



Clinical trial results:

Randomized phase II trial of erlotinib (TARCEVA®) or intermittent administration of erlotinib and docetaxel as second-line after chemotherapy failure in male ex-smokers with locally advanced or metastatic non-small cell lung cancer (NSCLC)

Summary

EudraCT number	2010-020229-42
Trial protocol	IT
Global end of trial date	29 July 2014

Results information

Result version number	v1 (current)
This version publication date	23 April 2016
First version publication date	23 April 2016

Trial information

Trial identification

Sponsor protocol code	ML21869
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01204697
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	Roche Trial Information Hotline, F. Hoffmann-La Roche AG, 41 61 6878333, global.trial_information@roche.com
Scientific contact	Roche Trial Information Hotline, F. Hoffmann-La Roche AG, 41 61 6878333, global.trial_information@roche.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	29 July 2014
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	29 July 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of erlotinib and erlotinib combined with docetaxel in ex-smoker participants with squamous NSCLC by using progression-free rate (PFR) at 6 months as primary endpoint.

Protection of trial subjects:

The study was conducted under the provisions of the Declaration of Helsinki, and in accordance with the International Conference on Harmonization (ICH) Consolidated Guideline on Good Clinical Practice (GCP).

The study protocol, protocol amendment, patient information leaflet and informed consent documents were submitted to the Independent Ethics Committee (IEC) of each center participating in the study prior to any study-related procedure was started. The study protocol was approved by the local IEC of each center participating in the study.

Prior to study start, participants were given a full explanation of the aims of the study, the benefits, potential discomforts and risks of taking part in the study. Before any study procedure was started, study participants were also given a written explanation of the study procedures in the study information sheet and informed consent was obtained.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 November 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Italy: 74
Worldwide total number of subjects	74
EEA total number of subjects	74

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)	24
From 65 to 84 years	50
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Due to difficulties in enrolment, the study was prematurely interrupted with 74 participants enrolled in total (all were randomized).

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 received erlotinib (Tarceva) at a dose of 150 milligram per day (mg/day) orally as monotherapy, up to progressive disease (PD), death, or unacceptable toxicity.

Arm type	Experimental
Investigational medicinal product name	Erlotinib
Investigational medicinal product code	
Other name	Tarceva
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received erlotinib at a dose of 150 mg/day orally as monotherapy, up to PD, death, or unacceptable toxicity.

Arm title	Docetaxel and erlotinib
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Arm description:

Participants received docetaxel at a dose of 75 milligram per square meter (mg/m²) as an intravenous infusion on Day 1 of each 3-week cycle, and erlotinib at a dose of 150 mg/day orally from Day 2 to Day 16 of each 3-week cycle for 4 cycles, administered in absence of PD, death, or unacceptable toxicity. Following the 4 cycles, erlotinib 150 mg/day was administered orally as monotherapy up to PD, death or unacceptable toxicity.

Arm type	Experimental
Investigational medicinal product name	Erlotinib
Investigational medicinal product code	
Other name	Tarceva
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received erlotinib at a dose of 150 mg/day orally as monotherapy, up to PD, death, or unacceptable toxicity.

Investigational medicinal product name	Docetaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received docetaxel at a dose of 75 mg/m² as an intravenous infusion on Day 1 of each 3-

week cycle for 4 cycles, in absence of PD, death, or unacceptable toxicity.

Number of subjects in period 1	Erlotinib	Docetaxel and erlotinib
Started	36	38
Treated	36	37
Completed	5	2
Not completed	31	36
Consent withdrawn by subject	2	4
Randomized, but not treated	-	1
Death	26	27
Lost to follow-up	3	4

Baseline characteristics

Reporting groups

Reporting group title	Erlotinib
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Reporting group description:

Participants received erlotinib (Tarceva) at a dose of 150 milligram per day (mg/day) orally as monotherapy, up to progressive disease (PD), death, or unacceptable toxicity.

Reporting group title	Docetaxel and erlotinib
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Reporting group description:

Participants received docetaxel at a dose of 75 milligram per square meter (mg/m²) as an intravenous infusion on Day 1 of each 3-week cycle, and erlotinib at a dose of 150 mg/day orally from Day 2 to Day 16 of each 3-week cycle for 4 cycles, administered in absence of PD, death, or unacceptable toxicity. Following the 4 cycles, erlotinib 150 mg/day was administered orally as monotherapy up to PD, death or unacceptable toxicity.

Reporting group values	Erlotinib	Docetaxel and erlotinib	Total
Number of subjects	36	38	74
Age categorical Units: Subjects			

Age continuous			
Data for Age continuous were reported for treated (73) participants only.			
Units: years			
arithmetic mean	68.4	65.9	
standard deviation	± 8.3	± 8.1	-
Gender categorical Units: Subjects			
Female	0	1	1
Male	36	36	72
Not available	0	1	1

End points

End points reporting groups

Reporting group title	Erlotinib
Reporting group description:	
Participants received erlotinib (Tarceva) at a dose of 150 milligram per day (mg/day) orally as monotherapy, up to progressive disease (PD), death, or unacceptable toxicity.	
Reporting group title	Docetaxel and erlotinib
Reporting group description:	
Participants received docetaxel at a dose of 75 milligram per square meter (mg/m ²) as an intravenous infusion on Day 1 of each 3-week cycle, and erlotinib at a dose of 150 mg/day orally from Day 2 to Day 16 of each 3-week cycle for 4 cycles, administered in absence of PD, death, or unacceptable toxicity. Following the 4 cycles, erlotinib 150 mg/day was administered orally as monotherapy up to PD, death or unacceptable toxicity.	

Primary: Percentage of Participants Free From Disease Progression or Death at 6 Months

End point title	Percentage of Participants Free From Disease Progression or Death at 6 Months ^[1]
End point description:	
According to Response Evaluation Criteria in Solid Tumors (RECIST) Version 1.1, progressive Disease (PD) is defined as: for Target Lesions - At least a 20 percent (%) increase in the sum of diameters of target lesions, taking as reference the smallest sum on study (this includes the baseline sum if that is the smallest on study). In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 millimeter (mm). (Note: the appearance of one or more new lesions is also considered progression). For Non-Target Lesions - Unequivocal progression of existing non-target lesions. (Note: the appearance of one or more new lesions is also considered progression). Analysis was performed on Full Analysis Set (FAS) defined as all randomized participants who received at least one dose of study medication. Participants were analyzed according to treatment received.	
End point type	Primary
End point timeframe:	
Month 6	

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: Statistical hypothesis testing was not planned for this study. Therefore, only descriptive statistical methods were applied and reported.

End point values	Erlotinib	Docetaxel and erlotinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	37		
Units: percentage of participants				
number (confidence interval 95%)	8.3 (0 to 17.4)	8.1 (0 to 16.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free Survival (PFS)

End point title	Progression-free Survival (PFS)
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End point description:

Progression-free Survival (PFS) was defined as the interval (in days) between the date of randomization and the first documentation of progressive disease or death from any cause. Participants alive and progression-free were considered as censored at the date of the last tumor assessment when the participant was known to be progression-free. Participants without postbaseline tumor assessment, but known to be alive, were censored at the time of randomization. $PFS\ (days) = (Date\ of\ Event - Date\ of\ Randomization) + 1$. PFS was assessed using the KaplanMeier method. Detailed definition of PD is provided in Outcome Measure "Percentage of Participants Free From Disease Progression or Death at 6 Months". Analysis was performed on FAS population.

End point type	Secondary
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End point timeframe:

From randomization until progressive disease or death, assessed up to 18 months

End point values	Erlotinib	Docetaxel and erlotinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	37		
Units: months				
median (confidence interval 95%)	2.33 (2.13 to 4.13)	2.82 (2.3 to 3.97)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)
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End point description:

Overall survival (OS) was defined as the interval (in days) between the date of randomization and death from any cause. Participants alive at the time of the analysis were censored at the date they were last known to be alive. OS was assessed using the KaplanMeier method. Analysis was performed on FAS population.

End point type	Secondary
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End point timeframe:

From randomization until death, assessed up to 18 months

End point values	Erlotinib	Docetaxel and erlotinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	37		
Units: months				
median (confidence interval 95%)	5.61 (3.54 to 8.69)	8.95 (6.13 to 10.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With a Best Overall Response of Complete Response (CR) or Partial Response (PR)

End point title	Percentage of Participants With a Best Overall Response of Complete Response (CR) or Partial Response (PR)
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End point description:

Best overall response (CR or PR) was defined as the best response recorded from the start of the treatment until disease progression (PD). Best response in this trial was defined as the best response observed at any post-treatment visits. According to RECIST Version 1.1, CR was defined as complete disappearance of all target lesions and non-target disease, with the exception of nodal disease. All nodes, both target and non-target, must decrease to normal (short axis less than [$<$] 10 mm). No new lesions. PR was defined as greater than or equal to [$\geq$] 30% decrease under baseline of the sum of diameters of all target lesions. The short axis was used in the sum for target nodes, while the longest diameter was used in the sum for all other target lesions. No unequivocal progression of non-target disease. No new lesions. Analysis was performed on FAS population.

End point type	Secondary
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End point timeframe:

From randomization until progressive disease or death, assessed up to 18 months

End point values	Erlotinib	Docetaxel and erlotinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	37		
Units: percentage of participants				
number (confidence interval 95%)	2.8 (0 to 8.15)	8.1 (0 to 16.9)		

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
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End point description:

Disease control was defined as PR, CR, or SD. Participants who did not achieve a CR or PR or SD were counted as nonresponders in the analysis of disease control. According to RECIST Version 1.1, SD was defined as not qualifying for CR, PR, and PD. Detailed definitions of CR and PR are provided in Outcome Measure "Percentage of Participants With a Best Overall Response of Complete Response (CR) or Partial Response (PR)". Analysis was performed on FAS population.

End point type	Secondary
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End point timeframe:

From randomization until progressive disease or death, assessed up to 18 months

End point values	Erlotinib	Docetaxel and erlotinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	37		
Units: percentage of participants				
number (confidence interval 95%)	41.7 (25.6 to 57.8)	37.8 (22.2 to 53.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DoR)

End point title	Duration of Response (DoR)
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End point description:

Duration of response (DoR) was defined as the interval (in days) from first documentation of a response (CR/PR depending on which occurred first) to the date of the first documentation of disease progression or death from any cause. Participants presenting a response were considered as censored at the date of the last assessment with a documentation of non-progression. DoR (days) = (Date of PD/death - Date of CR/PR) + 1. Assessments were performed according to RECIST Version 1.1. DoR was assessed using the KaplanMeier method. Detailed definitions of CR and PR are provided in Outcome Measure "Percentage of Participants With a Best Overall Response of Complete Response (CR) or Partial Response (PR)". Analysis was performed on FAS population. 99999 = Not estimable because the only participant evaluable was censored.

End point type	Secondary
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End point timeframe:

From randomization until progressive disease or death, assessed up to 18 months

End point values	Erlotinib	Docetaxel and erlotinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1 ^[2]	3 ^[3]		
Units: months				
median (confidence interval 95%)	99999 (99999 to 99999)	8.69 (1.87 to 10.8)		

Notes:

[2] - Number of participants analyzed signifies participants who had a best overall response of CR or PR.

[3] - Number of participants analyzed signifies participants who had a best overall response of CR or PR.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 18 months

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	13.0
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Reporting groups

Reporting group title	Erlotinib
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Reporting group description:

Participants received erlotinib (Tarceva) at a dose of 150 milligram per day (mg/day) orally as monotherapy, up to progressive disease (PD), death, or unacceptable toxicity.

Reporting group title	Docetaxel and erlotinib
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Reporting group description:

Participants received docetaxel at a dose of 75 milligram per square meter (mg/m²) as an intravenous infusion on Day 1 of each 3-week cycle, and erlotinib at a dose of 150 mg/day orally from Day 2 to Day 16 of each 3-week cycle for 4 cycles, administered in absence of PD, death, or unacceptable toxicity. Following the 4 cycles, erlotinib 150 mg/day was administered orally as monotherapy up to PD, death or unacceptable toxicity.

Serious adverse events	Erlotinib	Docetaxel and erlotinib	
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 36 (41.67%)	10 / 37 (27.03%)	
number of deaths (all causes)	26	27	
number of deaths resulting from adverse events			
Vascular disorders			
Angiopathy			
subjects affected / exposed	1 / 36 (2.78%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac tamponade			
subjects affected / exposed	1 / 36 (2.78%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Febrile neutropenia			

subjects affected / exposed	0 / 36 (0.00%)	4 / 37 (10.81%)	
occurrences causally related to treatment / all	0 / 0	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	0 / 36 (0.00%)	2 / 37 (5.41%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	1 / 1	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 36 (2.78%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device dislocation			
subjects affected / exposed	1 / 36 (2.78%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	1 / 36 (2.78%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Mucosal inflammation			
subjects affected / exposed	0 / 36 (0.00%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Performance status decreased			
subjects affected / exposed	1 / 36 (2.78%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Uncoded			
subjects affected / exposed	0 / 36 (0.00%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			

Anaphylactic reaction			
subjects affected / exposed	0 / 36 (0.00%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 36 (0.00%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 36 (2.78%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Gastrointestinal ulcer haemorrhage			
subjects affected / exposed	1 / 36 (2.78%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 36 (2.78%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cough			
subjects affected / exposed	1 / 36 (2.78%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Dyspnoea			
subjects affected / exposed	3 / 36 (8.33%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Haemoptysis			
subjects affected / exposed	2 / 36 (5.56%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Lung disorder			
subjects affected / exposed	1 / 36 (2.78%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory acidosis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 36 (0.00%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	1 / 36 (2.78%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	1 / 36 (2.78%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 36 (0.00%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Sepsis			
subjects affected / exposed	0 / 36 (0.00%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			

subjects affected / exposed	1 / 36 (2.78%)	0 / 37 (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			
Cachexia			
subjects affected / exposed	1 / 36 (2.78%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Dehydration			
subjects affected / exposed	2 / 36 (5.56%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus inadequate control			
subjects affected / exposed	1 / 36 (2.78%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Erlotinib	Docetaxel and erlotinib	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	32 / 36 (88.89%)	35 / 37 (94.59%)	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 36 (0.00%)	3 / 37 (8.11%)	
occurrences (all)	0	3	
Nervous system disorders			
Coordination abnormal			
subjects affected / exposed	0 / 36 (0.00%)	2 / 37 (5.41%)	
occurrences (all)	0	2	
Dysgeusia			
subjects affected / exposed	2 / 36 (5.56%)	0 / 37 (0.00%)	
occurrences (all)	2	0	
Neuropathy peripheral			

subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	2 / 37 (5.41%) 2	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 36 (11.11%)	3 / 37 (8.11%)	
occurrences (all)	4	4	
Leukopenia			
subjects affected / exposed	0 / 36 (0.00%)	2 / 37 (5.41%)	
occurrences (all)	0	3	
Neutropenia			
subjects affected / exposed	0 / 36 (0.00%)	9 / 37 (24.32%)	
occurrences (all)	0	11	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	8 / 36 (22.22%)	10 / 37 (27.03%)	
occurrences (all)	8	11	
Chest pain			
subjects affected / exposed	5 / 36 (13.89%)	0 / 37 (0.00%)	
occurrences (all)	5	0	
Mucosal inflammation			
subjects affected / exposed	0 / 36 (0.00%)	5 / 37 (13.51%)	
occurrences (all)	0	9	
Pyrexia			
subjects affected / exposed	4 / 36 (11.11%)	6 / 37 (16.22%)	
occurrences (all)	6	6	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 36 (0.00%)	2 / 37 (5.41%)	
occurrences (all)	0	2	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 36 (5.56%)	0 / 37 (0.00%)	
occurrences (all)	2	0	
Abdominal pain upper			
subjects affected / exposed	3 / 36 (8.33%)	0 / 37 (0.00%)	
occurrences (all)	3	0	

Diarrhoea			
subjects affected / exposed	9 / 36 (25.00%)	14 / 37 (37.84%)	
occurrences (all)	15	21	
Dyspepsia			
subjects affected / exposed	0 / 36 (0.00%)	2 / 37 (5.41%)	
occurrences (all)	0	2	
Dysphagia			
subjects affected / exposed	2 / 36 (5.56%)	0 / 37 (0.00%)	
occurrences (all)	2	0	
Nausea			
subjects affected / exposed	2 / 36 (5.56%)	3 / 37 (8.11%)	
occurrences (all)	2	3	
Vomiting			
subjects affected / exposed	0 / 36 (0.00%)	5 / 37 (13.51%)	
occurrences (all)	0	5	
Hepatobiliary disorders			
Hypertransaminasaemia			
subjects affected / exposed	3 / 36 (8.33%)	0 / 37 (0.00%)	
occurrences (all)	3	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 36 (11.11%)	0 / 37 (0.00%)	
occurrences (all)	5	0	
Dyspnoea			
subjects affected / exposed	3 / 36 (8.33%)	7 / 37 (18.92%)	
occurrences (all)	4	7	
Epistaxis			
subjects affected / exposed	0 / 36 (0.00%)	2 / 37 (5.41%)	
occurrences (all)	0	2	
Haemoptysis			
subjects affected / exposed	3 / 36 (8.33%)	0 / 37 (0.00%)	
occurrences (all)	4	0	
Productive cough			
subjects affected / exposed	0 / 36 (0.00%)	2 / 37 (5.41%)	
occurrences (all)	0	2	
Skin and subcutaneous tissue disorders			

Dry skin			
subjects affected / exposed	2 / 36 (5.56%)	0 / 37 (0.00%)	
occurrences (all)	2	0	
Erythema			
subjects affected / exposed	3 / 36 (8.33%)	0 / 37 (0.00%)	
occurrences (all)	3	0	
Pruritus			
subjects affected / exposed	2 / 36 (5.56%)	0 / 37 (0.00%)	
occurrences (all)	2	0	
Rash			
subjects affected / exposed	16 / 36 (44.44%)	12 / 37 (32.43%)	
occurrences (all)	26	22	
Urticaria			
subjects affected / exposed	0 / 36 (0.00%)	2 / 37 (5.41%)	
occurrences (all)	0	2	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 36 (5.56%)	0 / 37 (0.00%)	
occurrences (all)	2	0	
Neck pain			
subjects affected / exposed	2 / 36 (5.56%)	0 / 37 (0.00%)	
occurrences (all)	2	0	
Infections and infestations			
Folliculitis			
subjects affected / exposed	2 / 36 (5.56%)	0 / 37 (0.00%)	
occurrences (all)	2	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 36 (5.56%)	3 / 37 (8.11%)	
occurrences (all)	2	4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 January 2011	Substantial changes in study design and conduct

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.

None reported

Notes: