Clinical trial results:
This is a multinational, multicenter, randomized, open-label, Phase 3 study. 452 patients were randomized in a 1:1 ratio to receive dacomitinib (PF-00299804) and gefitinib.

Summary

EudraCT number	2012-004977-23
Trial protocol	ES IT PL
Global end of trial date	27 January 2022

Results information

Result version number	v2 (current)
This version publication date	28 December 2022
First version publication date	25 October 2018
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	A7471050

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, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., +1 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., +1 8007181021, 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	Interim
Date of interim/final analysis	29 October 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 January 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This is a multinational, multicenter, randomized, open-label, Phase 3 study comparing the efficacy and safety of treatment with dacomitinib (PF-00299804) to treatment with gefitinib in patients with locally advanced or metastatic non-small cell lung cancer, with epidermal growth factor receptor EGFR-activating mutation (s).

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 Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (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 subjects.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 May 2013
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy, Safety
Long term follow-up duration	80 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	China: 231
Country: Number of subjects enrolled	Spain: 53
Country: Number of subjects enrolled	Hong Kong: 4
Country: Number of subjects enrolled	Italy: 42
Country: Number of subjects enrolled	Japan: 83
Country: Number of subjects enrolled	Korea, Republic of: 27
Country: Number of subjects enrolled	Poland: 12
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:

This is a multinational, multicenter, randomized, open-label, Phase 3 study. 452 subjects were randomized to receive dacomitinib and gefitinib. After data cutoff (DCO) of 13 May 2019 , 11 subjects remained to continue dacomitinib treatment. All 11 subjects were discontinued from the study by last subject last visit (LSLV) date on 27 Jan 2022.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Dacomitinib

Arm description:

Subjects received 45 mg of dacomitinib tablets orally once daily in each treatment cycle of 28 days, up to a maximum of 48 months 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:

Dacomitinib was adminstered at 45 mg orally once daily in each treatment cycle of 28 days, up to a maximum of 48 months

Arm title	Gefitinib

Arm description:

Subjects received 250 mg of gefitinib tablets orally once daily in each treatment cycle of 28 days, for maximum of 48 months 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	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Gefitinib was adminstered at 250 mg orally once daily in each treatment cycle of 28 days, up to a maximum of 48 months

Number of subjects in period 1	Dacomitinib	Gefitinib
Started	227	225
Treated	227	224
Completed	0	0
Not completed	227	225
Adverse event, serious fatal	133	152
Consent withdrawn by subject	20	14
Disease progression	5	-
Did not meet eligibility criteria	-	3
Study terminated by sponsor	5	-
Lost to follow-up	6	7
Completed the follow-up period and other reasons	58	49

Baseline characteristics

Reporting groups	
Reporting group title	Dacomitinib
Reporting group description:	
Subjects received 45 mg of dacomitinib tablets orally once daily in each treatment cycle of 28 days, up to a maximum of 48 months 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, for maximum of 48 months 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			
<65 years	133	140	273
>=65 years - <75 years	66	64	130
>=75 years	28	21	49
Age Continuous Units: years			
arithmetic mean	61.2	60.9	
standard deviation	± 11.26	± 10.17	-
Sex: Female, Male Units: subjects			
Female	146	125	271
Male	81	100	181
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	227	225	452
Unknown or Not Reported	0	0	0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	170	176	346
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	0	1
White	56	49	105
More than one race	0	0	0
Unknown or Not Reported	0	0	0

Subject analysis sets	
Subject analysis set title	Dacomitinib
Subject analysis set type	Intention-to-treat

Subject analysis set description:

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

Subject analysis set title	Gefitinib
Subject analysis set type	Intention-to-treat

Subject analysis set description:

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

Subject analysis set title	Dacomitinib (ongoing at DCO)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

DCO was the protocol-defined cutoff at 48 months from first dosing of the last enrolled subject (13 May 2019). At the DCO, 11 subjects were ongoing in the dacomitinib arm and continued study treatment until disease progression, intolerable toxicities, withdrawal, death, or study terminated by sponsor, whichever occurred first. The 11 subjects were analyzed for adverse events after LSLV on 27 Jan 2022.

Reporting group values	Dacomitinib	Gefitinib	Dacomitinib (ongoing at DCO)
Number of subjects	227	225	11
Age categorical Units: subjects			
<65 years	133	140	
>=65 years - <75 years	66	64	
>=75 years	28	21	
Age Continuous Units: years			
arithmetic mean	61.2	60.9	
standard deviation	± 11.26	± 10.17	±
Sex: Female, Male Units: subjects			
Female	146	125	
Male	81	100	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	227	225	
Unknown or Not Reported	0	0	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	170	176	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	1	0	
White	56	49	
More than one race	0	0	
Unknown or Not Reported	0	0	

End points

End points reporting groups

Reporting group title	Dacomitinib

Reporting group description:

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

Subject analysis set title	Dacomitinib
Subject analysis set type	Intention-to-treat

Subject analysis set description:

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

Subject analysis set title	Gefitinib
Subject analysis set type	Intention-to-treat

Subject analysis set description:

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

Subject analysis set title	Dacomitinib (ongoing at DCO)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

DCO was the protocol-defined cutoff at 48 months from first dosing of the last enrolled subject (13 May 2019). At the DCO, 11 subjects were ongoing in the dacomitinib arm and continued study treatment until disease progression, intolerable toxicities, withdrawal, death, or study terminated by sponsor, whichever occurred first. The 11 subjects were analyzed for adverse events after LSLV on 27 Jan 2022.

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:

PFS: time from randomization to date of progression of disease (PD) as determined by IRC review or death due to any cause, whichever occurred first. PD: >=20% increase in sum of diameters of target lesions (TLs), referring smallest sum on study, sum must be an absolute increase of >=5 mm, appearance of >=1 new lesions; unequivocal progression of existing non TLs. Overall tumor burden increased sufficiently to merit discontinuation of therapy. In presence of stable disease or partial response in target disease; for new lesions: appearance of any new unequivocal malignant lesion indicated PD. Intent to Treat Population (ITT) population included all randomized subjects, with study treatment assignment designated according to initial randomization, regardless of whether subjects received study treatment or a different treatment from that to which they were randomized.

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%)				
Kaplan-meier estimates of time to event quartiles	14.7 (11.1 to 16.6)	9.2 (9.1 to 11.0)		

Statistical analyses

Statistical analysis title	Dacomtinib versus Gefitinib
Comparison groups	Gefitinib v Dacomitinib
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: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

OS was defined as the time from randomization to the date of death for any cause. In the absence of confirmation of death, survival time was censored at the last date the subject was known to be alive. OS (month)=[death date or last known alive date - randomization date + 1]/30.4375. ITT population included all randomized subjects, with study treatment assignment designated according to initial randomization, regardless of whether subjects received study treatment or a different treatment from that to which they were randomized.

End point type	Secondary

End point timeframe:

From randomization until death or last date known to be alive (up to 48 months after the first dose date of the last enrolled subjects)

End point values	Dacomitinib	Gefitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	227	225		
Units: months				
median (confidence interval 95%)	34.1 (29.5 to 39.8)	27.0 (24.4 to 31.6)		

Statistical analyses

Statistical analysis title	Dacomitinib versus Gefitinib
Comparison groups	Dacomitinib v Gefitinib
Number of subjects included in analysis	452
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0077
Method	1-sided stratified log-rank test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.748
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.591
upper limit	0.947

Secondary: OS at 30 months (OS30m)

End point title	OS at 30 months (OS30m)

End point description:

OS30m was defined as the probability of a subject being alive at 30 months from date of randomization. ITT population included all randomized subjects, with study treatment assignment designated according to initial randomization, regardless of whether subjects received study treatment or a different treatment from that to which they were randomized.

End point type	Secondary

End point timeframe:

up to 30 months from randomization

End point values	Dacomitinib	Gefitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	227	225		
Units: probability of survival				
number (confidence interval 95%)	56.4 (49.6 to 62.7)	45.7 (39.0 to 52.2)		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

PFS: time from randomization to date of PD as determined by IRC review or death due to any cause, whichever occurred first. PD: >=20% increase in sum of diameters of TLs, referring smallest sum on study, sum must be an absolute increase of >=5 mm, appearance of >=1 new lesions; unequivocal progression of existing non TLs. Overall tumor burden increased sufficiently to merit discontinuation of therapy. In presence of stable disease or partial response in target disease; for new lesions: appearance of any new unequivocal malignant lesion indicated PD. ITT population included all randomized subjects, with study treatment assignment designated according to initial randomization, regardless of whether subjects received study treatment or a different treatment from that to which they were randomized.

End point type	Secondary

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 versus Gefitinib
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	0.622
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

End point description:

BOR for CR/PR:>=1 objective status (OBS) of CR/PR before PD; SD:>=1 OBS of stable >=8 weeks (wks). PD:OBS of PD within 12 wks treatment; indeterminate:PD not within 12 wks post treatment & no other response category applies. RECIST v1.1, CR:disappearance of all target lesions (TLs), non TLs;any pathological lymph nodes (LN) must reduce in short axis to <10 mm; normalization of tumour marker level, for non TL all LN <10 mm short axis; PR:>=30% decrease in sum of diameters of TLs. SD:neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD. PD:>=20% increase in sum of diameters of TLs, sum increase >=5 mm, appearance of >=1 new lesions;unequivocal progression of existing non TLs. ITT population included all randomized subjects, with study treatment assignment designated according to initial randomization, regardless of whether subjects received study treatment or a different treatment from that to which they were randomized.

End point type	Secondary

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		
Stable disease	30	27		
Progressive disease	12	15		
Indeterminate	15	22		

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

End point description:

BOR for CR/PR:>=1 objective status (OBS) of CR/PR before PD; SD:>=1 OBS of stable >=8 weeks (wks). PD:OBS of PD within 12 wks treatment; indeterminate:PD not within 12 wks post treatment & no other response category applies. RECIST v1.1, CR:disappearance of all target lesions (TLs), non TLs;any pathological lymph nodes (LN) must reduce in short axis to <10 mm; normalization of tumour marker level, for non TL all LN <10 mm short axis; PR:>=30% decrease in sum of diameters of TLs. SD:neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD. PD:>=20% increase in sum of diameters of TLs, sum increase >=5 mm, appearance of >=1 new lesions;unequivocal progression of existing non TLs. ITT population included all randomized subjects, with study treatment assignment designated according to initial randomization, regardless of whether subjects received study treatment or a different treatment from that to which they were randomized.

End point type	Secondary

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		
Stable disease	38	49		
Progressive disease	9	11		
Indeterminate	9	7		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DoR)

End point title	Duration of Response (DoR)

End point description:

DoR was defined as time from first documentation of objective response(CR or PR)to date of PD/death from any cause. CR: disappearance of all target lesions (TLs), non TLs; any pathological lymph nodes (LN) must reduce in short axis to <10 mm; normalization of tumour marker level, for non TL all LN must be <10 mm short axis; PR:>=30% decrease in sum of diameters of TLs, referring baseline sum diameters. PD:>=20% increase in sum of diameters of TLs, sum must be an absolute increase of >=5 mm, appearance of >=1 new lesions; unequivocal progression of existing non TLs. DoR was recorded based on IRC review and investigator's assessment and summarized for subgroup of subjects with objective disease response. ITT population included all randomized subjects, with study treatment assignment designated according to initial randomization, regardless of whether subjects received study treatment or a different treatment from that to which they were randomized.

End point type	Secondary

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	14.8 (12.0 to 17.4)	8.3 (7.4 to 9.2)		
DoR: Investigator assessment	15.9 (13.8 to 17.6)	9.2 (8.2 to 11.0)		

Statistical analyses

Statistical analysis title	Dacomitinib versus Gefitinib

Statistical analysis description:

Comparison of dacomitinib vs gefitinib based on IRC review

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 versus Gefitinib
Statistical analysis description:	
Comparison of dacomitinib vs gefitinib based on Investigator assessment	
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	0.545
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.418
upper limit	0.711

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

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

End point description:

Percentage of subjects with a BOR of either CR or PR based on IRC review recorded from the start of treatment until disease progression based on RECIST v1.1. CR: disappearance of all target lesions (TLs), non TLs; any pathological lymph nodes (LN) must reduce in short axis to <10 mm; normalization of tumour marker level, for non TL all LN must be non-pathological in size (<10 mm short axis); PR:>=30% decrease in sum of diameters of TLs, referring baseline sum diameters. PD:>=20% increase in sum of diameters of TLs, referring smallest sum on study, sum must be an absolute increase of >=5 mm, appearance of >=1 new lesions; unequivocal progression of existing non TLs. ITT population included all randomized subjects, with study treatment assignment designated according to initial randomization, regardless of whether subjects received study treatment or a different treatment from that to which they were randomized.

End point type	Secondary

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

Statistical analysis title	Dacomitinib versus Gefitinib
Comparison groups	Dacomitinib v Gefitinib
Number of subjects included in analysis	452
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1942
Method	Cochran-Mantel-Haenszel

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

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

End point description:

Percentage of subjects with a BOR of either CR or PR based on investigator assessment recorded from the start of treatment until disease progression based on RECIST v1.1. CR: disappearance of all target lesions (TLs), non TLs; any pathological lymph nodes (LN) must reduce in short axis to <10 mm; normalization of tumour marker level, for non TL all LN must be non-pathological in size (<10 mm short axis); PR:>=30% decrease in sum of diameters of TLs, referring baseline sum diameters. PD:>=20% increase in sum of diameters of TLs, referring smallest sum on study, sum must be an absolute increase of >=5 mm, appearance of >=1 new lesions; unequivocal progression of existing non TLs. ITT population included all randomized subjects, with study treatment assignment designated according to initial randomization, regardless of whether subjects received study treatment or a different treatment from that to which they were randomized.

End point type	Secondary

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

Statistical analysis title	Dacomitinib versus Gefitinib
Comparison groups	Dacomitinib v Gefitinib
Number of subjects included in analysis	452
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0924
Method	Cochran-Mantel-Haenszel

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)

End point description:

An AE was any untoward medical occurrence in a subject who received study drug without regard to possibility of causal relationship. AEs included both serious and non- serious adverse events. An 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. 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

End point timeframe:

From baseline until 28-35 days after the last dose for the subjects who have completed the study. The 11 subjects were followed until the event has resolved, returned to baseline, has been deemed irreversible, or death, whichever occured first

End point values	Dacomitinib	Gefitinib	Dacomitinib (ongoing at DCO)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	227	224	11	
Units: subjects				
TEAEs	226	220	11	
SAEs	69	53	4	

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

End point description:

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. Grade 1=mild; Grade 2=moderate; Grade 3=severe; Grade 4=life-threatening; Grade 5=death related to AE. 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

End point timeframe:

From baseline up to 28-35 days after last dose of study drug (up to 48 months after the first dose date of the last enrolled subjects)

End point values	Dacomitinib	Gefitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	227	224		
Units: subjects				
Anaemia (Grade 3)	5	6		
Haemoglobin increased(Grade 3)	0	1		
Lymphopenia (Grade 3)	13	6		
Neutrophil count (absolute) (Grade 3)	0	2		
WBC count (Grade 3)	1	1		
Alanine aminotransferase increased (Grade 3)	5	26		
Alanine aminotransferase increased (Grade 4)	0	3		
Aspartate aminotransferase increased (Grade 3)	2	15		
Aspartate aminotransferase increased (Grade 4)	0	3		
Alkaline phosphatase increased (Grade 3)	2	5		
Bilirubin increased (total) (Grade 3)	1	1		
Creatinine increased (Grade 3)	1	1		
Hypercalcemia (Grade 3)	1	0		
Hyperglycemia (Grade 3)	2	5		
Hyperkalemia (Grade 3)	0	1		
Hyperkalemia (Grade 4)	0	2		
Hypermagnesemia (Grade 3)	9	7		
Hypocalcemia (Grade 3)	3	4		
Hypoglycemia (Grade 3)	0	2		
Hypoglycemia (Grade 4)	1	0		
Hypokalemia (Grade 3)	13	5		
Hypokalemia (Grade 4)	2	0		

Hypomagnesemia (Grade 3)	2	0		
Hyponatremia (Grade 3)	5	4		
Hyponatremia (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

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 outcome measure. 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

End point timeframe:

From baseline up to 28-35 days after last dose of study drug (up to 48 months after the first dose date of the last enrolled subjects)

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

End point description:

Criteria for vital signs abnormalities: postbaseline pulse rate less than (<) 50 beats per minute (bpm) or greater than (>)130 bpm and maximum increase from baseline in pulse rate >=30 bpm and maximum decrease from baseline in pulse rate <=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. And MDB in diastolic BP<=40 mmHg. Only categories with at least 1 subject with abnormality are reported in this outcome measure. 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

End point timeframe:

From baseline up to 28-35 days after last dose of study drug (up to 48 months after the first dose date of the last enrolled subjects)

End point values	Dacomitinib	Gefitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	227[1]	224[2]		
Units: subjects				
MIB in systolic BP >=40 mmHg	16	22		
MDB in systolic BP <=-60 mmHg	0	1		
MIB in diastolic BP >=20 mmHg	42	44		
MDB in diastolic BP >-40 and <=-20mmHg	51	53		
MDB in diastolic BP <=-40 mmHg	0	1		
Maximum post baseline pulse rate >130 bpm	2	2		
Minimum post baseline pulse rate <50 bpm	3	0		
MIB in pulse rate >=30 bpm	16	12		
MDB in pulse rate <=-30 bpm	17	15		
MIB in body weight >=10%	28	42		
MDB in body weight <=-10%	46	32		

Notes:

[1] - Nnumber of subjects with values for BP, pulse rate and body weight were 224,226 and 225.

[2] - Nnumber of subjects with values for BP, pulse rate and body weight were all 223.

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)

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 msec. 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. 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. Number of subjects analyzed signifies number of subjects who were evaluable for this specified outcome measure.

End point type	Secondary

End point timeframe:

From baseline up to 28-35 days after last dose of study drug (up to 48 months after the first dose date of the last enrolled subjects)

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)

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. Number of subjects analyzed signifies number of subjects who were evaluable for this specified outcome measure.

End point type	Secondary

End point timeframe:

From baseline 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

End point description:

HRQOL was measured by standardized questionnaires (European Organization for Research and Treatment of Cancer (EORTC)) quality of life questionnaires (OLQ-C30) and its lung cancer module (QLQ-LC13). TTD in pain (chest, arm/shoulder), dyspnea, fatigue or cough was defined as time between baseline 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. Subjects reported outcomes (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:

Baseline 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 versus Gefitinib
Comparison groups	Dacomitinib v Gefitinib
Number of subjects included in analysis	448
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1641
Method	Unstratified Log-rank Test
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)

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. Number of subjects analyzed signifies number of subjects

who were evaluable for this specified outcome measure.

End point type	Secondary

End point timeframe:

From Cycle 1 Day 1 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				
arithmetic 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

End point description:

Cmax was defined as maximum observed plasma concentration and can be observed directly from data. Pharmacokinetic (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 outcome measure was planned to be analyzed in Chinese subgroup only.

End point type	Secondary

End point timeframe:

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

End point values	Dacomitinib	Gefitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	0[3]		
Units: nanogram per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
Dacomitinib	84.19 (± 21.90)	()		
PF-05199265	12.77 (± 7.58)	()		

Notes:

[3] - Cmax was only estimated for dacomitinib and its major circulating metabolite PF-05199265.

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 (Tmax) of Dacomitinib and its Metabolite PF-05199265

End point description:

Tmax was defined as time to first occurrence of Cmax and can be observed directly from data as time of first occurrence. 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 outcome measure was planned to be analyzed in Chinese subgroup only.

End point type	Secondary

End point timeframe:

Pre-dose and 2, 4, 6, 8, and 24 hours post-dose (sample collection time points had window of +/- 10% of nominal time) on Cycle 2 Day 1 (Day 29)

End point values	Dacomitinib	Gefitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	0[4]		
Units: hour				
median (full range (min-max))				
Dacomitinib	4.03 (2.0 to 24.0)	(to)		
PF-05199265	6.0 (0.0 to 25.0)	(to)		

Notes:

[4] - Tmax was only estimated for dacomitinib and its major circulating metabolite PF-05199265.

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration-Time Curve From Time Zero (0) to end of Dosing Interval (AUCtau) of Dacomitinib and its Metabolite PF-05199265

End point title	Area Under the Plasma Concentration-Time Curve From Time Zero (0) to end of Dosing Interval (AUCtau) of Dacomitinib and its Metabolite PF-05199265

End point description:

AUCtau was defined as area under the plasma concentration-time curve over dosing interval tau and was determined by Linear/Log trapezoidal method. 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 outcome measure was planned to be analyzed in Chinese subgroup only.

End point type	Secondary

End point timeframe:

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

End point values	Dacomitinib	Gefitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	0[5]		
Units: nanogram*hour/milliliter (ng*hr/mL)				
arithmetic mean (standard deviation)				
Dacomitinib	1712.08 (± 413.61)	()		
PF-05199265	278.47 (± 163.53)	()		

Notes:

[5] - AUCtau was only estimated for dacomitinib and its major circulating metabolite PF-05199265.

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

End point description:

Cavg was defined as averaged plasma concentration at steady state, and was calculated as AUCtau/tau. 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 outcome measure was planned to be analyzed in Chinese subgroup only.

End point type	Secondary

End point timeframe:

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

End point values	Dacomitinib	Gefitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	0[6]		
Units: ng/mL				
arithmetic mean (standard deviation)				
Dacomitinib	71.33 (± 17.23)	()		
PF-05199265	11.60 (± 6.81)	()		

Notes:

[6] - Cavg was only estimated for dacomitinib and its major circulating metabolite PF-05199265.

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

End point description:

Cmin was defined as minimum observed plasma concentration and can be observed directly from data. 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 outcome measure was planned to be analyzed in Chinese subgroup only.

End point type	Secondary

End point timeframe:

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

End point values	Dacomitinib	Gefitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	0[7]		
Units: ng/mL				
arithmetic mean (standard deviation)				
Dacomitinib	60.64 (± 14.85)	()		
PF-05199265	10.49 (± 6.26)	()		

Notes:

[7] - Cmin was only estimated for dacomitinib and its major circulating metabolite PF-05199265.

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

End point description:

Fluctuation coefficient between trough and peak plasma concentration was determined as Cmax-Ctrough divided by Cavg, where Cmax was the maximum observed concentration within the dosing interval, Ctrough was the observed concentration prior to dose administration and Cavg 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 outcome measure was planned to be analyzed in Chinese subgroup only.

End point type	Secondary

End point timeframe:

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

End point values	Dacomitinib	Gefitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	0[8]		
Units: Fluctuation coefficient				
arithmetic mean (standard deviation)				
Dacomitinib	0.2883 (± 0.1460)	()		

PF-05199265	0.1105 (± 0.0827)	()		

Notes:

[8] - DF was only estimated for dacomitinib and its major circulating metabolite PF-05199265.

Statistical analyses

No statistical analyses for this end point

Secondary: Pre-dose Plasma Concentrations (Ctrough) of Dacomitinib and its Metabolite PF-05199265

End point title	Pre-dose Plasma Concentrations (Ctrough) of Dacomitinib and its Metabolite PF-05199265

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 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 outcome measure was planned to be analyzed in Chinese subgroup only.

End point type	Secondary

End point timeframe:

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

End point values	Dacomitinib	Gefitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	188	0[9]		
Units: ng/mL				
arithmetic mean (standard deviation)				
Cycle 2 Day 1: Dacomitinib	70.24 (± 27.16)	()		
Cycle 3 Day 1: Dacomitinib	68.34 (± 25.80)	()		
Cycle 4 Day 1: Dacomitinib	68.16 (± 25.49)	()		
Cycle 5 Day 1: Dacomitinib	64.50 (± 25.52)	()		
Cycle 6 Day 1: Dacomitinib	61.68 (± 22.58)	()		
Cycle 2 Day 1: PF-05199265	13.20 (± 8.55)	()		
Cycle 3 Day 1: PF-05199265	14.42 (± 9.10)	()		
Cycle 4 Day 1: PF-05199265	13.70 (± 8.33)	()		
Cycle 5 Day 1: PF-05199265	12.48 (± 6.69)	()		
Cycle 6 Day 1: PF-05199265	13.05 (± 6.52)	()		

Notes:

[9] - Cthrough was only estimated for dacomitinib and its major circulating metabolite PF-05199265.

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Clearance (CL) of Dacomitinib

End point title	Apparent Clearance (CL) of Dacomitinib

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 outcome measure was planned to be analyzed in Chinese subgroup only.

End point type	Secondary

End point timeframe:

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

End point values	Dacomitinib	Gefitinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	0[10]		
Units: Liter/hour				
arithmetic mean (standard deviation)	27.61 (± 5.97)	()		

Notes:

[10] - CL was only estimated for dacomitinib and its major circulating metabolite PF-05199265.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From baseline until 28-35 days after the last dose for the subjects completed the study by DCO.
For the 11 subjects were followed until the event has resolved, returned to baseline, has been deemed irreversible, or until death (up to 80 months)

Adverse event reporting additional description:

The same event may appear as both an AE and a SAE. 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

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	Dacomitinib

Reporting group description:

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

Reporting group title	Dacomitinib (ongoing at DCO)

Reporting group description:

DCO was the protocol-defined cutoff at 48 months from first dosing of the last enrolled subject (13 May 2019). At the DCO, 11 subjects were ongoing in the dacomitinib arm and continued study treatment until disease progression, intolerable toxicities, withdrawal, death, or study terminated by sponsor, whichever occurred first. The 11 subjects were analyzed for adverse events after LSLV on 27 Jan 2022.

Reporting group title	Gefitinib

Reporting group description:

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

Serious adverse events	Dacomitinib	Dacomitinib (ongoing at DCO)	Gefitinib
Total subjects affected by serious adverse events			
subjects affected / exposed	69 / 227 (30.40%)	4 / 11 (36.36%)	53 / 224 (23.66%)
number of deaths (all causes)	133	1	152
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 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic myeloid leukaemia			

subjects affected / exposed	1 / 227 (0.44%)	0 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant neoplasm progression			
subjects affected / exposed	0 / 227 (0.00%)	0 / 11 (0.00%)	2 / 224 (0.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Pancreatic carcinoma			
subjects affected / exposed	0 / 227 (0.00%)	0 / 11 (0.00%)	1 / 224 (0.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to meninges			
subjects affected / exposed	2 / 227 (0.88%)	0 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Cancer pain			
subjects affected / exposed	0 / 227 (0.00%)	0 / 11 (0.00%)	1 / 224 (0.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 227 (0.44%)	0 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	9 / 227 (3.96%)	0 / 11 (0.00%)	12 / 224 (5.36%)
occurrences causally related to treatment / all	0 / 9	0 / 0	0 / 12
deaths causally related to treatment / all	0 / 9	0 / 0	0 / 12
Death			
subjects affected / exposed	1 / 227 (0.44%)	0 / 11 (0.00%)	1 / 224 (0.45%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	1 / 1	0 / 0	1 / 1

Multiple organ dysfunction syndrome			
subjects affected / exposed	1 / 227 (0.44%)	0 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	1 / 227 (0.44%)	0 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	1 / 227 (0.44%)	0 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	0 / 227 (0.00%)	0 / 11 (0.00%)	1 / 224 (0.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	5 / 227 (2.20%)	0 / 11 (0.00%)	2 / 224 (0.89%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Haemoptysis			
subjects affected / exposed	2 / 227 (0.88%)	0 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	2 / 227 (0.88%)	0 / 11 (0.00%)	1 / 224 (0.45%)
occurrences causally related to treatment / all	1 / 3	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	2 / 227 (0.88%)	0 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Dyspnoea			
subjects affected / exposed	1 / 227 (0.44%)	0 / 11 (0.00%)	4 / 224 (1.79%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Respiratory failure			
subjects affected / exposed	2 / 227 (0.88%)	0 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Interstitial lung disease			
subjects affected / exposed	1 / 227 (0.44%)	0 / 11 (0.00%)	1 / 224 (0.45%)
occurrences causally related to treatment / all	1 / 1	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	1 / 227 (0.44%)	0 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchospasm			
subjects affected / exposed	0 / 227 (0.00%)	0 / 11 (0.00%)	1 / 224 (0.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Organising pneumonia			
subjects affected / exposed	0 / 227 (0.00%)	0 / 11 (0.00%)	1 / 224 (0.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 227 (0.00%)	0 / 11 (0.00%)	1 / 224 (0.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	0 / 227 (0.00%)	0 / 11 (0.00%)	1 / 224 (0.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			

Alanine aminotransferase increased			
subjects affected / exposed	0 / 227 (0.00%)	0 / 11 (0.00%)	1 / 224 (0.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 227 (0.00%)	0 / 11 (0.00%)	1 / 224 (0.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic enzyme increased			
subjects affected / exposed	0 / 227 (0.00%)	0 / 11 (0.00%)	2 / 224 (0.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	6 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Facial bones fracture			
subjects affected / exposed	1 / 227 (0.44%)	0 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	1 / 227 (0.44%)	0 / 11 (0.00%)	1 / 224 (0.45%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	1 / 227 (0.44%)	0 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Spinal fracture			
subjects affected / exposed	1 / 227 (0.44%)	0 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Extradural haematoma			
subjects affected / exposed	0 / 227 (0.00%)	0 / 11 (0.00%)	1 / 224 (0.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Subdural haematoma			
subjects affected / exposed	0 / 227 (0.00%)	0 / 11 (0.00%)	2 / 224 (0.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	1 / 227 (0.44%)	1 / 11 (9.09%)	1 / 224 (0.45%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ligament injury			
subjects affected / exposed	1 / 227 (0.44%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ligament rupture			
subjects affected / exposed	1 / 227 (0.44%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Concussion			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac tamponade			
subjects affected / exposed	1 / 227 (0.44%)	0 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arteriosclerosis coronary artery			
subjects affected / exposed	0 / 227 (0.00%)	0 / 11 (0.00%)	1 / 224 (0.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	1 / 227 (0.44%)	0 / 11 (0.00%)	3 / 224 (1.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1

Cerebral venous thrombosis			
subjects affected / exposed	1 / 227 (0.44%)	0 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord compression			
subjects affected / exposed	1 / 227 (0.44%)	0 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 227 (0.00%)	0 / 11 (0.00%)	1 / 224 (0.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cognitive disorder			
subjects affected / exposed	0 / 227 (0.00%)	0 / 11 (0.00%)	1 / 224 (0.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 227 (0.00%)	0 / 11 (0.00%)	1 / 224 (0.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post herpetic neuralgia			
subjects affected / exposed	0 / 227 (0.00%)	0 / 11 (0.00%)	1 / 224 (0.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorder			
subjects affected / exposed	0 / 227 (0.00%)	0 / 11 (0.00%)	1 / 224 (0.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Leukocytosis			
subjects affected / exposed	1 / 227 (0.44%)	0 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			

subjects affected / exposed	1 / 227 (0.44%)	0 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Keratitis			
subjects affected / exposed	1 / 227 (0.44%)	0 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cataract			
subjects affected / exposed	1 / 227 (0.44%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	5 / 227 (2.20%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	9 / 9	4 / 4	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	2 / 227 (0.88%)	0 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal distension			
subjects affected / exposed	1 / 227 (0.44%)	0 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer haemorrhage			
subjects affected / exposed	1 / 227 (0.44%)	0 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	2 / 227 (0.88%)	0 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mouth haemorrhage			

subjects affected / exposed	1 / 227 (0.44%)	0 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	1 / 227 (0.44%)	0 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	1 / 227 (0.44%)	0 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 227 (0.44%)	0 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspepsia			
subjects affected / exposed	0 / 227 (0.00%)	0 / 11 (0.00%)	1 / 224 (0.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematochezia			
subjects affected / exposed	0 / 227 (0.00%)	0 / 11 (0.00%)	1 / 224 (0.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal obstruction			
subjects affected / exposed	0 / 227 (0.00%)	0 / 11 (0.00%)	1 / 224 (0.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	1 / 227 (0.44%)	0 / 11 (0.00%)	1 / 224 (0.45%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Liver injury			

subjects affected / exposed	2 / 227 (0.88%)	0 / 11 (0.00%)	1 / 224 (0.45%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug-induced liver injury			
subjects affected / exposed	1 / 227 (0.44%)	0 / 11 (0.00%)	1 / 224 (0.45%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bile duct stone			
subjects affected / exposed	0 / 227 (0.00%)	0 / 11 (0.00%)	1 / 224 (0.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 227 (0.00%)	0 / 11 (0.00%)	1 / 224 (0.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangitis			
subjects affected / exposed	0 / 227 (0.00%)	0 / 11 (0.00%)	1 / 224 (0.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	1 / 227 (0.44%)	0 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug eruption			
subjects affected / exposed	1 / 227 (0.44%)	0 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash maculo-papular			
subjects affected / exposed	1 / 227 (0.44%)	0 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Decubitus ulcer			

subjects affected / exposed	0 / 227 (0.00%)	0 / 11 (0.00%)	1 / 224 (0.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 227 (0.88%)	0 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureterolithiasis			
subjects affected / exposed	0 / 227 (0.00%)	0 / 11 (0.00%)	1 / 224 (0.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	1 / 227 (0.44%)	0 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	1 / 227 (0.44%)	0 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal pain			
subjects affected / exposed	1 / 227 (0.44%)	0 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 227 (0.00%)	0 / 11 (0.00%)	1 / 224 (0.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Polymyalgia rheumatica			
subjects affected / exposed	0 / 227 (0.00%)	0 / 11 (0.00%)	1 / 224 (0.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Infections and infestations			
Pneumonia			
subjects affected / exposed	5 / 227 (2.20%)	0 / 11 (0.00%)	2 / 224 (0.89%)
occurrences causally related to treatment / all	3 / 10	0 / 0	2 / 3
deaths causally related to treatment / all	0 / 2	0 / 0	1 / 1
Respiratory tract infection			
subjects affected / exposed	2 / 227 (0.88%)	0 / 11 (0.00%)	1 / 224 (0.45%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	2 / 227 (0.88%)	0 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	2 / 227 (0.88%)	0 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopulmonary aspergillosis			
subjects affected / exposed	1 / 227 (0.44%)	0 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	1 / 227 (0.44%)	0 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia urinary tract infection			
subjects affected / exposed	1 / 227 (0.44%)	0 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 227 (0.44%)	0 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			

subjects affected / exposed	1 / 227 (0.44%)	0 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infection			
subjects affected / exposed	1 / 227 (0.44%)	0 / 11 (0.00%)	1 / 224 (0.45%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	1 / 227 (0.44%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	0 / 227 (0.00%)	0 / 11 (0.00%)	1 / 224 (0.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis bacterial			
subjects affected / exposed	1 / 227 (0.44%)	0 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media chronic			
subjects affected / exposed	1 / 227 (0.44%)	0 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 227 (1.32%)	0 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	2 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	1 / 227 (0.44%)	0 / 11 (0.00%)	0 / 224 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malnutrition			

subjects affected / exposed	1 / 227 (0.44%)	0 / 11 (0.00%)	1 / 224 (0.45%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Hyponatraemia			
subjects affected / exposed	0 / 227 (0.00%)	0 / 11 (0.00%)	2 / 224 (0.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Dacomitinib	Dacomitinib (ongoing at DCO)	Gefitinib
Total subjects affected by non-serious adverse events			
subjects affected / exposed	224 / 227 (98.68%)	11 / 11 (100.00%)	217 / 224 (96.88%)
Vascular disorders			
Hypertension			
subjects affected / exposed	19 / 227 (8.37%)	2 / 11 (18.18%)	21 / 224 (9.38%)
occurrences (all)	66	17	58
Ischaemia			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	32 / 227 (14.10%)	1 / 11 (9.09%)	30 / 224 (13.39%)
occurrences (all)	74	2	59
Chest pain			
subjects affected / exposed	19 / 227 (8.37%)	3 / 11 (27.27%)	27 / 224 (12.05%)
occurrences (all)	36	13	33
Mucosal inflammation			
subjects affected / exposed	21 / 227 (9.25%)	0 / 11 (0.00%)	8 / 224 (3.57%)
occurrences (all)	38	0	9
Fatigue			
subjects affected / exposed	26 / 227 (11.45%)	1 / 11 (9.09%)	20 / 224 (8.93%)
occurrences (all)	47	2	30
Pyrexia			

subjects affected / exposed	22 / 227 (9.69%)	3 / 11 (27.27%)	18 / 224 (8.04%)
occurrences (all)	28	5	20
Oedema peripheral			
subjects affected / exposed	13 / 227 (5.73%)	0 / 11 (0.00%)	7 / 224 (3.13%)
occurrences (all)	15	0	9
Pain			
subjects affected / exposed	16 / 227 (7.05%)	3 / 11 (27.27%)	14 / 224 (6.25%)
occurrences (all)	21	4	17
Mass			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Immune system disorders			
Immune system disorder			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Pelvic fluid collection			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Vulvovaginal rash			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	47 / 227 (20.70%)	5 / 11 (45.45%)	46 / 224 (20.54%)
occurrences (all)	84	20	74
Dyspnoea			
subjects affected / exposed	31 / 227 (13.66%)	1 / 11 (9.09%)	29 / 224 (12.95%)
occurrences (all)	49	6	59
Nasal inflammation			
subjects affected / exposed	15 / 227 (6.61%)	0 / 11 (0.00%)	3 / 224 (1.34%)
occurrences (all)	22	0	5
Epistaxis			
subjects affected / exposed	22 / 227 (9.69%)	3 / 11 (27.27%)	5 / 224 (2.23%)
occurrences (all)	26	3	5
Haemoptysis			

subjects affected / exposed	10 / 227 (4.41%)	0 / 11 (0.00%)	13 / 224 (5.80%)
occurrences (all)	10	0	14
Productive cough			
subjects affected / exposed	10 / 227 (4.41%)	1 / 11 (9.09%)	12 / 224 (5.36%)
occurrences (all)	10	1	13
Catarrh			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	2	0
Oropharyngeal pain			
subjects affected / exposed	0 / 227 (0.00%)	3 / 11 (27.27%)	0 / 224 (0.00%)
occurrences (all)	0	4	0
Laryngeal pain			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Nasal mucosal disorder			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Dysphonia			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Nasal mucosal ulcer			
subjects affected / exposed	0 / 227 (0.00%)	2 / 11 (18.18%)	0 / 224 (0.00%)
occurrences (all)	0	2	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	32 / 227 (14.10%)	1 / 11 (9.09%)	33 / 224 (14.73%)
occurrences (all)	54	11	46
Anxiety			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	2	0
Depression			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Investigations			
Weight decreased			

subjects affected / exposed	67 / 227 (29.52%)	5 / 11 (45.45%)	43 / 224 (19.20%)
occurrences (all)	131	23	74
Aspartate aminotransferase increased			
subjects affected / exposed	49 / 227 (21.59%)	5 / 11 (45.45%)	84 / 224 (37.50%)
occurrences (all)	83	10	186
Alanine aminotransferase increased			
subjects affected / exposed	53 / 227 (23.35%)	7 / 11 (63.64%)	90 / 224 (40.18%)
occurrences (all)	94	16	209
Blood bilirubin increased			
subjects affected / exposed	19 / 227 (8.37%)	1 / 11 (9.09%)	20 / 224 (8.93%)
occurrences (all)	40	1	40
Blood alkaline phosphatase increased			
subjects affected / exposed	16 / 227 (7.05%)	2 / 11 (18.18%)	8 / 224 (3.57%)
occurrences (all)	21	2	17
Gamma-glutamyltransferase increased			
subjects affected / exposed	17 / 227 (7.49%)	3 / 11 (27.27%)	19 / 224 (8.48%)
occurrences (all)	22	4	37
White blood cell count decreased			
subjects affected / exposed	6 / 227 (2.64%)	1 / 11 (9.09%)	14 / 224 (6.25%)
occurrences (all)	11	5	23
Weight increased			
subjects affected / exposed	11 / 227 (4.85%)	3 / 11 (27.27%)	19 / 224 (8.48%)
occurrences (all)	39	8	55
Haemoglobin decreased			
subjects affected / exposed	14 / 227 (6.17%)	0 / 11 (0.00%)	5 / 224 (2.23%)
occurrences (all)	42	0	9
Blood lactate dehydrogenase increased			
subjects affected / exposed	8 / 227 (3.52%)	1 / 11 (9.09%)	12 / 224 (5.36%)
occurrences (all)	12	1	14
Blood creatinine increased			
subjects affected / exposed	0 / 227 (0.00%)	3 / 11 (27.27%)	0 / 224 (0.00%)
occurrences (all)	0	6	0
Blood uric acid increased			

subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Blood albumin decreased			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	11	0
Eosinophil count increased			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Glomerular filtration rate decreased			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Blood glucose increased			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Neutrophil count decreased			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Neutrophil count increased			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Blood potassium decreased			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	2	0
Platelet count decreased			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Platelet count increased			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Fall			

subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Skin abrasion			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Sinus tachycardia			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	15 / 227 (6.61%)	0 / 11 (0.00%)	11 / 224 (4.91%)
occurrences (all)	32	0	12
Paraesthesia			
subjects affected / exposed	15 / 227 (6.61%)	1 / 11 (9.09%)	11 / 224 (4.91%)
occurrences (all)	34	3	14
Headache			
subjects affected / exposed	17 / 227 (7.49%)	1 / 11 (9.09%)	21 / 224 (9.38%)
occurrences (all)	19	1	23
Dizziness			
subjects affected / exposed	12 / 227 (5.29%)	2 / 11 (18.18%)	17 / 224 (7.59%)
occurrences (all)	13	2	21
Hypoaesthesia			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Vertebral artery stenosis			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Sciatica			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	27 / 227 (11.89%)	5 / 11 (45.45%)	18 / 224 (8.04%)
occurrences (all)	51	16	47

Leukocytosis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Leukopenia			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Deafness			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Dry eye			
subjects affected / exposed	12 / 227 (5.29%)	3 / 11 (27.27%)	8 / 224 (3.57%)
occurrences (all)	13	3	8
Cataract			
subjects affected / exposed	0 / 227 (0.00%)	2 / 11 (18.18%)	0 / 224 (0.00%)
occurrences (all)	0	2	0
Corneal erosion			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Keratitis			
alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Eye pruritus			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Periorbital oedema			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Trichiasis			

subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	199 / 227 (87.67%)	10 / 11 (90.91%)	125 / 224 (55.80%)
occurrences (all)	629	46	259
Stomatitis			
subjects affected / exposed	99 / 227 (43.61%)	6 / 11 (54.55%)	41 / 224 (18.30%)
occurrences (all)	260	22	75
Nausea			
subjects affected / exposed	45 / 227 (19.82%)	3 / 11 (27.27%)	50 / 224 (22.32%)
occurrences (all)	70	10	68
Constipation			
subjects affected / exposed	32 / 227 (14.10%)	2 / 11 (18.18%)	29 / 224 (12.95%)
occurrences (all)	52	3	36
Mouth ulceration			
subjects affected / exposed	32 / 227 (14.10%)	3 / 11 (27.27%)	14 / 224 (6.25%)
occurrences (all)	56	6	17
Aphthous ulcer			
subjects affected / exposed	13 / 227 (5.73%)	0 / 11 (0.00%)	6 / 224 (2.68%)
occurrences (all)	17	0	7
Vomiting			
subjects affected / exposed	22 / 227 (9.69%)	0 / 11 (0.00%)	29 / 224 (12.95%)
occurrences (all)	28	0	39
Oral pain			
subjects affected / exposed	13 / 227 (5.73%)	4 / 11 (36.36%)	1 / 224 (0.45%)
occurrences (all)	23	6	1
Abdominal pain			
subjects affected / exposed	14 / 227 (6.17%)	0 / 11 (0.00%)	13 / 224 (5.80%)
occurrences (all)	15	0	18
Dysphagia			
subjects affected / exposed	10 / 227 (4.41%)	1 / 11 (9.09%)	12 / 224 (5.36%)
occurrences (all)	24	2	18
Abdominal pain upper			
subjects affected / exposed	10 / 227 (4.41%)	0 / 11 (0.00%)	14 / 224 (6.25%)
occurrences (all)	13	0	16

Angular cheilitis			
subjects affected / exposed	12 / 227 (5.29%)	0 / 11 (0.00%)	2 / 224 (0.89%)
occurrences (all)	15	0	6
Dry mouth			
alternative dictionary used: MedDRA 24.1			
subjects affected / exposed	0 / 227 (0.00%)	2 / 11 (18.18%)	0 / 224 (0.00%)
occurrences (all)	0	3	0
Abdominal pain lower			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Toothache			
subjects affected / exposed	0 / 227 (0.00%)	2 / 11 (18.18%)	0 / 224 (0.00%)
occurrences (all)	0	2	0
Chapped lips			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Glossodynia			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	2	0
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	0 / 227 (0.00%)	2 / 11 (18.18%)	0 / 224 (0.00%)
occurrences (all)	0	4	0
Cholelithiasis			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	112 / 227 (49.34%)	3 / 11 (27.27%)	64 / 224 (28.57%)
occurrences (all)	369	9	112
Dry skin			
subjects affected / exposed	64 / 227 (28.19%)	0 / 11 (0.00%)	39 / 224 (17.41%)
occurrences (all)	108	0	50
Alopecia			
subjects affected / exposed	53 / 227 (23.35%)	4 / 11 (36.36%)	29 / 224 (12.95%)
occurrences (all)	80	6	44

Pruritus			
subjects affected / exposed	47 / 227 (20.70%)	3 / 11 (27.27%)	33 / 224 (14.73%)
occurrences (all)	69	4	52
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	33 / 227 (14.54%)	2 / 11 (18.18%)	7 / 224 (3.13%)
occurrences (all)	67	2	8
Rash			
subjects affected / exposed	41 / 227 (18.06%)	2 / 11 (18.18%)	26 / 224 (11.61%)
occurrences (all)	107	5	34
Rash maculo-papular			
subjects affected / exposed	29 / 227 (12.78%)	4 / 11 (36.36%)	27 / 224 (12.05%)
occurrences (all)	109	17	47
Dermatitis			
subjects affected / exposed	25 / 227 (11.01%)	1 / 11 (9.09%)	9 / 224 (4.02%)
occurrences (all)	68	4	13
Skin fissures			
subjects affected / exposed	21 / 227 (9.25%)	1 / 11 (9.09%)	7 / 224 (3.13%)
occurrences (all)	38	1	10
Acne			
subjects affected / exposed	19 / 227 (8.37%)	0 / 11 (0.00%)	13 / 224 (5.80%)
occurrences (all)	66	0	18
Erythema			
subjects affected / exposed	14 / 227 (6.17%)	1 / 11 (9.09%)	3 / 224 (1.34%)
occurrences (all)	26	1	4
Drug eruption			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Eczema			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Nail disorder			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Hirsutism			

subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Pain of skin			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Papule			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Skin ulcer			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	3	0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	34 / 227 (14.98%)	5 / 11 (45.45%)	26 / 224 (11.61%)
occurrences (all)	61	12	44
Musculoskeletal pain			
subjects affected / exposed	26 / 227 (11.45%)	2 / 11 (18.18%)	31 / 224 (13.84%)
occurrences (all)	68	2	46
Back pain			
subjects affected / exposed	26 / 227 (11.45%)	3 / 11 (27.27%)	37 / 224 (16.52%)
occurrences (all)	31	4	48
Arthralgia			
subjects affected / exposed	19 / 227 (8.37%)	2 / 11 (18.18%)	14 / 224 (6.25%)
occurrences (all)	36	11	18
Intervertebral disc protrusion			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	0 / 227 (0.00%)	2 / 11 (18.18%)	0 / 224 (0.00%)
occurrences (all)	0	3	0
Periarthritis			

subjects affected / exposed	0 / 227 (0.00%)	2 / 11 (18.18%)	0 / 224 (0.00%)
occurrences (all)	0	2	0
Joint swelling			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Paronychia			
subjects affected / exposed	140 / 227 (61.67%)	9 / 11 (81.82%)	45 / 224 (20.09%)
occurrences (all)	413	24	92
Upper respiratory tract infection			
subjects affected / exposed	36 / 227 (15.86%)	5 / 11 (45.45%)	29 / 224 (12.95%)
occurrences (all)	66	12	48
Conjunctivitis			
subjects affected / exposed	46 / 227 (20.26%)	3 / 11 (27.27%)	10 / 224 (4.46%)
occurrences (all)	64	4	11
Nasopharyngitis			
subjects affected / exposed	26 / 227 (11.45%)	3 / 11 (27.27%)	20 / 224 (8.93%)
occurrences (all)	48	6	29
Rash pustular			
subjects affected / exposed	15 / 227 (6.61%)	2 / 11 (18.18%)	3 / 224 (1.34%)
occurrences (all)	63	5	6
Urinary tract infection			
subjects affected / exposed	14 / 227 (6.17%)	0 / 11 (0.00%)	8 / 224 (3.57%)
occurrences (all)	22	0	10
Folliculitis			
subjects affected / exposed	12 / 227 (5.29%)	1 / 11 (9.09%)	4 / 224 (1.79%)
occurrences (all)	22	1	5
Bronchitis			
subjects affected / exposed	0 / 227 (0.00%)	2 / 11 (18.18%)	0 / 224 (0.00%)
occurrences (all)	0	2	0
Gingivitis			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0

Pharyngotonsillitis			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Otitis externa			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Skin infection			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Nasal vestibulitis			
subjects affected / exposed	0 / 227 (0.00%)	2 / 11 (18.18%)	0 / 224 (0.00%)
occurrences (all)	0	2	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	73 / 227 (32.16%)	2 / 11 (18.18%)	58 / 224 (25.89%)
occurrences (all)	139	13	88
Hypokalaemia			
subjects affected / exposed	25 / 227 (11.01%)	2 / 11 (18.18%)	13 / 224 (5.80%)
occurrences (all)	57	7	17
Hypoalbuminaemia			
subjects affected / exposed	12 / 227 (5.29%)	1 / 11 (9.09%)	10 / 224 (4.46%)
occurrences (all)	24	1	14
Hyponatraemia			
subjects affected / exposed	12 / 227 (5.29%)	0 / 11 (0.00%)	8 / 224 (3.57%)
occurrences (all)	18	0	10
Hyperuricaemia			
subjects affected / exposed	0 / 227 (0.00%)	2 / 11 (18.18%)	0 / 224 (0.00%)
occurrences (all)	0	2	0
Hyperlipidaemia			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	3	0
Hypernatraemia			

subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0
Hypocalcaemia			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	2	0
Tetany			
subjects affected / exposed	0 / 227 (0.00%)	1 / 11 (9.09%)	0 / 224 (0.00%)
occurrences (all)	0	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 June 2013	1. Included 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. Updated 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 2014	1. Removed the planned IA of PFS and modified related statistical considerations; 2. Shortened the period from screening to randomization in China; required confirmation of adenocarcinoma histo- and/or cytopathology, by the local laboratory prior to screening for all patients; 3. Added statement that a tumor specimen must be available for retrospective central laboratory confirmation for EGFR mutation (ex-China) and adenocarcinoma (all); 4. Clarified conditions for discontinuation of study treatment; 5. Clarified that patients who had PD 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; 6. Implemented retrospective CYP2D6 genotyping for all patients treated in the dacomitinib arm; 7. Provided further guidance on treatment and management of common AEs; 8. 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 subejcts was to include survival status and subsequent cancer therapies; 9. 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.
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; 2. Clarified that no IA was planned for the primary endpoint; 3. Added language describing when and how the analysis of the primary endpoint was to be conducted; 4. Added language describing when and how an interim and a final analysis of the secondary endpoint of OS was to be conducted.

08 February 2018	1. Study design was clarified to indicate that dacomitinib patients treated for 48 months may continue dacomitinib treatment beyond 48 months through either the Pfizer compassionate use program, transfer onto a local rollover study (applies to patients in Japan only), or through continuation of dacomitinib on this study (applies to patients in China only), if allowed under local law, until disease progression, or unacceptable toxicity, or the study was terminated by Sponsor, whichever occurred first. 2. Study procedures, schedule of activities, and safety/efficacy assessments were added or amended to include patients who will be treated on dacomitinib beyond 48 months.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported