Clinical trial results:
An open-label, multi-center study to evaluate the efficacy of nilotinib in adult patients with gastrointestinal stromal tumors resistant to imatinib and sunitinib

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com/CtrdWeb/home.novfor complete trial results

Summary

EudraCT number	2008-000357-35
Trial protocol	DE IT GB
Global end of trial date	16 July 2014

Results information

Result version number	v1 (current)
This version publication date	07 July 2018
First version publication date	07 July 2018

Trial information

Trial identification

Sponsor protocol code	CAMN107DDE05

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
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	16 July 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 July 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the preliminary efficacy of nilotinib in pretreated patients with unresectable or metastatic GIST. Efficacy was defined as SD, partial response (PR) or complete response (CR) during the first 4 months according to Response Evaluation Criteria in Solid Tumors (RECIST) criteria

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	28 November 2008
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 97
Country: Number of subjects enrolled	Italy: 28
Worldwide total number of subjects	125
EEA total number of subjects	125

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)	75
From 65 to 84 years	50

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were enrolled in 19 centers in 2 countries: 12 centers in Germany and 7 centers in Italy A total of 133 patients were screened for this study, 125 were treated and 83 discontinued prior to study completion

Pre-assignment

Screening details:

The study population consisted of adult patients with unresectable or metastatic GIST, showing progression of disease on both imatinib and/or sunitinib, or demonstrating intolerance to imatinib and/or sunitinib.

Period 1

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

Arms

Arm title	Nilotinib
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Nilotinib
Investigational medicinal product code	AMN107
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

The dose of nilotinib was 800 mg (as 400 mg bid).

Number of subjects in period 1	Nilotinib
Started	125
Completed	42
Not completed	83
Adverse event, serious fatal	4
Consent withdrawn by subject	6
Adverse event, non-fatal	14
Progressive Disease	49
No longer required	2
New Cancer Therapy	2
Abnormal Lab Value	1
Lost to follow-up	2
Missing reason for discon	1
Lack of efficacy	2

Baseline characteristics

Reporting groups	
Reporting group title	Nilotinib

Reporting group description: -

Reporting group values	Nilotinib	Total	
Number of subjects	125	125	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	75	75	
From 65-84 years	50	50	
85 years and over	0	0	
Age Continuous Units: years			
arithmetic mean	60		
standard deviation	± 12.1	-	
Gender, Male/Female Units: participants			
Female	46	46	
Male	79	79	

End points

End points reporting groups

Reporting group title	Nilotinib

Reporting group description: -

Primary: Percent of patients achieving Stable Disease (SD)

End point title	Percent of patients achieving Stable Disease (SD)[1]

End point description:

End point type	Primary

End point timeframe:

During the first 4 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: one arm open label study, no comparison to other dose or arm possible

End point values	Nilotinib			
Subject group type	Reporting group			
Number of subjects analysed	125			
Units: % participants				
number (not applicable)	48.8			

Statistical analyses

No statistical analyses for this end point

Primary: Percent of patients achieving Partial Response (PR)

End point title	Percent of patients achieving Partial Response (PR)[2]

End point description:

End point type	Primary

End point timeframe:

during the first 4 months

Notes:

[2] - 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: one arm open label study, no comparison to other dose or arm possible

End point values	Nilotinib			
Subject group type	Reporting group			
Number of subjects analysed	125			
Units: percentage of participants	0			

Statistical analyses

No statistical analyses for this end point

Primary: Percent of patients achieving Complete response (CR)

End point title	Percent of patients achieving Complete response (CR)[3]

End point description:

End point type	Primary

End point timeframe:

during the first 4 months

Notes:

[3] - 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: one arm open label study, no comparison to other dose or arm possible

End point values	Nilotinib			
Subject group type	Reporting group			
Number of subjects analysed	125			
Units: percentage of participants	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to overall response (CR or PR): Intent to treat population

End point title	Time to overall response (CR or PR): Intent to treat population

End point description:

End point type	Secondary

End point timeframe:

24 weeks and 52 weeks

End point values	Nilotinib			
Subject group type	Reporting group			
Number of subjects analysed	125			
Units: days				
number (not applicable)				
24 weeks	92			
52 weeks	92			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to overall response (CR or PR): per protocol population

End point title	Time to overall response (CR or PR): per protocol population

End point description:

End point type	Secondary

End point timeframe:

24 weeks and 52 weeks

End point values	Nilotinib			
Subject group type	Reporting group			
Number of subjects analysed	98			
Units: days				
number (not applicable)				
24 weeks	91.2			
52 weeks	91.2			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to tumor progression

End point title	Time to tumor progression

End point description:

Time to tumor progression defined as the time from start of treatment to observed tumor progression (censoring for death without progression) as stated in the original protocol was not evaluated.

End point type	Secondary

End point timeframe:

during the first 4 months

End point values	Nilotinib			
Subject group type	Reporting group			
Number of subjects analysed	125			
Units: days	999			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of overall response

End point title	Duration of overall response

End point description:

End point type	Secondary

End point timeframe:
during 12 months

End point values	Nilotinib			
Subject group type	Reporting group			
Number of subjects analysed	125			
Units: days				
median (confidence interval 95%)	1331 (366 to 9999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival

End point title	Overall survival

End point description:
The OS could not be calculated due to the high number of censored cases.

End point type	Secondary

End point timeframe:
during 12 months

End point values	Nilotinib			
Subject group type	Reporting group			
Number of subjects analysed	125			
Units: days	999			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression free survival (PFS) of the patients who were included due to an intolerability of a prior treatment.

End point title	Progression free survival (PFS) of the patients who were included due to an intolerability of a prior treatment.

End point description:

End point type	Secondary

End point timeframe:

during 12 months

End point values	Nilotinib			
Subject group type	Reporting group			
Number of subjects analysed	125			
Units: days				
number (confidence interval 95%)	110 (64 to 118)			

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:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Nilotinib

Reporting group description:

Nilotinib

Serious adverse events	Nilotinib		
Total subjects affected by serious adverse events			
subjects affected / exposed	57 / 125 (45.60%)		
number of deaths (all causes)	12		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	3 / 125 (2.40%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Metastases to lung			
subjects affected / exposed	1 / 125 (0.80%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neoplasm progression			
subjects affected / exposed	1 / 125 (0.80%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tumour haemorrhage			

subjects affected / exposed	1 / 125 (0.80%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tumour pain			
subjects affected / exposed	3 / 125 (2.40%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Arterial occlusive disease			
subjects affected / exposed	1 / 125 (0.80%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Peripheral arterial occlusive disease			
subjects affected / exposed	1 / 125 (0.80%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 125 (0.80%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Chest pain			
subjects affected / exposed	1 / 125 (0.80%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Chills			
subjects affected / exposed	1 / 125 (0.80%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Condition aggravated			
subjects affected / exposed	2 / 125 (1.60%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Device occlusion				
subjects affected / exposed	2 / 125 (1.60%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Disease progression				
subjects affected / exposed	5 / 125 (4.00%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Fatigue				
subjects affected / exposed	3 / 125 (2.40%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	0 / 0			
General physical health deterioration				
subjects affected / exposed	3 / 125 (2.40%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Multi-organ failure				
subjects affected / exposed	1 / 125 (0.80%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Obstruction				
subjects affected / exposed	1 / 125 (0.80%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	5 / 125 (4.00%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Chronic obstructive pulmonary disease				
subjects affected / exposed	1 / 125 (0.80%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			

Dyspnoea				
subjects affected / exposed	1 / 125 (0.80%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	1 / 125 (0.80%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				
Amylase increased				
subjects affected / exposed	1 / 125 (0.80%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Blood creatinine increased				
subjects affected / exposed	1 / 125 (0.80%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
C-reactive protein increased				
subjects affected / exposed	2 / 125 (1.60%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Electrocardiogram QT prolonged				
subjects affected / exposed	1 / 125 (0.80%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Lipase increased				
subjects affected / exposed	2 / 125 (1.60%)			
occurrences causally related to treatment / all	3 / 3			
deaths causally related to treatment / all	0 / 0			
Weight decreased				
subjects affected / exposed	2 / 125 (1.60%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural				

complications			
Concussion			
subjects affected / exposed	1 / 125 (0.80%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lip injury			
subjects affected / exposed	1 / 125 (0.80%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	1 / 125 (0.80%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Angina unstable			
subjects affected / exposed	1 / 125 (0.80%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Aortic valve stenosis			
subjects affected / exposed	1 / 125 (0.80%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation			
subjects affected / exposed	1 / 125 (0.80%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac failure			
subjects affected / exposed	1 / 125 (0.80%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Coronary artery stenosis			
subjects affected / exposed	1 / 125 (0.80%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Myocardial infarction			
subjects affected / exposed	2 / 125 (1.60%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Intercostal neuralgia			
subjects affected / exposed	1 / 125 (0.80%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 125 (3.20%)		
occurrences causally related to treatment / all	3 / 4		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	7 / 125 (5.60%)		
occurrences causally related to treatment / all	0 / 9		
deaths causally related to treatment / all	0 / 0		
Abdominal pain upper			
subjects affected / exposed	1 / 125 (0.80%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal wall mass			
subjects affected / exposed	1 / 125 (0.80%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ascites			
subjects affected / exposed	2 / 125 (1.60%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Constipation			

subjects affected / exposed	3 / 125 (2.40%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	1 / 125 (0.80%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Flatulence				
subjects affected / exposed	1 / 125 (0.80%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lower gastrointestinal haemorrhage				
subjects affected / exposed	1 / 125 (0.80%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Melaena				
subjects affected / exposed	1 / 125 (0.80%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Mesenteric haemorrhage				
subjects affected / exposed	1 / 125 (0.80%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	2 / 125 (1.60%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Pancreatitis acute				
subjects affected / exposed	1 / 125 (0.80%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Subileus				

subjects affected / exposed	1 / 125 (0.80%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	5 / 125 (4.00%)		
occurrences causally related to treatment / all	1 / 5		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	1 / 125 (0.80%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cholestasis			
subjects affected / exposed	1 / 125 (0.80%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatotoxicity			
subjects affected / exposed	1 / 125 (0.80%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hyperbilirubinaemia			
subjects affected / exposed	1 / 125 (0.80%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	1 / 125 (0.80%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal failure			
subjects affected / exposed	2 / 125 (1.60%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Renal failure acute			

subjects affected / exposed	1 / 125 (0.80%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ureteric stenosis				
subjects affected / exposed	1 / 125 (0.80%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary retention				
subjects affected / exposed	1 / 125 (0.80%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary tract obstruction				
subjects affected / exposed	1 / 125 (0.80%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Breast abscess				
subjects affected / exposed	1 / 125 (0.80%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infected skin ulcer				
subjects affected / exposed	1 / 125 (0.80%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Infection				
subjects affected / exposed	1 / 125 (0.80%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	1 / 125 (0.80%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rectal abscess				

subjects affected / exposed	1 / 125 (0.80%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sinusitis			
subjects affected / exposed	1 / 125 (0.80%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Staphylococcal infection			
subjects affected / exposed	1 / 125 (0.80%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	1 / 125 (0.80%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	1 / 125 (0.80%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Decreased appetite			
subjects affected / exposed	1 / 125 (0.80%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyperglycaemia			
subjects affected / exposed	1 / 125 (0.80%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyperkalaemia			
subjects affected / exposed	1 / 125 (0.80%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Nilotinib		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	107 / 125 (85.60%)		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	8 / 125 (6.40%)		
occurrences (all)	10		
Blood alkaline phosphatase increased			
subjects affected / exposed	16 / 125 (12.80%)		
occurrences (all)	17		
Lipase increased			
subjects affected / exposed	7 / 125 (5.60%)		
occurrences (all)	8		
C-reactive protein increased			
subjects affected / exposed	9 / 125 (7.20%)		
occurrences (all)	9		
Transaminases increased			
subjects affected / exposed	7 / 125 (5.60%)		
occurrences (all)	8		
Weight decreased			
subjects affected / exposed	13 / 125 (10.40%)		
occurrences (all)	13		
Nervous system disorders			
Headache			
subjects affected / exposed	14 / 125 (11.20%)		
occurrences (all)	16		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	14 / 125 (11.20%)		
occurrences (all)	18		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	44 / 125 (35.20%)		
occurrences (all)	47		

Asthenia subjects affected / exposed occurrences (all)	10 / 125 (8.00%) 12		
Oedema peripheral subjects affected / exposed occurrences (all)	17 / 125 (13.60%) 18		
Pyrexia subjects affected / exposed occurrences (all)	19 / 125 (15.20%) 23		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	28 / 125 (22.40%) 34		
Abdominal pain upper subjects affected / exposed occurrences (all)	7 / 125 (5.60%) 8		
Constipation subjects affected / exposed occurrences (all)	30 / 125 (24.00%) 30		
Diarrhoea subjects affected / exposed occurrences (all)	16 / 125 (12.80%) 17		
Flatulence subjects affected / exposed occurrences (all)	13 / 125 (10.40%) 13		
Vomiting subjects affected / exposed occurrences (all)	21 / 125 (16.80%) 25		
Nausea subjects affected / exposed occurrences (all)	28 / 125 (22.40%) 31		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	8 / 125 (6.40%) 8		
Dyspnoea			

subjects affected / exposed occurrences (all)	8 / 125 (6.40%) 8		
Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all) Dry skin subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all)	 10 / 125 (8.00%) 10 21 / 125 (16.80%) 24 10 / 125 (8.00%) 10 10 / 125 (8.00%) 11		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) Arthralgia subjects affected / exposed occurrences (all) Myalgia subjects affected / exposed occurrences (all) Muscle spasms subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all)	 11 / 125 (8.80%) 13 8 / 125 (6.40%) 8 10 / 125 (8.00%) 12 9 / 125 (7.20%) 10 11 / 125 (8.80%) 14		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	 12 / 125 (9.60%) 16		
Metabolism and nutrition disorders			

Decreased appetite subjects affected / exposed occurrences (all)	18 / 125 (14.40%) 18		
Hypophosphataemia subjects affected / exposed occurrences (all)	7 / 125 (5.60%) 8		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 January 2009	• Additional laboratory evaluations were added to the protocol (visit 4b, day 45). All patients were seen on every 2nd week in the first two months of the study to control the hematology parameters. The additional measurements could also be performed at the general practitioner.
08 January 2010	• The exclusion section concerning oral, implantable or injectable contraceptives was edited specifying that hormonal contraception was not defined as appropriate contraception, since it may be affected by cytochrome P450 interactions.
29 January 2010	• The visit schedule for responding patients in the follow-up period was modified to allow for patients to continue to be followed every three months until tumor progression.
10 June 2011	• CAMN107DDE05 trial enrollment was prematurely stopped in accordance to a Novartis decision taken on May 5, 2011. The protocol was amended such that all patients who were receiving nilotinib and considered by the investigators to be deriving benefit had the option of further receiving nilotinib until disease progression. For Germany, those patients continued to be treated with nilotinib as foreseen by the protocol until disease progression. For Italy, patients deriving benefit from a treatment with nilotinib had the option to complete the core phase of this trial. After completion of the core phase, those patients still deriving benefit were transferred to a local compassionate use program allowing a treatment with nilotinib until disease progression. • The objectives to compare RECIST and Choi criteria for response and time-to-event variables and to provide patients with unresectable or metastatic GIST showing progression with nilotinib until registration of the drug for this disease were deleted. • The evaluation of the primary endpoints was modified to be done with local radiologist interpretations collected by the investigator in the eCRF instead of a central radiologist. • The time point of the primary safety and efficacy analysis was set to the time all patients who were still receiving study drug had completed 4 months of treatment (or discontinued prematurely). • In addition, changes to the statistical analysis section were implemented due to the premature stop of trial enrollment. These changes pertained to the sample size calculation, CI (Clopper-Pearson method) used and deletion of analysis by Choi criteria.
06 January 2014	• At the time of the Amendment, only two patients with metastatic GIST were currently benefiting from the nilotinib treatment within the CAMN107DDE05 trial in Germany. Changes were implemented to move these patients to study CAM107DDE06 to allow the closure of study CAMN107DDE05. • The post-text supplement was amended to update the list of cytochrome P450 3A4 inducers and inhibitors and the list of agents that prolong QT interval. • The background and the safety information of the protocol were updated according to the Investigator's Brochure v 9.0, safety cut-off 30-Apr-2013

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.

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com/CtrdWeb/home.novfor complete trial result

Notes: