Clinical trial results:
A Randomized Phase 2 Trial of PF-00299804 Versus Erlotinib for the Treatment of Advanced Non-Small Cell Lung Cancer After Failure of at Least 1 Prior Chemotherapy Regimen

Summary

EudraCT number	2008-005235-14
Trial protocol	ES GB
Global end of trial date	15 August 2014

Results information

Result version number	v1
This version publication date	31 May 2016
First version publication date	12 August 2015

Trial information

Trial identification

Sponsor protocol code	A7471028

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00769067
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer, Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 800-718-1021, ClinicalTrials.gov_Inquiries@pfizer.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	15 August 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 August 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study was a Phase 2, open-label study to evaluate dacomitinib relative to erlotinib in the clinical setting for which erlotinib received approval for treatment of advanced Non Small Cell Lung Cancer (NSCLC) after failure of at least 1 prior chemotherapy regimen. In addition to the clinical safety and efficacy of dacomitinib, this study seeked to better understand the prognostic and predictive factors associated with advanced NSCLC, including both clinical factors (smoking, histology, sex, and race/ethnicity) and biomarkers (including epidermal growth factor receptor [EGFR], other human epidermal growth factor receptor [HER] family members, and v-Ki-ras2 Kirsten rat sarcoma viral oncogene homolog [KRAS] genetic changes).

Protection of trial subjects:

This study was conducted in compliance with the ethical principles originating in or derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. In addition, all local regulatory requirements were followed, in particular, those affording greater protection to the safety of trial participants.

The final protocol and any amendments were reviewed and approved by the Institutional Review Board(s) (IRB) and/or Independent Ethics Committee(s) (IEC) at each of the investigational centres participating in the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 November 2008
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	Australia: 16
Country: Number of subjects enrolled	Brazil: 25
Country: Number of subjects enrolled	Canada: 6
Country: Number of subjects enrolled	Hong Kong: 7
Country: Number of subjects enrolled	Korea, Republic of: 26
Country: Number of subjects enrolled	Puerto Rico: 1
Country: Number of subjects enrolled	Singapore: 5
Country: Number of subjects enrolled	Taiwan: 6
Country: Number of subjects enrolled	United States: 33
Country: Number of subjects enrolled	Poland: 29
Country: Number of subjects enrolled	Spain: 18
Country: Number of subjects enrolled	United Kingdom: 15

Worldwide total number of subjects	187
EEA total number of subjects	62

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)	125
From 65 to 84 years	61
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants were screened to ensure evidence of advanced non-small cell lung cancer (NSCLC), tumour tissue from either an original diagnostic biopsy or a recently obtained biopsy, left ventricular ejection fraction (LVEF) determination and satisfactory haematology, blood chemistry, coagulation and urine results within 7 days of start of treatment.

Period 1

Period 1 title	Overall Trial (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:

Erlotinib 150 milligram (mg) tablet orally once daily continuously in 28-day cycles until unacceptable toxicity, tumour progression or death.

Arm type	Active comparator
Investigational medicinal product name	Erlotinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

150 mg daily (at about the same time of each day) continuously in 28-day cycles until unacceptable toxicity, tumor progression or death.

Arm title	Dacomitinib

Arm description:

Dacomitinib (PF-00299804) 45 mg tablet orally once daily continuously in 28-day cycles until unacceptable toxicity, tumour progression or death.

Arm type	Experimental
Investigational medicinal product name	Dacomitinib
Investigational medicinal product code	
Other name	PF-00299804
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

45 mg daily (at about the same time of each day) continuously in 28-day cycles until unacceptable toxicity, tumor progression or death.

Number of subjects in period 1	Erlotinib	Dacomitinib
Started	94	93
Treated	94	93
Completed	0	0
Not completed	94	93
Death	89	86
Unspecified	1	3
Study Terminated by Sponsor	1	3
Lost to follow-up	3	1

Baseline characteristics

Reporting groups	
Reporting group title	Erlotinib
Reporting group description:	
Erlotinib 150 milligram (mg) tablet orally once daily continuously in 28-day cycles until unacceptable toxicity, tumour progression or death.	
Reporting group title	Dacomitinib
Reporting group description:	
Dacomitinib (PF-00299804) 45 mg tablet orally once daily continuously in 28-day cycles until unacceptable toxicity, tumour progression or death.	

Reporting group values	Erlotinib	Dacomitinib	Total
Number of subjects	94	93	187
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	60.1	59.9	
standard deviation	± 11.96	± 9.46	-
Gender categorical Units: Subjects			
Female	38	38	76
Male	56	55	111

End points

End points reporting groups

Reporting group title	Erlotinib
Reporting group description:	
Erlotinib 150 milligram (mg) tablet orally once daily continuously in 28-day cycles until unacceptable toxicity, tumour progression or death.	
Reporting group title	Dacomitinib
Reporting group description:	
Dacomitinib (PF-00299804) 45 mg tablet orally once daily continuously in 28-day cycles until unacceptable toxicity, tumour progression or death.	
Subject analysis set title	Dacomitinib
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Dacomitinib (PF-00299804) 45 mg tablet orally once daily continuously in 28-day cycles until unacceptable toxicity, tumour progression or death.	

Primary: Progression-Free Survival (PFS)

End point title	Progression-Free Survival (PFS)[1]
End point description:	
PFS: Time in weeks from randomization to date of objective disease progression or death due to any cause, whichever occurred first. PFS was calculated as (first event date or last known event-free date [if the event date unavailable] minus the date of randomization plus 1) divided by 7. Objective progression was defined using Response Evaluation Criteria in Solid Tumors (RECIST), as at least 20 percent (%) increase in the sum of longest dimensions (LDs) of target lesions, taking as reference the smallest sum of LD recorded since the treatment started and/or unequivocal progression of existing non-target lesions and/or appearance of 1 or more new lesions.	
End point type	Primary
End point timeframe:	
Baseline until disease progression or death, assessed at Cycle 2, 3, 4, 5, 6, thereafter every other cycle up to end of treatment (121 weeks), followed by every 8 weeks >284 weeks.	

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: The baseline period arm for dacomitinib includes only those subjects treated (i.e. the safety population). This outcome measure was analysed for all subjects randomised (i.e. the intention-to-treat [ITT] population).

End point values	Erlotinib	Dacomitinib		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	94[2]	94[3]		
Units: Weeks				
median (confidence interval 95%)	8.3 (7.9 to 11.7)	12.4 (8.1 to 16.1)		

Notes:

[2] - Reporting group = ITT population (i.e. all randomised participants)

[3] - Reporting group = ITT population

Statistical analyses

Statistical analysis title	Statistical Analysis of PFS

Statistical analysis description:

Total 128 events (progression/death) provided 80% power to detect a hazard ratio (HR) of 1.45 (erlotinib versus dacomitinib arm) with 1-sided alpha=0.10. This represented a 45% improvement in true median PFS. HR and 95% confidence interval estimated from stratified Cox regression; 2-sided p-value was based on stratified log-rank test with EGFR status, KRAS status, and baseline Eastern

Cooperative Oncology Group (ECOG) as stratification factors.

Comparison groups	Erlotinib v Dacomitinib
Number of subjects included in analysis	188
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.012 [4]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.657
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.472
upper limit	0.914

Notes:

[4] - 2-Sided
Point estimate of HR and its 95% CI were Dacomitinib vs Erlotinib

Secondary: Categorical Summary of Overall Scale Change in European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30)

End point title	Categorical Summary of Overall Scale Change in European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30)

End point description:

EORTC QLQ-C30: included global health status/quality of life (QoL), functional (Fn) scales (physical, role, cognitive, emotional, and social), symptom scales (fatigue, pain, nausea/vomiting), and single items (dyspnoea, appetite loss, insomnia, constipation, diarrhoea, and financial difficulties). Scores were averaged, transformed to 0-100 scale; higher score for Global Qol/Fn scales=better level of QoL/functioning or higher score for symptom scales/items=greater degree of symptoms. Overall scale change is categorized as Improved (if average scales change from baseline: for Global QoL/Fn scales >=10; for symptom scale/item <=-10), Worsened (if average scales change from baseline: for Global QoL/Fn scales <=-10; for symptom scale/item >=10), and Stable (if average scales change from baseline >-10 but <10 for Global QoL/Fn scales and symptom scale/item) and participants in each category are reported.

End point type	Secondary

End point timeframe:

Baseline up to Cycle 44 (Week 188)

End point values	Erlotinib	Dacomitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	88[5]	90[6]		
Units: Participants				
Global QoL: Improved (n= 85, 85)	14	11		
Global QoL: Worsened (n= 85, 85)	36	34		
Global QoL: Stable (n= 85, 85)	35	40		
Physical Functioning: Improved (n= 86, 88)	12	14		
Physical Functioning: Worsened (n= 86, 88)	25	24		
Physical Functioning: Stable (n= 86, 88)	49	50		
Role Functioning: Improved (n= 86, 88)	18	22		
Role Functioning: Worsened (n= 86, 88)	38	31		

Role Functioning: Stable (n= 86, 88)	30	35		
Cognitive Functioning: Improved (n= 86, 85)	13	15		
Cognitive Functioning: Worsened (n= 86, 85)	21	21		
Cognitive Functioning: Stable (n= 86, 85)	52	49		
Emotional Functioning: Improved (n= 86, 85)	11	21		
Emotional Functioning: Worsened (n= 86, 85)	27	26		
Emotional Functioning: Stable (n= 86, 85)	48	38		
Social Functioning: Improved (n= 86, 85)	24	30		
Social Functioning: Worsened (n= 86, 85)	30	19		
Social Functioning: Stable (n= 86, 85)	32	36		
Fatigue: Improved (n= 86, 87)	18	21		
Fatigue: Worsened (n= 86, 87)	38	35		
Fatigue: Stable (n= 86, 87)	30	31		
Pain: Improved (n= 86, 87)	19	19		
Pain: Worsened (n= 86, 87)	30	34		
Pain: Stable (n= 86, 87)	37	34		
Nausea and Vomiting: Improved (n= 86, 87)	13	13		
Nausea and Vomiting: Worsened (n= 86, 87)	27	26		
Nausea and Vomiting: Stable (n= 86, 87)	46	48		
Dyspnea: Improved (n= 86, 88)	23	25		
Dyspnea: Worsened (n= 86, 88)	26	25		
Dyspnea: Stable (n= 86, 88)	37	38		
Loss of Appetite: Improved (n= 85, 87)	17	19		
Loss of Appetite: Worsened (n= 85, 87)	41	43		
Loss of Appetite: Stable (n= 85, 87)	27	25		
Insomnia: Improved (n= 86, 87)	23	22		
Insomnia: Worsened (n= 86, 87)	32	33		
Insomnia: Stable (n= 86, 87)	31	32		
Constipation: Improved (n= 86, 85)	25	32		
Constipation: Worsened (n= 86, 85)	16	13		
Constipation: Stable (n= 86, 85)	45	40		
Diarrhea: Improved (n= 86, 85)	6	4		
Diarrhea: Worsened (n= 86, 85)	52	67		
Diarrhea: Stable (n= 86, 85)	28	14		
Financial Difficulties: Improved (n= 85, 86)	18	17		
Financial Difficulties: Worsened (n= 85, 86)	21	17		
Financial Difficulties: Stable (n= 85, 86)	46	51		

Notes:

[5] - Reporting group = ITT population

[6] - Reporting group = ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Categorical Summary of Overall Scale Change in EORTC QLQ Lung Cancer Module (LC13)

End point title	Categorical Summary of Overall Scale Change in EORTC QLQ Lung Cancer Module (LC13)

End point description:

QLQ-LC13 consisted of 13 questions relating to disease symptoms specific to lung cancer and treatment side effects typical of treatment with chemotherapy and radiotherapy. The 13 questions comprised 1 multi-item scale for dyspnoea and 10 single-item symptoms and side effects (coughing, haemoptysis, sore mouth, dysphagia, peripheral neuropathy, alopecia, chest pain, arm pain, other pain, and medicine for pain). Scores averaged, transformed to 0-100 scale; higher symptom score = greater degree of symptoms. Overall scale change was categorized as Improved (if average scales change from baseline <=-10), Worsened (if average scales change from baseline >=10), and Stable (if average scales change from baseline >-10 but <10) and participants in each category are reported.

End point type	Secondary

End point timeframe:

Baseline up to Cycle 44 (Week 188)

End point values	Erlotinib	Dacomitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	88[7]	89[8]		
Units: Participants				
Dyspnoea: Improved (n= 85, 87)	18	24		
Dyspnoea: Worsened (n= 85, 87)	29	20		
Dyspnoea: Stable (n= 85, 87)	38	43		
Coughing: Improved (n= 85, 87)	24	37		
Coughing: Worsened (n= 85, 87)	20	20		
Coughing: Stable (n= 85, 87)	41	30		
Haemoptysis: Improved (n= 85, 86)	5	8		
Haemoptysis: Worsened (n= 85, 86)	10	10		
Haemoptysis: Stable (n= 85, 86)	70	68		
Sore mouth: Improved (n= 85, 87)	3	5		
Sore mouth: Worsened (n= 85, 87)	38	58		
Sore mouth: Stable (n= 85, 87)	44	24		
Dysphagia: Improved (n= 85, 87)	7	6		
Dysphagia: Worsened (n= 85, 87)	24	35		
Dysphagia: Stable (n= 85, 87)	54	46		
Peripheral: Improved (n= 85, 87)	22	27		
Peripheral: Worsened (n= 85, 87)	23	20		
Peripheral: Stable (n= 85, 87)	40	40		
Alopecia: Improved (n= 84, 87)	20	21		
Alopecia: Worsened (n= 84, 87)	13	21		
Alopecia: Stable (n= 84, 87)	51	45		
Pain in chest: Improved (n= 85, 87)	26	30		
Pain in chest: Worsened (n= 85, 87)	21	13		
Pain in chest: Stable (n= 85, 87)	38	44		
Pain in arm or Shoulder: Improved (n= 85, 87)	19	28		
Pain in arm or Shoulder: Worsened (n= 85, 87)	27	17		

Pain in arm or Shoulder: Stable (n= 85, 87)	39	42		
Pain in other parts: Improved (n= 83, 86)	26	23		
Pain in other parts: Worsened (n= 83, 86)	27	28		
Pain in other parts: Stable (n= 83, 86)	30	35		

Notes:

[7] - Reporting group = ITT population

[8] - Reporting group = ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Dermatology Life Quality Index (DLQI)

End point title	Dermatology Life Quality Index (DLQI)

End point description:

DLQI: 10-item questionnaire to measure how much the participant's skin problem has impacted their life over the previous week on following 6 domains: symptoms/feelings (2 questions), daily activities (2 questions), leisure (2 questions), work/school (1 question), personal relationships (2 questions), and treatment (1 question). All questions were answered on a 4-point Likert scale ranging from 0 (not at all/not relevant) to 3 (very much/prevented work or studying). The DLQI total evaluable score was calculated by summing the score of each question and ranged from 0 to 30, where higher scores indicated more quality of life impairment. 9999 = SD could not be determined since n=1 or 0, 999 = arithmetic mean could not be determined since n=1 or 0.

End point type	Secondary

End point timeframe:

Cycle (C) 1 Day (D) 1 (baseline), C1D10-14, D1 of subsequent cycles up to C44

End point values	Erlotinib	Dacomitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	87[9]	91[10]		
Units: Units on a scale				
arithmetic mean (standard deviation)				
C1D1 (n= 87, 91)	0.7 (± 1.97)	0.88 (± 2.38)		
C1D10-14 (n=68, 81)	4.35 (± 6.25)	3.06 (± 4.94)		
C2D1 (n= 80, 82)	5.16 (± 6.29)	3.91 (± 4.07)		
C3D1 (n= 63, 63)	4.08 (± 5.67)	5.52 (± 6.65)		
C4D1 (n= 39, 43)	3.97 (± 4.59)	5.95 (± 6.38)		
C5D1 (n= 25, 38)	3.56 (± 3.61)	5.37 (± 6.08)		
C6D1 (n= 16, 27)	4.13 (± 4.8)	5.37 (± 6.67)		
C7D1 (n= 13, 27)	4.38 (± 4.07)	4.93 (± 6.54)		
C8D1 (n= 11, 24)	4.64 (± 3.14)	5.33 (± 6.23)		
C9D1 (n= 11, 19)	3.82 (± 3.34)	4.84 (± 5.76)		
C10D1 (n= 11, 17)	3.36 (± 3.04)	5.88 (± 7.37)		
C11D1 (n= 10, 15)	5.6 (± 5.13)	6.73 (± 7.57)		
C12D1 (n= 7, 14)	6.71 (± 5.62)	5.5 (± 6.99)		
C13D1 (n= 7, 13)	5.57 (± 4.08)	5.08 (± 7.9)		
C14D1 (n= 6, 12)	6 (± 3.95)	6 (± 7.35)		
C15D1 (n= 6, 12)	4.67 (± 3.78)	5.92 (± 7.4)		
C16D1 (n= 5, 11)	5.4 (± 3.91)	5.36 (± 8.18)		

C17D1 (n= 4, 11)	5 (± 4.24)	5.55 (± 7.85)		
C18D1 (n= 4, 10)	3 (± 2.16)	7.3 (± 9.08)		
C19D1 (n= 4, 9)	4.5 (± 2.38)	7.22 (± 7.73)		
C20D1 (n= 2, 10)	3.5 (± 3.54)	6.5 (± 8.57)		
C21D1 (n= 2, 9)	3.5 (± 2.12)	7.33 (± 7.76)		
C22D1 (n= 1, 7)	1 (± 9999)	2.14 (± 3.67)		
C23D1 (n= 1, 7)	1 (± 9999)	3.71 (± 3.99)		
C24D1 (n= 1, 7)	3 (± 9999)	2.57 (± 4.08)		
C25D1 (n= 1, 6)	8 (± 9999)	2.83 (± 4.45)		
C26D1 (n= 0, 6)	999 (± 9999)	2.67 (± 4.13)		
C27D1 (n= 0, 6)	999 (± 9999)	3.33 (± 3.98)		
C28D1 (n= 0, 6)	999 (± 9999)	3.17 (± 3.82)		
C29D1 (n= 0, 6)	999 (± 9999)	5.33 (± 4.59)		
C30D1 (n= 0, 5)	999 (± 9999)	4.2 (± 5.12)		
C31D1 (n= 0, 5)	999 (± 9999)	4.2 (± 4.97)		
C32D1 (n= 0, 4)	999 (± 9999)	2.75 (± 2.5)		
C33D1 (n= 0, 4)	999 (± 9999)	3 (± 2.94)		
C34D1 (n= 0, 2)	999 (± 9999)	4 (± 1.41)		
C35D1 (n= 0, 2)	999 (± 9999)	12.5 (± 13.44)		
C36D1 (n= 0, 2)	999 (± 9999)	1.5 (± 2.12)		
C37D1 (n= 0, 2)	999 (± 9999)	1.5 (± 2.12)		
C38D1 (n= 0, 2)	999 (± 9999)	0.5 (± 0.71)		
C39D1 (n= 0, 2)	999 (± 9999)	0 (± 0)		
C40D1 (n= 0, 2)	999 (± 9999)	0.5 (± 0.71)		
C41D1 (n= 0, 2)	999 (± 9999)	0 (± 0)		
C42D1 (n= 0, 2)	999 (± 9999)	0.5 (± 0.71)		
C43D1 (n= 0, 1)	999 (± 9999)	3 (± 9999)		
C44D1 (n= 0, 0)	999 (± 9999)	999 (± 999)		

Notes:

[9] - Reporting group = ITT population

[10] - Reporting group = ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Objective Response

End point title	Percentage of Participants With Objective Response[11]

End point description:

Percentage of participants with objective response based on assessment of confirmed complete response (CR) or confirmed partial response (PR) according to RECIST version 1.0. CR: disappearance of all target and non-target lesions. PR: at least 30% decrease in sum of the LDs of target lesions, taking as reference the baseline sum LD. Confirmed responses are those that persist on repeat imaging study at least 4 weeks after initial documentation of response.

End point type	Secondary

End point timeframe:

Baseline until disease progression or death, assessed at Cycle 2, 3, 4, 5, 6, thereafter every other cycle up to end of treatment (121 weeks), followed by every 8 weeks >284 weeks

Notes:

[11] - 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: The baseline period arm for dacomitinib includes only those subjects treated (i.e. the safety population). This outcome measure was analysed for all subjects randomised (i.e. the intention-to-treat [ITT] population).

End point values	Erlotinib	Dacomitinib		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	94[12]	94[13]		
Units: percent				
number (confidence interval 95%)	5.3 (1.7 to 12)	17 (10 to 26.2)		

Notes:

[12] - Reporting group = ITT population

[13] - Reporting group = ITT population

Statistical analyses

Statistical analysis title	Statistical Analysis of Objective Response
Comparison groups	Erlotinib v Dacomitinib
Number of subjects included in analysis	188
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.011 [14]
Method	Chi-squared

Notes:

[14] - 2-Sided

Secondary: Best Overall Response (BOR)

End point title	Best Overall Response (BOR)[15]

End point description:

Number of participants with BOR according to RECIST version 1.0: CR= disappearance of all target and non-target lesions. PR= at least 30% decrease in sum of LDs of target lesion, taking as reference baseline sum LD. Stable/no response= neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest sum of LDs since treatment started. Objective progression= at least a 20% increase in sum of LDs of target lesions, taking as reference the smallest sum of LDs recorded since treatment started and/or unequivocal progression of existing nontarget lesions and/or appearance of 1 or more new lesions.

End point type	Secondary

End point timeframe:

Baseline until disease progression or death, assessed at Cycle 2, 3, 4, 5, 6, thereafter every other cycle up to end of treatment (121 weeks), followed by every 8 weeks >284 weeks

Notes:

[15] - 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: The baseline period arm for dacomitinib includes only those subjects treated (i.e. the safety population). This outcome measure was analysed for all subjects randomised (i.e. the intention-to-treat [ITT] population).

End point values	Erlotinib	Dacomitinib		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	94[16]	94[17]		
Units: Participants				
Complete Response	0	1		
Partial Response	5	15		
Stable/No Response	37	32		
Objective Progression	49	30		
Indeterminate	3	16		

Notes:

[16] - Reporting group = ITT population

[17] - Reporting group = ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DR)

End point title	Duration of Response (DR)

End point description:

Time in weeks from first documentation of objective tumour response to objective tumour progression or symptomatic deterioration or death due to any cause, whichever occurred first. Duration of tumour response was calculated as (the date of the first documentation of objective tumour progression or symptomatic deterioration or death due to any cause or last known progression-free date [if none of the event dates available] minus the date of the first CR or PR [which ever occurred first] that was subsequently confirmed plus 1) divided by 7. DR was calculated for the subgroup of participants with a confirmed objective tumour response.

End point type	Secondary

End point timeframe:

Baseline until disease progression or death, assessed at Cycle 2, 3, 4, 5, 6, thereafter every other cycle up to end of treatment (121 weeks), followed by every 8 weeks >284 weeks

End point values	Erlotinib	Dacomitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5[18]	16[19]		
Units: Weeks				
median (confidence interval 95%)	40.1 (24.7 to 72)	71.9 (23.6 to 112.1)		

Notes:

[18] - Reporting group = sub-set of ITT population who had a confirmed objective tumour response (CR or PR)

[19] - Reporting group = sub-set of ITT population who had a confirmed objective tumour response (CR or PR)

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)[20]

End point description:

Time in weeks from randomization to date of death due to any cause. OS was calculated as (the death date or last known alive date (if death date unavailable) minus the date of randomization plus 1) divided by 7.

End point type	Secondary

End point timeframe:

Baseline until end of treatment (15 August 2014); followed up every 8 weeks after discontinuation from study treatment.

Notes:

[20] - 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: The baseline period arm for dacomitinib includes only those subjects treated (i.e. the safety population). This outcome measure was analysed for all subjects randomised (i.e. the intention-to-treat [ITT] population).

End point values	Erlotinib	Dacomitinib		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	94[21]	94[22]		
Units: Weeks				
median (confidence interval 95%)	32.3 (24 to 40.3)	41.4 (30.4 to 48.1)		

Notes:

[21] - Reporting group = ITT population

[22] - Reporting group = ITT population

Statistical analyses

Statistical analysis title	Statistical Analysis of Overall Survival
Comparison groups	Erlotinib v Dacomitinib
Number of subjects included in analysis	188
Analysis specification	Pre-specified
Analysis type	other[23]
P-value	= 0.252 [24]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.822
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.587
upper limit	1.151

Notes:

[23] - HR and its 95% confidence interval were estimated from stratified Cox Regression and 2-sided p-value was based on the stratified log-rank test with EGFR status, KRAS status and baseline ECOG as stratification factors.
[24] - 2-Sided
Point estimate of HR and its 95% CI were Dacomitinib vs Erlotinib

Other pre-specified: Number of Participants with KRAS and EGFR Status and EGFR T790M Mutation

End point title	Number of Participants with KRAS and EGFR Status and EGFR T790M Mutation[25]

End point description:

Tumour tissue were analysed at a sponsor-designated laboratory to investigate KRAS and EGFR status (wild type or mutated). Participants who did not provide samples for central laboratory analysis confirmation were classified as "unknown". Additionally blood specimens were analysed at a sponsor-designated laboratory for T790M mutation in EGFR. EGFR T790M mutation is counted under EGFR Status: Mutant category.

End point type	Other pre-specified

End point timeframe:

Baseline

Notes:

[25] - 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: The baseline period arm for dacomitinib includes only those subjects treated (i.e. the safety population). This outcome measure was analysed for all subjects randomised (i.e. the intention-to-treat [ITT] population).

End point values	Erlotinib	Dacomitinib		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	94[26]	94[27]		
Units: Participants				
EGFR Status: Wild Type	65	58		
EGFR Status: Mutant	11	19		
EGFR T790M Mutation	0	2		
EGFR Status: Unknown	18	17		
KRAS Status: Wild Type	64	57		
KRAS Status: Mutant	14	17		
KRAS Status: Unknown	16	20		

Notes:

[26] - Reporting group = ITT population

[27] - Reporting group = ITT population

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Soluble Protein Biomarkers Level

End point title	Soluble Protein Biomarkers Level

End point description:

Blood specimens were analysed at a sponsor-designated laboratory for analysis of shed proteins/receptors related to HER signalling (EGFR, HER-2, Epithelial-cadherin [E-cadherin]). The data collection after C12D1 was not performed, as there were too few participants across both treatment arms after C12D1.

End point type	Other pre-specified

End point timeframe:

C1D1 (baseline), D1 of each subsequent cycle up to end of treatment (up to 121 weeks)

End point values	Erlotinib	Dacomitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	76[28]	73[29]		
Units: nanogram(s) per millilitre (ng/mL)				
arithmetic mean (standard deviation)				
EGFR, C1D1 (n= 65, 66)	49.88 (± 7.513)	49.44 (± 9.286)		
EGFR, C2D1 (n= 76, 73)	48.87 (± 6.985)	41.29 (± 8.132)		
EGFR, C3D1 (n= 43, 53)	51.28 (± 6.925)	42.39 (± 8.072)		
EGFR, C4D1 (n= 26, 39)	49.49 (± 8.41)	41.9 (± 8.793)		

EGFR, C5D1 (n= 16, 29)	48.58 (± 5.801)	41.97 (± 7.974)		
EGFR, C6D1 (n= 15, 27)	50.32 (± 7.073)	42.82 (± 8.014)		
EGFR, C7D1 (n= 13, 26)	52.16 (± 7.449)	43.16 (± 9.13)		
EGFR, C8D1 (n= 10, 21)	54.74 (± 10.73)	44.78 (± 9.673)		
EGFR, C9D1 (n= 8, 17)	55.38 (± 12.888)	47.89 (± 10.854)		
EGFR, C10D1 (n= 10, 17)	54.57 (± 9.244)	48.12 (± 13.105)		
EGFR, C11D1 (n= 7, 14)	59.63 (± 14.624)	50.9 (± 13.667)		
EGFR, C12D1 (n= 6, 13)	57.65 (± 11.503)	52.39 (± 12.976)		
HER2, C1D1 (n= 65,66)	10.89 (± 15.44)	8.39 (± 2.05)		
HER2, C2D1 (n= 76,73)	9.17 (± 4.946)	6.42 (± 2.12)		
HER2, C3D1 (n= 43,53)	9.26 (± 6.383)	6.17 (± 1.703)		
HER2, C4D1 (n= 26,39)	9.51 (± 6.958)	6.29 (± 1.716)		
HER2, C5D1 (n= 16,29)	7.7 (± 1.79)	5.96 (± 1.342)		
HER2, C6D1 (n= 15,27)	7.45 (± 2.414)	6.34 (± 1.428)		
HER2, C7D1 (n= 13,26)	8.07 (± 2.262)	6.47 (± 1.773)		
HER2, C8D1 (n= 10,21)	7.28 (± 1.279)	7.15 (± 3.168)		
HER2, C9D1 (n= 8,17)	7.32 (± 1.204)	6.87 (± 2.205)		
HER2, C10D1 (n= 10,17)	7.49 (± 1.618)	7.25 (± 2.883)		
HER2, C11D1 (n= 7,14)	7.76 (± 1.735)	6.56 (± 1.333)		
HER2, C12D1 (n= 6,13)	7.15 (± 1.57)	6.57 (± 1.587)		
E-cadherin, C1D1 (n= 65, 66)	51.71 (± 14.63)	56.13 (± 22.694)		
E-cadherin, C2D1 (n= 76. 73)	41.46 (± 14.982)	45.4 (± 18.149)		
E-cadherin, C3D1 (n= 43, 53)	42.58 (± 13.284)	42.28 (± 17.81)		
E-cadherin, C4D1 (n= 26, 39)	40.51 (± 12.384)	40.15 (± 16.105)		
E-cadherin, C5D1 (n= 16, 29)	37.58 (± 9.951)	38.15 (± 10.913)		
E-cadherin, C6D1 (n= 15, 27)	36.78 (± 7.695)	39.16 (± 10.301)		
E-cadherin, C7D1 (n= 13, 26)	38.33 (± 9.675)	39.47 (± 11.977)		
E-cadherin, C8D1 (n= 10, 21)	43.6 (± 11.661)	40.94 (± 13.698)		
E-cadherin, C9D1 (n= 8,17)	40.26 (± 8.146)	38.97 (± 12.517)		
E-cadherin, C10D1 (n= 10, 17)	40.29 (± 15.742)	45.85 (± 12.244)		
E-cadherin, C11D1 (n= 7, 14)	35.9 (± 9.239)	39.44 (± 8.968)		
E-cadherin, C12D1 (n= 6, 13)	35.48 (± 8.637)	40.3 (± 12.433)		

Notes:

[28] - Reporting group = biomarker analysis population

[29] - Reporting group = biomarker analysis population

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Trough Plasma Concentration (Ctrough) of Dacomitinib (PF-00299804)

End point title	Trough Plasma Concentration (Ctrough) of Dacomitinib (PF-00299804)[30]

End point description:

Only participants from "Dacomitinib" treatment arm were planned to be analysed for this outcome.

End point type	Other pre-specified

End point timeframe:

C1D10-14, C2D1, C3D1, C4D1

Notes:

[30] - 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: Only participants from "Dacomitinib" treatment arm were planned to be analysed for this end point.

End point values	Dacomitinib			
Subject group type	Reporting group			
Number of subjects analysed	63[31]			
Units: ng /mL				
arithmetic mean (standard deviation)				
C1D10-14 (n= 63)	71.94 (± 37.496)			
C2D1 (n= 60)	65.5 (± 33.292)			
C3D1 (n= 44)	59.28 (± 30.089)			
C4D1 (n= 31)	57.79 (± 26.206)			

Notes:

[31] - Reporting group = Pharmacokinetic population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) were recorded from the time that the participant provided informed consent through and including 28 calendar days after the last administration of the investigational product.

Adverse event reporting additional description:

The same event may appear as both an AE and a serious AE (SAE). However, what is presented are distinct events. An event may be categorized as serious in 1 participant and as nonserious in another participant, or 1 participant may have experienced both a serious and nonserious event during the study.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	Erlotinib

Reporting group description:

Erlotinib 150 milligram (mg) tablet orally once daily continuously in 28-day cycles until unacceptable toxicity, tumor progression or death.

Reporting group title	Dacomitinib

Reporting group description:

Dacomitinib (PF-00299804) 45 mg tablet orally once daily continuously in 28-day cycles until unacceptable toxicity, tumor progression or death.

Serious adverse events	Erlotinib	Dacomitinib	
Total subjects affected by serious adverse events			
subjects affected / exposed	30 / 94 (31.91%)	34 / 93 (36.56%)	
number of deaths (all causes)	17	17	
number of deaths resulting from adverse events	2	2	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant pleural effusion			
subjects affected / exposed	0 / 94 (0.00%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 94 (1.06%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			

subjects affected / exposed	0 / 94 (0.00%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 94 (1.06%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cyst			
subjects affected / exposed	0 / 94 (0.00%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disease progression			
subjects affected / exposed	12 / 94 (12.77%)	9 / 93 (9.68%)	
occurrences causally related to treatment / all	0 / 12	0 / 9	
deaths causally related to treatment / all	0 / 12	0 / 9	
Fatigue			
subjects affected / exposed	0 / 94 (0.00%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	1 / 94 (1.06%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 94 (0.00%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			

subjects affected / exposed	1 / 94 (1.06%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cough			
subjects affected / exposed	0 / 94 (0.00%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	3 / 94 (3.19%)	8 / 93 (8.60%)	
occurrences causally related to treatment / all	0 / 3	0 / 8	
deaths causally related to treatment / all	0 / 1	0 / 0	
Haemoptysis			
subjects affected / exposed	1 / 94 (1.06%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	0 / 94 (0.00%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	1 / 1	
Pulmonary embolism			
subjects affected / exposed	3 / 94 (3.19%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	1 / 4	0 / 1	
deaths causally related to treatment / all	1 / 1	0 / 1	
Pulmonary haemorrhage			
subjects affected / exposed	0 / 94 (0.00%)	1 / 93 (1.08%)	
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	1 / 94 (1.06%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wheezing			

subjects affected / exposed	1 / 94 (1.06%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 94 (1.06%)	2 / 93 (2.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			
subjects affected / exposed	1 / 94 (1.06%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychotic disorder			
subjects affected / exposed	0 / 94 (0.00%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 94 (0.00%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	1 / 94 (1.06%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Altered state of consciousness			
subjects affected / exposed	0 / 94 (0.00%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 94 (1.06%)	0 / 93 (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			
Anaemia			
subjects affected / exposed	1 / 94 (1.06%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 94 (2.13%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	2 / 94 (2.13%)	2 / 93 (2.15%)	
occurrences causally related to treatment / all	2 / 2	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 94 (0.00%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nausea			
subjects affected / exposed	0 / 94 (0.00%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 94 (1.06%)	2 / 93 (2.15%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	0 / 94 (0.00%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Haematuria			

subjects affected / exposed	1 / 94 (1.06%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	0 / 94 (0.00%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure acute			
subjects affected / exposed	0 / 94 (0.00%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abscess			
subjects affected / exposed	0 / 94 (0.00%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	0 / 94 (0.00%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected dermal cyst			
subjects affected / exposed	1 / 94 (1.06%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 94 (0.00%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	0 / 94 (0.00%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parotitis			

subjects affected / exposed	1 / 94 (1.06%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	4 / 94 (4.26%)	6 / 93 (6.45%)	
occurrences causally related to treatment / all	3 / 7	2 / 8	
deaths causally related to treatment / all	1 / 2	1 / 2	
Pneumonia bacterial			
subjects affected / exposed	0 / 94 (0.00%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Sepsis			
subjects affected / exposed	0 / 94 (0.00%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin infection			
subjects affected / exposed	0 / 94 (0.00%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	1 / 94 (1.06%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Dehydration			
subjects affected / exposed	1 / 94 (1.06%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia			
subjects affected / exposed	1 / 94 (1.06%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemia			

subjects affected / exposed	0 / 94 (0.00%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Erlotinib	Dacomitinib	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	93 / 94 (98.94%)	93 / 93 (100.00%)	
Investigations			
Weight decreased			
subjects affected / exposed	13 / 94 (13.83%)	18 / 93 (19.35%)	
occurrences (all)	16	25	
Nervous system disorders			
Dizziness			
subjects affected / exposed	9 / 94 (9.57%)	3 / 93 (3.23%)	
occurrences (all)	9	4	
Dysgeusia			
subjects affected / exposed	7 / 94 (7.45%)	7 / 93 (7.53%)	
occurrences (all)	7	9	
Headache			
subjects affected / exposed	8 / 94 (8.51%)	3 / 93 (3.23%)	
occurrences (all)	9	4	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	5 / 94 (5.32%)	6 / 93 (6.45%)	
occurrences (all)	6	9	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	11 / 94 (11.70%)	13 / 93 (13.98%)	
occurrences (all)	13	18	
Chest pain			
subjects affected / exposed	13 / 94 (13.83%)	5 / 93 (5.38%)	
occurrences (all)	15	6	
Fatigue			

subjects affected / exposed	33 / 94 (35.11%)	24 / 93 (25.81%)	
occurrences (all)	41	30	
Mucosal inflammation			
subjects affected / exposed	7 / 94 (7.45%)	23 / 93 (24.73%)	
occurrences (all)	7	34	
Oedema peripheral			
subjects affected / exposed	4 / 94 (4.26%)	6 / 93 (6.45%)	
occurrences (all)	5	7	
Pain			
subjects affected / exposed	6 / 94 (6.38%)	5 / 93 (5.38%)	
occurrences (all)	6	6	
Eye disorders			
Dry eye			
subjects affected / exposed	3 / 94 (3.19%)	6 / 93 (6.45%)	
occurrences (all)	3	11	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	7 / 94 (7.45%)	2 / 93 (2.15%)	
occurrences (all)	8	4	
Cheilitis			
subjects affected / exposed	1 / 94 (1.06%)	5 / 93 (5.38%)	
occurrences (all)	1	18	
Constipation			
subjects affected / exposed	12 / 94 (12.77%)	9 / 93 (9.68%)	
occurrences (all)	12	10	
Diarrhoea			
subjects affected / exposed	46 / 94 (48.94%)	67 / 93 (72.04%)	
occurrences (all)	59	145	
Dry mouth			
subjects affected / exposed	8 / 94 (8.51%)	9 / 93 (9.68%)	
occurrences (all)	8	11	
Dyspepsia			
subjects affected / exposed	8 / 94 (8.51%)	3 / 93 (3.23%)	
occurrences (all)	9	4	
Mouth ulceration			

subjects affected / exposed	5 / 94 (5.32%)	3 / 93 (3.23%)	
occurrences (all)	5	3	
Nausea			
subjects affected / exposed	21 / 94 (22.34%)	20 / 93 (21.51%)	
occurrences (all)	24	23	
Stomatitis			
subjects affected / exposed	10 / 94 (10.64%)	27 / 93 (29.03%)	
occurrences (all)	14	38	
Vomiting			
subjects affected / exposed	14 / 94 (14.89%)	11 / 93 (11.83%)	
occurrences (all)	16	13	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	21 / 94 (22.34%)	17 / 93 (18.28%)	
occurrences (all)	24	24	
Dysphonia			
subjects affected / exposed	0 / 94 (0.00%)	6 / 93 (6.45%)	
occurrences (all)	0	8	
Dyspnoea			
subjects affected / exposed	16 / 94 (17.02%)	20 / 93 (21.51%)	
occurrences (all)	17	24	
Epistaxis			
subjects affected / exposed	2 / 94 (2.13%)	7 / 93 (7.53%)	
occurrences (all)	3	9	
Haemoptysis			
subjects affected / exposed	3 / 94 (3.19%)	9 / 93 (9.68%)	
occurrences (all)	3	11	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	11 / 94 (11.70%)	12 / 93 (12.90%)	
occurrences (all)	17	20	
Alopecia			
subjects affected / exposed	3 / 94 (3.19%)	9 / 93 (9.68%)	
occurrences (all)	4	12	
Dermatitis acneiform			

subjects affected / exposed	54 / 94 (57.45%)	60 / 93 (64.52%)	
occurrences (all)	77	124	
Dry skin			
subjects affected / exposed	15 / 94 (15.96%)	22 / 93 (23.66%)	
occurrences (all)	21	48	
Erythema multiforme			
subjects affected / exposed	4 / 94 (4.26%)	10 / 93 (10.75%)	
occurrences (all)	5	12	
Exfoliative rash			
subjects affected / exposed	14 / 94 (14.89%)	16 / 93 (17.20%)	
occurrences (all)	24	37	
Nail disorder			
subjects affected / exposed	1 / 94 (1.06%)	7 / 93 (7.53%)	
occurrences (all)	2	13	
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	5 / 94 (5.32%)	11 / 93 (11.83%)	
occurrences (all)	6	14	
Pruritus			
subjects affected / exposed	15 / 94 (15.96%)	14 / 93 (15.05%)	
occurrences (all)	18	27	
Skin fissures			
subjects affected / exposed	2 / 94 (2.13%)	9 / 93 (9.68%)	
occurrences (all)	3	20	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	5 / 94 (5.32%)	2 / 93 (2.15%)	
occurrences (all)	5	2	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	10 / 94 (10.64%)	11 / 93 (11.83%)	
occurrences (all)	10	12	
Pain in extremity			
subjects affected / exposed	2 / 94 (2.13%)	5 / 93 (5.38%)	
occurrences (all)	2	5	
Infections and infestations			

Conjunctivitis			
subjects affected / exposed	3 / 94 (3.19%)	9 / 93 (9.68%)	
occurrences (all)	4	10	
Paronychia			
subjects affected / exposed	8 / 94 (8.51%)	24 / 93 (25.81%)	
occurrences (all)	11	58	
Upper respiratory tract infection			
subjects affected / exposed	6 / 94 (6.38%)	3 / 93 (3.23%)	
occurrences (all)	6	5	
Urinary tract infection			
subjects affected / exposed	6 / 94 (6.38%)	5 / 93 (5.38%)	
occurrences (all)	6	6	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	29 / 94 (30.85%)	27 / 93 (29.03%)	
occurrences (all)	36	31	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 May 2013	Protocol Amendment 2 updated dosing language, allowed less frequent tumor assessment imaging for participants on therapy over 1 year (with Sponsor approval), provided information on the single reference safety documents used in the study, revised pregnancy/contraception language, updated dacomitinib concomitant medication guide for those drugs dependent on cytochrome P450 2D6 for metabolism and use of acid reducing agents, based on recent clinical pharmacology analyses, revised reporting of dose errors as AEs, included 3 additional strengths for dacomitinib film coated tablets (15, 30, and 45 mg), included clarifying language on active reporting period and necessity to report SAEs post-active reporting period to align with CT-3 and Food and Drug Administration Final Rule, updated instructions for evaluation of liver function changes and updated wording and format to align with changes in the Pfizer protocol template.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported