocol.

End point values	Erlotinib			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: hours				
geometric mean (confidence interval 95%)	2.1 (1.6 to 2.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent body cleareance (CL/F) of erlotinib

End point title	Apparent body cleareance (CL/F) of erlotinib[8]

End point description:

Pharmacokinetic parameters were determined from the serial plasma concentration data obtained for erlotinib. Apparent body clearance (CL/F) of erlotinib was measured at steady state on Day 14 using sparse sampling.

End point type	Secondary

End point timeframe:

Day 14 predose and 0.5 to 1.5 hours, 2 to 3 hours and 4 to 8 hours post-dose

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data values are not provided for the etoposide arm as the pharmacokinetic parameters were only measured for the investigative drug, and not for the comparator, as already pre-determined in the study plan/protocol.

End point values	Erlotinib			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: mL/m^2				
geometric mean (confidence interval 95%)	2922.1 (2233.4 to 3823.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent volume of Distribution (Vz/F) of erlotinib

End point title	Apparent volume of Distribution (Vz/F) of erlotinib[9]

End point description:

Pharmacokinetic parameters were determined from the serial plasma concentration data obtained for erlotinib. The apparent volume of distribtuion (Vz/F) of erlotinib was measured at steady state on day 14 using sparse sampling.

End point type	Secondary

End point timeframe:

Day 14 predose and 0.5 to 1.5 hours, 2 to 3 hours and 4 to 8 hours post-dose

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data values are not provided for the etoposide arm as the pharmacokinetic parameters were only measured for the investigative drug, and not for the comparator, as already pre-determined in the study plan/protocol.

End point values	Erlotinib			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: mL/m^2				
geometric mean (confidence interval 95%)	71628.5 (59572 to 86124.9)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the date of first dose of study drug until 30 days after last dose. The median time on treatment was 52 days for erlotinib and 58 days for etoposide.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13.0

Reporting groups

Reporting group title	Erlotinib
Reporting group description: -	
Reporting group title	Etoposide

Reporting group description: -

Serious adverse events	Erlotinib	Etoposide	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 13 (46.15%)	5 / 12 (41.67%)	
number of deaths (all causes)	3	6	
number of deaths resulting from adverse events	0		
Investigations			
Weight decreased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Nervous system disorders			
Convulsion			
subjects affected / exposed	2 / 13 (15.38%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Grand mal convulsion			

subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	0 / 13 (0.00%)	2 / 12 (16.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrocephalus			
subjects affected / exposed	2 / 13 (15.38%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Loss of consciousness			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis haemorrhagic			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Lower gastrointestinal haemorrhage			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary hesitation			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Lung infection			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			

subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypophosphataemia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Erlotinib	Etoposide	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 13 (100.00%)	11 / 12 (91.67%)	
Vascular disorders			
Epistaxis (vascular disorders)			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Hypertension			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Hypotension			
subjects affected / exposed	1 / 13 (7.69%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Vena cava thrombosis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Chills			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Fatigue			
subjects affected / exposed	3 / 13 (23.08%)	8 / 12 (66.67%)	
occurrences (all)	3	16	
Irritability			

subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Malaise			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Mucosal inflammation			
subjects affected / exposed	1 / 13 (7.69%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Oedema peripheral			
subjects affected / exposed	2 / 13 (15.38%)	1 / 12 (8.33%)	
occurrences (all)	2	2	
Pain			
subjects affected / exposed	2 / 13 (15.38%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
Pyrexia			
subjects affected / exposed	2 / 13 (15.38%)	4 / 12 (33.33%)	
occurrences (all)	3	5	
Immune system disorders			
Multiple allergies			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Breast enlargement			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Bronchospasm			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Cough			
subjects affected / exposed	2 / 13 (15.38%)	4 / 12 (33.33%)	
occurrences (all)	2	11	
Dyspnoea			
subjects affected / exposed	1 / 13 (7.69%)	2 / 12 (16.67%)	
occurrences (all)	1	2	
Epistaxis			

subjects affected / exposed	0 / 13 (0.00%)	3 / 12 (25.00%)	
occurrences (all)	0	3	
Nasal congestion			
subjects affected / exposed	1 / 13 (7.69%)	3 / 12 (25.00%)	
occurrences (all)	1	5	
Oropharyngeal pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Postnasal drip			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	2	
Productive cough			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Rhinitis allergic			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Rhinorrhoea			
subjects affected / exposed	1 / 13 (7.69%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Confusional state			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Depressed mood			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Depression			
subjects affected / exposed	0 / 13 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Insomnia			
subjects affected / exposed	0 / 13 (0.00%)	3 / 12 (25.00%)	
occurrences (all)	0	5	

Investigations			
Blood pressure increased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	3	
Blood urine present			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Heart rate increased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	3	
Neurophil count decreased			
subjects affected / exposed	1 / 13 (7.69%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Platelet count decreased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Urine output decreased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Weight decreased			
subjects affected / exposed	3 / 13 (23.08%)	2 / 12 (16.67%)	
occurrences (all)	3	3	
Weight increased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	3	
Injury, poisoning and procedural complications			
Anthropod bite			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Catheter site pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Contusion			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Fall			

subjects affected / exposed	1 / 13 (7.69%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Head injury			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Procedural complication			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Procedural pain			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Upper motor neurone lesion			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Ageusia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Amnesia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Ataxia			
subjects affected / exposed	2 / 13 (15.38%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
Cerebellar syndrome			
subjects affected / exposed	1 / 13 (7.69%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Coordination abnormal			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	4	
Cranial nerve disorder			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Dizziness			
subjects affected / exposed	1 / 13 (7.69%)	1 / 12 (8.33%)	
occurrences (all)	1	2	

Facial palsy			
subjects affected / exposed	1 / 13 (7.69%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Headache			
subjects affected / exposed	5 / 13 (38.46%)	7 / 12 (58.33%)	
occurrences (all)	10	16	
Hypersomnia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Hypoaesthesia			
subjects affected / exposed	1 / 13 (7.69%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Loss of consciousness			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Meningism			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Muscle spasticity			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Nervous system disorder			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Nystagmus			
subjects affected / exposed	3 / 13 (23.08%)	2 / 12 (16.67%)	
occurrences (all)	3	2	
Peripheral sensory neuropathy			
subjects affected / exposed	2 / 13 (15.38%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
Somnolence			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
Tongue paralysis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	3	

VIIth nerve paralysis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
VIth nerve paralysis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	3	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 13 (7.69%)	2 / 12 (16.67%)	
occurrences (all)	5	4	
Lymphopenia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	4	
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 13 (7.69%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Tinnitus			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Tympanic membrane perforation			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Diplopia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
Eye movement disorder			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Optic nerve disorder			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Strabismus			
subjects affected / exposed	0 / 13 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Vision blurred			

subjects affected / exposed	1 / 13 (7.69%)	1 / 12 (8.33%)	
occurrences (all)	1	2	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Abdominal pain			
subjects affected / exposed	2 / 13 (15.38%)	4 / 12 (33.33%)	
occurrences (all)	2	6	
Abdominal pain upper			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	3 / 13 (23.08%)	6 / 12 (50.00%)	
occurrences (all)	3	7	
Diarrhoea			
subjects affected / exposed	6 / 13 (46.15%)	4 / 12 (33.33%)	
occurrences (all)	6	13	
Dry mouth			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Gastritis			
subjects affected / exposed	1 / 13 (7.69%)	2 / 12 (16.67%)	
occurrences (all)	2	2	
Gastroesophageal reflux disease			
subjects affected / exposed	0 / 13 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	3	
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Lip ulceration			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Mouth ulceration			
subjects affected / exposed	1 / 13 (7.69%)	1 / 12 (8.33%)	
occurrences (all)	1	3	

Nausea			
subjects affected / exposed	3 / 13 (23.08%)	5 / 12 (41.67%)	
occurrences (all)	3	7	
Retching			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Stomatitis			
subjects affected / exposed	2 / 13 (15.38%)	1 / 12 (8.33%)	
occurrences (all)	2	3	
Vomiting			
subjects affected / exposed	6 / 13 (46.15%)	8 / 12 (66.67%)	
occurrences (all)	15	17	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 13 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Alopecia			
subjects affected / exposed	0 / 13 (0.00%)	4 / 12 (33.33%)	
occurrences (all)	0	7	
Dermatitis acneiform			
subjects affected / exposed	3 / 13 (23.08%)	0 / 12 (0.00%)	
occurrences (all)	9	0	
Dermatitis diaper			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Dry skin			
subjects affected / exposed	1 / 13 (7.69%)	2 / 12 (16.67%)	
occurrences (all)	1	3	
Erythema			
subjects affected / exposed	2 / 13 (15.38%)	0 / 12 (0.00%)	
occurrences (all)	3	0	
Hypoaethesia facial			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Nail discolouration			

subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Pain of skin			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	3	
Pruritus			
subjects affected / exposed	3 / 13 (23.08%)	0 / 12 (0.00%)	
occurrences (all)	3	0	
Purpura			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Rash			
subjects affected / exposed	4 / 13 (30.77%)	1 / 12 (8.33%)	
occurrences (all)	1	0	
Rash macular			
subjects affected / exposed	1 / 13 (7.69%)	2 / 12 (16.67%)	
occurrences (all)	1	2	
Rash maculo-papular			
subjects affected / exposed	2 / 13 (15.38%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
Rash papular			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Skin fissures			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
Skin hyperpigmentation			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Skin striae			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	3	
Skin ulcer			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Swelling face			

subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Bladder spasm			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Enuresis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Urinary incontinence			
subjects affected / exposed	1 / 13 (7.69%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Endocrine disorders			
Cushingoid			
subjects affected / exposed	0 / 13 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	3	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 13 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	4	
Back pain			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Muscle spasms			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Muscular weakness			
subjects affected / exposed	3 / 13 (23.08%)	2 / 12 (16.67%)	
occurrences (all)	3	5	
Myalgia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Neck pain			
subjects affected / exposed	1 / 13 (7.69%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Pain in extremity			

subjects affected / exposed	1 / 13 (7.69%)	4 / 12 (33.33%)	
occurrences (all)	1	7	
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Conjunctivitis infective			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Corneal infection			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Escherichia urinary tract infection			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Fungal skin infection			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Mucosal infection			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Nasophayngitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Otitis media			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Paronychia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
Pneumonia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Sinusitis			
subjects affected / exposed	0 / 13 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	3	

Upper respiratory tract infection			
subjects affected / exposed	0 / 13 (0.00%)	3 / 12 (25.00%)	
occurrences (all)	0	3	
Urinary tract infection			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 13 (15.38%)	2 / 12 (16.67%)	
occurrences (all)	2	4	
Dehydration			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Hyokalaemia			
subjects affected / exposed	0 / 13 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	4	

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 lack of efficacy criteria were met at the second interim analysis dated 15 Aug 2012. Per the DMC recommendation and FDA's agreement, the enrollment of patients in this study and Study OSI-774-206 was permanently closed.

Notes: