



Clinical trial results:

ARCHER 1050: A RANDOMIZED, OPEN-LABEL, PHASE 3, EFFICACY AND SAFETY STUDY OF DACOMITINIB (PF 00299804) VERSUS GEFITINIB FOR THE FIRST LINE TREATMENT OF LOCALLY ADVANCED OR METASTATIC NON SMALL CELL LUNG CANCER (NSCLC) IN SUBJECTS WITH EPIDERMAL GROWTH FACTOR RECEPTOR (EGFR) ACTIVATING MUTATION(S)

Summary

EudraCT number	2012-004977-23
Trial protocol	ES IT PL
Global end of trial date	

Results information

Result version number	v1
This version publication date	25 October 2018
First version publication date	25 October 2018

Trial information

Trial identification

Sponsor protocol code	DP312804
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01774721
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer, Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States,
Public contact	WRS Oncology Europe, Pfizer Italia S.r.l., 0039 0241498 636, paola.tozzi@pfizer.com
Scientific contact	WRS Oncology Europe, Pfizer Italia S.r.l., 0039 0241498 636, paola.tozzi@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	Interim
Date of interim/final analysis	15 February 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 July 2016
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that dacomitinib treatment was superior to gefitinib treatment with respect to Progression-Free Survival (PFS) as determined by blinded independent radiologic central (IRC) review, in the study population.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Council for Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 May 2013
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	48 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 12
Country: Number of subjects enrolled	Spain: 53
Country: Number of subjects enrolled	Italy: 42
Country: Number of subjects enrolled	China: 231
Country: Number of subjects enrolled	Hong Kong: 4
Country: Number of subjects enrolled	Japan: 83
Country: Number of subjects enrolled	Korea, Republic of: 27
Worldwide total number of subjects	452
EEA total number of subjects	107

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)	273
From 65 to 84 years	176
85 years and over	3

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of four hundred and fifty two subjects were enrolled at multiple centers in this study. The results reported are based on the data cut off date as of 29 July 2016.

Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Dacomitinib

Arm description:

Subjects received 45 milligram (mg) of dacomitinib tablets orally once daily in each treatment cycle of 28 days, up to a maximum duration of 48 months or until disease progression, intolerable toxicities, withdrawal, death, or investigator decision dictated by protocol compliance, whichever occurred first.

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

Dosage and administration details:

Subjects received 45 mg of dacomitinib tablets orally once daily in each treatment cycle of 28 days.

Arm title	Gefitinib
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Arm description:

Subjects received 250 mg of gefitinib tablets orally once daily, in each treatment cycle of 28 days, up to a maximum duration of 48 months or until disease progression, intolerable toxicities, withdrawal, death, or investigator decision dictated by protocol compliance, whichever occurred first.

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

Dosage and administration details:

Subjects received 250 mg of gefitinib tablets orally once daily, in each treatment cycle of 28 days.

Number of subjects in period 1	Dacomitinib	Gefitinib
Started	227	225
Treated	227	224
Completed	0	0
Not completed	227	225
Ongoing in study	136	120
Death	76	91
Did not meet eligibility criteria	-	3
Lost to follow-up	1	1
Withdrawal by subject	14	10

Baseline characteristics

Reporting groups

Reporting group title	Dacomitinib
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Reporting group description:

Subjects received 45 milligram (mg) of dacomitinib tablets orally once daily in each treatment cycle of 28 days, up to a maximum duration of 48 months or until disease progression, intolerable toxicities, withdrawal, death, or investigator decision dictated by protocol compliance, whichever occurred first.

Reporting group title	Gefitinib
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Reporting group description:

Subjects received 250 mg of gefitinib tablets orally once daily, in each treatment cycle of 28 days, up to a maximum duration of 48 months or until disease progression, intolerable toxicities, withdrawal, death, or investigator decision dictated by protocol compliance, whichever occurred first.

Reporting group values	Dacomitinib	Gefitinib	Total
Number of subjects	227	225	452
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	61.2 ± 11.26	60.9 ± 10.17	-
Gender categorical Units: Subjects			
Female	146	125	271
Male	81	100	181
Race (NIH/OMB) Units: Subjects			
Asian	170	176	346
Black or African American	1	0	1
White	56	49	105
Ethnicity (NIH/OMB) Units: Subjects			
Not Hispanic or Latino	227	225	452

End points

End points reporting groups

Reporting group title	Dacomitinib
Reporting group description: Subjects received 45 milligram (mg) of dacomitinib tablets orally once daily in each treatment cycle of 28 days, up to a maximum duration of 48 months or until disease progression, intolerable toxicities, withdrawal, death, or investigator decision dictated by protocol compliance, whichever occurred first.	
Reporting group title	Gefitinib
Reporting group description: Subjects received 250 mg of gefitinib tablets orally once daily, in each treatment cycle of 28 days, up to a maximum duration of 48 months or until disease progression, intolerable toxicities, withdrawal, death, or investigator decision dictated by protocol compliance, whichever occurred first.	

Primary: Progression Free Survival (PFS) Based on Independent Radiologic Central (IRC) Review

End point title	Progression Free Survival (PFS) Based on Independent Radiologic Central (IRC) Review
End point description: Time from randomization to date of progression of disease (PD) as determined by IRC review as per Response evaluation Criteria in solid tumors (RECIST) v1.1 criteria or death due to any cause, whichever occurred first. PD for target lesions: 20% increase in sum of diameters of target measurable lesions above smallest sum observed, with minimum absolute increase of 5 mm; for non-target lesions: unequivocal progression of pre-existing lesions. Overall tumor burden increased sufficiently to merit discontinuation of therapy. In presence of stable disease (did not achieve partial response, complete response or PD) or partial response ($\geq 30\%$ decrease under baseline of sum of diameters of all target measurable lesions, short diameter used in the sum for target nodes, longest diameter used in sum for all other target lesions) in target disease; for new lesions: appearance of any new unequivocal malignant lesion indicated PD. Intent to treat (ITT) analysis set.	
End point type	Primary
End point timeframe: Day 28 of Cycle 1, Cycle 2 then every 8 weeks until disease progression or death due to any cause, whichever occurred first (up to 48 months)	

End point values	Dacomitinib	Gefitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	227	225		
Units: months				
median (confidence interval 95%)	14.7 (11.1 to 16.6)	9.2 (9.1 to 11.0)		

Statistical analyses

Statistical analysis title	Dacomitinib vs Gefitinib
Statistical analysis description: Analysis of HR ratio was based on stratified Cox regression model.	
Comparison groups	Dacomitinib v Gefitinib

Number of subjects included in analysis	452
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	1-sided stratified log-rank test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.589
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.469
upper limit	0.739

Secondary: Progression Free Survival (PFS) Based on Investigator Assessment

End point title	Progression Free Survival (PFS) Based on Investigator Assessment
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End point description:

Time from randomization to date of PD as determined by investigator assessment as per RECIST v1.1 criteria or death due to any cause, whichever occurred first. PD for target lesions: 20% increase in sum of diameters of target measurable lesions above smallest sum observed, with minimum absolute increase of 5 mm; for non-target lesions: unequivocal progression of pre-existing lesions. Overall tumor burden increased sufficiently to merit discontinuation of therapy. In presence of stable disease (did not achieve partial response, complete response or PD) or partial response ($\geq 30\%$ decrease under baseline of sum of diameters of all target measurable lesions, short diameter used in the sum for target nodes, longest diameter used in sum for all other target lesions) in target disease; for new lesions: appearance of any new unequivocal malignant lesion indicated PD. ITT analysis set.

End point type	Secondary
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End point timeframe:

Day 28 of Cycle 1, Cycle 2 then every 8 weeks until disease progression or death due to any cause, whichever occurred first (up to 48 months)

End point values	Dacomitinib	Gefitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	227	225		
Units: months				
median (confidence interval 95%)	16.6 (12.9 to 18.4)	11.0 (9.4 to 12.1)		

Statistical analyses

Statistical analysis title	Dacomitinib vs Gefitinib
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Statistical analysis description:

Analysis of HR ratio was based on stratified Cox regression model.

Comparison groups	Dacomitinib v Gefitinib
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Number of subjects included in analysis	452
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	1-sided stratified log-rank test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.622
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.497
upper limit	0.779

Secondary: Number of Subjects With Best Overall Response (BOR) Based on IRC Review

End point title	Number of Subjects With Best Overall Response (BOR) Based on IRC Review
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End point description:

Number of subjects with BOR based on IRC review (complete response[CR] or confirmed partial response[PR]) was recorded from randomization until disease progression based on RECISTv1.1. CR for target lesion: disappearance of all target lesions with exception of nodal disease. All target nodes must decreased to normal size; for non-target lesions: disappearance of all non-target lesions and normalization of tumor marker levels. All lymph nodes must be 'normal' in size(<short axis <10 mm);for new lesions: repeated assessments of a new lesion if it was equivocal. PR: >=30% decrease under baseline of sum of all target measurable lesions, short diameter was used in sum for target nodes, longest diameter was used in sum for all other target lesions. PD was defined as 20% increase in sum of diameters of target measurable lesions above the smallest sum observed (over baseline if no decrease in the sum is observed during therapy), with a minimum absolute increase of 5 mm. ITT analysis set.

End point type	Secondary
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End point timeframe:

Day 28 of Cycle 1, Cycle 2 then every 8 weeks until disease progression (up to 48 months)

End point values	Dacomitinib	Gefitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	227	225		
Units: Subjects				
Complete response	12	4		
Partial response	158	157		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Best Overall Response (BOR) Based on Investigator Assessment

End point title	Number of Subjects With Best Overall Response (BOR) Based on Investigator Assessment
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End point description:

Number of subjects with BOR based on investigator assessment (CR or confirmed PR) was recorded from randomization until disease progression based on RECIST v1.1. CR for target lesion: disappearance of all target lesions with exception of nodal disease. All target nodes must decreased to normal size (short axis <10 mm); for non-target lesions: disappearance of all non-target lesions and normalization of tumor marker levels. All lymph nodes must be 'normal' in size (<short axis <10 mm); for new lesions: repeated assessments of a new lesion if it was equivocal. PR: $\geq 30\%$ decrease under baseline of sum of all target measurable lesions, short diameter was used in sum for target nodes, longest diameter was used in sum for all other target lesions. PD was defined as 20% increase in sum of diameters of target measurable lesions above the smallest sum observed (over baseline if no decrease in the sum is observed during therapy), with a minimum absolute increase of 5 mm. ITT analysis set.

End point type	Secondary
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End point timeframe:

Day 28 of Cycle 1, Cycle 2 then every 8 weeks until disease progression (up to 48 months)

End point values	Dacomitinib	Gefitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	227	225		
Units: Subjects				
Complete response	2	1		
Partial response	169	157		

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate (ORR) Based on IRC Review

End point title	Objective Response Rate (ORR) Based on IRC Review
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End point description:

Percentage of subjects with a BOR of either CR or PR based on IRC review recorded from randomization until disease progression based on RECIST v1.1. CR for target lesion: disappearance of all target lesions with exception of nodal disease. All target nodes must decreased to normal size (short axis <10 mm); for non-target lesions: disappearance of all non-target lesions and normalization of tumor marker levels. All lymph nodes must be 'normal' in size (<short axis <10 mm); for new lesions: repeated assessments of a new lesion if it was equivocal. PR: $\geq 30\%$ decrease under baseline of sum of all target measurable lesions, short diameter was used in sum for target nodes, longest diameter was used in sum for all other target lesions. PD was defined as 20% increase in sum of diameters of target measurable lesions above the smallest sum observed (over baseline if no decrease in the sum is observed during therapy), with a minimum absolute increase of 5 mm. ITT analysis set.

End point type	Secondary
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End point timeframe:

Day 28 of Cycle 1, Cycle 2 then every 8 weeks until disease progression (up to 48 months)

End point values	Dacomitinib	Gefitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	227	225		
Units: percentage of subjects				
number (confidence interval 95%)	74.9 (68.7 to 80.4)	71.6 (65.2 to 77.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate (ORR) Based on Investigator Assessment

End point title	Objective Response Rate (ORR) Based on Investigator Assessment
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End point description:

Percentage of subjects with a BOR of either CR or PR based on investigator assessment recorded from randomization until disease progression based on RECIST v1.1. CR for target lesion:disappearance of all target lesions with exception of nodal disease. All target nodes must decreased to normal size (short axis <10 mm); for non-target lesions:disappearance of all non-target lesions and normalization of tumor marker levels. All lymph nodes must be 'normal' in size (<short axis <10 mm); for new lesions: repeated assessments of a new lesion if it was equivocal. PR: >=30% decrease under baseline of sum of all target measurable lesions, short diameter was used in sum for target nodes, longest diameter was used in sum for all other target lesions. PD was defined as 20% increase in sum of diameters of target measurable lesions above the smallest sum observed (over baseline if no decrease in the sum is observed during therapy), with a minimum absolute increase of 5 mm.ITT analysis set.

End point type	Secondary
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End point timeframe:

Day 28 of Cycle 1, Cycle 2 then every 8 weeks until disease progression (up to 48 months)

End point values	Dacomitinib	Gefitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	227	225		
Units: percentage of subjects				
number (confidence interval 95%)	75.3 (69.2 to 80.8)	70.2 (63.8 to 76.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DoR)

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

It was defined as time from first documentation of objective response(CR or PR) to date of PD or death from any cause,whichever occurred first.CR for target lesion:disappearance of all target lesions with exception of nodal disease.All target nodes decreased to normal size;for non-target lesions:disappearance of all non-target lesions and normalization of tumor marker levels.All lymph nodes must be 'normal' in size(short axis <10 mm);for new lesions:repeated assessments of new lesion if it

equivocal.PR: $\geq 30\%$ decrease under baseline of sum of all target measurable lesions, short diameter used in sum for target nodes, longest diameter used in sum for all other target lesions. PD: 20% increase in sum of diameters of target measurable lesions above the smallest sum observed (over baseline if no decrease in sum is observed), with a minimum absolute increase of 5 mm. DoR was recorded based on IRC review and investigator's assessment. ITT analysis set. n = number evaluable for specific categories.

End point type	Secondary
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End point timeframe:

Day 28 of Cycle 1, Cycle 2 then every 8 weeks until disease progression or death due to any cause, whichever occurred first (up to 48 months)

End point values	Dacomitinib	Gefitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	227	225		
Units: months				
median (confidence interval 95%)				
DoR: IRC review (n = 170, 161)	14.8 (12.0 to 17.4)	8.3 (7.4 to 9.2)		
DoR: Investigator assessment (n = 171, 158)	15.9 (13.8 to 17.6)	9.2 (8.2 to 11.0)		

Statistical analyses

Statistical analysis title	Dacomitinib vs Gefitinib
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Statistical analysis description:

Comparison of dacomitinib vs gefitinib based on IRC review. Analysis of HR ratio was based on stratified Cox regression model.

Comparison groups	Dacomitinib v Gefitinib
Number of subjects included in analysis	452
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	1-sided stratified log-rank test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.403
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.307
upper limit	0.529

Statistical analysis title	Dacomitinib vs Gefitinib
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Statistical analysis description:

Comparison of dacomitinib vs gefitinib based on Investigator assessment. Analysis of HR ratio was based on stratified Cox regression model.

Comparison groups	Dacomitinib v Gefitinib
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Number of subjects included in analysis	452
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	1-sided stratified log-rank test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.545
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.418
upper limit	0.711

Secondary: Number of Subjects With Treatment-Emergent Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point title	Number of Subjects With Treatment-Emergent Adverse Events (AEs) and Serious Adverse Events (SAEs)
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End point description:

An AE was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. Treatment-emergent AEs were events between first dose of study drug and up to 28-35 days after last dose that were absent before treatment or that worsened relative to pretreatment state. AEs included both serious and non-serious. Safety analysis set included all subjects who received at least 1 dose of study medication, with treatment assignments designated according to actual study treatment received.

End point type	Secondary
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End point timeframe:

From baseline up to 28-35 days after last dose of study drug (up to 48 months)

End point values	Dacomitinib	Gefitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	227	224		
Units: Subjects				
AEs	226	220		
SAEs	62	50		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Laboratory Test Abnormalities of Grade 3 or Higher Severity Based on NCI CTCAE Version 4.03: Biochemistry and Haematology

End point title	Number of Subjects With Laboratory Test Abnormalities of Grade 3 or Higher Severity Based on NCI CTCAE Version 4.03: Biochemistry and Haematology
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End point description:

Laboratory parameters included haematological and biochemistry parameters. Haematology parameters included anaemia, activated partial thromboplastin time, haemoglobin, international normalized ratio, lymphocyte count, lymphopenia, neutrophils (absolute), platelets, prothrombin time and white blood cells. Biochemistry parameters included alanine aminotransferase (increased), alkaline phosphatase (increased), aspartate aminotransferase (increased), bilirubin (total), creatinine (increased), hypercalcaemia, hyperglycaemia, hyperkalaemia, hypermagnesaemia, hypernatraemia, hypoalbuminaemia, hypocalcaemia, hypoglycaemia, hypokalaemia, hypomagnesaemia, hyponatraemia. Test abnormalities were graded by AEs according to the Common Terminology Criteria for Adverse Events (NCI CTCAE) version 4.03 as Grade 1= mild; Grade 2= moderate; Grade 3= severe and Grade 4= life-threatening or disabling. Only categories with at least 1 subject with abnormality are reported in this endpoint. Safety analysis set.

End point type	Secondary
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End point timeframe:

From baseline up to 28-35 days after last dose of study drug (up to 48 months)

End point values	Dacomitinib	Gefitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	227	224		
Units: Subjects				
Anaemia (Grade 3)	2	6		
Haemoglobin (Grade 3)	0	1		
Lymphopenia (Grade 3)	13	6		
Lymphopenia (Grade 4)	1	0		
Neutrophil count (absolute) (Grade 3)	0	1		
WBC count (Grade 3)	1	1		
Alanine aminotransferase increased (Grade 3)	3	26		
Alanine aminotransferase increased (Grade 4)	0	2		
Aspartate aminotransferase increased (Grade 3)	1	15		
Aspartate aminotransferase increased (Grade 4)	0	2		
Alkaline phosphatase increased (Grade 3)	2	6		
Bilirubin increased (total) (Grade 3)	1	1		
Creatinine increased (Grade 3)	0	1		
Hypercalcaemia (Grade 3)	1	0		
Hyperglycaemia (Grade 3)	2	5		
Hyperkalaemia (Grade 4)	0	2		
Hypermagnesaemia (Grade 3)	7	6		
Hypocalcaemia (Grade 3)	3	4		
Hypoglycaemia (Grade 3)	0	2		
Hypoglycaemia (Grade 4)	1	0		
Hypokalaemia (Grade 3)	13	5		
Hypokalaemia (Grade 4)	2	0		
Hypomagnesaemia (Grade 3)	2	0		
Hyponatraemia (Grade 3)	6	5		
Hyponatraemia (Grade 4)	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Laboratory Test Abnormalities: Urinalysis

End point title	Number of Subjects With Laboratory Test Abnormalities: Urinalysis
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End point description:

Urinalysis parameter included urine protein, urine blood/haemoglobin, urine glucose and urine sediment. Test abnormalities was defined as deviation from normal range (higher or lower). Normal range of 24-hour urine protein test: less than 150 mg of protein per day, urine glucose: 0 to 0.8 mmol/L (millimole per liter), urine protein: 0 to 20 mg/dL (milligrams per deciliter). Urine blood/haemoglobin abnormality was defined as presence and absence of blood/haemoglobin in urine of subjects. Urine sediment abnormality was defined as the presence of any bacteria, casts, crystals, and epithelial cells. Only categories with at least 1 subject with abnormality are reported in this endpoint. Safety analysis set included all subjects who received at least 1 dose of study medication, with treatment assignments designated according to actual study treatment received.

End point type	Secondary
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End point timeframe:

From baseline up to 28-35 days after last dose of study drug (up to 48 months)

End point values	Dacomitinib	Gefitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	227	224		
Units: Subjects				
High Urine Protein	1	1		
Low Urine Glucose	1	0		
High Urine Blood/Haemoglobin	4	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinically Significant Abnormalities in Vital Signs

End point title	Number of Subjects With Clinically Significant Abnormalities in Vital Signs
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End point description:

Criteria for vital signs abnormalities: systolic pulse rate less than (<) 50 beats per minute (bpm) or greater than (>) 130 bpm and maximum increase or decrease from baseline in pulse rate of 30 bpm. Systolic blood pressure of maximum increase from baseline (MIB) ≥ 40 millimeters of mercury (mmHg), maximum decrease from baseline (MDB) in systolic blood pressure ≤ 60 mmHg. Diastolic blood pressure of MIB ≥ 20 mmHg and MDB in diastolic blood pressure ≥ 40 and ≤ 20 mmHg. Only categories with at least 1 subject with abnormality are reported in this endpoint. Safety analysis set

included all subjects who received at least 1 dose of study medication, with treatment assignments designated according to actual study treatment received.

End point type	Secondary
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End point timeframe:

From baseline up to 28-35 days after last dose of study drug (up to 48 months)

End point values	Dacomitinib	Gefitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	227	224		
Units: Subjects				
MIB in systolic BP ≥ 40 mmHg	13	20		
MDB in systolic BP ≤ -60 mmHg	0	1		
MIB in diastolic BP ≥ 20 mmHg	38	44		
MDB in diastolic BP > -40 and ≤ -20 mmHg	46	52		
MDB in diastolic BP ≤ -40 mmHg	0	1		
Maximum post baseline pulse rate > 130 bpm	2	2		
Minimum post baseline pulse rate < 50 bpm	2	0		
MIB in pulse rate ≥ 30 bpm	13	12		
MDB in pulse rate ≤ -30 bpm	17	16		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinically Significant Abnormality in Electrocardiogram (ECG)

End point title	Number of Subjects With Clinically Significant Abnormality in Electrocardiogram (ECG)
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End point description:

ECG parameters included corrected QT interval using Bazett's formula (QTcB) and corrected QT interval using Fridericia's formula (QTcF). ECG criteria for abnormality: absolute value 450 - < 480 msec, 480 - < 500 msec ≥ 500 . The number of subjects with potentially clinically significant ECG findings at any visit were reported. Safety analysis set included all subjects who received at least 1 dose of study medication, with treatment assignments designated according to actual study treatment received. Here, "N" (number of subjects analyzed) signifies subjects who were evaluable for this specified endpoint.

End point type	Secondary
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End point timeframe:

From baseline up to 28-35 days after last dose of study drug (up to 48 months)

End point values	Dacomitinib	Gefitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	217	7		
Units: Subjects				
QTcF Criteria: 450-<480	5	0		
QTcB Criteria: 450-<480	22	0		
QTcB Criteria: 480-<500	3	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Maximum Relative Decrease From Baseline >20% in Left Ventricular Ejection Fraction (LVEF)

End point title	Number of Subjects With Maximum Relative Decrease From Baseline >20% in Left Ventricular Ejection Fraction (LVEF)
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End point description:

An ejection fraction (EF) was the volumetric fraction of blood ejected from a ventricle of the heart with each heartbeat; it was a measure of the pumping efficiency of the heart. The EF of the left heart, known as the left ventricular ejection fraction, was a measure of the efficiency of pumping into the body's systemic circulation. Safety analysis set included all subjects who received at least 1 dose of study medication, with treatment assignments designated according to actual study treatment received. Here "N" signifies number of subjects who were evaluable for this specified endpoint.

End point type	Secondary
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End point timeframe:

From randomization up to 7 days of Cycle 4 (up to 91 days)

End point values	Dacomitinib	Gefitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	191	199		
Units: Subjects	5	5		

Statistical analyses

No statistical analyses for this end point

Secondary: Health Related Quality of Life (HRQOL): Time to Deterioration (TTD) in Pain, Dyspnea, Fatigue or Cough

End point title	Health Related Quality of Life (HRQOL): Time to Deterioration (TTD) in Pain, Dyspnea, Fatigue or Cough
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End point description:

HRQOL was measured by standardized questionnaires (European Organization for Research and Treatment of Cancer (EORTC)) quality of life questionnaires (QLQ-C30) and its lung cancer module (QLQ-LC13). TTD in pain (chest, arm/shoulder), dyspnea, fatigue or cough was defined as time between randomization and first occurrence of increase in score of 10 points or greater from baseline in any of these 4 symptoms for at least two consecutive cycles. For those who had not shown deterioration, the data was censored at the last date when the subjects completed an assessment for pain, dyspnea,

fatigue or cough. Patient reported outcome (PRO) analysis set included all enrolled subjects, who started treatment and completed a baseline PRO assessments and at least one post-baseline PRO assessment after the first dose.

End point type	Secondary
End point timeframe:	
Randomization until the end of treatment (up to 48 months)	

End point values	Dacomitinib	Gefitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	226	222		
Units: months				
median (confidence interval 95%)	3.8 (2.3 to 4.8)	6.6 (3.8 to 9.3)		

Statistical analyses

Statistical analysis title	Dacomitinib vs Gefitinib
Comparison groups	Dacomitinib v Gefitinib
Number of subjects included in analysis	448
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5327
Method	2-sided Hochberg adjusted p-value
Parameter estimate	Cox proportional hazard
Point estimate	1.173
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.928
upper limit	1.483

Secondary: Overall Mean Scores of Euro Quality of Life-5 Dimension Visual Analog Scale (EQ-5D VAS)

End point title	Overall Mean Scores of Euro Quality of Life-5 Dimension Visual Analog Scale (EQ-5D VAS)
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End point description:

The Euro Quality of Life-5 dimension (EQ-5D) is a brief self-administered, validated reliable generic health status instrument. EQ-5D general health status can also be measured by a visual analog scale (EQ-5D VAS). EQ-5D VAS measures the subject's self-rated health status on a scale from 0 (worst imaginable health state) to 100 (best imaginable health state). PRO analysis set included all enrolled subjects, who started treatment and completed a baseline PRO assessments and at least one post-baseline PRO assessment after the first dose.

End point type	Secondary
End point timeframe:	
From Cycle 1 to 41 (up to 48 months)	

End point values	Dacomitinib	Gefitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	224	221		
Units: units on a scale				
least squares mean (confidence interval 95%)	73.3869 (71.608 to 75.166)	77.6923 (75.895 to 79.490)		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Plasma Concentration (Cmax) of Dacomitinib and Its Metabolite PF-05199265

End point title	Maximum Observed Plasma Concentration (Cmax) of Dacomitinib and Its Metabolite PF-05199265 ^[1]
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End point description:

PK analysis set included all subjects who were treated with dacomitinib with at least 1 measured plasma concentration and were dose-compliant (who received 45 mg dacomitinib daily without interruptions/dose reductions for at least 14 days prior to day of data collection). This endpoint was planned to be analyzed in Chinese subgroup only.

End point type	Secondary
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End point timeframe:

Pre-dose and 2, 4, 6, 8, and 24 hours post-dose on Cycle 2 Day 1 (Day 29)

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: Descriptive analysis was planned to be reported for Dacomitinib arm only.

End point values	Dacomitinib			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: nanogram per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
Dacomitinib	84.19 (± 21.90)			
PF-05199265	12.77 (± 7.58)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Reach Maximum Observed Plasma Concentration (Tmax) of Dacomitinib and Its Metabolite PF-05199265

End point title	Time to Reach Maximum Observed Plasma Concentration
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End point description:

PK analysis set included all subjects who were treated with dacomitinib with at least 1 measured plasma concentration and were dose-compliant (who received 45 mg dacomitinib daily without interruptions/dose reductions for at least 14 days prior to day of data collection). This endpoint was planned to be analyzed in Chinese subgroup only.

End point type	Secondary
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End point timeframe:

Pre-dose and 2, 4, 6, 8, and 24 hours post-dose on Cycle 2 Day 1 (Day 29)

Notes:

[2] - 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: Descriptive analysis was planned to be reported for Dacomitinib arm only.

End point values	Dacomitinib			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: hour				
median (full range (min-max))				
Dacomitinib	4.03 (2.0 to 24.0)			
PF-05199265	6.0 (0.0 to 25.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration-Time Curve From Time 0 to End of Dosing Interval (AUC_{tau}) of Dacomitinib and Its Metabolite PF-05199265

End point title	Area Under the Plasma Concentration-Time Curve From Time 0 to End of Dosing Interval (AUC _{tau}) of Dacomitinib and Its Metabolite PF-05199265 ^[3]
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End point description:

PK analysis set included all subjects who were treated with dacomitinib with at least 1 measured plasma concentration and were dose-compliant (who received 45 mg dacomitinib daily without interruptions/dose reductions for at least 14 days prior to day of data collection). This endpoint was planned to be analyzed in Chinese subgroup only.

End point type	Secondary
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End point timeframe:

Pre-dose and 2, 4, 6, 8, and 24 hours post-dose on Cycle 2 Day 1 (Day 29)

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Descriptive analysis was planned to be reported for Dacomitinib arm only.

End point values	Dacomitinib			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: nanogram*hour/milliliter (ng*hr/mL)				
arithmetic mean (standard deviation)				

Dacomitinib	1712.08 (± 413.61)			
PF-05199265	278.47 (± 163.53)			

Statistical analyses

No statistical analyses for this end point

Secondary: Averaged Plasma Concentration at Steady State (Cavg) of Dacomitinib and Its Metabolite PF-05199265

End point title	Averaged Plasma Concentration at Steady State (Cavg) of Dacomitinib and Its Metabolite PF-05199265 ^[4]
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End point description:

PK analysis set included all subjects who were treated with dacomitinib with at least 1 measured plasma concentration and were dose-compliant (who received 45 mg dacomitinib daily without interruptions/dose reductions for at least 14 days prior to day of data collection). This endpoint was planned to be analyzed in Chinese subgroup only.

End point type	Secondary
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End point timeframe:

Pre-dose and 2, 4, 6, 8, and 24 hours post-dose on Cycle 2 Day 1 (Day 29)

Notes:

[4] - 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: Descriptive analysis was planned to be reported for Dacomitinib arm only.

End point values	Dacomitinib			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: ng/mL				
arithmetic mean (standard deviation)				
Dacomitinib	71.33 (± 17.23)			
PF-05199265	11.60 (± 6.81)			

Statistical analyses

No statistical analyses for this end point

Secondary: Minimum Observed Plasma Concentration (Cmin) of Dacomitinib and Its Metabolite PF-05199265

End point title	Minimum Observed Plasma Concentration (Cmin) of Dacomitinib and Its Metabolite PF-05199265 ^[5]
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End point description:

PK analysis set included all subjects who were treated with dacomitinib with at least 1 measured plasma concentration and were dose-compliant (who received 45 mg dacomitinib daily without interruptions/dose reductions for at least 14 days prior to day of data collection). This endpoint was planned to be analyzed in Chinese subgroup only.

End point type	Secondary
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End point timeframe:

Pre-dose and 2, 4, 6, 8, and 24 hours post-dose on Cycle 2 Day 1 (Day 29)

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive analysis was planned to be reported for Dacomitinib arm only.

End point values	Dacomitinib			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: ng/mL				
arithmetic mean (standard deviation)				
Dacomitinib	60.64 (± 14.85)			
PF-05199265	10.49 (± 6.26)			

Statistical analyses

No statistical analyses for this end point

Secondary: Fluctuation Coefficient Between Trough and Peak Plasma Concentration (DF) of Dacomitinib and Its Metabolite PF-05199265

End point title	Fluctuation Coefficient Between Trough and Peak Plasma Concentration (DF) of Dacomitinib and Its Metabolite PF-05199265 ^[6]
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End point description:

Fluctuation coefficient between trough and peak plasma concentration was determined as C_{max}-C_{trough} divided by C_{avg}, where C_{max} was the maximum observed concentration within the dosing interval, C_{trough} was the observed concentration prior to dose administration and C_{avg} was averaged plasma concentration at steady state. PK analysis set included all subjects who were treated with dacomitinib with at least 1 measured plasma concentration and were dose-compliant (who received 45 mg dacomitinib daily without interruptions/dose reductions for at least 14 days prior to day of data collection). This endpoint was planned to be analyzed in Chinese subgroup only.

End point type	Secondary
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End point timeframe:

Pre-dose and 2, 4, 6, 8, and 24 hours post-dose on Cycle 2 Day 1 (Day 29)

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive analysis was planned to be reported for Dacomitinib arm only.

End point values	Dacomitinib			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: Fluctuation coefficient				
arithmetic mean (standard deviation)				
Dacomitinib	0.2883 (± 0.1460)			
PF-05199265	0.1105 (± 0.0827)			

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Clearance (CL) of Dacomitinib

End point title	Apparent Clearance (CL) of Dacomitinib ^[7]
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End point description:

Drug clearance was a quantitative measure of the rate at which a drug substance was removed from the blood (rate at which a drug is metabolized or eliminated by normal biological processes). PK analysis set included all subjects who were treated with dacomitinib with at least 1 measured plasma concentration and were dose-compliant (who received 45 mg dacomitinib daily without interruptions/dose reductions for at least 14 days prior to day of data collection). This endpoint was planned to be analyzed in Chinese subgroup only.

End point type	Secondary
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End point timeframe:

Pre-dose and 2, 4, 6, 8, and 24 hours post-dose on Cycle 2 Day 1 (Day 29)

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Descriptive analysis was planned to be reported for Dacomitinib arm only.

End point values	Dacomitinib			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: Liter/hour (L/h)				
arithmetic mean (standard deviation)	27.61 (± 5.97)			

Statistical analyses

No statistical analyses for this end point

Secondary: Pre-dose Plasma Concentrations (C_{trough}) of Dacomitinib and Its Metabolite PF-05199265

End point title	Pre-dose Plasma Concentrations (C _{trough}) of Dacomitinib and Its Metabolite PF-05199265 ^[8]
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End point description:

Trough plasma concentration was defined as the measured concentration at the end of a dosing interval at steady state (taken directly before next administration). PK analysis set included all subjects who were treated with dacomitinib with at least one measured plasma concentration and were dose-compliant. Dose-compliant subjects were those who received 45 mg dacomitinib daily without interruptions or dose reductions for at least 14 days prior to the day of data collection. Here, n signifies number of subjects evaluable at specified time points only.

End point type	Secondary
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End point timeframe:

Pre-dose on Day 1 of Cycle 2, 3, 4, 5 and 6

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive analysis was planned to be reported for Dacomitinib arm only.

End point values	Dacomitinib			
Subject group type	Reporting group			
Number of subjects analysed	188			
Units: ng/mL				
arithmetic mean (standard deviation)				
Cycle 2 Day 1: Dacomitinib (n =176)	70.24 (± 27.16)			
Cycle 3 Day 1: Dacomitinib (n =143)	68.34 (± 25.80)			
Cycle 4 Day 1: Dacomitinib (n =112)	68.16 (± 25.49)			
Cycle 5 Day 1: Dacomitinib (n =85)	64.50 (± 25.52)			
Cycle 6 Day 1: Dacomitinib (n =74)	61.68 (± 22.58)			
Cycle 2 Day 1: PF-05199265 (n =176)	13.20 (± 8.55)			
Cycle 3 Day 1: PF-05199265 (n =143)	14.42 (± 9.10)			
Cycle 4 Day 1: PF-05199265 (n =112)	13.70 (± 8.33)			
Cycle 5 Day 1: PF-05199265 (n =85)	12.48 (± 6.69)			
Cycle 6 Day 1: PF-05199265 (n =74)	13.05 (± 6.52)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From baseline until 35 days after the last dose of study drug (up to 40 months)

Adverse event reporting additional description:

The same event may appear as both an AE and a SAE. However, what is presented are distinct events. An event may be categorized as serious in one subject and as non-serious in another subject, or one subject may have experienced both a serious and non-serious event during the study.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.1
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Reporting groups

Reporting group title	Dacomitinib
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Reporting group description:

Subjects received 45 mg of dacomitinib tablets orally once daily in each treatment cycle of 28 days, up to a maximum duration of 48 months or until disease progression, intolerable toxicities, withdrawal, death, or investigator decision dictated by protocol compliance, whichever occurred first.

Reporting group title	Gefitinib
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Reporting group description:

Subjects received 250 mg of gefitinib tablets orally once daily, in each treatment cycle of 28 days, up to a maximum duration of 48 months or until disease progression, intolerable toxicities, withdrawal, death, or investigator decision dictated by protocol compliance, whichever occurred first.

Serious adverse events	Dacomitinib	Gefitinib	
Total subjects affected by serious adverse events			
subjects affected / exposed	62 / 227 (27.31%)	50 / 224 (22.32%)	
number of deaths (all causes)	76	91	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 227 (0.44%)	0 / 224 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic myeloid leukaemia			
subjects affected / exposed	1 / 227 (0.44%)	0 / 224 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to meninges			

subjects affected / exposed	1 / 227 (0.44%)	0 / 224 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant neoplasm progression			
subjects affected / exposed	0 / 227 (0.00%)	1 / 224 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Pancreatic carcinoma			
subjects affected / exposed	0 / 227 (0.00%)	1 / 224 (0.45%)	
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 / 227 (0.44%)	0 / 224 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	8 / 227 (3.52%)	11 / 224 (4.91%)	
occurrences causally related to treatment / all	0 / 8	0 / 11	
deaths causally related to treatment / all	0 / 9	0 / 11	
Multiple organ dysfunction syndrome			
subjects affected / exposed	1 / 227 (0.44%)	1 / 224 (0.45%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	1 / 227 (0.44%)	0 / 224 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 227 (0.44%)	0 / 224 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

General physical health deterioration			
subjects affected / exposed	0 / 227 (0.00%)	1 / 224 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Death			
subjects affected / exposed	1 / 227 (0.44%)	1 / 224 (0.45%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	1 / 1	1 / 1	
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	5 / 227 (2.20%)	2 / 224 (0.89%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Haemoptysis			
subjects affected / exposed	2 / 227 (0.88%)	0 / 224 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	2 / 227 (0.88%)	1 / 224 (0.45%)	
occurrences causally related to treatment / all	1 / 3	1 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumothorax			
subjects affected / exposed	2 / 227 (0.88%)	0 / 224 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	2 / 227 (0.88%)	0 / 224 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Dyspnoea			
subjects affected / exposed	1 / 227 (0.44%)	4 / 224 (1.79%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 2	

Interstitial lung disease			
subjects affected / exposed	1 / 227 (0.44%)	1 / 224 (0.45%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 227 (0.44%)	0 / 224 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchospasm			
subjects affected / exposed	0 / 227 (0.00%)	1 / 224 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Organising pneumonia			
subjects affected / exposed	0 / 227 (0.00%)	1 / 224 (0.45%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 227 (0.00%)	1 / 224 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			
subjects affected / exposed	0 / 227 (0.00%)	1 / 224 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 227 (0.00%)	1 / 224 (0.45%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 227 (0.00%)	1 / 224 (0.45%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hepatic enzyme increased subjects affected / exposed	0 / 227 (0.00%)	2 / 224 (0.89%)	
occurrences causally related to treatment / all	0 / 0	6 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Facial bones fracture subjects affected / exposed	1 / 227 (0.44%)	0 / 224 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture subjects affected / exposed	1 / 227 (0.44%)	1 / 224 (0.45%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose subjects affected / exposed	1 / 227 (0.44%)	0 / 224 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture subjects affected / exposed	1 / 227 (0.44%)	0 / 224 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extradural haematoma subjects affected / exposed	0 / 227 (0.00%)	1 / 224 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma subjects affected / exposed	0 / 227 (0.00%)	2 / 224 (0.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture subjects affected / exposed	0 / 227 (0.00%)	1 / 224 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiac disorders			
Cardiac tamponade			
subjects affected / exposed	1 / 227 (0.44%)	0 / 224 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerosis coronary artery			
subjects affected / exposed	0 / 227 (0.00%)	1 / 224 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	1 / 227 (0.44%)	2 / 224 (0.89%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 1	
Cerebral venous thrombosis			
subjects affected / exposed	1 / 227 (0.44%)	0 / 224 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord compression			
subjects affected / exposed	1 / 227 (0.44%)	0 / 224 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	0 / 227 (0.00%)	1 / 224 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cognitive disorder			
subjects affected / exposed	0 / 227 (0.00%)	1 / 224 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	0 / 227 (0.00%)	1 / 224 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Post herpetic neuralgia			
subjects affected / exposed	0 / 227 (0.00%)	1 / 224 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Leukocytosis			
subjects affected / exposed	1 / 227 (0.44%)	0 / 224 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Keratitis			
subjects affected / exposed	1 / 227 (0.44%)	0 / 224 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	5 / 227 (2.20%)	0 / 224 (0.00%)	
occurrences causally related to treatment / all	9 / 9	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Abdominal pain			
subjects affected / exposed	2 / 227 (0.88%)	0 / 224 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal distension			
subjects affected / exposed	1 / 227 (0.44%)	0 / 224 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer haemorrhage			
subjects affected / exposed	1 / 227 (0.44%)	0 / 224 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			

subjects affected / exposed	1 / 227 (0.44%)	0 / 224 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mouth haemorrhage			
subjects affected / exposed	1 / 227 (0.44%)	0 / 224 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatitis			
subjects affected / exposed	1 / 227 (0.44%)	0 / 224 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 227 (0.44%)	0 / 224 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspepsia			
subjects affected / exposed	0 / 227 (0.00%)	1 / 224 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	1 / 227 (0.44%)	0 / 224 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematochezia			
subjects affected / exposed	0 / 227 (0.00%)	1 / 224 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal obstruction			
subjects affected / exposed	0 / 227 (0.00%)	1 / 224 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Liver injury			

subjects affected / exposed	2 / 227 (0.88%)	1 / 224 (0.45%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug-induced liver injury			
subjects affected / exposed	1 / 227 (0.44%)	1 / 224 (0.45%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct stone			
subjects affected / exposed	0 / 227 (0.00%)	1 / 224 (0.45%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	0 / 227 (0.00%)	1 / 224 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	1 / 227 (0.44%)	0 / 224 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug eruption			
subjects affected / exposed	1 / 227 (0.44%)	0 / 224 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash maculo-papular			
subjects affected / exposed	1 / 227 (0.44%)	0 / 224 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decubitus ulcer			
subjects affected / exposed	0 / 227 (0.00%)	1 / 224 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			

Acute kidney injury			
subjects affected / exposed	1 / 227 (0.44%)	0 / 224 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			
subjects affected / exposed	0 / 227 (0.00%)	1 / 224 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	1 / 227 (0.44%)	0 / 224 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			
subjects affected / exposed	1 / 227 (0.44%)	0 / 224 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal pain			
subjects affected / exposed	1 / 227 (0.44%)	0 / 224 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	0 / 227 (0.00%)	1 / 224 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polymyalgia rheumatica			
subjects affected / exposed	0 / 227 (0.00%)	1 / 224 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	5 / 227 (2.20%)	2 / 224 (0.89%)	
occurrences causally related to treatment / all	1 / 8	2 / 3	
deaths causally related to treatment / all	0 / 2	1 / 1	

Respiratory tract infection			
subjects affected / exposed	2 / 227 (0.88%)	1 / 224 (0.45%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	2 / 227 (0.88%)	0 / 224 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 227 (0.44%)	0 / 224 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopulmonary aspergillosis			
subjects affected / exposed	1 / 227 (0.44%)	0 / 224 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Diverticulitis			
subjects affected / exposed	1 / 227 (0.44%)	0 / 224 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia urinary tract infection			
subjects affected / exposed	1 / 227 (0.44%)	0 / 224 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 227 (0.44%)	0 / 224 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	1 / 227 (0.44%)	0 / 224 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			

subjects affected / exposed	1 / 227 (0.44%)	0 / 224 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	0 / 227 (0.00%)	1 / 224 (0.45%)	
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	1 / 227 (0.44%)	1 / 224 (0.45%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 227 (0.88%)	0 / 224 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	1 / 227 (0.44%)	0 / 224 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malnutrition			
subjects affected / exposed	1 / 227 (0.44%)	1 / 224 (0.45%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hyponatraemia			
subjects affected / exposed	0 / 227 (0.00%)	2 / 224 (0.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Dacomitinib	Gefitinib	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	224 / 227 (98.68%)	217 / 224 (96.88%)	
Investigations			
Weight decreased			
subjects affected / exposed	58 / 227 (25.55%)	37 / 224 (16.52%)	
occurrences (all)	100	54	
Alanine aminotransferase increased			
subjects affected / exposed	44 / 227 (19.38%)	88 / 224 (39.29%)	
occurrences (all)	75	201	
Aspartate aminotransferase increased			
subjects affected / exposed	42 / 227 (18.50%)	81 / 224 (36.16%)	
occurrences (all)	62	169	
Blood bilirubin increased			
subjects affected / exposed	20 / 227 (8.81%)	19 / 224 (8.48%)	
occurrences (all)	40	37	
Blood alkaline phosphatase increased			
subjects affected / exposed	14 / 227 (6.17%)	7 / 224 (3.13%)	
occurrences (all)	18	16	
Gamma-glutamyltransferase increased			
subjects affected / exposed	14 / 227 (6.17%)	20 / 224 (8.93%)	
occurrences (all)	16	37	
White blood cell count decreased			
subjects affected / exposed	6 / 227 (2.64%)	14 / 224 (6.25%)	
occurrences (all)	8	20	
Weight increased			
subjects affected / exposed	5 / 227 (2.20%)	12 / 224 (5.36%)	
occurrences (all)	13	27	
Vascular disorders			
Hypertension			
subjects affected / exposed	13 / 227 (5.73%)	10 / 224 (4.46%)	
occurrences (all)	15	15	
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	16 / 227 (7.05%)	11 / 224 (4.91%)	
occurrences (all)	33	12	

Paraesthesia subjects affected / exposed occurrences (all)	16 / 227 (7.05%) 32	11 / 224 (4.91%) 14	
Headache subjects affected / exposed occurrences (all)	14 / 227 (6.17%) 16	19 / 224 (8.48%) 22	
Dizziness subjects affected / exposed occurrences (all)	11 / 227 (4.85%) 12	17 / 224 (7.59%) 18	
Blood and lymphatic system disorders			
Anaemia	Additional description: Same event may appear as both an adverse event and serious adverse event. However, what is presented are distinct events. An event may be categorized as serious in one subject and as non-serious in another, or a subject may have experienced both a se		
subjects affected / exposed occurrences (all)	22 / 227 (9.69%) 41	16 / 224 (7.14%) 41	
General disorders and administration site conditions			
Asthenia subjects affected / exposed occurrences (all)	29 / 227 (12.78%) 62	28 / 224 (12.50%) 55	
Chest pain subjects affected / exposed occurrences (all)	22 / 227 (9.69%) 35	32 / 224 (14.29%) 41	
Fatigue subjects affected / exposed occurrences (all)	21 / 227 (9.25%) 37	19 / 224 (8.48%) 29	
Mucosal inflammation subjects affected / exposed occurrences (all)	21 / 227 (9.25%) 37	8 / 224 (3.57%) 9	
Pyrexia subjects affected / exposed occurrences (all)	19 / 227 (8.37%) 24	17 / 224 (7.59%) 18	
Oedema peripheral subjects affected / exposed occurrences (all)	13 / 227 (5.73%) 15	7 / 224 (3.13%) 9	
Pain subjects affected / exposed occurrences (all)	11 / 227 (4.85%) 12	12 / 224 (5.36%) 15	

Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	198 / 227 (87.22%)	125 / 224 (55.80%)	
occurrences (all)	576	253	
Stomatitis			
subjects affected / exposed	99 / 227 (43.61%)	40 / 224 (17.86%)	
occurrences (all)	254	74	
Nausea			
subjects affected / exposed	43 / 227 (18.94%)	49 / 224 (21.88%)	
occurrences (all)	68	63	
Constipation			
subjects affected / exposed	30 / 227 (13.22%)	31 / 224 (13.84%)	
occurrences (all)	48	38	
Mouth ulceration			
subjects affected / exposed	28 / 227 (12.33%)	13 / 224 (5.80%)	
occurrences (all)	46	16	
Vomiting			
subjects affected / exposed	20 / 227 (8.81%)	29 / 224 (12.95%)	
occurrences (all)	24	37	
Aphthous ulcer			
subjects affected / exposed	13 / 227 (5.73%)	6 / 224 (2.68%)	
occurrences (all)	17	7	
Oral pain			
subjects affected / exposed	12 / 227 (5.29%)	1 / 224 (0.45%)	
occurrences (all)	23	1	
Abdominal pain			
subjects affected / exposed	10 / 227 (4.41%)	12 / 224 (5.36%)	
occurrences (all)	12	17	
Dysphagia			
subjects affected / exposed	10 / 227 (4.41%)	12 / 224 (5.36%)	
occurrences (all)	20	18	
Abdominal pain upper			
subjects affected / exposed	9 / 227 (3.96%)	14 / 224 (6.25%)	
occurrences (all)	11	16	
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	48 / 227 (21.15%)	42 / 224 (18.75%)	
occurrences (all)	65	67	
Dyspnoea			
subjects affected / exposed	29 / 227 (12.78%)	28 / 224 (12.50%)	
occurrences (all)	40	56	
Epistaxis			
subjects affected / exposed	21 / 227 (9.25%)	5 / 224 (2.23%)	
occurrences (all)	24	5	
Nasal inflammation			
subjects affected / exposed	15 / 227 (6.61%)	3 / 224 (1.34%)	
occurrences (all)	22	5	
Haemoptysis			
subjects affected / exposed	10 / 227 (4.41%)	13 / 224 (5.80%)	
occurrences (all)	10	13	
Productive cough			
subjects affected / exposed	9 / 227 (3.96%)	12 / 224 (5.36%)	
occurrences (all)	9	13	
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	111 / 227 (48.90%)	64 / 224 (28.57%)	
occurrences (all)	360	112	
Dry skin			
subjects affected / exposed	63 / 227 (27.75%)	38 / 224 (16.96%)	
occurrences (all)	105	49	
Alopecia			
subjects affected / exposed	53 / 227 (23.35%)	28 / 224 (12.50%)	
occurrences (all)	79	43	
Pruritus			
subjects affected / exposed	45 / 227 (19.82%)	32 / 224 (14.29%)	
occurrences (all)	67	48	
Rash			
subjects affected / exposed	40 / 227 (17.62%)	24 / 224 (10.71%)	
occurrences (all)	97	31	
Palmar-plantar erythrodysaesthesia syndrome			

subjects affected / exposed	33 / 227 (14.54%)	7 / 224 (3.13%)	
occurrences (all)	58	8	
Rash maculo-papular			
subjects affected / exposed	28 / 227 (12.33%)	27 / 224 (12.05%)	
occurrences (all)	99	46	
Dermatitis			
subjects affected / exposed	25 / 227 (11.01%)	9 / 224 (4.02%)	
occurrences (all)	67	13	
Skin fissures			
subjects affected / exposed	21 / 227 (9.25%)	6 / 224 (2.68%)	
occurrences (all)	35	7	
Acne			
subjects affected / exposed	20 / 227 (8.81%)	13 / 224 (5.80%)	
occurrences (all)	66	18	
Erythema			
subjects affected / exposed	12 / 227 (5.29%)	3 / 224 (1.34%)	
occurrences (all)	23	4	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	24 / 227 (10.57%)	33 / 224 (14.73%)	
occurrences (all)	36	46	
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	31 / 227 (13.66%)	26 / 224 (11.61%)	
occurrences (all)	50	42	
Musculoskeletal pain			
subjects affected / exposed	26 / 227 (11.45%)	28 / 224 (12.50%)	
occurrences (all)	59	38	
Back pain			
subjects affected / exposed	18 / 227 (7.93%)	34 / 224 (15.18%)	
occurrences (all)	23	44	
Arthralgia			
subjects affected / exposed	16 / 227 (7.05%)	15 / 224 (6.70%)	
occurrences (all)	20	22	
Infections and infestations			

Paronychia			
subjects affected / exposed	140 / 227 (61.67%)	45 / 224 (20.09%)	
occurrences (all)	395	88	
Conjunctivitis			
subjects affected / exposed	43 / 227 (18.94%)	9 / 224 (4.02%)	
occurrences (all)	55	10	
Upper respiratory tract infection			
subjects affected / exposed	27 / 227 (11.89%)	28 / 224 (12.50%)	
occurrences (all)	44	45	
Nasopharyngitis			
subjects affected / exposed	21 / 227 (9.25%)	19 / 224 (8.48%)	
occurrences (all)	37	27	
Rash pustular			
subjects affected / exposed	14 / 227 (6.17%)	3 / 224 (1.34%)	
occurrences (all)	63	6	
Urinary tract infection			
subjects affected / exposed	14 / 227 (6.17%)	8 / 224 (3.57%)	
occurrences (all)	21	10	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	69 / 227 (30.40%)	56 / 224 (25.00%)	
occurrences (all)	126	83	
Hypokalaemia			
subjects affected / exposed	22 / 227 (9.69%)	13 / 224 (5.80%)	
occurrences (all)	51	17	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 June 2013	1) To include subjects who had evidence of both EGFR -activating mutations (exon 19 deletion and L858R mutation in exon 21) within a tumor specimen (allowing for the presence of the T790M mutation in exon 20). 2) To update emerging information on dacomitinib PK characteristics and metabolism in subjects and implemented related changes in the dosing instructions and concomitant medications.3) Provided instructions for preparation of tumor tissue specimens for EGFR mutational analysis and pathology/histology study to ensure that sufficient tumor specimens would be available for protocol-required testing; clarified that confirmation of adenocarcinoma histology and presence of an EGFR-activating mutation in tumor tissue were required for eligibility screening. 4) Stated that CYP2D6 genotyping would be performed in patients treated in the dacomitinib arm who were undergoing multiple PK sampling on C2D1. 5) Stated that dacomitinib could be dosed with or without food; added that concomitant use of proton-pump inhibitors and H ₂ antagonists with dacomitinib should be avoided if possible. 6) Clarified that potential dose reductions to manage treatment-related toxicity applied only to dacomitinib (not gefitinib); added guidelines for interruption and resumption of gefitinib dosing for management of toxicity.
01 October 2013	Expanded eligibility to subjects with recurrent NSCLC (in addition to those with newly diagnosed disease), if there was a disease-free interval of at least 12 months' duration between completion of prior systemic therapy (neoadjuvant/adjuvant chemotherapy and/or combined modality chemotherapy/radiation therapy) and recurrence of NSCLC.
30 June 2015	1) Extended the maximum duration of study participation (including long-term follow-up for progression and survival) to 48 months from date of first dose of study treatment per the current protocol (changed from 32 months), to improve the potential to obtain at least 201 overall survival (OS) events.
04 November 2015	1) Clarified that patients who had PD per RECIST v1.1 confirmed by IRC review, and for whom the investigator believed it was in their best interest to continue on their respective study therapy, would be allowed to continue on their respective study therapy with or without concomitant local therapy. 2) Clarified follow-up procedures for subjects who continued on their respective study therapy after disease progression assessed by IRC review; specified that long-term follow-up for all subjects was to include survival status and subsequent cancer therapies. 3) Clarified inclusion criterion: In the case of subjects with recurrent NSCLC who had received prior neoadjuvant/adjuvant chemotherapy, the tumor specimen was to be obtained at the time of recurrence after completion of neoadjuvant/adjuvant therapy. 3)Implemented retrospective CYP2D6 genotyping for all subjects treated in the dacomitinib arm that provided specific consent to participate.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Data for overall survival is not reported at Primary completion date and will be reported after the study completion date.

Notes: