Clinical trial results:
A multicenter, randomized, double-blind, placebo-controlled, Phase II trial evaluating the safety and efficacy of dovitinib combined with fulvestrant, in post-menopausal patients with human epidermal growth factor receptor 2 negative (HER2-) and hormone receptor positive (HR+) breast cancer that have evidence of disease progression on or after prior endocrine therapy.

Summary

EudraCT number	2011-001230-42
Trial protocol	AT ES HU BE IT NL PL
Global end of trial date	03 April 2015

Results information

Result version number	v1 (current)
This version publication date	11 June 2016
First version publication date	11 June 2016

Trial information

Trial identification

Sponsor protocol code	CTKI258A2210

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01528345
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111,
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	03 April 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 April 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess the treatment effect of dovitinib in combination with fulvestrant vs. fulvestrant plus placebo on progression-free survival (PFS) per local Investigator assessment in patients with HER2-, HR+, LA/mBC that have evidence of disease progression on or after prior endocrine therapy for each of the 2 groups, namely:
- FGF Pathway amplified
- Regardless of FGF pathway amplification status

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 April 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 8
Country: Number of subjects enrolled	Austria: 4
Country: Number of subjects enrolled	Belgium: 10
Country: Number of subjects enrolled	Brazil: 1
Country: Number of subjects enrolled	France: 16
Country: Number of subjects enrolled	Hungary: 9
Country: Number of subjects enrolled	Italy: 13
Country: Number of subjects enrolled	Netherlands: 4
Country: Number of subjects enrolled	Russian Federation: 5
Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	Taiwan: 7
Country: Number of subjects enrolled	United States: 17
Worldwide total number of subjects	97
EEA total number of subjects	59

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)	52
From 65 to 84 years	45
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Prior to dosing, all patients who fulfilled all inclusion/exclusion criteria were randomized to one of the two treatment groups in a ratio of 1:1.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Fulvestrant + Dovitinib active

Arm description:

Fulvestrant in combination with the study drug Dovitinib.

Arm type	Experimental
Investigational medicinal product name	Dovitinib
Investigational medicinal product code	TKI258
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Active Dovitinib (in tablet form) taken orally at a dose of 500 mg (i.e., 5 x 100mg tablets) on a 5 days on/2 days off dosing schedule

Investigational medicinal product name	Fulvestrant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Fulvestrant (in solution) injected intramuscularly at a dose of 500 mg once on Week 1 Day 1, Week 3 Day 1 and Week 5 Day 1 and subsequently once every 4 weeks on Day 1 of the week.

Arm title	Fulvestrant + Dovitinib placebo

Arm description:

Fulvestrant in combination with a placebo matching Dovitinib.

Arm type	Placebo
Investigational medicinal product name	Dovitinib Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Dovitinib Placebo (in tablet form) taken orally at a dose of 500 mg (i.e., 5 x 100mg tablets) on a 5 days on/2 days off dosing schedule

Number of subjects in period 1	Fulvestrant + Dovitinib active	Fulvestrant + Dovitinib placebo
Started	47	50
Completed	0	0
Not completed	47	50
Adverse event, serious fatal	1	1
Adverse event, non-fatal	10	1
Non-compliance with study treatment	1	-
Progressive Disease	26	40
Subject/Guardian Decision	5	-
Study Terminated by Sponsor	4	8

Baseline characteristics

Reporting groups	
Reporting group title	Fulvestrant + Dovitinib active
Reporting group description:	
Fulvestrant in combination with the study drug Dovitinib.	
Reporting group title	Fulvestrant + Dovitinib placebo
Reporting group description:	
Fulvestrant in combination with a placebo matching Dovitinib.	

Reporting group values	Fulvestrant + Dovitinib active	Fulvestrant + Dovitinib placebo	Total
Number of subjects	47	50	97
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	25	27	52
From 65-84 years	22	23	45
85 years and over	0	0	0
Age Continuous | Units: Years			
arithmetic mean	63.5	61.7	
standard deviation	± 9.02	± 9.51	-
Gender, Male/Female Units: Participants			
Female	47	50	97
Male	0	0	0

End points

End points reporting groups

Reporting group title	Fulvestrant + Dovitinib active
Reporting group description: Fulvestrant in combination with the study drug Dovitinib.	
Reporting group title	Fulvestrant + Dovitinib placebo
Reporting group description: Fulvestrant in combination with a placebo matching Dovitinib.	

Primary: Progression Free Survival (PFS) based on Investigator assessment

End point title	Progression Free Survival (PFS) based on Investigator assessment
End point description: Efficacy criteria were therefore achieved in FGF amplified patients. In consideration of the smaller than planned number of events (only 18 events against the planned 50 events) results are to be interpreted with caution as only indicative and requiring further exploration. For the FGF non-amplified patients, where the target number of PFS events was achieved, the study passed the futility analysis (i.e. dovitinib plus fulvestrant treatment was not rejected as futile).	
End point type	Primary
End point timeframe: Every 8 weeks assessed up to 34 months	

End point values	Fulvestrant + Dovitinib active	Fulvestrant + Dovitinib placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	50		
Units: Months				
median (confidence interval 95%)				
All patients (n: 30, 34)	5.5 (3.8 to 14)	5.5 (3.5 to 10.7)		
FGF amplified patients (n: 9, 9)	10.9 (3.5 to 16.5)	5.5 (3.5 to 16.4)		
FGF non-amplified patients (n: 21, 25)	5.5 (3.8 to 16.8)	5.5 (1.9 to 12.8)		

Statistical analyses

Statistical analysis title	progression free survival: All Patients
Comparison groups	Fulvestrant + Dovitinib placebo v Fulvestrant + Dovitinib active

Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.681
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.406
upper limit	1.143

Secondary: Overall Response Rate (ORR)

End point title	Overall Response Rate (ORR)

End point description:

ORR was defined as the percentage of patients with a best overall response of Complete Response (CR) or Partial Response (PR) as per RECIST. Responses include: Complete Response: Disappearance of all non-nodal target lesions; Partial Response: At least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of diameters; Progressive Disease: At least a 20% increase in the sum of diameter of all measured target lesions, taking as reference the smallest sum of diameter of all target lesions recorded at or after baseline; Stable Disease: Neither sufficient shrinkage to qualify for PR or CR nor an increase in lesions which would qualify for PD; Unknown (UNK) Progression has not been documented and one or more target lesions have not been assessed or have been assessed using a different method than baseline.

End point type	Secondary

End point timeframe:

Every 8 weeks assessed up to 34 months

End point values	Fulvestrant + Dovitinib active	Fulvestrant + Dovitinib placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	50		
Units: Percentage of participants				
number (not applicable)				
All patients	27.7	10		
FGF amplified patients	20	12.5		
FGF non-amplified patients	31.3	8.8		

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 the date of the first documented response (CR or PR) to the date of the first documented or death due to disease. If a patient does not have a progression event, DOR will be censored on the date of the last adequate tumor assessment. This outcome measure was not analyzed as the study was terminated before duration of response could be analyzed.

End point type	Secondary

End point timeframe:

From date of first documented efficacy response (CR or PR) to time of documented progression (PD) whichever comes first, assessed up to 24 months

End point values	Fulvestrant + Dovitinib active	Fulvestrant + Dovitinib placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[1]	0[2]		
Units: Months				
number (not applicable)				

Notes:

[1] - This outcome measure was not analyzed as the study was terminated.

[2] - This outcome measure was not analyzed as the study was terminated

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS) using Kaplan- Meier method

End point title	Overall Survival (OS) using Kaplan- Meier method

End point description:

OS was defined as the time from the date of randomization to the date of death from any cause. If a patient is not known to have died at the date of analysis cut-off, the OS will be censored at the last date of contact. The Upper Limit of confidence interval is not estimable as there were too few events (not enough patients died by the data cutoff date for database lock). 99999.9 represents not applicable data and used as place holder to avoid system error because EudraCT system is not accepting "NA" for not available/not applicable data.

End point type	Secondary

End point timeframe:

From date of randomization to date of death from any cause whichever comes first, assessed up to 34 months

End point values	Fulvestrant + Dovitinib active	Fulvestrant + Dovitinib placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	50		
Units: Months				
median (confidence interval 95%)	99999.9 (18.6 to 99999.9)	25.9 (18.4 to 99999.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with adverse events as a measure of safety

End point title	Number of participants with adverse events as a measure of safety

End point description:

The type, frequency and severity of adverse events, laboratory values, and Electrocardiograms (ECGs) experienced by patients will be assessed according to Common Terminology Criteria for Adverse Events. The study enrollment was terminated early due to challenges in enrolling patients with FGF amplified status. See safety section for safety details.

End point type	Secondary

End point timeframe:

Screening, Week 2, Week 4 and approximately every 4 weeks during treatment period (approximately 34 months)

End point values	Fulvestrant + Dovitinib active	Fulvestrant + Dovitinib placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47[3]	50[4]		
Units: Participants	47	50		

Notes:

[3] - This outcome measure was not analyzed as the study was terminated.

[4] - This outcome measure was not analyzed as the study was terminated.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to worsening of ECOG performance status

End point title	Time to worsening of ECOG performance status

End point description:

Eastern Cooperative Oncology Group (ECOG) Performance Status (scales and criteria used by doctors and researchers to assess how a patient's disease is progressing and assess how the disease affects the daily living abilities of the patient.) This outcome measure was not analyzed as the study was terminated before duration of response could be analyzed.

End point type	Secondary

End point timeframe:

Screening, Every 4 weeks during treatment period, and every 8 weeks during follow-up (approximately 9-12 months)

End point values	Fulvestrant + Dovitinib active	Fulvestrant + Dovitinib placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[5]	0[6]		
Units: Months				
number (not applicable)				

Notes:

[5] - This outcome measure was not analyzed as the study was terminated

[6] - This outcome measure was not analyzed as the study was terminated

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All adverse events reported in this record are from date of First Patient First Treatment until Last Patient Last Visit.

Adverse event reporting additional description:

Adverse events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All adverse events reported in this record are from date of First Patient First Treatment until Last Patient Last Visit.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Fulvestrant + Dovitinib placebo

Reporting group description:

Fulvestrant in combination with a placebo matching Dovitinib.

Reporting group title	Fulvestrant + Dovitinib active

Reporting group description:

Fulvestrant in combination with the study drug Dovitinib.

Serious adverse events	Fulvestrant + Dovitinib placebo	Fulvestrant + Dovitinib active	
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 50 (20.00%)	14 / 47 (29.79%)	
number of deaths (all causes)	2	2	
number of deaths resulting from adverse events	1	1	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
CERVIX CARCINOMA			
subjects affected / exposed	0 / 50 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
MALIGNANT MELANOMA			
subjects affected / exposed	1 / 50 (2.00%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
DEEP VEIN THROMBOSIS			

subjects affected / exposed	0 / 50 (0.00%)	2 / 47 (4.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOTENSION			
subjects affected / exposed	1 / 50 (2.00%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
HYPERTENSIVE CRISIS			
subjects affected / exposed	1 / 50 (2.00%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERIPHERAL ARTERY THROMBOSIS			
subjects affected / exposed	0 / 50 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
DEVICE BREAKAGE			
subjects affected / exposed	1 / 50 (2.00%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GENERAL PHYSICAL HEALTH DETERIORATION			
subjects affected / exposed	0 / 50 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERPYREXIA			
subjects affected / exposed	1 / 50 (2.00%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	1 / 50 (2.00%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal			

disorders			
LARYNGOSPASM			
subjects affected / exposed	1 / 50 (2.00%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PLEURAL EFFUSION			
subjects affected / exposed	1 / 50 (2.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PULMONARY EMBOLISM			
subjects affected / exposed	1 / 50 (2.00%)	3 / 47 (6.38%)	
occurrences causally related to treatment / all	0 / 1	2 / 3	
deaths causally related to treatment / all	0 / 1	1 / 1	
Injury, poisoning and procedural complications			
FEMUR FRACTURE			
subjects affected / exposed	1 / 50 (2.00%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
PERICARDIAL EFFUSION			
subjects affected / exposed	0 / 50 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
ISCHAEMIC CEREBRAL INFARCTION			
subjects affected / exposed	0 / 50 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
THROMBOCYTOPENIA			
subjects affected / exposed	0 / 50 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
CONSTIPATION			

subjects affected / exposed	1 / 50 (2.00%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIARRHOEA			
subjects affected / exposed	1 / 50 (2.00%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LUMBAR HERNIA			
subjects affected / exposed	0 / 50 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
OESOPHAGEAL VARICES HAEMORRHAGE			
subjects affected / exposed	0 / 50 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PANCREATITIS			
subjects affected / exposed	1 / 50 (2.00%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VARICES OESOPHAGEAL			
subjects affected / exposed	0 / 50 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
BILE DUCT OBSTRUCTION			
subjects affected / exposed	1 / 50 (2.00%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERBILIRUBINAEMIA			
subjects affected / exposed	0 / 50 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			

PIGMENTATION DISORDER			
subjects affected / exposed	0 / 50 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
ARTHRITIS			
subjects affected / exposed	0 / 50 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
BONE PAIN			
subjects affected / exposed	0 / 50 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SPINAL PAIN			
subjects affected / exposed	1 / 50 (2.00%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
INFECTION			
subjects affected / exposed	0 / 50 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA			
subjects affected / exposed	0 / 50 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
TOOTH ABSCESS			
subjects affected / exposed	1 / 50 (2.00%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
DEHYDRATION			

subjects affected / exposed	0 / 50 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Fulvestrant + Dovitinib placebo	Fulvestrant + Dovitinib active	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	45 / 50 (90.00%)	47 / 47 (100.00%)	
Vascular disorders			
HOT FLUSH			
subjects affected / exposed	3 / 50 (6.00%)	4 / 47 (8.51%)	
occurrences (all)	4	4	
HYPERTENSION			
subjects affected / exposed	4 / 50 (8.00%)	13 / 47 (27.66%)	
occurrences (all)	5	32	
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	11 / 50 (22.00%)	18 / 47 (38.30%)	
occurrences (all)	17	23	
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	2 / 50 (4.00%)	3 / 47 (6.38%)	
occurrences (all)	2	3	
FATIGUE			
subjects affected / exposed	13 / 50 (26.00%)	16 / 47 (34.04%)	
occurrences (all)	16	20	
MALAISE			
subjects affected / exposed	1 / 50 (2.00%)	4 / 47 (8.51%)	
occurrences (all)	1	4	
OEDEMA PERIPHERAL			
subjects affected / exposed	3 / 50 (6.00%)	3 / 47 (6.38%)	
occurrences (all)	4	3	
PYREXIA			
subjects affected / exposed	5 / 50 (10.00%)	6 / 47 (12.77%)	
occurrences (all)	7	8	

PAIN			
subjects affected / exposed	0 / 50 (0.00%)	4 / 47 (8.51%)	
occurrences (all)	0	7	
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	6 / 50 (12.00%)	7 / 47 (14.89%)	
occurrences (all)	6	7	
DYSPNOEA			
subjects affected / exposed	6 / 50 (12.00%)	8 / 47 (17.02%)	
occurrences (all)	7	8	
OROPHARYNGEAL PAIN			
subjects affected / exposed	0 / 50 (0.00%)	3 / 47 (6.38%)	
occurrences (all)	0	3	
Psychiatric disorders			
INSOMNIA			
subjects affected / exposed	4 / 50 (8.00%)	6 / 47 (12.77%)	
occurrences (all)	4	6	
Investigations			
BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	1 / 50 (2.00%)	11 / 47 (23.40%)	
occurrences (all)	1	12	
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	4 / 50 (8.00%)	10 / 47 (21.28%)	
occurrences (all)	4	12	
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	5 / 50 (10.00%)	15 / 47 (31.91%)	
occurrences (all)	5	16	
GAMMA-GLUTAMYLTRANSFERASE INCREASED			
subjects affected / exposed	4 / 50 (8.00%)	9 / 47 (19.15%)	
occurrences (all)	6	9	
LIPASE INCREASED			
subjects affected / exposed	3 / 50 (6.00%)	3 / 47 (6.38%)	
occurrences (all)	4	3	
WEIGHT DECREASED			

subjects affected / exposed	3 / 50 (6.00%)	7 / 47 (14.89%)	
occurrences (all)	3	8	
WEIGHT INCREASED			
subjects affected / exposed	3 / 50 (6.00%)	1 / 47 (2.13%)	
occurrences (all)	3	1	
Nervous system disorders			
AGEUSIA			
subjects affected / exposed	0 / 50 (0.00%)	3 / 47 (6.38%)	
occurrences (all)	0	3	
DIZZINESS			
subjects affected / exposed	2 / 50 (4.00%)	4 / 47 (8.51%)	
occurrences (all)	3	4	
DYSGEUSIA			
subjects affected / exposed	1 / 50 (2.00%)	15 / 47 (31.91%)	
occurrences (all)	1	16	
HEADACHE			
subjects affected / exposed	3 / 50 (6.00%)	17 / 47 (36.17%)	
occurrences (all)	4	26	
PARAESTHESIA			
subjects affected / exposed	3 / 50 (6.00%)	2 / 47 (4.26%)	
occurrences (all)	3	2	
SYNCOPE			
subjects affected / exposed	0 / 50 (0.00%)	5 / 47 (10.64%)	
occurrences (all)	0	8	
Blood and lymphatic system disorders			
LEUKOPENIA			
subjects affected / exposed	0 / 50 (0.00%)	3 / 47 (6.38%)	
occurrences (all)	0	5	
ANAEMIA			
subjects affected / exposed	4 / 50 (8.00%)	9 / 47 (19.15%)	
occurrences (all)	4	10	
NEUTROPENIA			
subjects affected / exposed	0 / 50 (0.00%)	7 / 47 (14.89%)	
occurrences (all)	0	8	
Ear and labyrinth disorders			

EAR PAIN			
subjects affected / exposed	0 / 50 (0.00%)	5 / 47 (10.64%)	
occurrences (all)	0	5	
VERTIGO			
subjects affected / exposed	0 / 50 (0.00%)	6 / 47 (12.77%)	
occurrences (all)	0	6	
Eye disorders			
LACRIMATION INCREASED			
subjects affected / exposed	0 / 50 (0.00%)	6 / 47 (12.77%)	
occurrences (all)	0	6	
DRY EYE			
subjects affected / exposed	0 / 50 (0.00%)	5 / 47 (10.64%)	
occurrences (all)	0	6	
VISION BLURRED			
subjects affected / exposed	0 / 50 (0.00%)	3 / 47 (6.38%)	
occurrences (all)	0	3	
Gastrointestinal disorders			
ABDOMINAL DISTENSION			
subjects affected / exposed	3 / 50 (6.00%)	4 / 47 (8.51%)	
occurrences (all)	3	4	
ABDOMINAL PAIN			
subjects affected / exposed	5 / 50 (10.00%)	8 / 47 (17.02%)	
occurrences (all)	5	10	
ABDOMINAL PAIN UPPER			
subjects affected / exposed	3 / 50 (6.00%)	10 / 47 (21.28%)	
occurrences (all)	3	12	
CONSTIPATION			
subjects affected / exposed	5 / 50 (10.00%)	8 / 47 (17.02%)	
occurrences (all)	5	9	
DIARRHOEA			
subjects affected / exposed	15 / 50 (30.00%)	37 / 47 (78.72%)	
occurrences (all)	18	91	
DRY MOUTH			
subjects affected / exposed	1 / 50 (2.00%)	5 / 47 (10.64%)	
occurrences (all)	1	6	
DYSPEPSIA			

subjects affected / exposed	0 / 50 (0.00%)	12 / 47 (25.53%)	
occurrences (all)	0	15	
GASTRITIS			
subjects affected / exposed	0 / 50 (0.00%)	3 / 47 (6.38%)	
occurrences (all)	0	4	
NAUSEA			
subjects affected / exposed	11 / 50 (22.00%)	34 / 47 (72.34%)	
occurrences (all)	13	65	
VOMITING			
subjects affected / exposed	4 / 50 (8.00%)	27 / 47 (57.45%)	
occurrences (all)	4	73	
STOMATITIS			
subjects affected / exposed	2 / 50 (4.00%)	10 / 47 (21.28%)	
occurrences (all)	2	11	
Skin and subcutaneous tissue disorders			
DERMATITIS ACNEIFORM			
subjects affected / exposed	0 / 50 (0.00%)	3 / 47 (6.38%)	
occurrences (all)	0	3	
ALOPECIA			
subjects affected / exposed	1 / 50 (2.00%)	4 / 47 (8.51%)	
occurrences (all)	1	5	
DRY SKIN			
subjects affected / exposed	2 / 50 (4.00%)	9 / 47 (19.15%)	
occurrences (all)	2	11	
PRURITUS			
subjects affected / exposed	2 / 50 (4.00%)	3 / 47 (6.38%)	
occurrences (all)	2	3	
RASH			
subjects affected / exposed	3 / 50 (6.00%)	16 / 47 (34.04%)	
occurrences (all)	3	22	
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	9 / 50 (18.00%)	7 / 47 (14.89%)	
occurrences (all)	11	9	
BACK PAIN			

subjects affected / exposed	9 / 50 (18.00%)	7 / 47 (14.89%)	
occurrences (all)	12	8	
MUSCLE SPASMS			
subjects affected / exposed	1 / 50 (2.00%)	3 / 47 (6.38%)	
occurrences (all)	1	3	
BONE PAIN			
subjects affected / exposed	4 / 50 (8.00%)	3 / 47 (6.38%)	
occurrences (all)	5	3	
MUSCULAR WEAKNESS			
subjects affected / exposed	0 / 50 (0.00%)	4 / 47 (8.51%)	
occurrences (all)	0	4	
MYALGIA			
subjects affected / exposed	1 / 50 (2.00%)	5 / 47 (10.64%)	
occurrences (all)	1	5	
MUSCULOSKELETAL PAIN			
subjects affected / exposed	3 / 50 (6.00%)	4 / 47 (8.51%)	
occurrences (all)	3	4	
PAIN IN EXTREMITY			
subjects affected / exposed	3 / 50 (6.00%)	9 / 47 (19.15%)	
occurrences (all)	5	13	
SPINAL PAIN			
subjects affected / exposed	1 / 50 (2.00%)	3 / 47 (6.38%)	
occurrences (all)	1	3	
Infections and infestations			
CONJUNCTIVITIS			
subjects affected / exposed	3 / 50 (6.00%)	3 / 47 (6.38%)	
occurrences (all)	3	3	
NASOPHARYNGITIS			
subjects affected / exposed	1 / 50 (2.00%)	3 / 47 (6.38%)	
occurrences (all)	1	3	
URINARY TRACT INFECTION			
subjects affected / exposed	4 / 50 (8.00%)	2 / 47 (4.26%)	
occurrences (all)	9	3	
Metabolism and nutrition disorders			
DECREASED APPETITE			

subjects affected / exposed	8 / 50 (16.00%)	13 / 47 (27.66%)	
occurrences (all)	9	17	
HYPERKALAEMIA			
subjects affected / exposed	2 / 50 (4.00%)	3 / 47 (6.38%)	
occurrences (all)	2	3	
HYPERGLYCAEMIA			
subjects affected / exposed	1 / 50 (2.00%)	3 / 47 (6.38%)	
occurrences (all)	1	4	
HYPERTRIGLYCERIDAEMIA			
subjects affected / exposed	1 / 50 (2.00%)	8 / 47 (17.02%)	
occurrences (all)	1	9	
HYPOCALCAEMIA			
subjects affected / exposed	1 / 50 (2.00%)	3 / 47 (6.38%)	
occurrences (all)	1	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 June 2012	The protocol was amended to provide the new information from the results of the recently completed food effect study, which allowed Dovitinib to be taken with food. In addition, the protocol amendment introduced minor changes or clarifications to some topics as a result of discussions held at the Investigators Meeting and with the Study Steering Committee, and questions raised during the regulatory review of the protocol in some countries as well.
19 July 2013	The protocol was amended to allow FGF amplification testing prior to progression on endocrine therapy.
21 March 2014	Because of the slow enrollment of FGF amplified patients, the protocol was amended to add a futility interim analysis for FGF amplified patients so that decisions about FGF amplified patients could be made earlier.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

The study enrollment was terminated early due to challenges in enrolling.

Notes: