Clinical trial results:
A Randomised Placebo-Controlled Phase II Study of Continuous Maintenance Treatment with BIBF 1120 Following Chemotherapy in Patients with Relapsed Ovarian Cancer

Summary

EudraCT number	2005-002427-14
Trial protocol	GB
Global end of trial date	18 March 2014

Results information

Result version number	v2 (current)
This version publication date	15 May 2019
First version publication date	01 August 2015
Version creation reason	• Changes to summary attachments Updates in synopsis
Summary attachment (see zip file)	Synopsis (1199.9_U10-2880-01-DS_CO.pdf)

Trial information

Trial identification

Sponsor protocol code	1199.9

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00710762
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Boehringer Ingelheim
Sponsor organisation address	Binger Strasse 173, Ingelheim am Rhein, Germany, 55216
Public contact	QRPE Processes and Systems Coordination Clinical Trial Information Disclosure, Boehringer Ingelheim Pharma GmbH & Co. KG, +1 800243 0127, clintriage.rdg@boehringer-ingelheim.com
Scientific contact	QRPE Processes and Systems Coordination Clinical Trial Information Disclosure, Boehringer Ingelheim Pharma GmbH & Co. KG, +1 800243 0127, clintriage.rdg@boehringer-ingelheim.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	17 July 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 March 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to estimate the Progression Free Survival Rates (PFS) of patients with relapsed ovarian cancer after 9 months of continuous treatment with either BIBF 1120 or matching placebo.

Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were entered in the study. All subjects were free to withdraw from the clinical trial at any time for any reason given. If a subject continued to take trial medication, close monitoring was adhered to and all adverse events recorded. Rules were implemented in all trials whereby doses would be reduced if required. Thereafter, if further events were reported, the subject would be withdrawn from the trial. Symptomatic treatment of tumour associated symptoms were allowed throughout.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 March 2006
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 89
Worldwide total number of subjects	89
EEA total number of subjects	89

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)	59
From 65 to 84 years	30
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Of the 84 randomised patients, 43 Nintedanib and 40 placebo treated patients were included in all analyses. 1 patient was excluded from analyses as she had received both trial treatments at different times(she was randomised to placebo but was initially treated for 1 treatment cycle with Nintedanib due to a dispensing error then 2 treatment cycles)

Period 1

Period 1 title	Treatment period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Nintedanib

Arm description:

Patients were treated with 250mg nintedanib twice daily.
43 patients were included in the analyses instead of 44 patients in nintedanib arm as one patient was excluded after drug administration due to important protocol violation. Consequently, number of subjects that started is 44 but only 43 reported (to match the numbers in the baseline characteristics)

Arm type	Experimental
Investigational medicinal product name	BIBF 1120
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

Patients were treated with 250mg nintedanib twice daily

Arm title	Placebo

Arm description:

Patients were treated with matching placebo twice daily

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

Patients were treated with matching placebo twice daily

Number of subjects in period 1[1]	Nintedanib	Placebo
Started	43	40
Completed	5	0
Not completed	38	40
Adverse Event other disease worsening	2	1
Other Adverse Event	7	7
Reason other than those listed	1	2
Lost to follow-up	1	-
Progressive disease	27	30

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Baseline characteristics are based on the patients who were randomised after successfully completing the screening period and received at least one of the trial medication.

Baseline characteristics

Reporting groups	
Reporting group title	Nintedanib
Reporting group description:	
Patients were treated with 250mg nintedanib twice daily. 43 patients were included in the analyses instead of 44 patients in nintedanib arm as one patient was excluded after drug administration due to important protocol violation. Consequently, number of subjects that started is 44 but only 43 reported (to match the numbers in the baseline characteristics)	
Reporting group title	Placebo
Reporting group description:	
Patients were treated with matching placebo twice daily	

Reporting group values	Nintedanib	Placebo	Total
Number of subjects	43	40	83
Age categorical Units: Subjects			
Age continuous			
One patient in the placebo arm has been excl			
Units: years			
arithmetic mean	58.4	61.3	
standard deviation	± 9.5	± 9.1	-
Gender categorical Units: Subjects			
Female	43	40	83
Male	0	0	0

End points

End points reporting groups

Reporting group title	Nintedanib

Reporting group description:

Patients were treated with 250mg nintedanib twice daily.
43 patients were included in the analyses instead of 44 patients in nintedanib arm as one patient was excluded after drug administration due to important protocol violation. Consequently, number of subjects that started is 44 but only 43 reported (to match the numbers in the baseline characteristics)

Reporting group title	Placebo

Reporting group description:

Patients were treated with matching placebo twice daily

Primary: PFS Rate at 36 Weeks (After 9 Months)

End point title	PFS Rate at 36 Weeks (After 9 Months)[1]

End point description:

The rate (probability) of being progression free at Week 36. Progression Free Survival (PFS) was defined according to RECIST version 1.0 from the time of first study drug administration to the first time of either objective tumour progression, the appearance of ≥1 new tumour lesion(s), occurrence or significant progression of malignant ascites, tumour related death, or the time when patients were censored at last known follow up. The rate is the Kaplan- Meier estimated percent probability.

End point type	Primary

End point timeframe:

36 weeks (after 9 months)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This endpoint was evaluated only descriptively. Thus, no statistical hypothiesis test were tested.

End point values	Nintedanib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43[2]	40[3]		
Units: percent probability of PFS				
median (confidence interval 95%)	15.6 (3.8 to 27.3)	2.9 (0 to 8.4)		

Notes:

[2] - Treated set.

[3] - Treated set.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Tumour Progression

End point title	Time to Tumour Progression

End point description:

Time to Tumour Progression according to RECIST version 1.0 , CA-125 (ovarian tumour marker) levels and RECIST + CA-125 levels.
For CA-125, progressive disease was defined on the basis of progressive serial elevations of CA-125 according to the following criteria:
Patients with elevated CA-125 pre-treatment and normalisation of CA-125 had to show evidence of CA-125 levels ≥2 x ULN on 2 occasions at least 1 week apart, or Patients with elevated CA-125 pre-

treatment that never normalised had to show evidence of CA-125 levels ≥2 x the nadir value on 2 occasions at least 1 week apart. or Patients with CA-125 in the normal range pre-treatment had to show evidence of CA-125 levels ≥2 x ULN on 2 occasions at least 1 week apart.
Composite (RECIST+CA-125) endpoint is the RECIST progressive disease (PD) if it occurred or the CA-125 PD if it occurred in the absence of RECIST PD.

End point type	Secondary

End point timeframe:

9 months

End point values	Nintedanib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43[4]	40[5]		
Units: days				
median (confidence interval 95%)				
according to RECIST and CA-125	83 (78 to 149)	84 (78 to 87)		
according to CA-125	85 (79 to 149)	86 (67 to 113)		
according to RECIST	143 (82 to 175)	85 (78 to 89)		

Notes:

[4] - Treated set

[5] - Treated set

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Death

End point title	Time to Death

End point description:

This end point was not determined as no patients died during the trial.

End point type	Secondary

End point timeframe:

9 months

End point values	Nintedanib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[6]	0[7]		
Units: days				
median (confidence interval 95%)	(to)	(to)		

Notes:

[6] - This end point was not determined as no patients died during the trial.

[7] - This end point was not determined as no patients died during the trial.

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence and Intensity of Adverse Events With Grading According CTCAE

End point title	Incidence and Intensity of Adverse Events With Grading According CTCAE

End point description:

Incidence and intensity of Adverse Events with grading according to the Common Terminology Criteria for Adverse Events (CTCAE version 3.0).

End point type	Secondary

End point timeframe:

First drug administration until 28 days after last drug administration,up until 309 days

End point values	Nintedanib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43[8]	40[9]		
Units: percentage of participants				
number (not applicable)				
CTCAE grade 1	2.3	25		
CTCAE grade 2	34.9	42.5		
CTCAE grade 3	53.5	25		
CTCAE grade 4	7	2.5		
CTCAE grade 5	0	0		

Notes:

[8] - Treated set

[9] - Treated set

Statistical analyses

No statistical analyses for this end point

Secondary: PFS Rate at 12 Weeks (After 3 Months) and 24 Weeks (After 6 Months)

End point title	PFS Rate at 12 Weeks (After 3 Months) and 24 Weeks (After 6 Months)

End point description:

The rate (probability) of being progression free at Week 12 and Week 24. Progression Free Survival (PFS) was defined according to RECIST version 1.0 from the time of first study drug administration to the first time of either objective tumour progression, the appearance of ≥1 new tumour lesion(s), occurrence or significant progression of malignant ascites, tumour related death, or the time when patients were censored at last known follow up. The rate is the Kaplan- Meier estimated percent probability.

End point type	Secondary

End point timeframe:

12 weeks (after 3 months) and 24 weeks (after 6 months)

End point values	Nintedanib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43[10]	40[11]		
Units: percent probability of PFS				
median (confidence interval 95%)				
at 24 weeks (after 6 months)	26.7 (12.5 to 40.8)	17.3 (5.2 to 29.4)		
at 12 weeks (after 3 months)	45.3 (29.5 to 61.2)	46.2 (30.5 to 61.8)		

Notes:

[10] - Treated set

[11] - Treated set

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Relevant Abnormalities for Laboratory Parameters

End point title	Clinical Relevant Abnormalities for Laboratory Parameters

End point description:

Clinical Relevant Abnormalities for laboratory parameters. Any new or clinically relevant worsening of baseline conditions was reported as Adverse Events.

End point type	Secondary

End point timeframe:

First drug administration until 28 days after last drug administration, up until 309 days

End point values	Nintedanib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43[12]	40[13]		
Units: Percentage of participants				
number (not applicable)				
Alanine aminotransferase increased	37.2	7.5		
Gamma-glutamyltransferase increased	30.2	2.5		
Aspartate aminotransferase increased	25.6	2.5		
Blood alkaline phosphatase increased	7	5		
Blood lactate dehydrogenase increased	4.7	0		
Blood alkaline phosphatase	0	2.5		
Blood alkaline phosphatase abnormal	2.3	2.5		
Lymphocyte count decreased	0	2.5		
Vitamin B12 decreased	0	2.5		
Alanine aminotransferase abnormal	2.3	0		
Blood lactate dehydrogenase abnormal	2.3	0		
Gamma-glutamyltransferase abnormal	2.3	0		
Neutrophil count decreased	2.3	0		
White blood cells urine positive	2.3	0		
Blood pressure increased	0	2.5		
Electrocardiogram T wave amplitude decreased	0	2.5		
Liver function test abnormal	2.3	0		

Notes:
[12] - Treated set
[13] - Treated set

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
First drug administration until 28 days after last drug administration, up until 309 days	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	11.1
Reporting groups	
Reporting group title	Nintedanib
Reporting group description:	
Patients were treated with 250mg nintedanib twice daily	
Reporting group title	Placebo
Reporting group description:	
Patients were treated with matching placebo twice daily	

Serious adverse events	Nintedanib	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 43 (32.56%)	10 / 40 (25.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 43 (2.33%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 43 (2.33%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 43 (2.33%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gamma-glutamyltransferase increased			

subjects affected / exposed	1 / 43 (2.33%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung neoplasm			
subjects affected / exposed	0 / 43 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuroendocrine tumour			
subjects affected / exposed	0 / 43 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 43 (2.33%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Pancytopenia			
subjects affected / exposed	0 / 43 (0.00%)	1 / 40 (2.50%)	
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			
Pyrexia			
subjects affected / exposed	1 / 43 (2.33%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 43 (2.33%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			

subjects affected / exposed	4 / 43 (9.30%)	2 / 40 (5.00%)	
occurrences causally related to treatment / all	2 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	6 / 43 (13.95%)	5 / 40 (12.50%)	
occurrences causally related to treatment / all	0 / 6	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	1 / 43 (2.33%)	0 / 40 (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	3 / 43 (6.98%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	2 / 43 (4.65%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 43 (2.33%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	1 / 43 (2.33%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	1 / 43 (2.33%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			

subjects affected / exposed	5 / 43 (11.63%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	3 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pleuritic pain			
subjects affected / exposed	1 / 43 (2.33%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 43 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Abnormal behaviour			
subjects affected / exposed	1 / 43 (2.33%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Agitation			
subjects affected / exposed	1 / 43 (2.33%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Confusional state			
subjects affected / exposed	1 / 43 (2.33%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delusion			
subjects affected / exposed	1 / 43 (2.33%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	0 / 43 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Mood altered			
subjects affected / exposed	0 / 43 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Catheter related infection			
subjects affected / exposed	0 / 43 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 43 (2.33%)	0 / 40 (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			
Anorexia			
subjects affected / exposed	1 / 43 (2.33%)	0 / 40 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	0 / 43 (0.00%)	1 / 40 (2.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Nintedanib	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	42 / 43 (97.67%)	37 / 40 (92.50%)	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	16 / 43 (37.21%)	3 / 40 (7.50%)	
occurrences (all)	20	3	
Aspartate aminotransferase increased			
subjects affected / exposed	10 / 43 (23.26%)	1 / 40 (2.50%)	
occurrences (all)	12	1	

Gamma-glutamyltransferase increased			
subjects affected / exposed	12 / 43 (27.91%)	1 / 40 (2.50%)	
occurrences (all)	12	1	
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 43 (11.63%)	2 / 40 (5.00%)	
occurrences (all)	5	2	
Hot flush			
subjects affected / exposed	3 / 43 (6.98%)	3 / 40 (7.50%)	
occurrences (all)	3	3	
Nervous system disorders			
Dizziness			
subjects affected / exposed	4 / 43 (9.30%)	4 / 40 (10.00%)	
occurrences (all)	4	4	
Headache			
subjects affected / exposed	6 / 43 (13.95%)	4 / 40 (10.00%)	
occurrences (all)	6	4	
Lethargy			
subjects affected / exposed	4 / 43 (9.30%)	4 / 40 (10.00%)	
occurrences (all)	4	4	
Paraesthesia			
subjects affected / exposed	1 / 43 (2.33%)	4 / 40 (10.00%)	
occurrences (all)	1	4	
Neuropathy peripheral			
subjects affected / exposed	0 / 43 (0.00%)	3 / 40 (7.50%)	
occurrences (all)	0	3	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	12 / 43 (27.91%)	11 / 40 (27.50%)	
occurrences (all)	17	12	
Oedema peripheral			
subjects affected / exposed	1 / 43 (2.33%)	3 / 40 (7.50%)	
occurrences (all)	1	3	
Ear and labyrinth disorders			
Tinnitus			

subjects affected / exposed	3 / 43 (6.98%)	1 / 40 (2.50%)	
occurrences (all)	3	1	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	3 / 43 (6.98%)	1 / 40 (2.50%)	
occurrences (all)	3	1	
Abdominal pain			
subjects affected / exposed	23 / 43 (53.49%)	15 / 40 (37.50%)	
occurrences (all)	36	17	
Constipation			
subjects affected / exposed	9 / 43 (20.93%)	11 / 40 (27.50%)	
occurrences (all)	10	13	
Diarrhoea			
subjects affected / exposed	33 / 43 (76.74%)	14 / 40 (35.00%)	
occurrences (all)	105	22	
Dyspepsia			
subjects affected / exposed	3 / 43 (6.98%)	1 / 40 (2.50%)	
occurrences (all)	4	1	
Flatulence			
subjects affected / exposed	5 / 43 (11.63%)	4 / 40 (10.00%)	
occurrences (all)	5	4	
Nausea			
subjects affected / exposed	32 / 43 (74.42%)	13 / 40 (32.50%)	
occurrences (all)	65	21	
Rectal haemorrhage			
subjects affected / exposed	3 / 43 (6.98%)	1 / 40 (2.50%)	
occurrences (all)	4	1	
Stomatitis			
subjects affected / exposed	5 / 43 (11.63%)	1 / 40 (2.50%)	
occurrences (all)	6	1	
Vomiting			
subjects affected / exposed	23 / 43 (53.49%)	9 / 40 (22.50%)	
occurrences (all)	52	10	
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	6 / 43 (13.95%)	1 / 40 (2.50%)	
occurrences (all)	6	1	
Dyspnoea			
subjects affected / exposed	5 / 43 (11.63%)	3 / 40 (7.50%)	
occurrences (all)	6	3	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 43 (0.00%)	6 / 40 (15.00%)	
occurrences (all)	0	6	
Alopecia			
subjects affected / exposed	2 / 43 (4.65%)	4 / 40 (10.00%)	
occurrences (all)	2	5	
Rash			
subjects affected / exposed	3 / 43 (6.98%)	5 / 40 (12.50%)	
occurrences (all)	3	6	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 43 (4.65%)	4 / 40 (10.00%)	
occurrences (all)	2	4	
Insomnia			
subjects affected / exposed	0 / 43 (0.00%)	3 / 40 (7.50%)	
occurrences (all)	0	3	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 43 (11.63%)	6 / 40 (15.00%)	
occurrences (all)	7	6	
Back pain			
subjects affected / exposed	2 / 43 (4.65%)	8 / 40 (20.00%)	
occurrences (all)	2	8	
Muscle spasms			
subjects affected / exposed	2 / 43 (4.65%)	4 / 40 (10.00%)	
occurrences (all)	2	6	
Pain in extremity			
subjects affected / exposed	4 / 43 (9.30%)	2 / 40 (5.00%)	
occurrences (all)	4	2	

Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	6 / 43 (13.95%)	2 / 40 (5.00%)	
occurrences (all)	6	2	
Infection			
subjects affected / exposed	3 / 43 (6.98%)	1 / 40 (2.50%)	
occurrences (all)	4	2	
Upper respiratory tract infection			
subjects affected / exposed	4 / 43 (9.30%)	3 / 40 (7.50%)	
occurrences (all)	4	3	
Urinary tract infection			
subjects affected / exposed	4 / 43 (9.30%)	4 / 40 (10.00%)	
occurrences (all)	5	4	
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	11 / 43 (25.58%)	6 / 40 (15.00%)	
occurrences (all)	14	6	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 October 2005	Amendment no. 1, documented new preclinical (phototoxicity) data that had become available since the preparation of the original study protocol.
04 January 2006	Amendment no. 2, documented a rewording of inclusion criteria for clarification, following the suggestion of a study investigator, and the correction of a typographical error with regard to the description of the packages of study medication.
26 January 2006	Amendment no. 3, documented administrative changes and a clarification of the data collection procedures for patients who continued into the treatment extension period and the subsequent analyses of such data.

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.

From Nov2009-Mar2014,there was 1 patient who continued taking Nintedanib on compassionate use programme,but due to limited data collected for compassionate use patients,no further analyses/reanalyses were deemed necessary and no new AE data recorded

Notes: