Clinical trial results:
Randomized phase II study to compare vinorelbine in combination with the mTOR inhibitor everolimus versus vinorelbine monotherapy for second-line treatment in advanced breast cancer

Summary

EudraCT number	2011-001024-38
Trial protocol	DE
Global end of trial date	31 October 2016

Results information

Result version number	v1 (current)
This version publication date	09 July 2022
First version publication date	09 July 2022

Trial information

Trial identification

Sponsor protocol code	AIO-MAM-0110

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01520103
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AIO-Studien-gGmbH
Sponsor organisation address	Kuno-Fischer-Str. 8, Berlin, Germany,
Public contact	info@aio-studien-ggmbh.de, AIO-Studien-gGmbH, info@aio-studien-ggmbh.de
Scientific contact	info@aio-studien-ggmbh.de, AIO-Studien-gGmbH, info@aio-studien-ggmbh.de

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	09 June 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 October 2016
Global end of trial reached?	Yes
Global end of trial date	31 October 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary study goal was the evaluation of Progression-free survival (PFS).

Protection of trial subjects:

This study was planned, analyzed and conducted according to the study protocol and in accordance with the International Conference on Harmonization (ICH) ‚Guideline for Good Clinical Practice E6(R1)', CPMP/ICH/135/95, based on the principles of the Declaration of Helsinki (1964) and its October 1996 amendment (Somerset West, South Africa). The study was duly conducted in compliance with the German Arzneimittelgesetz (AMG; German Drug Law), and the corresponding Directive 2001/20/EC. Subjects were fully informed regarding all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the subject.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 December 2011
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	Germany: 133
Worldwide total number of subjects	133
EEA total number of subjects	133

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)	74
From 65 to 84 years	58

85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited between December 2011 and October 2016 at 32 study sites in Germany.

Pre-assignment

Screening details:

154 patients were screened, of which 138 were randomized. 5 patients refused study participation after randomization.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm 1 - Vinorelbine + Everolimus

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Vinorelbine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

In both treatment arms, vinorelbine was adminstered at 25 mg/m² on days 1, 8, and 15 of a q3w treatment cycle.

Investigational medicinal product name	Everolimus
Investigational medicinal product code	
Other name	Afinitor
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Everolimus was dosed at 5 mg daily.

Arm title	Arm 2 - Vinorelbine

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Vinorelbine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

In both treatment arms, vinorelbine was adminstered at 25 mg/m² on days 1, 8, and 15 of a q3w treatment cycle.

Number of subjects in period 1	Arm 1 - Vinorelbine + Everolimus	Arm 2 - Vinorelbine
Started	68	65
Completed	68	65

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	133	133	
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)	74	74	
From 65-84 years	58	58	
85 years and over	1	1	
Gender categorical Units: Subjects			
Female	133	133	
Male	0	0	

End points

End points reporting groups

Reporting group title	Arm 1 - Vinorelbine + Everolimus
Reporting group description: -	
Reporting group title	Arm 2 - Vinorelbine
Reporting group description: -	

Primary: Progression-free survival

End point title	Progression-free survival
End point description:	
Tumor assessments were performed at screening and subsequently after start of study treatment every nine weeks. The primary endpoint analysis of PFS was done at 111 events.	
End point type	Primary
End point timeframe:	
PFS was calculated from date of randomization. Patients were followed for disease progression until End of Study. Patients for whom no date of death was recorded were censored at last date of contact.	

End point values	Arm 1 - Vinorelbine + Everolimus	Arm 2 - Vinorelbine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	65		
Units: Months				
median (confidence interval 95%)	4.08 (2.78 to 6.32)	4.21 (3.03 to 6.35)		

Statistical analyses

Statistical analysis title	Statistical analysis of primary endpoint PFS
Comparison groups	Arm 1 - Vinorelbine + Everolimus v Arm 2 - Vinorelbine
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.977
Method	Logrank
Parameter estimate	Cox proportional hazard
Point estimate	1.006
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.691
upper limit	1.464

Secondary: Overall survival

End point title	Overall survival

End point description:

End point type	Secondary

End point timeframe:

OS was calculated from date of randomization. Patients were followed for survival until End of Study. Patients for whom no date of death was recorded were censored at last date of contact.

End point values	Arm 1 - Vinorelbine + Everolimus	Arm 2 - Vinorelbine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	65		
Units: Months				
median (confidence interval 95%)	17.3 (12.47 to 19.34)	14.8 (11.2 to 22.43)		

Statistical analyses

No statistical analyses for this end point

Secondary: PFS rate at 6 months

End point title	PFS rate at 6 months

End point description:

End point type	Secondary

End point timeframe:

For this endpoint, disease status (progressed/not progressed) at six months post randomization was evaluated.

End point values	Arm 1 - Vinorelbine + Everolimus	Arm 2 - Vinorelbine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	65		
Units: Percentage of patients without PD				
number (confidence interval 95%)	41.1 (28.81 to 52.98)	40.5 (27.65 to 52.90)		

Statistical analyses

No statistical analyses for this end point

Secondary: Best overall response

End point title	Best overall response

End point description:

Best overall response was not different between the treatment arms.

End point type	Secondary

End point timeframe:

Participants were tracked for response from randomization until End of Study. For each patient, the best response from the start of treatment until disease progression was counted towards this endpoint.

End point values	Arm 1 - Vinorelbine + Everolimus	Arm 2 - Vinorelbine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	65		
Units: Best response per patient				
CR	0	1		
PR	8	11		
SD	18	15		
PD	33	32		
Non-CR/Non-PD	2	0		
Not evaluable	1	0		
Not evaluated	6	6		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were recorded from day of first study treatment until 30 days after last study treatment.

Adverse event reporting additional description:

The section dedicated to the reporting of non-serious adverse events contains, for this trial, reports of ALL adverse events, serious and non-serious, as isolated data for non-serious events only is not readily retrievable.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	Arm 1 - Vinorelbine + Everolimus
Reporting group description: -	
Reporting group title	Arm 2 - Vinorelbine

Reporting group description: -

Serious adverse events	Arm 1 - Vinorelbine + Everolimus	Arm 2 - Vinorelbine	
Total subjects affected by serious adverse events			
subjects affected / exposed	28 / 68 (41.18%)	23 / 65 (35.38%)	
number of deaths (all causes)	47	43	
number of deaths resulting from adverse events	6	5	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	4 / 68 (5.88%)	1 / 65 (1.54%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
Metastases to peritoneum			
subjects affected / exposed	1 / 68 (1.47%)	0 / 65 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Neoplasm progression			
subjects affected / exposed	0 / 68 (0.00%)	1 / 65 (1.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Vascular disorders			

Deep vein thrombosis			
subjects affected / exposed	0 / 68 (0.00%)	1 / 65 (1.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			
subjects affected / exposed	0 / 68 (0.00%)	1 / 65 (1.54%)	
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			
Asthenia			
subjects affected / exposed	1 / 68 (1.47%)	0 / 65 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	1 / 68 (1.47%)	0 / 65 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Disease progression			
subjects affected / exposed	1 / 68 (1.47%)	1 / 65 (1.54%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Fatigue			
subjects affected / exposed	2 / 68 (2.94%)	0 / 65 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	5 / 68 (7.35%)	2 / 65 (3.08%)	
occurrences causally related to treatment / all	2 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	3 / 68 (4.41%)	2 / 65 (3.08%)	
occurrences causally related to treatment / all	1 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 68 (0.00%)	1 / 65 (1.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 68 (1.47%)	0 / 65 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	2 / 68 (2.94%)	1 / 65 (1.54%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung disorder			
subjects affected / exposed	0 / 68 (0.00%)	1 / 65 (1.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 68 (1.47%)	3 / 65 (4.62%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	3 / 68 (4.41%)	0 / 65 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 68 (1.47%)	2 / 65 (3.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Psychiatric disorders			
Mood altered			

subjects affected / exposed	1 / 68 (1.47%)	0 / 65 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 68 (0.00%)	1 / 65 (1.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transaminases increased			
subjects affected / exposed	0 / 68 (0.00%)	1 / 65 (1.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Thoracic vertebral fracture			
subjects affected / exposed	0 / 68 (0.00%)	1 / 65 (1.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	1 / 68 (1.47%)	0 / 65 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Coronary artery disease			
subjects affected / exposed	0 / 68 (0.00%)	1 / 65 (1.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular dysfunction			
subjects affected / exposed	0 / 68 (0.00%)	1 / 65 (1.54%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Right ventricular failure			

subjects affected / exposed	1 / 68 (1.47%)	0 / 65 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 68 (0.00%)	1 / 65 (1.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 68 (0.00%)	2 / 65 (3.08%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Agranulocytosis			
subjects affected / exposed	1 / 68 (1.47%)	0 / 65 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	0 / 68 (0.00%)	1 / 65 (1.54%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	1 / 68 (1.47%)	1 / 65 (1.54%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	1 / 68 (1.47%)	0 / 65 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 68 (0.00%)	1 / 65 (1.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastrointestinal disorders			
Anal fistula			
subjects affected / exposed	0 / 68 (0.00%)	1 / 65 (1.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	2 / 68 (2.94%)	0 / 65 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 68 (1.47%)	0 / 65 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Faecaloma			
subjects affected / exposed	1 / 68 (1.47%)	0 / 65 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis erosive			
subjects affected / exposed	0 / 68 (0.00%)	1 / 65 (1.54%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			
subjects affected / exposed	1 / 68 (1.47%)	0 / 65 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	1 / 68 (1.47%)	1 / 65 (1.54%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Nausea			
subjects affected / exposed	3 / 68 (4.41%)	0 / 65 (0.00%)	
occurrences causally related to treatment / all	3 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatitis			

subjects affected / exposed	1 / 68 (1.47%)	0 / 65 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	2 / 68 (2.94%)	0 / 65 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	1 / 68 (1.47%)	0 / 65 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Prerenal failure			
subjects affected / exposed	0 / 68 (0.00%)	1 / 65 (1.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	0 / 68 (0.00%)	1 / 65 (1.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteric compression			
subjects affected / exposed	0 / 68 (0.00%)	1 / 65 (1.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract obstruction			
subjects affected / exposed	0 / 68 (0.00%)	1 / 65 (1.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	0 / 68 (0.00%)	1 / 65 (1.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infections and infestations			
Device related infection			
subjects affected / exposed	0 / 68 (0.00%)	1 / 65 (1.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile infection			
subjects affected / exposed	1 / 68 (1.47%)	1 / 65 (1.54%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngitis			
subjects affected / exposed	0 / 68 (0.00%)	1 / 65 (1.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mastitis			
subjects affected / exposed	0 / 68 (0.00%)	1 / 65 (1.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic infection			
subjects affected / exposed	1 / 68 (1.47%)	0 / 65 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ophthalmic herpes zoster			
subjects affected / exposed	1 / 68 (1.47%)	0 / 65 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	4 / 68 (5.88%)	2 / 65 (3.08%)	
occurrences causally related to treatment / all	4 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	3 / 68 (4.41%)	0 / 65 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth abscess			

subjects affected / exposed	1 / 68 (1.47%)	0 / 65 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 68 (1.47%)	1 / 65 (1.54%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 68 (0.00%)	1 / 65 (1.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 68 (1.47%)	1 / 65 (1.54%)	
occurrences causally related to treatment / all	1 / 1	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	Arm 1 - Vinorelbine + Everolimus	Arm 2 - Vinorelbine	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	68 / 68 (100.00%)	64 / 65 (98.46%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	4 / 68 (5.88%)	1 / 65 (1.54%)	
occurrences (all)	4	1	
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 68 (7.35%)	1 / 65 (1.54%)	
occurrences (all)	5	1	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	8 / 68 (11.76%)	4 / 65 (6.15%)	
occurrences (all)	9	4	
Chills			

subjects affected / exposed	5 / 68 (7.35%)	6 / 65 (9.23%)	
occurrences (all)	9	6	
Fatigue			
subjects affected / exposed	26 / 68 (38.24%)	27 / 65 (41.54%)	
occurrences (all)	31	29	
General physical health deterioration			
subjects affected / exposed	6 / 68 (8.82%)	6 / 65 (9.23%)	
occurrences (all)	6	7	
Mucosal inflammation			
subjects affected / exposed	7 / 68 (10.29%)	4 / 65 (6.15%)	
occurrences (all)	8	6	
Oedema peripheral			
subjects affected / exposed	4 / 68 (5.88%)	3 / 65 (4.62%)	
occurrences (all)	4	3	
Pain			
subjects affected / exposed	4 / 68 (5.88%)	11 / 65 (16.92%)	
occurrences (all)	4	15	
Pyrexia			
subjects affected / exposed	15 / 68 (22.06%)	8 / 65 (12.31%)	
occurrences (all)	15	13	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	12 / 68 (17.65%)	5 / 65 (7.69%)	
occurrences (all)	13	5	
Dyspnoea			
subjects affected / exposed	13 / 68 (19.12%)	10 / 65 (15.38%)	
occurrences (all)	15	12	
Epistaxis			
subjects affected / exposed	12 / 68 (17.65%)	2 / 65 (3.08%)	
occurrences (all)	13	2	
Pneumonitis			
subjects affected / exposed	4 / 68 (5.88%)	0 / 65 (0.00%)	
occurrences (all)	4	0	
Psychiatric disorders			

Depression			
subjects affected / exposed	4 / 68 (5.88%)	3 / 65 (4.62%)	
occurrences (all)	4	3	
Insomnia			
subjects affected / exposed	4 / 68 (5.88%)	1 / 65 (1.54%)	
occurrences (all)	4	1	
Sleep disorder			
subjects affected / exposed	4 / 68 (5.88%)	7 / 65 (10.77%)	
occurrences (all)	4	8	
Investigations			
Weight decreased			
subjects affected / exposed	2 / 68 (2.94%)	6 / 65 (9.23%)	
occurrences (all)	2	6	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	4 / 68 (5.88%)	0 / 65 (0.00%)	
occurrences (all)	4	0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	5 / 68 (7.35%)	7 / 65 (10.77%)	
occurrences (all)	5	10	
Dysgeusia			
subjects affected / exposed	7 / 68 (10.29%)	1 / 65 (1.54%)	
occurrences (all)	7	1	
Headache			
subjects affected / exposed	10 / 68 (14.71%)	9 / 65 (13.85%)	
occurrences (all)	11	11	
Paraesthesia			
subjects affected / exposed	7 / 68 (10.29%)	4 / 65 (6.15%)	
occurrences (all)	7	4	
Peripheral sensory neuropathy			
subjects affected / exposed	4 / 68 (5.88%)	6 / 65 (9.23%)	
occurrences (all)	4	6	
Polyneuropathy			
subjects affected / exposed	2 / 68 (2.94%)	4 / 65 (6.15%)	
occurrences (all)	2	4	
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	26 / 68 (38.24%)	20 / 65 (30.77%)	
occurrences (all)	31	27	
Leukopenia			
subjects affected / exposed	30 / 68 (44.12%)	21 / 65 (32.31%)	
occurrences (all)	49	40	
Neutropenia			
subjects affected / exposed	40 / 68 (58.82%)	27 / 65 (41.54%)	
occurrences (all)	95	75	
Thrombocytopenia			
subjects affected / exposed	9 / 68 (13.24%)	2 / 65 (3.08%)	
occurrences (all)	11	2	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	5 / 68 (7.35%)	4 / 65 (6.15%)	
occurrences (all)	7	4	
Abdominal pain upper			
subjects affected / exposed	5 / 68 (7.35%)	7 / 65 (10.77%)	
occurrences (all)	9	9	
Aphthous ulcer			
subjects affected / exposed	4 / 68 (5.88%)	0 / 65 (0.00%)	
occurrences (all)	6	0	
Constipation			
subjects affected / exposed	13 / 68 (19.12%)	16 / 65 (24.62%)	
occurrences (all)	13	18	
Diarrhoea			
subjects affected / exposed	17 / 68 (25.00%)	8 / 65 (12.31%)	
occurrences (all)	26	10	
Dysphagia			
subjects affected / exposed	4 / 68 (5.88%)	0 / 65 (0.00%)	
occurrences (all)	5	0	
Nausea			
subjects affected / exposed	20 / 68 (29.41%)	21 / 65 (32.31%)	
occurrences (all)	25	27	
Stomatitis			

subjects affected / exposed	21 / 68 (30.88%)	5 / 65 (7.69%)	
occurrences (all)	28	8	
Vomiting			
subjects affected / exposed	8 / 68 (11.76%)	9 / 65 (13.85%)	
occurrences (all)	11	10	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	7 / 68 (10.29%)	9 / 65 (13.85%)	
occurrences (all)	7	10	
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	4 / 68 (5.88%)	1 / 65 (1.54%)	
occurrences (all)	4	1	
Rash			
subjects affected / exposed	5 / 68 (7.35%)	4 / 65 (6.15%)	
occurrences (all)	6	6	
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	1 / 68 (1.47%)	4 / 65 (6.15%)	
occurrences (all)	1	4	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 68 (7.35%)	2 / 65 (3.08%)	
occurrences (all)	5	4	
Back pain			
subjects affected / exposed	9 / 68 (13.24%)	3 / 65 (4.62%)	
occurrences (all)	11	3	
Bone pain			
subjects affected / exposed	5 / 68 (7.35%)	7 / 65 (10.77%)	
occurrences (all)	5	7	
Muscle spasms			
subjects affected / exposed	4 / 68 (5.88%)	5 / 65 (7.69%)	
occurrences (all)	7	6	
Myalgia			
subjects affected / exposed	5 / 68 (7.35%)	2 / 65 (3.08%)	
occurrences (all)	5	2	
Pain in extremity			

subjects affected / exposed	5 / 68 (7.35%)	6 / 65 (9.23%)	
occurrences (all)	5	6	
Infections and infestations			
Bronchitis			
subjects affected / exposed	5 / 68 (7.35%)	4 / 65 (6.15%)	
occurrences (all)	6	4	
Nasopharyngitis			
subjects affected / exposed	6 / 68 (8.82%)	6 / 65 (9.23%)	
occurrences (all)	7	8	
Pneumonia			
subjects affected / exposed	6 / 68 (8.82%)	2 / 65 (3.08%)	
occurrences (all)	6	2	
Urinary tract infection			
subjects affected / exposed	7 / 68 (10.29%)	9 / 65 (13.85%)	
occurrences (all)	7	10	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	9 / 68 (13.24%)	10 / 65 (15.38%)	
occurrences (all)	10	11	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 December 2011	The study was initially designed as a single-arm trial investigating vinorelbine + everolimus combination treatment. With this substantial protocol amendment, a vinorelbine monotheray arm was added. Based on ecent results from another trial, the underlying rationale was to assess possible synergistic effects of combined chemotherapy. The targeted number of study subjects and study sites was increased to accommodate the new design. No patients had been enrolled into the study at the time of the amendment.
12 May 2016	With this amendment, the patient accrual target was reduced, as recruitment had decreased over the course of the study, and the initial target could not be reached within a realistic time frame. In addition, study duration was reduced from 12 to 7 months of post-treatment follow-up for the last treated patient.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/31115844