



Clinical trial results:

Randomized, Placebo-controlled, Double-blind Phase 1b/2 Study of U3-1287 (AMG 888) in Combination with Erlotinib in EGFR Treatment Naive Subjects with Advanced Non-Small Cell Lung Cancer (NSCLC) Who Have Progressed on at Least One Prior Chemotherapy

Summary

EudraCT number	2010-021082-74
Trial protocol	DE BE LT HU GB BG AT SI IT
Global end of trial date	06 December 2013

Results information

Result version number	v1 (current)
This version publication date	09 April 2016
First version publication date	09 April 2016

Trial information

Trial identification

Sponsor protocol code	U31287-A-U201
-----------------------	---------------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01211483
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Daiichi Sankyo Development Limited
Sponsor organisation address	Chiltern Place, Chalfont Park, Gerrards Cross, United Kingdom, SL90BG
Public contact	Clinical Trial Information , Daiichi Sankyo Development Limited, +44 1753482800, info@dsd-eu.com
Scientific contact	Clinical Trial Information , Daiichi Sankyo Development Limited, +44 1753482800, info@dsd-eu.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	22 September 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 November 2013
Global end of trial reached?	Yes
Global end of trial date	06 December 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Phase 1b Portion

- To evaluate the safety and tolerability of the combination of patritumab and erlotinib in subjects with advanced or metastatic NSCLC.
- To determine the recommended dose of patritumab for Phase 2 study (RP2D) in combination with erlotinib.

Phase II Portion

- To evaluate progression-free survival (PFS) among all randomized subjects treated with erlotinib in combination with high and low doses of patritumab compared to erlotinib plus placebo.
- To evaluate the safety profile of the combination of patritumab and erlotinib.

Protection of trial subjects:

The study was conducted in compliance with ethical principles that have their origin in the Declarations of Helsinki, the International Conference on Harmonisation (ICH) consolidated Guideline E6 for Good Clinical Practice (GCP) (CPMP/ICH/135/95), and applicable regulatory requirement(s):

- European Commission Directive (2001/20/EC Apr 2001) and/or
- European Commission Directive (2005/28/EC Apr 2005) and/or
- United States (US) Food and Drug Administration (FDA) GCP Regulations: Code of Federal Regulations (CFR) Title 21, parts 11, 50, 54, 56, and 312 as appropriate and/or
- Other applicable local regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 September 2010
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	Israel: 7
Country: Number of subjects enrolled	Slovenia: 1
Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	Austria: 1
Country: Number of subjects enrolled	Belgium: 13
Country: Number of subjects enrolled	Bulgaria: 8
Country: Number of subjects enrolled	Germany: 92
Country: Number of subjects enrolled	Hungary: 15
Country: Number of subjects enrolled	Italy: 4

Country: Number of subjects enrolled	Lithuania: 7
Country: Number of subjects enrolled	Ukraine: 18
Country: Number of subjects enrolled	United States: 31
Country: Number of subjects enrolled	Romania: 21
Worldwide total number of subjects	222
EEA total number of subjects	166

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)	133
From 65 to 84 years	88
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects, after having the study explained to them by the Investigator or designee, gave voluntary and signed informed consent before participating in any study procedures.

Period 1

Period 1 title	Baseline and Treatment (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo + Erlotinib

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Placebo was administered IV every 3 weeks

Investigational medicinal product name	Erlotinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

150mg/day erlotinib taken in the morning, at the same time of each day, 1 hour before or 2 hours after a meal.

Arm title	Patritumab 18 mg/kg + Erlotinib
------------------	---------------------------------

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Patritumab
Investigational medicinal product code	U3-1287
Other name	AMG 888
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patritumab infusions were administered every 3 weeks. Patritumab was administered as a continuous intravenous infusion over 60 minutes (\pm 10 minutes). Infusion times could be extended to a maximum of 120 minutes for subjects unable to tolerate the 60 minute infusion.

Investigational medicinal product name	Erlotinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet

Routes of administration	Oral use
--------------------------	----------

Dosage and administration details:

150mg/day erlotinib taken in the morning, at the same time of each day, 1 hour before or 2 hours after a meal.

Arm title	Patritumab 9 mg/kg + Erlotinib
------------------	--------------------------------

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Patritumab
Investigational medicinal product code	U3-1287
Other name	AMG 888
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patritumab infusions were administered every 3 weeks. Patritumab was administered as a continuous intravenous infusion over 60 minutes (\pm 10 minutes). Infusion times could be extended to a maximum of 120 minutes for subjects unable to tolerate the 60 minute infusion.

Investigational medicinal product name	Erlotinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

150mg/day erlotinib taken in the morning, at the same time of each day, 1 hour before or 2 hours after a meal.

Arm title	Patritumab 18 mg/kg + Erlotinib Phase Ib
------------------	--

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Patritumab
Investigational medicinal product code	U3-1287
Other name	AMG 888
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patritumab infusions were administered every 3 weeks. Patritumab was administered as a continuous intravenous infusion over 60 minutes (\pm 10 minutes). Infusion times could be extended to a maximum of 120 minutes for subjects unable to tolerate the 60 minute infusion.

Investigational medicinal product name	Erlotinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

150mg/day erlotinib taken in the morning, at the same time of each day, 1 hour before or 2 hours after a meal.

Number of subjects in period 1	Placebo + Erlotinib	Patritumab 18 mg/kg + Erlotinib	Patritumab 9 mg/kg + Erlotinib
Started	71	72	72
Phase Ib	0	0	0
Phase II	71	72	72
Completed	0	0	0
Not completed	71	72	72
Adverse event, serious fatal	4	8	2
Enrolled/randomized but Not Dosed	-	2	1
Consent withdrawn by subject	3	1	3
Adverse event, non-fatal	7	11	8
Other	3	4	7
Progressive Disease	53	46	48
Ongoing on the treatment	1	-	3

Number of subjects in period 1	Patritumab 18 mg/kg + Erlotinib Phase Ib
Started	7
Phase Ib	7
Phase II	0
Completed	0
Not completed	7
Adverse event, serious fatal	-
Enrolled/randomized but Not Dosed	-
Consent withdrawn by subject	-
Adverse event, non-fatal	-
Other	-
Progressive Disease	7
Ongoing on the treatment	-

Baseline characteristics

Reporting groups

Reporting group title	Baseline and Treatment
-----------------------	------------------------

Reporting group description: -

Reporting group values	Baseline and Treatment	Total	
Number of subjects	222	222	
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)	133	133	
From 65-84 years	88	88	
85 years and over	1	1	
Gender categorical			
Units: Subjects			
Female	87	87	
Male	135	135	

End points

End points reporting groups

Reporting group title	Placebo + Erlotinib
Reporting group description: -	
Reporting group title	Patritumab 18 mg/kg + Erlotinib
Reporting group description: -	
Reporting group title	Patritumab 9 mg/kg + Erlotinib
Reporting group description: -	
Reporting group title	Patritumab 18 mg/kg + Erlotinib Phase Ib
Reporting group description: -	

Primary: Progression Free Survival - Time to event (months)

End point title	Progression Free Survival - Time to event (months) ^[1]
End point description:	

End point type	Primary
End point timeframe:	
16 months	

Notes:

[1] - 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: Progression-Free Survival was not assessed in the Phase IB portion of the study, the objective of this portion being to evaluate the safety and tolerability of the combination of patritumab and erlotinib in subjects with advanced or metastatic NSCLC and determine the recommended dose of patritumab for the Phase 2 in combination with erlotinib.

End point values	Placebo + Erlotinib	Patritumab 18 mg/kg + Erlotinib	Patritumab 9 mg/kg + Erlotinib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	71 ^[2]	70 ^[3]	71 ^[4]	
Units: Months				
median (confidence interval 95%)	1.6 (1.4 to 2.6)	1.4 (1.3 to 2.7)	2.5 (1.5 to 3)	

Notes:

[2] - 59 subjects had an event

[3] - 58 subjects had an event

[4] - 52 subjects had an event

Statistical analyses

Statistical analysis title	Stratified log-rank linear trend test for the dose
Comparison groups	Placebo + Erlotinib v Patritumab 18 mg/kg + Erlotinib v Patritumab 9 mg/kg + Erlotinib
Number of subjects included in analysis	212
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.9166
Method	Logrank

Statistical analysis title	Progression-Free Survival Pairwise Comparisons
Comparison groups	Placebo + Erlotinib v Patritumab 18 mg/kg + Erlotinib
Number of subjects included in analysis	141
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.978
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.674
upper limit	1.42

Statistical analysis title	Progression-Free Survival Pairwise Comparisons
Comparison groups	Placebo + Erlotinib v Patritumab 9 mg/kg + Erlotinib
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.523
upper limit	1.131

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs were reported from time of Informed Consent to EOT visit assessment and up to 53 days after the last dose of U3-1287, or, if U3-1287 was discontinued earlier or if subject received erlotinib alone, up to 30 days after the last dose of erlotinib

Adverse event reporting additional description:

AEs may have been directly observed, reported spontaneously by the subject or by questioning the subject at each study visit.

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	13.0
--------------------	------

Reporting groups

Reporting group title	Placebo + Erlotinib
-----------------------	---------------------

Reporting group description: -

Reporting group title	U3-1287 9 mg/kg + Erlotinib
-----------------------	-----------------------------

Reporting group description: -

Reporting group title	U3-1287 18 mg/kg + Erlotinib
-----------------------	------------------------------

Reporting group description: -

Serious adverse events	Placebo + Erlotinib	U3-1287 9 mg/kg + Erlotinib	U3-1287 18 mg/kg + Erlotinib
Total subjects affected by serious adverse events			
subjects affected / exposed	24 / 71 (33.80%)	24 / 71 (33.80%)	35 / 70 (50.00%)
number of deaths (all causes)	53	53	62
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 71 (0.00%)	2 / 71 (2.82%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastatic pain			
subjects affected / exposed	0 / 71 (0.00%)	0 / 71 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bile duct cancer			
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Metastases to central nervous system			
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to bone			
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	0 / 71 (0.00%)	0 / 71 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Jugular vein thrombosis			
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
General physical health deterioration			
subjects affected / exposed	1 / 71 (1.41%)	2 / 71 (2.82%)	4 / 70 (5.71%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaise			
subjects affected / exposed	0 / 71 (0.00%)	0 / 71 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	0 / 71 (0.00%)	0 / 71 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthenia			

subjects affected / exposed	1 / 71 (1.41%)	1 / 71 (1.41%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multi-organ failure			
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Puncture site pain			
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	5 / 70 (7.14%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 5
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 4
Dyspnoea			
subjects affected / exposed	2 / 71 (2.82%)	2 / 71 (2.82%)	3 / 70 (4.29%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pulmonary embolism			

subjects affected / exposed	3 / 71 (4.23%)	0 / 71 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Alveolitis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 71 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchial haemorrhage			
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Cough			
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary haemorrhage			
subjects affected / exposed	0 / 71 (0.00%)	0 / 71 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atelectasis			
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oropharyngeal pain			

subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 71 (0.00%)	0 / 71 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 71 (0.00%)	0 / 71 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prothrombin time prolonged			
subjects affected / exposed	0 / 71 (0.00%)	0 / 71 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood bilirubin increased			
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine increased			
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weight decreased			
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural			

complications			
Femur fracture			
subjects affected / exposed	0 / 71 (0.00%)	0 / 71 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural pain			
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skeletal injury			
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardio-respiratory arrest			
subjects affected / exposed	2 / 71 (2.82%)	1 / 71 (1.41%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 2	0 / 1	0 / 1
Acute myocardial infarction			
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 71 (0.00%)	0 / 71 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cardiovascular insufficiency			
subjects affected / exposed	0 / 71 (0.00%)	0 / 71 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cor pulmonale			
subjects affected / exposed	0 / 71 (0.00%)	0 / 71 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Ventricular fibrillation			
subjects affected / exposed	0 / 71 (0.00%)	0 / 71 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorder			
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Brain oedema			
subjects affected / exposed	0 / 71 (0.00%)	0 / 71 (0.00%)	2 / 70 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Convulsion			
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Grand mal convulsion			
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia of malignant disease			
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphadenopathy			
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Neutropenia			
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 71 (0.00%)	0 / 71 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Panophthalmitis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 71 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 71 (1.41%)	5 / 71 (7.04%)	4 / 70 (5.71%)
occurrences causally related to treatment / all	0 / 1	0 / 5	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 71 (0.00%)	2 / 71 (2.82%)	3 / 70 (4.29%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	1 / 71 (1.41%)	1 / 71 (1.41%)	2 / 70 (2.86%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 71 (0.00%)	0 / 71 (0.00%)	2 / 70 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Dysphagia			

subjects affected / exposed	0 / 71 (0.00%)	2 / 71 (2.82%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 71 (0.00%)	0 / 71 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 71 (0.00%)	0 / 71 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 71 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varices oesophageal			
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash			

subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	2 / 70 (2.86%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash generalised			
subjects affected / exposed	0 / 71 (0.00%)	2 / 71 (2.82%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin ulcer			
subjects affected / exposed	0 / 71 (0.00%)	0 / 71 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dermatitis acneiform			
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 71 (0.00%)	0 / 71 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure acute			
subjects affected / exposed	0 / 71 (0.00%)	0 / 71 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 71 (0.00%)	0 / 71 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain			
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Musculoskeletal chest pain			
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis of jaw			
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	3 / 71 (4.23%)	3 / 71 (4.23%)	3 / 70 (4.29%)
occurrences causally related to treatment / all	0 / 3	0 / 5	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Cellulitis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 71 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia sepsis			
subjects affected / exposed	0 / 71 (0.00%)	0 / 71 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile infection			
subjects affected / exposed	0 / 71 (0.00%)	0 / 71 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin infection			
subjects affected / exposed	0 / 71 (0.00%)	0 / 71 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			

subjects affected / exposed	0 / 71 (0.00%)	0 / 71 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	1 / 71 (1.41%)	1 / 71 (1.41%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infection			
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 71 (1.41%)	1 / 71 (1.41%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	0 / 71 (0.00%)	0 / 71 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Decreased appetite			
subjects affected / exposed	1 / 71 (1.41%)	1 / 71 (1.41%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	1 / 71 (1.41%)	0 / 71 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Placebo + Erlotinib	U3-1287 9 mg/kg + Erlotinib	U3-1287 18 mg/kg + Erlotinib
Total subjects affected by non-serious adverse events			
subjects affected / exposed	69 / 71 (97.18%)	70 / 71 (98.59%)	69 / 70 (98.57%)
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	13 / 71 (18.31%)	22 / 71 (30.99%)	18 / 70 (25.71%)
occurrences (all)	18	27	24
General physical health deterioration			
subjects affected / exposed	7 / 71 (9.86%)	10 / 71 (14.08%)	11 / 70 (15.71%)
occurrences (all)	8	10	14
Oedema peripheral			
subjects affected / exposed	4 / 71 (5.63%)	9 / 71 (12.68%)	9 / 70 (12.86%)
occurrences (all)	4	10	9
Pyrexia			
subjects affected / exposed	4 / 71 (5.63%)	6 / 71 (8.45%)	8 / 70 (11.43%)
occurrences (all)	4	7	9
Asthenia			
subjects affected / exposed	6 / 71 (8.45%)	4 / 71 (5.63%)	7 / 70 (10.00%)
occurrences (all)	9	4	8
Mucosal inflammation			
subjects affected / exposed	2 / 71 (2.82%)	6 / 71 (8.45%)	4 / 70 (5.71%)
occurrences (all)	2	7	4
Non-cardiac chest pain			
subjects affected / exposed	5 / 71 (7.04%)	1 / 71 (1.41%)	5 / 70 (7.14%)
occurrences (all)	5	1	5
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	12 / 71 (16.90%)	17 / 71 (23.94%)	12 / 70 (17.14%)
occurrences (all)	14	19	14
Cough			
subjects affected / exposed	11 / 71 (15.49%)	11 / 71 (15.49%)	5 / 70 (7.14%)
occurrences (all)	16	13	5
Dysphonia			

subjects affected / exposed	1 / 71 (1.41%)	7 / 71 (9.86%)	2 / 70 (2.86%)
occurrences (all)	1	7	2
Respiratory failure			
subjects affected / exposed	2 / 71 (2.82%)	0 / 71 (0.00%)	6 / 70 (8.57%)
occurrences (all)	2	0	6
Epistaxis			
subjects affected / exposed	2 / 71 (2.82%)	6 / 71 (8.45%)	6 / 70 (8.57%)
occurrences (all)	2	6	8
Productive cough			
subjects affected / exposed	4 / 71 (5.63%)	6 / 71 (8.45%)	3 / 70 (4.29%)
occurrences (all)	5	7	3
Haemoptysis			
subjects affected / exposed	5 / 71 (7.04%)	3 / 71 (4.23%)	5 / 70 (7.14%)
occurrences (all)	5	3	5
Oropharyngeal pain			
subjects affected / exposed	3 / 71 (4.23%)	4 / 71 (5.63%)	0 / 70 (0.00%)
occurrences (all)	4	4	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	4 / 71 (5.63%)	1 / 71 (1.41%)	0 / 70 (0.00%)
occurrences (all)	5	1	0
Insomnia			
subjects affected / exposed	1 / 71 (1.41%)	4 / 71 (5.63%)	2 / 70 (2.86%)
occurrences (all)	1	4	2
Investigations			
Weight decreased			
subjects affected / exposed	8 / 71 (11.27%)	16 / 71 (22.54%)	10 / 70 (14.29%)
occurrences (all)	11	17	14
Nervous system disorders			
Brain oedema			
subjects affected / exposed	2 / 71 (2.82%)	0 / 71 (0.00%)	4 / 70 (5.71%)
occurrences (all)	2	0	4
Dizziness			
subjects affected / exposed	2 / 71 (2.82%)	4 / 71 (5.63%)	1 / 70 (1.43%)
occurrences (all)	2	4	1
Blood and lymphatic system disorders			

Anaemia subjects affected / exposed occurrences (all)	5 / 71 (7.04%) 7	6 / 71 (8.45%) 10	7 / 70 (10.00%) 11
Anaemia of malignant disease subjects affected / exposed occurrences (all)	1 / 71 (1.41%) 1	1 / 71 (1.41%) 1	5 / 70 (7.14%) 5
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	2 / 71 (2.82%) 3	4 / 71 (5.63%) 4	5 / 70 (7.14%) 5
Eye disorders Conjunctivitis subjects affected / exposed occurrences (all)	2 / 71 (2.82%) 6	5 / 71 (7.04%) 7	4 / 70 (5.71%) 4
Lacrimation increased subjects affected / exposed occurrences (all)	0 / 71 (0.00%) 0	5 / 71 (7.04%) 5	0 / 70 (0.00%) 0
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	23 / 71 (32.39%) 40	50 / 71 (70.42%) 65	47 / 70 (67.14%) 66
Nausea subjects affected / exposed occurrences (all)	14 / 71 (19.72%) 14	17 / 71 (23.94%) 24	26 / 70 (37.14%) 29
Vomiting subjects affected / exposed occurrences (all)	5 / 71 (7.04%) 12	7 / 71 (9.86%) 7	18 / 70 (25.71%) 22
Constipation subjects affected / exposed occurrences (all)	4 / 71 (5.63%) 4	10 / 71 (14.08%) 12	9 / 70 (12.86%) 9
Abdominal pain subjects affected / exposed occurrences (all)	3 / 71 (4.23%) 4	9 / 71 (12.68%) 10	9 / 70 (12.86%) 10
Abdominal pain upper subjects affected / exposed occurrences (all)	8 / 71 (11.27%) 9	5 / 71 (7.04%) 5	5 / 70 (7.14%) 5
Dysphagia			

subjects affected / exposed	2 / 71 (2.82%)	7 / 71 (9.86%)	0 / 70 (0.00%)
occurrences (all)	2	7	0
Stomatitis			
subjects affected / exposed	0 / 71 (0.00%)	3 / 71 (4.23%)	6 / 70 (8.57%)
occurrences (all)	0	3	6
Dyspepsia			
subjects affected / exposed	1 / 71 (1.41%)	5 / 71 (7.04%)	3 / 70 (4.29%)
occurrences (all)	1	6	3
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	28 / 71 (39.44%)	38 / 71 (53.52%)	35 / 70 (50.00%)
occurrences (all)	55	60	58
Dry skin			
subjects affected / exposed	6 / 71 (8.45%)	12 / 71 (16.90%)	5 / 70 (7.14%)
occurrences (all)	9	14	5
Rash generalised			
subjects affected / exposed	4 / 71 (5.63%)	8 / 71 (11.27%)	8 / 70 (11.43%)
occurrences (all)	4	16	11
Dermatitis acneiform			
subjects affected / exposed	7 / 71 (9.86%)	6 / 71 (8.45%)	4 / 70 (5.71%)
occurrences (all)	12	9	6
Alopecia			
subjects affected / exposed	4 / 71 (5.63%)	4 / 71 (5.63%)	6 / 70 (8.57%)
occurrences (all)	4	5	6
Pruritus			
subjects affected / exposed	4 / 71 (5.63%)	6 / 71 (8.45%)	3 / 70 (4.29%)
occurrences (all)	5	6	3
Decubitus ulcer			
subjects affected / exposed	0 / 71 (0.00%)	1 / 71 (1.41%)	5 / 70 (7.14%)
occurrences (all)	0	1	6
Skin fissures			
subjects affected / exposed	1 / 71 (1.41%)	3 / 71 (4.23%)	5 / 70 (7.14%)
occurrences (all)	1	3	5
Night sweats			
subjects affected / exposed	4 / 71 (5.63%)	2 / 71 (2.82%)	1 / 70 (1.43%)
occurrences (all)	4	3	1

Pruritus generalised subjects affected / exposed occurrences (all)	0 / 71 (0.00%) 0	4 / 71 (5.63%) 5	2 / 70 (2.86%) 4
Musculoskeletal and connective tissue disorders			
Back pain subjects affected / exposed occurrences (all)	4 / 71 (5.63%) 4	3 / 71 (4.23%) 3	6 / 70 (8.57%) 6
Pain in extremity subjects affected / exposed occurrences (all)	1 / 71 (1.41%) 1	6 / 71 (8.45%) 10	4 / 70 (5.71%) 5
Musculoskeletal pain subjects affected / exposed occurrences (all)	4 / 71 (5.63%) 6	3 / 71 (4.23%) 3	4 / 70 (5.71%) 4
Musculoskeletal chest pain subjects affected / exposed occurrences (all)	3 / 71 (4.23%) 3	4 / 71 (5.63%) 7	3 / 70 (4.29%) 3
Infections and infestations			
Paronychia subjects affected / exposed occurrences (all)	1 / 71 (1.41%) 1	5 / 71 (7.04%) 5	8 / 70 (11.43%) 8
Oral candidiasis subjects affected / exposed occurrences (all)	0 / 71 (0.00%) 0	6 / 71 (8.45%) 6	3 / 70 (4.29%) 3
Urinary tract infection subjects affected / exposed occurrences (all)	2 / 71 (2.82%) 2	4 / 71 (5.63%) 8	5 / 70 (7.14%) 6
Nasopharyngitis subjects affected / exposed occurrences (all)	2 / 71 (2.82%) 3	5 / 71 (7.04%) 8	0 / 70 (0.00%) 0
Pneumonia subjects affected / exposed occurrences (all)	5 / 71 (7.04%) 5	4 / 71 (5.63%) 10	4 / 70 (5.71%) 4
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	14 / 71 (19.72%) 17	17 / 71 (23.94%) 21	18 / 70 (25.71%) 19

Hypokalaemia			
subjects affected / exposed	3 / 71 (4.23%)	11 / 71 (15.49%)	12 / 70 (17.14%)
occurrences (all)	3	14	17
Dehydration			
subjects affected / exposed	1 / 71 (1.41%)	4 / 71 (5.63%)	5 / 70 (7.14%)
occurrences (all)	4	4	6
Hyponatraemia			
subjects affected / exposed	3 / 71 (4.23%)	1 / 71 (1.41%)	4 / 70 (5.71%)
occurrences (all)	3	1	5
Hypomagnesaemia			
subjects affected / exposed	0 / 71 (0.00%)	4 / 71 (5.63%)	0 / 70 (0.00%)
occurrences (all)	0	5	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 January 2011	<ol style="list-style-type: none">1. An exclusion criterion to exclude subjects with a history of hypersensitivity to any of the study drugs or any excipients was added.2. The window for the end-of-treatment visit was revised to 53 to 60 days after the last dose of study drug to ensure safety follow-up for at least 5 times the elimination half-life of U3-1287.3. The extension phase of the protocol was deleted.4. An independent Data Monitoring Committee (DMC) was to be established prior to the last subject in the Phase 1b portion of the study completing 1 cycle of treatment.

Notes:

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.

Results released at ASCO: J Clin Oncol 32:5s, 2014 (suppl; abstr 8045)
--

Notes:

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/26137564>