Clinical trial results:
A Study to Assess the Incidence of Mutations in the Tyrosine Kinase Domain of the Epidermal Growth Factor Receptor in UK Patients with Newly Diagnosed Locally Advanced or Metastatic Non-Small Cell Lung Cancer and to Investigate the Quality of Life of These Patients Undergoing First-Line Monotherapy with Erlotinib (Tarceva®).

Summary

EudraCT number	2010-021120-96
Trial protocol	GB
Global end of trial date	07 May 2014

Results information

Result version number	v1 (current)
This version publication date	25 February 2016
First version publication date	25 February 2016

Trial information

Trial identification

Sponsor protocol code	ML25279

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01250119
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, CH-4070, Basel, Switzerland,
Public contact	Roche Trial Information Hotline, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.com
Scientific contact	Roche Trial Information Hotline, F. Hoffmann-La Roche AG, 41 616878333, 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	14 July 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 May 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to assess the prevalence of Epidermal Growth Factor Receptor (EGFR) exon 19 deletion or exon 21 mutation in Non-Small Cell Lung Cancer (NSCLC) participants tested in the United Kingdom (UK).

Protection of trial subjects:

The study was conducted in full conformance with the principles of the Declaration of Helsinki. The study also adhered to the principles outlined in the Guideline for Good Clinical Practice (GCP) International Conference on Harmonisation (ICH) Tripartite Guideline (January 1977) and with local UK law. The investigators ensured compliance with the European Union (EU) Clinical Trial Directive (2001/20/EC).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 May 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 688
Worldwide total number of subjects	688
EEA total number of subjects	688

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)	243
From 65 to 84 years	424
85 years and over	21

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

During the Diagnostic Phase, Screening period was from Day -28 to Day -14 and during the Treatment Phase, Screening period was from Day -14 to Day -1.

Period 1

Period 1 title	Diagnostic Phase
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Non-Small-Cell Lung Cancer (NSCLC) Group

Arm description:

During the Diagnostic Phase participants newly diagnosed with recurrent or metastatic NSCLC were tested for Epidermal Growth Factor Receptor (EGFR) exon 19 deletions or exon 21 (L858R) mutations.

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:

Erlotinib was administered on an outpatient basis at a fixed dose of 150 mg as a single daily oral dose.

Number of subjects in period 1	Non-Small-Cell Lung Cancer (NSCLC) Group
Started	688
Completed	575
Not completed	113
Participants not tested	44
Failed to produce a test results	69

Period 2

Period 2 title	Treatment Phase
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Erlotinib 150 milligrams per day (mg/day)

Arm description:

During the Treatment Phase participants found to have a tumor with EGFR exon 19 deletion or exon 21 (L858R) mutations received erlotinib 150 mg/day as a single oral dose until progressive disease (PD), death, unacceptable toxicity or withdrawal of consent.

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:

Erlotinib was administered on an outpatient basis at a fixed dose of 150 mg as a single daily oral dose.

Number of subjects in period 2[1]	Erlotinib 150 milligrams per day (mg/day)
Started	41
Completed	0
Not completed	41
Adverse event, serious fatal	2
Consent withdrawn by subject	1
Adverse event, non-fatal	2
Unknown reason	4
Progressive disease	32

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: During the first period (Diagnostic Phase) participants were tested to determine the presence of EGFR exon 19 deletions or exon 21 (L858R) mutations. Only participants who tested positive for exon 19 deletions or exon 21 (L858R) mutations were included in the second period (Treatment Phase). Out of 52 participants with positive EGFR mutation test result, only 41 participants were treated.

Baseline characteristics

Reporting groups	
Reporting group title	Non-Small-Cell Lung Cancer (NSCLC) Group

Reporting group description:

During the Diagnostic Phase participants newly diagnosed with recurrent or metastatic NSCLC were tested for Epidermal Growth Factor Receptor (EGFR) exon 19 deletions or exon 21 (L858R) mutations.

Reporting group values	Non-Small-Cell Lung Cancer (NSCLC) Group	Total	
Number of subjects	688	688	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 68 ± 10	 -	
Gender categorical Units: Subjects			
Female	299	299	
Male	389	389	

End points

End points reporting groups

Reporting group title	Non-Small-Cell Lung Cancer (NSCLC) Group
Reporting group description:	
During the Diagnostic Phase participants newly diagnosed with recurrent or metastatic NSCLC were tested for Epidermal Growth Factor Receptor (EGFR) exon 19 deletions or exon 21 (L858R) mutations.	
Reporting group title	Erlotinib 150 milligrams per day (mg/day)
Reporting group description:	
During the Treatment Phase participants found to have a tumor with EGFR exon 19 deletion or exon 21 (L858R) mutations received erlotinib 150 mg/day as a single oral dose until progressive disease (PD), death, unacceptable toxicity or withdrawal of consent.	
Subject analysis set title	EGFR Positive
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All participants who tested positive for EGFR mutations were included in this group.	
Subject analysis set title	EGFR Negative
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All participants who tested negative for EGFR mutations were included in this group.	
Subject analysis set title	EGFR Positive and Negative
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants who tested either positive or negative foe EGFR mutations were included in this group.	

Primary: Percentage of Participants Who Tested Positive for EGFR Mutations

End point title	Percentage of Participants Who Tested Positive for EGFR Mutations[1]
End point description:	
All participants newly diagnosed with recurrent or metastatic NSCLC were tested for EGFR exon 19 deletion or exon 21 mutations. Diagnostic population: All participants newly diagnosed with recurrent or metastatic NSCLC who entered the study and signed the consent form were included in this population.	
End point type	Primary
End point timeframe:	
14 days	

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: The primary endpoint in this study was to determine the percentage of participants who test positive for EGFR mutations in the diagnostic phase. Therefore only descriptive analyses were performed for this endpoint.

End point values	Non-Small-Cell Lung Cancer (NSCLC) Group			
Subject group type	Reporting group			
Number of subjects analysed	644[2]			
Units: percentage of participants				
number (not applicable)	8.1			

Notes:

[2] - Only participants who were tested for EGFR mutations were included in the analysis.

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With EGFR Mutations by Subgroup

End point title	Percentage of Participants With EGFR Mutations by Subgroup

End point description:

Incidence of EGFR mutations were summarized overall and with respect to different subgroups as follows: (1) equals (=) Histopathology, (2) = Stage of disease, (3) = Age at consent, (4) = Gender, (5) = Race, (6) = Smoking history. Only participants with a valid EGFR mutations test result were included in the analysis. Analysis was performed on the Diagnostic Population.

End point type	Primary

End point timeframe:

14 days

End point values	EGFR Positive	EGFR Negative		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	52	523		
Units: percentage of participants				
number (not applicable)				
(1) Squamous cell carcinoma	0	22.6		
(1) Adenocarcinoma	100	67.3		
(1) Bronchoalveolar carcinoma	0	1.7		
(1) Large cell carcinoma	0	0.6		
(1) Other	0	7.8		
(2) Unresectable Stage IIIB	1.9	11.9		
(2) Stage IIIB with malignant effusions	1.9	3.4		
(2) Stage IV	96.2	84.7		
(3) Less than 70 years	73.1	55.6		
(3) Greater than 70 years	26.9	44.4		
(4) Male	23.1	60.8		
(4) Female	76.9	39.2		
(5) Asian	13.5	2.9		
(5) Black	9.6	3.3		
(5) Caucasian	75	93.5		
(5) Other	1.9	0.4		
(6) Never smoked	44.2	7.8		
(6) Previous smoker	44.2	60.6		
(6) Current smoker	7.7	31		
(6) Missing	3.8	0.6		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	EGFR Positive v EGFR Negative

Number of subjects included in analysis	575
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0 [3]
Method	Wald Test

Notes:

[3] - Test for difference in incidence of EGFR mutations for each subgroup controlled for histopathology; Univariate analysis

Statistical analysis title	Statistical Analysis 2
Comparison groups	EGFR Positive v EGFR Negative
Number of subjects included in analysis	575
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1038 [4]
Method	Wald Test

Notes:

[4] - Test for difference in incidence of EGFR mutations for each subgroup controlled for histopathology; Multivariate analysis (6 main effects only).

Statistical analysis title	Statistical Analysis 3
Comparison groups	EGFR Positive v EGFR Negative
Number of subjects included in analysis	575
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0588 [5]
Method	Wald Test

Notes:

[5] - Test for difference in incidence of EGFR mutations for each subgroup controlled for stage of disease; Univariate analysis

Statistical analysis title	Statistical Analysis 4
Comparison groups	EGFR Positive v EGFR Negative
Number of subjects included in analysis	575
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4802 [6]
Method	Wald Test

Notes:

[6] - Test for difference in incidence of EGFR mutations for each subgroup controlled for stage of disease; Multivariate analysis (6 main effects only).

Statistical analysis title	Statistical Analysis 5
Comparison groups	EGFR Negative v EGFR Positive
Number of subjects included in analysis	575
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0147 [7]
Method	Wald Test

Notes:

[7] - Test for difference in incidence of EGFR mutations for each subgroup controlled for age at consent; Multivariate analysis (6 main effects only).

Statistical analysis title	Statistical Analysis 6
Comparison groups	EGFR Positive v EGFR Negative
Number of subjects included in analysis	575
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1181 [8]
Method	Wald Test

Notes:

[8] - Test for difference in incidence of EGFR mutations for each subgroup controlled for age at consent; Multivariate analysis (6 main effects only).

Statistical analysis title	Statistical Analysis 7
Comparison groups	EGFR Positive v EGFR Negative
Number of subjects included in analysis	575
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0 [9]
Method	Wald Test

Notes:

[9] - Test for difference in incidence of EGFR mutations for each subgroup controlled for gender; Univariate analysis.

Statistical analysis title	Statistical Analysis 8
Comparison groups	EGFR Positive v EGFR Negative
Number of subjects included in analysis	575
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0006 [10]
Method	Wald Test

Notes:

[10] - Test for difference in incidence of EGFR mutations for each subgroup controlled for gender; Multivariate analysis (6 main effects only).

Statistical analysis title	Statistical Analysis 9
Comparison groups	EGFR Positive v EGFR Negative
Number of subjects included in analysis	575
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0004 [11]
Method	Wald Test

Notes:

[11] - Test for difference in incidence of EGFR mutations for each subgroup controlled for race; Univariate analysis.

Statistical analysis title	Statistical Analysis 10
Comparison groups	EGFR Positive v EGFR Negative
Number of subjects included in analysis	575
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3371 [12]
Method	Wald Test

Notes:

[12] - Test for difference in incidence of EGFR mutations for each subgroup controlled for race; Multivariate analysis (6 main effects only).

Statistical analysis title	Statistical Analysis 11
Comparison groups	EGFR Positive v EGFR Negative
Number of subjects included in analysis	575
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0 [13]
Method	Wald Test

Notes:

[13] - Test for difference in incidence of EGFR mutations for each subgroup controlled for smoking history; Univariate analysis.

Statistical analysis title	Statistical Analysis 12
Comparison groups	EGFR Positive v EGFR Negative
Number of subjects included in analysis	575
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0001 [14]
Method	Wald Test

Notes:

[14] - Test for difference in incidence of EGFR mutations for each subgroup controlled for smoking history; Multivariate analysis (6 main effects only).

Secondary: Percentage of Participants With a Response by Best Objective Tumor Response

End point title	Percentage of Participants With a Response by Best Objective Tumor Response

End point description:

Best objective response was defined as the best response recorded from the start of treatment until disease progression/recurrence. Complete Response (CR): Disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to less than (<)10 millimeters (mm). Partial Response (PR): At least a 30 percent (%) decrease in the sum of diameters of target lesions, taking as reference the baseline sum of diameters. Progressive Disease (PD): At least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study (this may include the baseline sum). The sum must also demonstrate an absolute increase of at least 5 mm. Stable Disease (SD): Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD. Intention-to-treat (ITT) population: All participants in the target population who were eligible for treatment and who actually received one dose of treatment.

End point type	Secondary

End point timeframe:

Screening, Day 1 of each 6 week visit starting from Visit 3 until PD, Death, Unacceptable toxicity or Withdrawal of consent up to 34 months

End point values	Erlotinib 150 milligrams per day (mg/day)			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: percentage of participants				
number (not applicable)				
CR	0			

PR	84.8			
SD	9.1			
PD	6.1			

Statistical analyses

No statistical analyses for this end point

Secondary: Probability of Being Alive and Free of Progression by Timepoint

End point title	Probability of Being Alive and Free of Progression by Timepoint

End point description:

Progression Free Survival (PFS) was defined as the interval (number of days) from the trial treatment start date to the earlier of the date of the first tumor response assessment of PD or the date of death by any cause. Participants who experienced neither of these events or who were lost to followup at the time of the analysis were censored at date of last contact. PFS was summarized according to the Kaplan-Meier method. Analysis was performed on the ITT Population.

End point type	Secondary

End point timeframe:

Months 0, 3, 6, 9, 12, 15, and 18

End point values	Erlotinib 150 milligrams per day (mg/day)			
Subject group type	Reporting group			
Number of subjects analysed	41[15]			
Units: Probability of being alive				
number (confidence interval 95%)				
0 Months	1 (1 to 1)			
3 Months	0.97 (0.81 to 1)			
6 Months	0.94 (0.78 to 0.98)			
9 Months	0.73 (0.54 to 0.85)			
12 Months	0.54 (0.36 to 0.69)			
15 Months	0.37 (0.21 to 0.54)			
18 Months	0.22 (0.09 to 0.39)			

Notes:

[15] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Survival Time in Months

End point title	Survival Time in Months

End point description:

Duration of time in months from Screening until Death due to any cause. Analysis was performed on the ITT population.

End point type	Secondary

End point timeframe:

Baseline, Day 1 of each 6-week visit starting from Visit 3 until PD, Death, Unacceptable toxicity or Withdrawal of consent

End point values	Erlotinib 150 milligrams per day (mg/day)			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: months				
median (confidence interval 95%)	12.57 (10.1 to 16.53)			

Statistical analyses

No statistical analyses for this end point

Secondary: Quality of Life Assessment Using EuroQol(EQ) 5D Visual Analog Score (VAS) Instrument

End point title	Quality of Life Assessment Using EuroQol(EQ) 5D Visual Analog Score (VAS) Instrument

End point description:

he EQ-5D contains a descriptive system which measures 5 health dimensions: mobility, self-care, usual activity, pain/discomfort, and anxiety/depression. The EQ-5D also contains a visual analog scale (EQ-VAS), which records the respondent's self-rated health status on a vertical graduated visual analog scale in millimeters (mm) ranging from 0 (worst imaginable health state) to 100 (best imaginable health state). Analysis was performed on the ITT population.

End point type	Secondary

End point timeframe:

Screening, Baseline and Final or Withdrawal Visit up to 34 months

End point values	Erlotinib 150 milligrams per day (mg/day)			
Subject group type	Reporting group			
Number of subjects analysed	40[16]			
Units: mm				
arithmetic mean (standard deviation)				
Screening (n=40)	62.6 (± 23.5)			
Baseline (n=20)	65.4 (± 19.9)			
Final visit/Withdrawal (n=20)	63 (± 22.4)			
Change from Baseline Final visit(n=20)	-0.4 (± 22)			

Notes:

[16] - number (n) = number of participants analyzed at the specified visit.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Problems With Mobility as Assessed Using the EQ-5D

End point title	Percentage of Participants With Problems With Mobility as Assessed Using the EQ-5D

End point description:

The EQ-5D contains a descriptive system which measures 5 health dimensions: mobility, self-care, usual activity, pain/discomfort, and anxiety/depression. The participants were required to rate their mobility as the following categories: Category 1. I have no problems in walking about; Category 2. I have some problems in walking about; Category 3. I am confined to bed. Analysis was performed on the ITT Population.

End point type	Secondary

End point timeframe:

Baseline (Visit 1), Days 10 to 14 (Visit 2), Day 1 of every 6 weeks until PD, Death, Unacceptable toxicity or Withdrawal of consent up to 34 months

End point values	Erlotinib 150 milligrams per day (mg/day)			
Subject group type	Reporting group			
Number of subjects analysed	41[17]			
Units: percentage of participants				
number (not applicable)				
Screening Category 1 (n=41)	43.9			
Screening Category 2 (n=41)	56.1			
Screening Category 3 (n=41)	0			
Visit 01 Category 1 (n=20)	45			
Visit 01 Category 2 (n=20)	55			
Visit 01 Category 3 (n=20)	0			
Visit 02 Category 1 (n=33)	45.5			
Visit 02 Category 2 (n=33)	54.5			
Visit 02 Category 3 (n=33)	0			
Visit 03 Category 1 (n=30)	56.7			
Visit 03 Category 2 (n=30)	43.3			
Visit 03 Category 3 (n=30)	0			
Visit 04 Category 1 (n=29)	51.7			
Visit 04 Category 2 (n=29)	48.3			
Visit 04 Category 3 (n=29)	0			
Visit 05 Category 1 (n=33)	54.5			
Visit 05 Category 2 (n=33)	45.5			
Visit 05 Category 3 (n=33)	0			
Visit 06 Category 1 (n=31)	54.8			

Visit 06 Category 2 (n=31)	45.2			
Visit 06 Category 3 (n=31)	0			
Visit 07 Category 1 (n=29)	58.6			
Visit 07 Category 2 (n=29)	41.4			
Visit 07 Category 3 (n=29)	0			
Visit 08 Category 1 (n=27)	55.6			
Visit 08 Category 2 (n=27)	44.4			
Visit 08 Category 3 (n=27)	0			
Visit 09 Category 1 (n=24)	62.5			
Visit 09 Category 2 (n=24)	37.5			
Visit 09 Category 3 (n=24)	0			
Visit 10 Category 1 (n=21)	42.9			
Visit 10 Category 2 (n=21)	57.1			
Visit 10 Category 3 (n=21)	0			
Visit 11 Category 1 (n=13)	46.2			
Visit 11 Category 2 (n=13)	53.8			
Visit 11 Category 3 (n=13)	0			
Visit 12 Category 1 (n=11)	45.5			
Visit 12 Category 2 (n=11)	54.5			
Visit 12 Category 3 (n=11)	0			
Visit 13 Category 1 (n=9)	55.6			
Visit 13 Category 2 (n=9)	44.4			
Visit 13 Category 3 (n=9)	0			
Visit 14 Category 1 (n=8)	50			
Visit 14 Category 2 (n=8)	50			
Visit 14 Category 3 (n=8)	0			
Visit 15 Category 1 (n=5)	40			
Visit 15 Category 2 (n=5)	60			
Visit 15 Category 3 (n=5)	0			
Visit 16 Category 1 (n=4)	25			
Visit 16 Category 2 (n=4)	75			
Visit 16 Category 3 (n=4)	0			
Visit 17 Category 1 (n=4)	25			
Visit 17 Category 2 (n=4)	75			
Visit 17 Category 3 (n=4)	0			
Visit 18 Category 1 (n=3)	33.3			
Visit 18 Category 2 (n=3)	66.7			
Visit 18 Category 3 (n=3)	0			
Visit 19 Category 1 (n=2)	50			
Visit 19 Category 2 (n=2)	50			
Visit 19 Category 3 (n=2)	0			
Visit 20 Category 1 (n=2)	50			
Visit 20 Category 2 (n=2)	50			
Visit 20 Category 3 (n=2)	0			
Visit 21 Category 1 (n=2)	50			
Visit 21 Category 2 (n=2)	50			
Visit 21 Category 3 (n=2)	0			
Visit 22 Category 1 (n=1)	0			
Visit 22 Category 2 (n=1)	100			
Visit 22 Category 3 (n=1)	0			
Visit 23 Category 1 (n=1)	0			
Visit 23 Category 2 (n=1)	100			

Visit 23 Category 3 (n=1)	0			
Visit 24 Category 1 (n=1)	0			
Visit 24 Category 2 (n=1)	100			
Visit 24 Category 3 (n=1)	0			
Visit 25 Category 1 (n=1)	0			
Visit 25 Category 2 (n=1)	100			
Visit 25 Category 3 (n=1)	0			
Final visit/Withdraw Category 1 (n=21)	33.3			
Final visit/Withdraw Category 2 (n=21)	66.7			
Final visit/Withdraw Category 3 (n=21)	0			

Notes:

[17] - n = number of participants analyzed at for the given parameter at the specified visit.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Problems With Self-Care as Assessed Using the EQ-5D

End point title	Percentage of Participants With Problems With Self-Care as Assessed Using the EQ-5D

End point description:

The EQ-5D contains a descriptive system which measures 5 health dimensions: mobility, self-care, usual activity, pain/discomfort, and anxiety/depression. The participants were required to rate their self-care as the following categories: Category 1. I have no problems with self-care; Category 2. I have some problems washing or dressing myself; Category 3. I am unable to wash or dress myself. Analysis was performed on the ITT Population.

End point type	Secondary

End point timeframe:

Baseline (Visit 1), Days 10 to 14 (Visit 2), Day 1 of every 6 weeks until PD, Death, Unacceptable toxicity or Withdrawal of consent up to 34 months

End point values	Erlotinib 150 milligrams per day (mg/day)			
Subject group type	Reporting group			
Number of subjects analysed	41[18]			
Units: percentage of particvipants				
number (not applicable)				
Screening Category 1 (n=41)	78			
Screening Category 2 (n=41)	17.1			
Screening Category 3 (n=41)	4.9			
Visit 01 Category 1 (n=20)	80			
Visit 01 Category 2 (n=20)	20			
Visit 01 Category 3 (n=20)	0			
Visit 02 Category 1 (n=33)	81.8			
Visit 02 Category 2 (n=33)	18.2			
Visit 02 Category 3 (n=33)	0			
Visit 03 Category 1 (n=29)	86.2			
Visit 03 Category 2 (n=29)	13.8			
Visit 03 Category 3 (n=29)	0			

Visit 04 Category 1 (n=28)	82.1			
Visit 04 Category 2 (n=28)	17.9			
Visit 04 Category 3 (n=28)	0			
Visit 05 Category 1 (n=33)	78.8			
Visit 05 Category 2 (n=33)	21.2			
Visit 05 Category 3 (n=33)	0			
Visit 06 Category 1 (n=31)	83.9			
Visit 06 Category 2 (n=31)	16.1			
Visit 06 Category 3 (n=31)	0			
Visit 07 Category 1 (n=29)	79.3			
Visit 07 Category 2 (n=29)	20.7			
Visit 07 Category 3 (n=29)	0			
Visit 08 Category 1 (n=27)	85.2			
Visit 08 Category 2 (n=27)	14.8			
Visit 08 Category 3 (n=27)	0			
Visit 09 Category 1 (n=24)	75			
Visit 09 Category 2 (n=24)	25			
Visit 09 Category 3 (n=24)	0			
Visit 10 Category 1 (n=21)	71.4			
Visit 10 Category 2 (n=21)	28.6			
Visit 10 Category 3 (n=21)	0			
Visit 11 Category 1 (n=13)	61.5			
Visit 11 Category 2 (n=13)	38.5			
Visit 11 Category 3 (n=13)	0			
Visit 12 Category 1 (n=11)	54.5			
Visit 12 Category 2 (n=11)	45.5			
Visit 12 Category 3 (n=11)	0			
Visit 13 Category 1 (n=9)	55.6			
Visit 13 Category 2 (n=9)	44.4			
Visit 13 Category 3 (n=9)	0			
Visit 14 Category 1 (n=8)	62.5			
Visit 14 Category 2 (n=8)	37.5			
Visit 14 Category 3 (n=8)	0			
Visit 15 Category 1 (n=5)	40			
Visit 15 Category 2 (n=5)	60			
Visit 15 Category 3 (n=5)	0			
Visit 16 Category 1 (n=4)	50			
Visit 16 Category 2 (n=4)	50			
Visit 16 Category 3 (n=4)	0			
Visit 17 Category 1 (n=4)	50			
Visit 17 Category 2 (n=4)	50			
Visit 17 Category 3 (n=4)	0			
Visit 18 Category 1 (n=3)	33.3			
Visit 18 Category 2 (n=3)	66.7			
Visit 18 Category 3 (n=3)	0			
Visit 19 Category 1 (n=2)	50			
Visit 19 Category 2 (n=2)	50			
Visit 19 Category 3 (n=2)	0			
Visit 20 Category 1 (n=2)	50			
Visit 20 Category 2 (n=2)	50			
Visit 20 Category 3 (n=2)	0			
Visit 21 Category 1 (n=2)	50			

Visit 21 Category 2 (n=2)	50			
Visit 21 Category 3 (n=2)	0			
Visit 22 Category 1 (n=1)	100			
Visit 22 Category 2 (n=1)	0			
Visit 22 Category 3 (n=1)	0			
Visit 23 Category 1 (n=1)	0			
Visit 23 Category 2 (n=1)	100			
Visit 23 Category 3 (n=1)	0			
Visit 24 Category 1 (n=1)	0			
Visit 24 Category 2 (n=1)	100			
Visit 24 Category 3 (n=1)	0			
Visit 25 Category 1 (n=1)	0			
Visit 25 Category 2 (n=1)	100			
Visit 25 Category 3 (n=1)	0			
Final Visit/Withdraw Category 1 (n=21)	66.7			
Final Visit/Withdraw Category 2 (n=21)	33.3			
Final Visit/Withdraw Category 3 (n=21)	0			

Notes:

[18] - n = number of participants analyzed for the given parameter at the specified visit.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Problems With Usual Activities as Assessed Using the EQ-5D

End point title	Percentage of Participants With Problems With Usual Activities as Assessed Using the EQ-5D

End point description:

The EQ-5D contains a descriptive system which measures 5 health dimensions: mobility, self-care, usual activity, pain/discomfort, and anxiety/depression. The participants were required to rate their ability to perform usual activities as the following categories: Category 1. I have no problems with performing my usual activities; Category 2. I have some problems with performing my usual activities; Category 3. I am unable to perform my usual activities. Analysis was performed on the ITT Population.

End point type	Secondary

End point timeframe:

Baseline (Visit 1), Days 10 to 14 (Visit 2), Day 1 of every 6 weeks until PD, Death, Unacceptable toxicity or Withdrawal of consent up to 34 months

End point values	Erlotinib 150 milligrams per day (mg/day)			
Subject group type	Reporting group			
Number of subjects analysed	41[19]			
Units: percentage of psarticipants				
number (not applicable)				
Screening Category 1 (n=41)	39			
Screening Category 2 (n=41)	46.3			
Screening Category 3 (n=41)	14.6			
Visit 01 Category 1 (n=20)	40			
Visit 01 Category 2 (n=20)	50			

Visit 01 Category 3 (n=20)	10			
Visit 02 Category 1 (n=33)	36.4			
Visit 02 Category 2 (n=33)	60.6			
Visit 02 Category 3 (n=33)	3			
Visit 03 Category 1 (n=30)	40			
Visit 03 Category 2 (n=30)	53.3			
Visit 03 Category 3 (n=30)	6.7			
Visit 04 Category 1 (n=29)	51.7			
Visit 04 Category 2 (n=29)	44.8			
Visit 04 Category 3 (n=29)	3.4			
Visit 05 Category 1 (n=33)	51.5			
Visit 05 Category 2 (n=33)	48.5			
Visit 05 Category 3 (n=33)	0			
Visit 06 Category 1 (n=31)	45.2			
Visit 06 Category 2 (n=31)	54.8			
Visit 06 Category 3 (n=31)	0			
Visit 07 Category 1 (n=29)	48.3			
Visit 07 Category 2 (n=29)	51.7			
Visit 07 Category 3 (n=29)	0			
Visit 08 Category 1 (n=27)	40.7			
Visit 08 Category 2 (n=27)	59.3			
Visit 08 Category 3 (n=27)	0			
Visit 09 Category 1 (n=24)	33.3			
Visit 09 Category 2 (n=24)	66.7			
Visit 09 Category 3 (n=24)	0			
Visit 10 Category 1 (n=21)	38.1			
Visit 10 Category 2 (n=21)	61.9			
Visit 10 Category 3 (n=21)	0			
Visit 11 Category 1 (n=13)	30.8			
Visit 11 Category 2 (n=13)	69.2			
Visit 11 Category 3 (n=13)	0			
Visit 12 Category 1 (n=11)	27.3			
Visit 12 Category 2 (n=11)	72.7			
Visit 12 Category 3 (n=11)	0			
Visit 13 Category 1 (n=9)	22.2			
Visit 13 Category 2 (n=9)	77.8			
Visit 13 Category 3 (n=9)	0			
Visit 14 Category 1 (n=8)	37.5			
Visit 14 Category 2 (n=8)	62.5			
Visit 14 Category 3 (n=8)	0			
Visit 15 Category 1 (n=5)	20			
Visit 15 Category 2 (n=5)	80			
Visit 15 Category 3 (n=5)	0			
Visit 16 Category 1 (n=4)	25			
Visit 16 Category 2 (n=4)	75			
Visit 16 Category 3 (n=4)	0			
Visit 17 Category 1 (n=4)	25			
Visit 17 Category 2 (n=4)	75			
Visit 17 Category 3 (n=4)	0			
Visit 18 Category 1 (n=3)	33.3			
Visit 18 Category 2 (n=3)	66.7			
Visit 18 Category 3 (n=3)	0			

Visit 19 Category 1 (n=2)	50			
Visit 19 Category 2 (n=2)	50			
Visit 19 Category 3 (n=2)	0			
Visit 20 Category 1 (n=2)	50			
Visit 20 Category 2 (n=2)	50			
Visit 20 Category 3 (n=2)	0			
Visit 21 Category 1 (n=2)	50			
Visit 21 Category 2 (n=2)	50			
Visit 21 Category 3 (n=2)	0			
Visit 22 Category 1 (n=1)	0			
Visit 22 Category 2 (n=1)	100			
Visit 22 Category 3 (n=1)	0			
Visit 23 Category 1 (n=1)	0			
Visit 23 Category 2 (n=1)	100			
Visit 23 Category 3 (n=1)	0			
Visit 24 Category 1 (n=1)	0			
Visit 24 Category 2 (n=1)	100			
Visit 24 Category 3 (n=1)	0			
Visit 25 Category 1 (n=1)	0			
Visit 25 Category 2 (n=1)	100			
Visit 25 Category 3 (n=1)	0			
Final Visit/Withdrawal Category 1 (n=21)	33.3			
Final Visit/Withdrawal Category 2 (n=21)	61.9			
Final Visit/Withdrawal Category 3 (n=21)	4.8			

Notes:

[19] - n = number of participants analyzed for the given parameter at the specified visit.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Pain/Discomfort as Assessed Using the EQ-5D

End point title	Percentage of Participants With Pain/Discomfort as Assessed Using the EQ-5D

End point description:

The EQ-5D contains a descriptive system which measures 5 health dimensions: mobility, self-care, usual activity, pain/discomfort, and anxiety/depression. The participants were required to rate their pain as the following categories: Category 1. I have no pain or discomfort; Category 2. I have moderate pain or discomfort; Category 3. I have extreme pain or discomfort. Analysis was performed on the ITT Population.

End point type	Secondary

End point timeframe:

Baseline (Visit 1), Days 10 to 14 (Visit 2), Day 1 of every 6 weeks until PD, Death, Unacceptable toxicity or Withdrawal of consent up to 34 months

End point values	Erlotinib 150 milligrams per day (mg/day)			
Subject group type	Reporting group			
Number of subjects analysed	41[20]			
Units: percentage of participants				
number (not applicable)				
Screening Category 1 (n=41)	29.3			
Screening Category 2 (n=41)	63.4			
Screening Category 3 (n=41)	7.3			
Visit 01 Category 1 (n=20)	10			
Visit 01 Category 2 (n=20)	85			
Visit 01 Category 3 (n=20)	5			
Visit 02 Category 1 (n=32)	43.8			
Visit 02 Category 2 (n=32)	56.3			
Visit 02 Category 3 (n=32)	0			
Visit 03 Category 1 (n=30)	40			
Visit 03 Category 2 (n=30)	60			
Visit 03 Category 3 (n=30)	0			
Visit 04 Category 1 (n=29)	55.2			
Visit 04 Category 2 (n=29)	37.9			
Visit 04 Category 3 (n=29)	6.9			
Visit 05 Category 1 (n=33)	45.5			
Visit 05 Category 2 (n=33)	51.5			
Visit 05 Category 3 (n=33)	3			
Visit 06 Category 1 (n=31)	48.4			
Visit 06 Category 2 (n=31)	51.6			
Visit 06 Category 3 (n=31)	0			
Visit 07 Category 1 (n=29)	48.3			
Visit 07 Category 2 (n=29)	51.7			
Visit 07 Category 3 (n=29)	0			
Visit 08 Category 1 (n=27)	37			
Visit 08 Category 2 (n=27)	59.3			
Visit 08 Category 3 (n=27)	3.7			
Visit 09 Category 1 (n=24)	50			
Visit 09 Category 2 (n=24)	37.5			
Visit 09 Category 3 (n=24)	12.5			
Visit 10 Category 1 (n=21)	42.9			
Visit 10 Category 2 (n=21)	47.6			
Visit 10 Category 3 (n=21)	9.5			
Visit 11 Category 1 (n=13)	46.2			
Visit 11 Category 2 (n=13)	53.8			
Visit 11 Category 3 (n=13)	0			
Visit 12 Category 1 (n=11)	45.5			
Visit 12 Category 2 (n=11)	36.4			
Visit 12 Category 3 (n=11)	18.2			
Visit 13 Category 1 (n=9)	44.4			
Visit 13 Category 2 (n=9)	55.6			
Visit 13 Category 3 (n=9)	0			
Visit 14 Category 1 (n=8)	62.5			
Visit 14 Category 2 (n=8)	37.5			
Visit 14 Category 3 (n=8)	0			

Visit 15 Category 1 (n=5)	60			
Visit 15 Category 2 (n=5)	40			
Visit 15 Category 3 (n=5)	0			
Visit 16 Category 1 (n=4)	25			
Visit 16 Category 2 (n=4)	75			
Visit 16 Category 3 (n=4)	0			
Visit 17 Category 1 (n=4)	25			
Visit 17 Category 2 (n=4)	75			
Visit 17 Category 3 (n=4)	0			
Visit 18 Category 1 (n=3)	0			
Visit 18 Category 2 (n=3)	100			
Visit 18 Category 3 (n=3)	0			
Visit 19 Category 1 (n=2)	0			
Visit 19 Category 2 (n=2)	100			
Visit 19 Category 3 (n=2)	0			
Visit 20 Category 1 (n=2)	0			
Visit 20 Category 2 (n=2)	100			
Visit 20 Category 3 (n=2)	0			
Visit 21 Category 1 (n=2)	0			
Visit 21 Category 2 (n=2)	100			
Visit 21 Category 3 (n=2)	0			
Visit 22 Category 1 (n=1)	100			
Visit 22 Category 2 (n=1)	0			
Visit 22 Category 3 (n=1)	0			
Visit 23 Category 1 (n=1)	0			
Visit 23 Category 2 (n=1)	100			
Visit 23 Category 3 (n=1)	0			
Visit 24 Category 1 (n=1)	0			
Visit 24 Category 2 (n=1)	100			
Visit 24 Category 3 (n=1)	0			
Visit 25 Category 1 (n=1)	0			
Visit 25 Category 2 (n=1)	100			
Visit 25 Category 3 (n=1)	0			
Final Visit/Withdrawal Category 1 (n=21)	38.1			
Final Visit/Withdrawal Category 2 (n=21)	57.1			
Final Visit/Withdrawal Category 3 (n=21)	4.8			

Notes:

[20] - n = number of participants analyzed for the given parameter at the specified visit.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Anxiety/Depression as Assessed Using the EQ-5D

End point title	Percentage of Participants With Anxiety/Depression as Assessed Using the EQ-5D

End point description:

The EQ-5D contains a descriptive system which measures 5 health dimensions: mobility, self-care, usual activity, pain/discomfort, and anxiety/depression. The participants were required to rate their pain as

the following categories: Category 1. I am not anxious or depressed; Category 2. I am moderately anxious or depressed; Category 3. I am extremely anxious or depressed. Analysis was performed on the ITT Population.

End point type	Secondary

End point timeframe:

Baseline (Visit 1), Days 10 to 14 (Visit 2), Day 1 of every 6 weeks until PD, Death, Unacceptable toxicity or Withdrawal of consent up to 34 months

End point values	Erlotinib 150 milligrams per day (mg/day)			
Subject group type	Reporting group			
Number of subjects analysed	41[21]			
Units: percentage of participants				
number (not applicable)				
Screening Category 1 (n=40)	52.5			
Screening Category 2 (n=40)	37.5			
Screening Category 3 (n=40)	10			
Visit 01 Category 1 (n=19)	57.9			
Visit 01 Category 2 (n=19)	42.1			
Visit 01 Category 3 (n=19)	0			
Visit 02 Category 1 (n=33)	57.6			
Visit 02 Category 2 (n=33)	42.4			
Visit 02 Category 3 (n=33)	0			
Visit 03 Category 1 (n=30)	43.3			
Visit 03 Category 2 (n=30)	56.7			
Visit 03 Category 3 (n=30)	0			
Visit 04 Category 1 (n=29)	58.6			
Visit 04 Category 2 (n=29)	41.4			
Visit 04 Category 3 (n=29)	0			
Visit 05 Category 1 (n=33)	60.6			
Visit 05 Category 2 (n=33)	36.4			
Visit 05 Category 3 (n=33)	3			
Visit 06 Category 1 (n=31)	48.4			
Visit 06 Category 2 (n=31)	51.6			
Visit 06 Category 3 (n=31)	0			
Visit 07 Category 1 (n=29)	62.1			
Visit 07 Category 2 (n=29)	37.9			
Visit 07 Category 3 (n=29)	0			
Visit 08 Category 1 (n=27)	55.6			
Visit 08 Category 2 (n=27)	44.4			
Visit 08 Category 3 (n=27)	0			
Visit 09 Category 1 (n=24)	62.5			
Visit 09 Category 2 (n=24)	25			
Visit 09 Category 3 (n=24)	12.5			
Visit 10 Category 1 (n=21)	61.9			
Visit 10 Category 2 (n=21)	28.6			
Visit 10 Category 3 (n=21)	9.5			
Visit 11 Category 1 (n=13)	61.5			
Visit 11 Category 2 (n=13)	30.8			

Visit 11 Category 3 (n=13)	7.7			
Visit 12 Category 1 (n=11)	45.5			
Visit 12 Category 2 (n=11)	45.5			
Visit 12 Category 3 (n=11)	9.1			
Visit 13 Category 1 (n=9)	77.8			
Visit 13 Category 2 (n=9)	22.2			
Visit 13 Category 3 (n=9)	0			
Visit 14 Category 1 (n=8)	75			
Visit 14 Category 2 (n=8)	25			
Visit 14 Category 3 (n=8)	0			
Visit 15 Category 1 (n=5)	60			
Visit 15 Category 2 (n=5)	40			
Visit 15 Category 3 (n=5)	0			
Visit 16 Category 1 (n=4)	75			
Visit 16 Category 2 (n=4)	25			
Visit 16 Category 3 (n=4)	0			
Visit 17 Category 1 (n=4)	75			
Visit 17 Category 2 (n=4)	25			
Visit 17 Category 3 (n=4)	0			
Visit 18 Category 1 (n=3)	66.7			
Visit 18 Category 2 (n=3)	33.3			
Visit 18 Category 3 (n=3)	0			
Visit 19 Category 1 (n=2)	50			
Visit 19 Category 2 (n=2)	50			
Visit 19 Category 3 (n=2)	0			
Visit 20 Category 1 (n=2)	50			
Visit 20 Category 2 (n=2)	50			
Visit 20 Category 3 (n=2)	0			
Visit 21 Category 1 (n=2)	50			
Visit 21 Category 2 (n=2)	50			
Visit 21 Category 3 (n=2)	0			
Visit 22 Category 1 (n=1)	100			
Visit 22 Category 2 (n=1)	0			
Visit 22 Category 3 (n=1)	0			
Visit 23 Category 1 (n=1)	0			
Visit 23 Category 2 (n=1)	100			
Visit 23 Category 3 (n=1)	0			
Visit 24 Category 1 (n=1)	0			
Visit 24 Category 2 (n=1)	100			
Visit 24 Category 3 (n=1)	0			
Visit 25 Category 1 (n=1)	0			
Visit 25 Category 2 (n=1)	100			
Visit 25 Category 3 (n=1)	0			
Final Visit/Withdrawal Category 1 (n=21)	57.1			
Final Visit/Withdrawal Category 2 (n=21)	38.1			
Final Visit/Withdrawal Category 3 (n=21)	4.8			

Notes:

[21] - n = number of participants analyzed for the given parameter at the specified visit.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were recorded from Visit 1 (Baseline) until 30 days after the Final/Withdrawal Visit.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.1

Reporting groups

Reporting group title	Erlotinib

Reporting group description:

During the Treatment Phase participants found to have a tumour with EGFR exon 19 deletion or exon 21 (L858R) mutations received erlotinib 150 mg/day as a single oral dose until PD, death, unacceptable toxicity or withdrawal of consent.

Serious adverse events	Erlotinib		
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 41 (39.02%)		
number of deaths (all causes)	9		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Nervous system disorders			
Cerebral infarction			

subjects affected / exposed	1 / 41 (2.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Presyncope				
subjects affected / exposed	1 / 41 (2.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Spinal cord compression				
subjects affected / exposed	1 / 41 (2.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Thrombocytopenia				
subjects affected / exposed	1 / 41 (2.44%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Pyrexia				
subjects affected / exposed	2 / 41 (4.88%)			
occurrences causally related to treatment / all	3 / 4			
deaths causally related to treatment / all	0 / 0			
Ear and labyrinth disorders				
Vertigo				
subjects affected / exposed	1 / 41 (2.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal pain				
subjects affected / exposed	2 / 41 (4.88%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Constipation				

subjects affected / exposed	1 / 41 (2.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	1 / 41 (2.44%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal haemorrhage				
subjects affected / exposed	1 / 41 (2.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Respiratory, thoracic and mediastinal disorders				
Dyspnoea				
subjects affected / exposed	1 / 41 (2.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Interstitial lung disease				
subjects affected / exposed	1 / 41 (2.44%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				
subjects affected / exposed	1 / 41 (2.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonitis				
subjects affected / exposed	1 / 41 (2.44%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	1 / 41 (2.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Respiratory failure				

subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	1 / 41 (2.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Erlotinib		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	40 / 41 (97.56%)		
Investigations			
Pulmonary function test decreased			
subjects affected / exposed	6 / 41 (14.63%)		
occurrences (all)	8		
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	4 / 41 (9.76%)		
occurrences (all)	4		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	7 / 41 (17.07%)		
occurrences (all)	9		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	4 / 41 (9.76%)		
occurrences (all)	4		
Chest pain			

subjects affected / exposed	3 / 41 (7.32%)		
occurrences (all)	3		
Fatigue			
subjects affected / exposed	14 / 41 (34.15%)		
occurrences (all)	17		
Mucosal inflammation			
subjects affected / exposed	6 / 41 (14.63%)		
occurrences (all)	6		
Oedema peripheral			
subjects affected / exposed	7 / 41 (17.07%)		
occurrences (all)	10		
Pain			
subjects affected / exposed	3 / 41 (7.32%)		
occurrences (all)	3		
Eye disorders			
Conjunctivitis			
subjects affected / exposed	3 / 41 (7.32%)		
occurrences (all)	4		
Dry eye			
subjects affected / exposed	3 / 41 (7.32%)		
occurrences (all)	3		
Vision blurred			
subjects affected / exposed	3 / 41 (7.32%)		
occurrences (all)	3		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	5 / 41 (12.20%)		
occurrences (all)	5		
Abdominal pain upper			
subjects affected / exposed	3 / 41 (7.32%)		
occurrences (all)	3		
Constipation			
subjects affected / exposed	9 / 41 (21.95%)		
occurrences (all)	10		
Diarrhoea			

subjects affected / exposed	26 / 41 (63.41%)		
occurrences (all)	40		
Dyspepsia			
subjects affected / exposed	3 / 41 (7.32%)		
occurrences (all)	3		
Nausea			
subjects affected / exposed	11 / 41 (26.83%)		
occurrences (all)	14		
Oral pain			
subjects affected / exposed	5 / 41 (12.20%)		
occurrences (all)	5		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	10 / 41 (24.39%)		
occurrences (all)	11		
Dyspnoea			
subjects affected / exposed	5 / 41 (12.20%)		
occurrences (all)	7		
Epistaxis			
subjects affected / exposed	5 / 41 (12.20%)		
occurrences (all)	5		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	9 / 41 (21.95%)		
occurrences (all)	9		
Dermatitis acneiform			
subjects affected / exposed	5 / 41 (12.20%)		
occurrences (all)	5		
Dry skin			
subjects affected / exposed	13 / 41 (31.71%)		
occurrences (all)	15		
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	3 / 41 (7.32%)		
occurrences (all)	8		
Pruritus			

subjects affected / exposed	3 / 41 (7.32%)		
occurrences (all)	3		
Rash			
subjects affected / exposed	26 / 41 (63.41%)		
occurrences (all)	42		
Skin ulcer			
subjects affected / exposed	3 / 41 (7.32%)		
occurrences (all)	3		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	7 / 41 (17.07%)		
occurrences (all)	7		
Back pain			
subjects affected / exposed	6 / 41 (14.63%)		
occurrences (all)	8		
Muscle spasms			
subjects affected / exposed	4 / 41 (9.76%)		
occurrences (all)	5		
Musculoskeletal pain			
subjects affected / exposed	4 / 41 (9.76%)		
occurrences (all)	4		
Pain in extremity			
subjects affected / exposed	3 / 41 (7.32%)		
occurrences (all)	5		
Infections and infestations			
Cellulitis			
subjects affected / exposed	3 / 41 (7.32%)		
occurrences (all)	3		
Lower respiratory tract infection			
subjects affected / exposed	3 / 41 (7.32%)		
occurrences (all)	3		
Nasopharyngitis			
subjects affected / exposed	3 / 41 (7.32%)		
occurrences (all)	3		
Paronychia			

subjects affected / exposed	8 / 41 (19.51%)		
occurrences (all)	9		
Urinary tract infection			
subjects affected / exposed	3 / 41 (7.32%)		
occurrences (all)	3		
Oral candidiasis			
subjects affected / exposed	4 / 41 (9.76%)		
occurrences (all)	4		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	10 / 41 (24.39%)		
occurrences (all)	10		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 April 2011	This amendment clarified that participants with previous treatment with NSCLC with chemotherapy were not excluded if the chemotherapy was neo-adjuvant or adjuvant and was completed > 6 months prior to concent for the diagnostic phase of the study. Physical examination, vital signs and EQ-5D were added to the text on the 'final visit/withdrawal from study' assessments to make the text consistent with the table of assessments. Shelf life of erlotinib was updated to 4 years. RECIST criteria to be used was updated from version 1.0 to 1.1.
28 November 2012	A further approved indication for erlotinib was added. Introduction sections were updated to included additional publications. Administrative changes were documented. Number of participants to enter diagnostic phase was reduced from 1200 to 700. Number of participants to enter treatment phase was reduced from 120 to 60. It was specified that if the drug was to be destroyed it had to be done by a Roche approved vendor.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported