Clinical trial results:
A Randomized, Phase IIb/III Study of Ganetespib (STA-9090) in Combination with Docetaxel versus Docetaxel alone in Subjects with Stage IIIb or IV Non-Small Cell Lung Cancer

Summary

EudraCT number	2011-001084-42
Trial protocol	CZ DE GB HU ES BE PL
Global end of trial date	04 November 2015

Results information

Result version number	v1 (current)
This version publication date	02 April 2016
First version publication date	02 April 2016

Trial information

Trial identification

Sponsor protocol code	9090-08

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01348126
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Synta Pharmaceuticals Corp
Sponsor organisation address	45 Hartwell Avenue, Lexington, MA, United States, 02421
Public contact	VP Clinical Research, Synta Pharmaceuticals Corp, 001 781-541-7156 ,
Scientific contact	VP Clinical Research, Synta Pharmaceuticals Corp, 001 781-541-7156 ,

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	21 December 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	04 November 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Randomized multicenter, parallel group study of patients with Stage IIIB or IV NSCLC who failed 1 prior systemic therapy for advanced disease and had measurable disease, as defined by RECIST criteria .
Stage 1
• Evaluate progression-free survival (PFS) in subjects with non-small-cell lung cancer (NSCLC) with adenocarcinoma histology who present with elevated
baseline total lactate dehydrogenase (LDH), treated with the combination of ganetespib and docetaxel compared to docetaxel alone
• Evaluate PFS in subjects with KRAS mutated NSCLC.

Stage 2
• Assess OS in subjects with stage IIIB or IV NSCLC treated with the combination of ganetespib and docetaxel compared to docetaxel alone. Stage 2 (the Phase 3 portion of the study) was never implemented as a part of this study. The Phase 3 study, Protocol 9090-14 was initiated instead.

Protection of trial subjects:

All Investigators obtained Independent Ethics Committee (IEC) or Institutional Review Board (IRB) approval for this protocol and written informed consent prior to study initiation in adherence with 21 Code of Federal Regulations (CFR) 50 and 21 CFR 56.

This trial was designed and monitored in accordance with Sponsor procedures, which comply with the ethical principles of Good Clinical Practice (GCP) as required by the major regulatory authorities, and in accordance with the Declaration of Helsinki.

Prior to the start of any protocol-specific evaluations or screening procedures, the Investigator (or designated staff) explained the nature of the study and its risks and benefits to the patient (or the patient's legal representative). Each patient received an informed consent document with patient information. Patients were to be given ample time to read the information and the opportunity to ask questions. Informed consent was required to be obtained from each patient prior to performing any protocol-specific evaluations. One copy of the signed informed consent document was given to the patient, and another was
retained by the Investigator.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 June 2011
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	Poland: 20
Country: Number of subjects enrolled	Spain: 20
Country: Number of subjects enrolled	United Kingdom: 20

Country: Number of subjects enrolled	Belgium: 3
Country: Number of subjects enrolled	Czech Republic: 6
Country: Number of subjects enrolled	Germany: 25
Country: Number of subjects enrolled	Bosnia and Herzegovina: 23
Country: Number of subjects enrolled	Croatia: 14
Country: Number of subjects enrolled	Romania: 25
Country: Number of subjects enrolled	Serbia: 107
Country: Number of subjects enrolled	Ukraine: 33
Country: Number of subjects enrolled	Canada: 16
Country: Number of subjects enrolled	United States: 40
Country: Number of subjects enrolled	Russian Federation: 33
Worldwide total number of subjects	385
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)	272
From 65 to 84 years	111
85 years and over	2

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 685 patients with advanced NSCLC of all histologies were screened and 385 such patients were randomized.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Ganetespib + Docetaxel

Arm description:

On Day 1 of each 3-week treatment cycle, ganetespib (150 mg/m^2) and docetaxel (75 mg/m^2) were administered as separate 1-hour intravenous infusions. There was a 1-hour "rest" period following the end of the ganetespib infusion prior to docetaxel infusion. Ganetespib 150 mg/m^2 was administered again on Day 15 of each cycle.
Participating patients were to be treated until intolerability or disease progression.

Arm type	Experimental
Investigational medicinal product name	Ganetespib
Investigational medicinal product code	
Other name	STA-9090
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Ganetespib was infused over 60 minutes, approximately, at a dose of 150 mg/m^2 on Day 1 an Day 15 of each three week cycle. The amount of ganetespib to be administered was determined by calculating the patient's body surface area and was recalculated on Day 1 of each cycle during the course of the study.

Investigational medicinal product name	Docetaxel
Investigational medicinal product code	
Other name	Taxotere, Docecad
Pharmaceutical forms	Solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Docetaxel 75 mg/m^2 was administered on Day 1 of a 3-week treatment cycle by 1-hour intravenous infusion. The amount of docetaxel administered was determined by calculating the patient's body surface area and was recalculated on Day 1 of each cycle during the course of the study. Premedication for docetaxel followed the local institutional standard of care guidelines.

Arm title	Docetaxel

Arm description:

On Day 1 of each 3-week treatment cycle, docetaxel (75 mg/m^2) was administered as a 1-hour intravenous infusion. Participating patients were treated until intolerability or disease progression.

Arm type	Active comparator

Investigational medicinal product name	Docetaxel
Investigational medicinal product code	
Other name	Taxotere, Docecad
Pharmaceutical forms	Solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Docetaxel 75 mg/m^2 was administered on Day 1 of a 3-week treatment cycle by 1-hour intravenous infusion. The amount of docetaxel administered was determined by calculating the patient's body surface area and was recalculated on Day 1 of each cycle during the course of the study. Premedication for docetaxel followed the local institutional standard of care guidelines.

Number of subjects in period 1	Ganetespib + Docetaxel	Docetaxel
Started	197	188
Patients treated (>= 1 dose)	195	186
Completed	0	0
Not completed	197	188
Adverse event, serious fatal	16	17
Clinical progression	23	17
Consent withdrawn by subject	11	14
Adverse event, non-fatal	17	15
Symptomatic deterioration	12	4
Objective disease progression (RECIST)	102	80
Sponsor decision	2	-
Treatment completed	5	35
not specified	9	6

Baseline characteristics

Reporting groups	
Reporting group title	Ganetespib + Docetaxel
Reporting group description:	
On Day 1 of each 3-week treatment cycle, ganetespib (150 mg/m^2) and docetaxel (75 mg/m^2) were administered as separate 1-hour intravenous infusions. There was a 1-hour "rest" period following the end of the ganetespib infusion prior to docetaxel infusion. Ganetespib 150 mg/m^2 was administered again on Day 15 of each cycle. Participating patients were to be treated until intolerability or disease progression.	
Reporting group title	Docetaxel
Reporting group description:	
On Day 1 of each 3-week treatment cycle, docetaxel (75 mg/m^2) was administered as a 1-hour intravenous infusion. Participating patients were treated until intolerability or disease progression.	

Reporting group values	Ganetespib + Docetaxel	Docetaxel	Total
Number of subjects	197	188	385
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
arithmetic mean	60.7	59.9	
standard deviation	± 8.22	± 9.13	-
Gender categorical Units: Subjects			
Female	75	71	146
Male	122	117	239
Histology Units: Subjects			
Squamous Cell Carcinoma	34	25	59
Adenocarcinoma	158	156	314
Large Cell Carcinoma	1	2	3
Adenosquamous Carcinoma	2	3	5
Not Specified	2	2	4

End points

End points reporting groups

Reporting group title	Ganetespib + Docetaxel

Reporting group description:

On Day 1 of each 3-week treatment cycle, ganetespib (150 mg/m^2) and docetaxel (75 mg/m^2) were administered as separate 1-hour intravenous infusions. There was a 1-hour "rest" period following the end of the ganetespib infusion prior to docetaxel infusion. Ganetespib 150 mg/m^2 was administered again on Day 15 of each cycle.
Participating patients were to be treated until intolerability or disease progression.

Reporting group title	Docetaxel

Reporting group description:

On Day 1 of each 3-week treatment cycle, docetaxel (75 mg/m^2) was administered as a 1-hour intravenous infusion. Participating patients were treated until intolerability or disease progression.

Subject analysis set title	Ganetespib + Docetaxel: eLDH
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Includes subjects with baseline lactate dehydrogenase values above the normal range.
On Day 1 of each 3-week treatment cycle, ganetespib (150 mg/m^2) and docetaxel (75 mg/m^2) were administered as separate 1-hour intravenous infusions. There was a 1-hour "rest" period following the end of the ganetespib infusion prior to docetaxel infusion. Ganetespib 150 mg/m^2 was administered again on Day 15 of each cycle.
Participating patients were to be treated until intolerability or disease progression.

Subject analysis set title	Docetaxel: eLDH
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Includes subjects with baseline lactate dehydrogenase values above the normal range.
On Day 1 of each 3-week treatment cycle, docetaxel (75 mg/m^2) was administered as a 1-hour intravenous infusion. Participating patients were treated until intolerability or disease progression.

Subject analysis set title	Ganetespib + Docetaxel: mKRAS
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Includes subjects with mutated KRAS (V-Ki-ras2, Kirsten rat sarcoma viral oncogene homolog).
On Day 1 of each 3-week treatment cycle, ganetespib (150 mg/m^2) and docetaxel (75 mg/m^2) were administered as separate 1-hour intravenous infusions. There was a 1-hour "rest" period following the end of the ganetespib infusion prior to docetaxel infusion. Ganetespib 150 mg/m^2 was administered again on Day 15 of each cycle.
Participating patients were to be treated until intolerability or disease progression.

Subject analysis set title	Docetaxel: mKRAS
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Includes subjects with mutated KRAS (V-Ki-ras2, Kirsten rat sarcoma viral oncogene homolog).
On Day 1 of each 3-week treatment cycle, docetaxel (75 mg/m^2) was administered as a 1-hour intravenous infusion. Participating patients were treated until intolerability or disease progression.

Subject analysis set title	Ganetespib + Docetaxel: Adenocarcinoma
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Includes subjects with adenocarcinoma histology.
On Day 1 of each 3-week treatment cycle, ganetespib (150 mg/m^2) and docetaxel (75 mg/m^2) were administered as separate 1-hour intravenous infusions. There was a 1-hour "rest" period following the end of the ganetespib infusion prior to docetaxel infusion. Ganetespib 150 mg/m^2 was administered again on Day 15 of each cycle.
Participating patients were to be treated until intolerability or disease progression.

Subject analysis set title	Docetaxel: Adenocarcinoma
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Includes subjects with adenocarcinoma histology.

On Day 1 of each 3-week treatment cycle, docetaxel (75 mg/m^2) was administered as a 1-hour intravenous infusion. Participating patients were treated until intolerability or disease progression.

Primary: Kaplan-Meier Estimates for Progression Free Survival (PFS) in Adenocarcinoma Subjects with Elevated Baseline Serum Lactate Dehydrogenase (eLDH)

End point title	Kaplan-Meier Estimates for Progression Free Survival (PFS) in Adenocarcinoma Subjects with Elevated Baseline Serum Lactate Dehydrogenase (eLDH)

End point description:

PFS was measured from the date of randomization until disease progression or death from any cause in the absence of disease progression. Disease progression (PD) was defined as at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum of diameters on study. In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 mm.
The range for normal total LDH was 97 – 236 U/L and elevated LDH was total LDH ≥237 U/L.
Adenocarcinoma patients with eLDH enrolled after Amendment 3 contribute to this endpoint. This excludes the first 27 adenocarcinoma patients with eLDH whose data were used in an interim analysis that established this endpoint in Amendment 3.
Results from the 30 April 2014 data set.

End point type	Primary

End point timeframe:

Day 1 to 25 months

End point values	Ganetespib + Docetaxel	Docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44[1]	43[2]		
Units: months				
median (confidence interval 90%)	2.8 (1.4 to 3.5)	2.7 (1.4 to 3.9)		

Notes:

[1] - Randomized adenocarcinoma eLDH patients enrolled after Protocol Amendment 3

[2] - Randomized adenocarcinoma eLDH patients enrolled after Protocol Amendment 3

Statistical analyses

Statistical analysis title	PFS - adenocarcinoma eLDH population
Comparison groups	Ganetespib + Docetaxel v Docetaxel
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5949 [3]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.059
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.714
upper limit	1.571

Notes:

[3] - P-value was from a 1-sided stratified log rank test (strata: LDH, ECOG, smoking status, and interval between diagnosis of advanced disease and randomization)

Primary: Kaplan-Meier Estimates for Progression Free Survival (PFS) in Subjects with mKRAS

End point title	Kaplan-Meier Estimates for Progression Free Survival (PFS) in Subjects with mKRAS

End point description:

PFS was measured from the date of randomization until disease progression or death from any cause in the absence of disease progression. Disease progression (PD) was defined as at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum of diameters on study. In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 mm.
Mutations in the oncogene KRAS occur in approximately 20% of NSCLC tumors and therefore represent one of the largest molecularly profiled subsets of NSCLC patients.
Results from the 30 April 2014 data set.

End point type	Primary

End point timeframe:

Day 1 up to 25 months

End point values	Ganetespib + Docetaxel	Docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42[4]	47[5]		
Units: months				
median (confidence interval 90%)	3.9 (2.9 to 4.2)	3 (2.7 to 4.2)		

Notes:

[4] - Randomized mKRAS patients

[5] - Randomized mKRAS patients

Statistical analyses

Statistical analysis title	PFS - mKRAS population
Comparison groups	Ganetespib + Docetaxel v Docetaxel
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3865 [6]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.934
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.632
upper limit	1.379

Notes:

[6] - 1-sided Log-Rank P-value stratified by LDH, ECOG, smoking status, and interval between diagnosis of advanced disease and randomization.

Secondary: Kaplan-Meier Estimates for Progression Free Survival (PFS) in

Adenocarcinoma Subjects

End point title	Kaplan-Meier Estimates for Progression Free Survival (PFS) in Adenocarcinoma Subjects

End point description:

PFS was measured from the date of randomization until disease progression or death from any cause in the absence of disease progression. Disease progression (PD) was defined as at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum of diameters on study. In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 mm.
Statistical analyses include the effect of individual prognostic factors on PFS; sex, smoking status, baseline LDH, ECOG upon entry, interval since advanced NSCLC diagnosis, age, total baseline target lesions tumor size, and region.
Results from the 30 April 2014 data set.

End point type	Secondary

End point timeframe:

Day 1 up to 25 months

End point values	Ganetespib + Docetaxel	Docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	125[7]	128[8]		
Units: months				
median (confidence interval 90%)	4.5 (4.1 to 5.5)	3.2 (2.8 to 4.1)		

Notes:

[7] - Randomize patients with adenocarcinoma

[8] - Randomize patients with adenocarcinoma

Statistical analyses

Statistical analysis title	PFS - adenocarcinoma population
Comparison groups	Ganetespib + Docetaxel v Docetaxel
Number of subjects included in analysis	253
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1117 [9]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.846
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.672
upper limit	1.065

Notes:

[9] - Strata: ECOG PS (0 vs 1), screening total LDH levels (normal vs. elevated), smoking status (never smoked, current smoker, past smoker), and interval since initial diagnosis of advanced disease (≤6 vs. >6 months).

Statistical analysis title	PFS - adenocarcinoma population: Sex

Statistical analysis description:

Factor: Sex
Hazard ratio, 90% CI, and p-values for each factor were obtained from Cox PH model including only that factor as a covariate.

Comparison groups	Ganetespib + Docetaxel v Docetaxel
Number of subjects included in analysis	253
Analysis specification	Pre-specified
Analysis type	other[10]
P-value	= 0.7892 [11]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.419
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.122
upper limit	1.794

Notes:

[10] - Effect of the prognostic factor of sex (male vs female) on PFS.

[11] - p-value for the interaction term is from the Cox model containing only the predictor of interest, treatment, and their interaction.

Statistical analysis title	PFS - adenocarcinoma population: Smoking Status

Statistical analysis description:

Factor: Smoking status
Hazard ratio, 90% CI, and p-values for each factor were obtained from Cox PH model including only that factor as a covariate.

Comparison groups	Ganetespib + Docetaxel v Docetaxel
Number of subjects included in analysis	253
Analysis specification	Pre-specified
Analysis type	other[12]
P-value	= 0.4588 [13]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.605
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.459
upper limit	0.796

Notes:

[12] - Effect of the prognostic factor of smoking status (never vs. ever) on PFS.

[13] - p-value for the interaction term is from the Cox model containing only the predictor of interest, treatment, and their interaction.

Statistical analysis title	PFS - adenocarcinoma population: Baseline LDH

Statistical analysis description:

Factor: Baseline LDH
Hazard ratio, 90% CI, and p-values for each factor were obtained from Cox PH model including only that factor as a covariate.

Comparison groups	Ganetespib + Docetaxel v Docetaxel
Number of subjects included in analysis	253
Analysis specification	Pre-specified
Analysis type	other[14]
P-value	= 0.8009 [15]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.738

Confidence interval	
level	90 %
sides	2-sided
lower limit	1.352
upper limit	2.233

Notes:

[14] - Effect of the prognostic factor of baseline LDH (elevated vs. normal) on PFS.

[15] - p-value for the interaction term is from the Cox model containing only the predictor of interest, treatment, and their interaction.

Statistical analysis title	PFS - adenocarcinoma population: ECOG at entry

Statistical analysis description:

Factor: ECOG at entry
Hazard ratio, 90% CI, and p-values for each factor were obtained from Cox PH model including only that factor as a covariate.

Comparison groups	Ganetespib + Docetaxel v Docetaxel
Number of subjects included in analysis	253
Analysis specification	Pre-specified
Analysis type	other[16]
P-value	= 0.4755 [17]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.446
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.142
upper limit	1.832

Notes:

[16] - Effect of the prognostic factor of ECOG at entry (>=1 vs. 0) on PFS.

[17] - p-value for the interaction term is from the Cox model containing only the predictor of interest, treatment, and their interaction.

Statistical analysis title	PFS - adenocarcinoma population: time since NSCLC

Statistical analysis description:

Factor: Interval since advanced NSCLC diagnosis
Hazard ratio, 90% CI, and p-values for each factor were obtained from Cox PH model including only that factor as a covariate.

Comparison groups	Ganetespib + Docetaxel v Docetaxel
Number of subjects included in analysis	253
Analysis specification	Pre-specified
Analysis type	other[18]
P-value	= 0.1877 [19]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.781
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.608
upper limit	1.002

Notes:

[18] - Effect of the prognostic factor of Interval since advanced NSCLC diagnosis (>6 vs. <=6 months) on PFS.

[19] - p-value for the interaction term is from the Cox model containing only the predictor of interest, treatment, and their interaction.

Statistical analysis title	PFS - adenocarcinoma population: age

Statistical analysis description:

Factor: age
Hazard ratio, 90% CI, and p-values for each factor were obtained from Cox PH model including only that factor as a covariate.

Comparison groups	Ganetespib + Docetaxel v Docetaxel
Number of subjects included in analysis	253
Analysis specification	Pre-specified
Analysis type	other[20]
P-value	= 0.6136 [21]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.993
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.979
upper limit	1.006

Notes:

[20] - Effect of the prognostic factor of age (years) on PFS.

[21] - p-value for the interaction term is from the Cox model containing only the predictor of interest, treatment, and their interaction.

Statistical analysis title	PFS - adenocarcinoma population: tumor size

Statistical analysis description:

Factor: total baseline target lesions tumor size
Hazard ratio, 90% CI, and p-values for each factor were obtained from Cox PH model including only that factor as a covariate.

Comparison groups	Ganetespib + Docetaxel v Docetaxel
Number of subjects included in analysis	253
Analysis specification	Pre-specified
Analysis type	other[22]
P-value	= 0.4499 [23]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.005
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.003
upper limit	1.007

Notes:

[22] - Effect of the prognostic factor of total baseline target lesions tumor size (mm) on PFS.

[23] - p-value for the interaction term is from the Cox model containing only the predictor of interest, treatment, and their interaction.

Statistical analysis title	PFS - adenocarcinoma population: region

Statistical analysis description:

Factor: region
Hazard ratio, 90% CI, and p-values for each factor were obtained from Cox PH model including only that factor as a covariate.

Comparison groups	Ganetespib + Docetaxel v Docetaxel
Number of subjects included in analysis	253
Analysis specification	Pre-specified
Analysis type	other[24]
P-value	= 0.0459 [25]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.765
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.6
upper limit	0.976

Notes:

[24] - Effect of the prognostic factor of region (EEU vs. other) on PFS. EEU refers to Bosnia-Herzegovina, Croatia, Czech Republic, Poland, Romania, Russia, Serbia, and Ukraine. "Other" refers to all other countries.

[25] - p-value for the interaction term is from the Cox model containing only the predictor of interest, treatment, and their interaction.

Secondary: Kaplan-Meier Estimates for Overall Survival (OS) in Adenocarcinoma Subjects

End point title	Kaplan-Meier Estimates for Overall Survival (OS) in Adenocarcinoma Subjects

End point description:

Overall survival was defined as the time from randomization until death due to any cause. Subjects who were lost for follow-up were censored at the time of the last contact.
Statistical analyses include the effect of individual prognostic factors on PFS; sex, smoking status, baseline LDH, ECOG upon entry, interval since advanced NSCLC diagnosis, age, total baseline target lesions tumor size, and region.
Results from the 30 April 2014 data set.

End point type	Secondary

End point timeframe:

Day 1 up to 25 months

End point values	Ganetespib + Docetaxel	Docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	125[26]	128[27]		
Units: months				
median (confidence interval 90%)	10.2 (8 to 12.3)	8.4 (6.3 to 10.9)		

Notes:

[26] - Randomized patients with adenocarcinoma

[27] - Randomized patients with adenocarcinoma

Statistical analyses

Statistical analysis title	OS - adenocarcinoma population
Comparison groups	Ganetespib + Docetaxel v Docetaxel

Number of subjects included in analysis	253
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1502 [28]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.866
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.682
upper limit	1.1

Notes:

[28] - P-value was from a 1-sided stratified log rank test (strata: LDH, ECOG, smoking status, and interval between diagnosis of advanced disease and randomization)

Statistical analysis title	OS - adenocarcinoma population: Sex

Statistical analysis description:

Factor: Sex
Hazard ratio, 90% CI, and p-values for each factor were obtained from Cox PH model including only that factor as a covariate.

Comparison groups	Ganetespib + Docetaxel v Docetaxel
Number of subjects included in analysis	253
Analysis specification	Pre-specified
Analysis type	other[29]
P-value	= 0.695 [30]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.608
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.256
upper limit	2.057

Notes:

[29] - Effect of the prognostic factor of sex (male vs female) on OS.

[30] - p-value for the interaction term is from the Cox model containing only the predictor of interest, treatment, and their interaction.

Statistical analysis title	OS - adenocarcinoma population: Smoking Status

Statistical analysis description:

Factor: Smoking status
Hazard ratio, 90% CI, and p-values for each factor were obtained from Cox PH model including only that factor as a covariate.

Comparison groups	Ganetespib + Docetaxel v Docetaxel
Number of subjects included in analysis	253
Analysis specification	Pre-specified
Analysis type	other[31]
P-value	= 0.0571 [32]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.546

Confidence interval	
level	90 %
sides	2-sided
lower limit	0.404
upper limit	0.737

Notes:

[31] - Effect of the prognostic factor of smoking status (never vs. ever) on OS.

[32] - p-value for the interaction term is from the Cox model containing only the predictor of interest, treatment, and their interaction.

Statistical analysis title	OS - adenocarcinoma population: Baseline LDH

Statistical analysis description:

Factor: baseline LDH
Hazard ratio, 90% CI, and p-values for each factor were obtained from Cox PH model including only that factor as a covariate.

Comparison groups	Ganetespib + Docetaxel v Docetaxel
Number of subjects included in analysis	253
Analysis specification	Pre-specified
Analysis type	other[33]
P-value	= 0.1384 [34]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	2.215
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.72
upper limit	2.852

Notes:

[33] - Effect of the prognostic factor of baseline LDH (elevated vs. normal) on OS.

[34] - p-value for the interaction term is from the Cox model containing only the predictor of interest, treatment, and their interaction.

Statistical analysis title	OS - adenocarcinoma population: ECOG on Entry

Statistical analysis description:

Factor: EGOC on entry
Hazard ratio, 90% CI, and p-values for each factor were obtained from Cox PH model including only that factor as a covariate.

Comparison groups	Ganetespib + Docetaxel v Docetaxel
Number of subjects included in analysis	253
Analysis specification	Pre-specified
Analysis type	other[35]
P-value	= 0.9239 [36]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.71
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.334
upper limit	2.191

Notes:

[35] - Effect of the prognostic factor of ECOG score on entry (>=1 vs. 0) on OS.

[36] - p-value for the interaction term is from the Cox model containing only the predictor of interest, treatment, and their interaction.

Statistical analysis title	OS - adenocarcinoma population: Time since NSCLC

Statistical analysis description:

Factor: Interval since advanced NSCLC diagnosis
Hazard ratio, 90% CI, and p-values for each factor were obtained from Cox PH model including only that factor as a covariate.

Comparison groups	Ganetespib + Docetaxel v Docetaxel
Number of subjects included in analysis	253
Analysis specification	Pre-specified
Analysis type	other[37]
P-value	= 0.0367 [38]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.873
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.672
upper limit	1.134

Notes:

[37] - Effect of the prognostic factor of Interval since advanced NSCLC diagnosis (>6 vs. <=6 months) on OS.
[38] - p-value for the interaction term is from the Cox model containing only the predictor of interest, treatment, and their interaction.

Statistical analysis title	OS - adenocarcinoma population: Age

Statistical analysis description:

Factor: Age
Hazard ratio, 90% CI, and p-values for each factor were obtained from Cox PH model including only that factor as a covariate.

Comparison groups	Ganetespib + Docetaxel v Docetaxel
Number of subjects included in analysis	253
Analysis specification	Pre-specified
Analysis type	other[39]
P-value	= 0.6108 [40]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.009
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.995
upper limit	1.023

Notes:

[39] - Effect of the prognostic factor of age (years) on OS.

[40] - p-value for the interaction term is from the Cox model containing only the predictor of interest, treatment, and their interaction.

Statistical analysis title	OS - adenocarcinoma population: Tumor Size

Statistical analysis description:

Factor: total baseline target lesions tumor size
Hazard ratio, 90% CI, and p-values for each factor were obtained from Cox PH model including only that

factor as a covariate.

Comparison groups	Ganetespib + Docetaxel v Docetaxel
Number of subjects included in analysis	253
Analysis specification	Pre-specified
Analysis type	other[41]
P-value	= 0.7323 [42]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.007
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.004
upper limit	1.009

Notes:

[41] - Effect of the prognostic factor of total baseline target lesions tumor size (mm) on OS.

[42] - p-value for the interaction term is from the Cox model containing only the predictor of interest, treatment, and their interaction.

Statistical analysis title	OS - adenocarcinoma population: Region

Statistical analysis description:

Factor: region
Hazard ratio, 90% CI, and p-values for each factor were obtained from Cox PH model including only that factor as a covariate.

Comparison groups	Ganetespib + Docetaxel v Docetaxel
Number of subjects included in analysis	253
Analysis specification	Pre-specified
Analysis type	other[43]
P-value	= 0.0902 [44]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.884
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.688
upper limit	1.136

Notes:

[43] - Effect of the prognostic factor of region (EEU vs. other) on OS. EEU refers to Bosnia-Herzegovina, Croatia, Czech Republic, Poland, Romania, Russia, Serbia, and Ukraine. "Other" refers to all other countries.

[44] - p-value for the interaction term is from the Cox model containing only the predictor of interest, treatment, and their interaction.

Secondary: Kaplan-Meier Estimates for Overall Survival (OS) by Subpopulation

End point title	Kaplan-Meier Estimates for Overall Survival (OS) by Subpopulation

End point description:

Overall survival was defined as the time from randomization until death due to any cause. Subjects who were lost for follow-up were censored at the time of the last contact.
Results from the 30 April 2014 data set.

End point type	Secondary

End point timeframe:

Day 1 up to 25 months

End point values	Ganetespib + Docetaxel: eLDH	Docetaxel: eLDH	Ganetespib + Docetaxel: mKRAS	Docetaxel: mKRAS
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	44	43	42	47
Units: months				
median (confidence interval 90%)	6 (3.7 to 8)	5.1 (3.5 to 6.8)	7.6 (5.2 to 10.7)	6.4 (5.2 to 11.9)

Statistical analyses

Statistical analysis title	OS: eLDH

Statistical analysis description:

Hazard ratio and 90% CI were calculated using the Cox Proportional Hazard model with treatment as the only factor.

Comparison groups	Ganetespib + Docetaxel: eLDH v Docetaxel: eLDH
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2999 [45]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.883
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.599
upper limit	1.303

Notes:

[45] - P-value was from a 1-sided stratified log rank test.

Statistical analysis title	OS: mKRAS

Statistical analysis description:

Hazard ratio and 90% CI were calculated using the Cox Proportional Hazard model with treatment as the only factor.

Comparison groups	Ganetespib + Docetaxel: mKRAS v Docetaxel: mKRAS
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7551 [46]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.183

Confidence interval	
level	90 %
sides	2-sided
lower limit	0.793
upper limit	1.765

Notes:

[46] - P-value was from a 1-sided stratified log rank test.

Secondary: Overall Survival (OS) Rate at 12 Months by Subpopulation

End point title	Overall Survival (OS) Rate at 12 Months by Subpopulation

End point description:

Overall survival was defined as the time from randomization until death due to any cause and measured up to 12 months. Subjects who were lost for follow-up were censored at the time of the last contact. 90% CI and p-value were from Greenwood approximation.
Results from the 30 April 2014 data set.

End point type	Secondary

End point timeframe:

Day 1 up to 12 months

End point values	Ganetespib + Docetaxel: eLDH	Docetaxel: eLDH	Ganetespib + Docetaxel: mKRAS	Docetaxel: mKRAS
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	44	43	42	47
Units: percentage of participants				
number (confidence interval 90%)	24.1 (14.1 to 35.7)	17.4 (9 to 28)	28.6 (17.8 to 40.3)	37.4 (25.8 to 49)

End point values	Ganetespib + Docetaxel: Adenocarcinoma	Docetaxel: Adenocarcinoma		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	125	128		
Units: percentage of participants				
number (confidence interval 90%)	44.2 (36.8 to 51.4)	38.8 (31.5 to 45.9)		

Statistical analyses

Statistical analysis title	OS at 12 Months: eLDH
Comparison groups	Ganetespib + Docetaxel: eLDH v Docetaxel: eLDH

Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2242
Method	Greenwood approximation

Statistical analysis title	OS at 12 Months: mKRAS
Comparison groups	Ganetespib + Docetaxel: mKRAS v Docetaxel: mKRAS
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1874
Method	Greenwood approximation

Statistical analysis title	OS at 12 Months: Adenocarcinoma
Comparison groups	Docetaxel: Adenocarcinoma v Ganetespib + Docetaxel: Adenocarcinoma
Number of subjects included in analysis	253
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1908
Method	Greenwood approximation

Secondary: Tumor Response by Subpopulation

End point title	Tumor Response by Subpopulation

End point description:

Tumor response rate was measured two ways using modified RECIST 1.1:
1) Objective Response Rate (ORR) which is the sum of subjects whose best response was a complete response or a partial response.
2) Disease Control Rate (DCR) at >=18 weeks. DCR is the sum of subjects whose best response of a complete or partial response or stable disease lasted for >=18 weeks.
A complete response was the disappearance (or normalization) of all target lesions. A partial response was at least 30% decrease in the sum of diameters of target lesions taking as reference the baseline sum of diameters. Stable disease was neither sufficient shrinkage to qualify for partial response nor sufficient increase to qualify for progressive disease.
Results from the 30 April 2014 data set.

End point type	Secondary

End point timeframe:

Day 1 up to 12 months

End point values	Ganetespib + Docetaxel: eLDH	Docetaxel: eLDH	Ganetespib + Docetaxel: mKRAS	Docetaxel: mKRAS
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	44	43	42	47
Units: percentage of participants				
number (confidence interval 90%)				
Objective Response Rate	9.1 (3.2 to 19.6)	9.3 (3.2 to 20)	11.9 (4.8 to 23.4)	10.6 (4.3 to 21.1)
Disease Control Rate >=18 weeks	22.7 (12.9 to 35.5)	20.9 (11.4 to 33.7)	28.6 (17.4 to 42.1)	34 (22.7 to 47)

End point values	Ganetespib + Docetaxel: Adenocarcinoma	Docetaxel: Adenocarcinoma		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	125	128		
Units: percentage of participants				
number (confidence interval 90%)				
Objective Response Rate	22.4 (16.4 to 29.4)	13.3 (8.6 to 19.3)		
Disease Control Rate >=18 weeks	44.8 (37.2 to 52.5)	33.6 (26.7 to 41.1)		

Statistical analyses

Statistical analysis title	ORR: eLDH
Comparison groups	Ganetespib + Docetaxel: eLDH v Docetaxel: eLDH
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.656 [47]
Method	Fisher exact

Notes:

[47] - One-sided p-values are from Fisher's exact test.

Statistical analysis title	DCR >=18 weeks: eLDH
Comparison groups	Ganetespib + Docetaxel: eLDH v Docetaxel: eLDH
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.523 [48]
Method	Fisher exact

Notes:

[48] - One-sided p-values are from Fisher's exact test.

Statistical analysis title	ORR: mKRAS

Comparison groups	Ganetespib + Docetaxel: mKRAS v Docetaxel: mKRAS
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.556 [49]
Method	Fisher exact

Notes:

[49] - One-sided p-values are from Fisher's exact test.

Statistical analysis title	DCR >=18 weeks: mKRAS
Comparison groups	Ganetespib + Docetaxel: mKRAS v Docetaxel: mKRAS
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.783 [50]
Method	Fisher exact

Notes:

[50] - One-sided p-values are from Fisher's exact test.

Statistical analysis title	ORR: Adenocarcinoma
Comparison groups	Ganetespib + Docetaxel: Adenocarcinoma v Docetaxel: Adenocarcinoma
Number of subjects included in analysis	253
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.041 [51]
Method	Fisher exact

Notes:

[51] - One-sided p-values are from Fisher's exact test.

Statistical analysis title	DCR >=18 weeks: Adenocarcinoma
Comparison groups	Ganetespib + Docetaxel: Adenocarcinoma v Docetaxel: Adenocarcinoma
Number of subjects included in analysis	253
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.045 [52]
Method	Fisher exact

Notes:

[52] - One-sided p-values are from Fisher's exact test.

Secondary: Change in Quality of Life from Baseline to End of Treatment Based on	
End point title	Change in Quality of Life from Baseline to End of Treatment Based on

End point description:

The European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) is a questionnaire that includes the following sub-scales:
- global health status,
- functional scales (physical functioning, role functioning, emotional functioning, cognitive functioning, and social activity), and
- symptom scales (fatigue, nausea and vomiting, and pain) and symptom single items (dyspnoea, insomnia, appetite loss, constipation, diarrhoea and financial difficulties).

Scores are averaged for each scale and transformed to 0-100 scale; higher score indicates better quality of life on global health status and functional scales and worse quality of life on symptom scales and financial difficulty scale.
Results from the 30 April 2014 data set.

End point type	Secondary

End point timeframe:

Day 1 up to 25 months

End point values	Ganetespib + Docetaxel: Adenocarcinoma	Docetaxel: Adenocarcinoma		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	125	128		
Units: units on a scale				
arithmetic mean (standard deviation)				
Global Health status	-5.8 (± 20.56)	-2.2 (± 18.65)		
F: Physical functioning	-7.6 (± 16.47)	-4.9 (± 17.52)		
F: Role functioning	-10.5 (± 24.56)	-4.7 (± 27.1)		
F: Emotional functioning	1 (± 22.36)	-1.2 (± 21.74)		
F: Cognitive functioning	-4.3 (± 18.44)	-5.3 (± 22.23)		
F: Social functioning	-3.7 (± 26.34)	-3.6 (± 28.69)		
S: Fatigue	6 (± 21.41)	6.5 (± 21.86)		
S: Nausea and vomiting	3.9 (± 19.62)	4.5 (± 20.39)		
S: Pain	2.3 (± 24.39)	-2.7 (± 26.06)		
S: Dyspnea	8.9 (± 26.85)	1.4 (± 25.16)		
S: Insomnia	10.4 (± 28.22)	-0.7 (± 23.69)		
S: Appetite loss	4.3 (± 27.32)	4 (± 25.6)		
S: Constipation	-1.1 (± 22.11)	2.2 (± 19.65)		
S: Diarrhea	9.9 (± 21.21)	1.8 (± 12.47)		
S: Financial difficulties	2.2 (± 26.38)	1.4 (± 28.78)		

Statistical analyses

No statistical analyses for this end point

Secondary: Participants with Treatment-Emergent Adverse Events (AEs)

End point title	Participants with Treatment-Emergent Adverse Events (AEs)

End point description:

At each summarization level, a patient is counted once if the patient reported one or more events.

National Cancer Institute (NCI) Common Terminology Criteria (NCI-CTCAE V4) is a scale of the severity of the AE. CTCAE grade 3 is severe (the AE is intolerable and disrupts normal daily activities, may require additional therapy or hospitalization, and/or discontinuation of the study drug), and grade 4 is life threatening (the AE exposes the subject to risk of death at the time of the event; it does not refer to an event that may have caused death if the event was more severe).

Results from the 02 December 2015 dataset.

End point type	Secondary

End point timeframe:
Day 1 up to 25 months

End point values	Ganetespib + Docetaxel	Docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	195[53]	186[54]		
Units: participants				
>=1 AE	190	171		
>= 1 AE with CTCAE grade 3 or 4	142	116		
>=1 serious AE	78	54		
>=1 AE leading to dose reduction	33	18		
>=1 AE leading to delayed dose	90	23		
>=1 AE leading to study drug d/c	28	14		
>=1 serious AE leading to study drug d/c	14	8		
>=1 SAE leading to hospitalization	61	36		
>=1 AE with outcome of death	36	24		

Notes:
[53] - All NSCLC treated patients
[54] - All NSCLC treated patients

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Day 1 up to 25 months	
Adverse event reporting additional description:	
Results from the 1 December 2015 data set.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups	
Reporting group title	Docetaxel
Reporting group description:	
On Day 1 of each 3-week treatment cycle, docetaxel (75 mg/m^2) was administered as a 1-hour intravenous infusion. Participating patients were treated until intolerability or disease progression.	
Reporting group title	Ganetespib + Docetaxel
Reporting group description:	
On Day 1 of each 3-week treatment cycle, ganetespib (150 mg/m^2) and docetaxel (75 mg/m^2) were administered as separate 1-hour intravenous infusions. There was a 1-hour "rest" period following the end of the ganetespib infusion prior to docetaxel infusion. Ganetespib 150 mg/m^2 was administered again on Day 15 of each cycle. Participating patients were to be treated until intolerability or disease progression.	

Serious adverse events	Docetaxel	Ganetespib + Docetaxel	
Total subjects affected by serious adverse events			
subjects affected / exposed	54 / 186 (29.03%)	78 / 195 (40.00%)	
number of deaths (all causes)	153	159	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 186 (0.00%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial tumour haemorrhage			
subjects affected / exposed	1 / 186 (0.54%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Metastases to central nervous system			

subjects affected / exposed	1 / 186 (0.54%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Metastases to meninges			
subjects affected / exposed	1 / 186 (0.54%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasm progression			
subjects affected / exposed	9 / 186 (4.84%)	9 / 195 (4.62%)	
occurrences causally related to treatment / all	0 / 10	0 / 10	
deaths causally related to treatment / all	0 / 9	0 / 9	
Vascular disorders			
Embolism			
subjects affected / exposed	1 / 186 (0.54%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Peripheral embolism			
subjects affected / exposed	1 / 186 (0.54%)	0 / 195 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Phlebitis			
subjects affected / exposed	0 / 186 (0.00%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Superior vena cava syndrome			
subjects affected / exposed	0 / 186 (0.00%)	3 / 195 (1.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 3	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 186 (0.54%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Death			
subjects affected / exposed	1 / 186 (0.54%)	0 / 195 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Multi-organ failure			
subjects affected / exposed	0 / 186 (0.00%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	1 / 1	
Pain			
subjects affected / exposed	0 / 186 (0.00%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 186 (0.54%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden cardiac death			
subjects affected / exposed	2 / 186 (1.08%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
Sudden death			
subjects affected / exposed	2 / 186 (1.08%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 186 (0.54%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Social circumstances			
Social stay hospitalisation			
subjects affected / exposed	0 / 186 (0.00%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 186 (0.00%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 186 (0.00%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	3 / 186 (1.61%)	2 / 195 (1.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Haemoptysis			
subjects affected / exposed	0 / 186 (0.00%)	5 / 195 (2.56%)	
occurrences causally related to treatment / all	0 / 0	1 / 6	
deaths causally related to treatment / all	0 / 0	0 / 2	
Pleural effusion			
subjects affected / exposed	2 / 186 (1.08%)	2 / 195 (1.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	1 / 186 (0.54%)	0 / 195 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	0 / 186 (0.00%)	2 / 195 (1.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	6 / 186 (3.23%)	6 / 195 (3.08%)	
occurrences causally related to treatment / all	1 / 6	0 / 7	
deaths causally related to treatment / all	0 / 3	0 / 3	

Pulmonary haemorrhage			
subjects affected / exposed	1 / 186 (0.54%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Pulmonary oedema			
subjects affected / exposed	0 / 186 (0.00%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Respiratory failure			
subjects affected / exposed	1 / 186 (0.54%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 186 (0.00%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			
subjects affected / exposed	1 / 186 (0.54%)	0 / 195 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Weight decreased			
subjects affected / exposed	0 / 186 (0.00%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	1 / 186 (0.54%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			

subjects affected / exposed	0 / 186 (0.00%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 186 (0.00%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	0 / 186 (0.00%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardio-respiratory arrest			
subjects affected / exposed	1 / 186 (0.54%)	0 / 195 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiovascular insufficiency			
subjects affected / exposed	0 / 186 (0.00%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Myocardial infarction			
subjects affected / exposed	1 / 186 (0.54%)	0 / 195 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Nervous system disorders			
Cerebral ischaemia			
subjects affected / exposed	0 / 186 (0.00%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Dizziness			
subjects affected / exposed	0 / 186 (0.00%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalized tonic-clonic seizure			

subjects affected / exposed	1 / 186 (0.54%)	0 / 195 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuralgia			
subjects affected / exposed	1 / 186 (0.54%)	0 / 195 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	1 / 186 (0.54%)	0 / 195 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Somnolence			
subjects affected / exposed	1 / 186 (0.54%)	0 / 195 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 186 (0.00%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo CNS origin			
subjects affected / exposed	0 / 186 (0.00%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 186 (0.00%)	3 / 195 (1.54%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	8 / 186 (4.30%)	17 / 195 (8.72%)	
occurrences causally related to treatment / all	9 / 9	19 / 19	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			

subjects affected / exposed	5 / 186 (2.69%)	5 / 195 (2.56%)	
occurrences causally related to treatment / all	5 / 5	5 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	1 / 186 (0.54%)	0 / 195 (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 pain			
subjects affected / exposed	0 / 186 (0.00%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 186 (0.54%)	6 / 195 (3.08%)	
occurrences causally related to treatment / all	1 / 1	6 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis			
subjects affected / exposed	0 / 186 (0.00%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Gastritis			
subjects affected / exposed	1 / 186 (0.54%)	0 / 195 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematemesis			
subjects affected / exposed	0 / 186 (0.00%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Mallory-Weiss syndrome			
subjects affected / exposed	1 / 186 (0.54%)	0 / 195 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			

subjects affected / exposed	1 / 186 (0.54%)	0 / 195 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 186 (0.00%)	2 / 195 (1.03%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			
subjects affected / exposed	0 / 186 (0.00%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatitis			
subjects affected / exposed	1 / 186 (0.54%)	0 / 195 (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	1 / 186 (0.54%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 186 (0.54%)	0 / 195 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	1 / 186 (0.54%)	0 / 195 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 186 (0.54%)	0 / 195 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Bone pain			
subjects affected / exposed	0 / 186 (0.00%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			
subjects affected / exposed	0 / 186 (0.00%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 186 (0.00%)	1 / 195 (0.51%)	
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	0 / 186 (0.00%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchitis			
subjects affected / exposed	2 / 186 (1.08%)	2 / 195 (1.03%)	
occurrences causally related to treatment / all	0 / 3	3 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 186 (0.54%)	0 / 195 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	0 / 186 (0.00%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			
subjects affected / exposed	1 / 186 (0.54%)	0 / 195 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes simplex encephalitis			

subjects affected / exposed	1 / 186 (0.54%)	0 / 195 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Influenza			
subjects affected / exposed	0 / 186 (0.00%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Lower respiratory tract infection			
subjects affected / exposed	0 / 186 (0.00%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	1 / 186 (0.54%)	2 / 195 (1.03%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic sepsis			
subjects affected / exposed	1 / 186 (0.54%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	6 / 186 (3.23%)	8 / 195 (4.10%)	
occurrences causally related to treatment / all	3 / 8	3 / 8	
deaths causally related to treatment / all	0 / 0	0 / 2	
Respiratory tract infection			
subjects affected / exposed	2 / 186 (1.08%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 186 (0.00%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			

subjects affected / exposed	0 / 186 (0.00%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 186 (0.00%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 186 (0.54%)	1 / 195 (0.51%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 186 (0.00%)	2 / 195 (1.03%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	1 / 186 (0.54%)	3 / 195 (1.54%)	
occurrences causally related to treatment / all	1 / 1	3 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	1 / 186 (0.54%)	0 / 195 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Docetaxel	Ganetespib + Docetaxel	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	164 / 186 (88.17%)	183 / 195 (93.85%)	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	5 / 186 (2.69%)	11 / 195 (5.64%)	
occurrences (all)	8	16	

Aspartate aminotransferase increased			
subjects affected / exposed	4 / 186 (2.15%)	15 / 195 (7.69%)	
occurrences (all)	7	26	
Weight decreased			
subjects affected / exposed	6 / 186 (3.23%)	13 / 195 (6.67%)	
occurrences (all)	6	16	
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	5 / 186 (2.69%)	11 / 195 (5.64%)	
occurrences (all)	7	21	
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	14 / 186 (7.53%)	14 / 195 (7.18%)	
occurrences (all)	24	26	
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 186 (3.23%)	16 / 195 (8.21%)	
occurrences (all)	7	23	
Neuropathy peripheral			
subjects affected / exposed	10 / 186 (5.38%)	10 / 195 (5.13%)	
occurrences (all)	13	19	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	28 / 186 (15.05%)	46 / 195 (23.59%)	
occurrences (all)	45	111	
Leukopenia			
subjects affected / exposed	16 / 186 (8.60%)	19 / 195 (9.74%)	
occurrences (all)	34	59	
Neutropenia			
subjects affected / exposed	76 / 186 (40.86%)	83 / 195 (42.56%)	
occurrences (all)	202	255	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	20 / 186 (10.75%)	37 / 195 (18.97%)	
occurrences (all)	42	72	
Chest pain			

subjects affected / exposed	9 / 186 (4.84%)	11 / 195 (5.64%)	
occurrences (all)	13	13	
Fatigue			
subjects affected / exposed	48 / 186 (25.81%)	59 / 195 (30.26%)	
occurrences (all)	60	99	
Oedema peripheral			
subjects affected / exposed	11 / 186 (5.91%)	18 / 195 (9.23%)	
occurrences (all)	14	24	
Pyrexia			
subjects affected / exposed	19 / 186 (10.22%)	18 / 195 (9.23%)	
occurrences (all)	23	26	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	14 / 186 (7.53%)	19 / 195 (9.74%)	
occurrences (all)	18	21	
Diarrhoea			
subjects affected / exposed	28 / 186 (15.05%)	86 / 195 (44.10%)	
occurrences (all)	33	271	
Nausea			
subjects affected / exposed	33 / 186 (17.74%)	45 / 195 (23.08%)	
occurrences (all)	49	89	
Stomatitis			
subjects affected / exposed	13 / 186 (6.99%)	17 / 195 (8.72%)	
occurrences (all)	21	23	
Vomiting			
subjects affected / exposed	14 / 186 (7.53%)	23 / 195 (11.79%)	
occurrences (all)	18	34	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	22 / 186 (11.83%)	20 / 195 (10.26%)	
occurrences (all)	30	28	
Dyspnoea			
subjects affected / exposed	23 / 186 (12.37%)	38 / 195 (19.49%)	
occurrences (all)	33	59	
Haemoptysis			

subjects affected / exposed	6 / 186 (3.23%)	11 / 195 (5.64%)	
occurrences (all)	9	18	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	30 / 186 (16.13%)	38 / 195 (19.49%)	
occurrences (all)	33	42	
Rash			
subjects affected / exposed	10 / 186 (5.38%)	17 / 195 (8.72%)	
occurrences (all)	11	26	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	7 / 186 (3.76%)	18 / 195 (9.23%)	
occurrences (all)	8	22	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	12 / 186 (6.45%)	17 / 195 (8.72%)	
occurrences (all)	21	31	
Back pain			
subjects affected / exposed	14 / 186 (7.53%)	17 / 195 (8.72%)	
occurrences (all)	17	22	
Myalgia			
subjects affected / exposed	7 / 186 (3.76%)	11 / 195 (5.64%)	
occurrences (all)	11	13	
Pain in extremity			
subjects affected / exposed	5 / 186 (2.69%)	12 / 195 (6.15%)	
occurrences (all)	5	15	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	24 / 186 (12.90%)	37 / 195 (18.97%)	
occurrences (all)	31	54	
Hyperglycaemia			
subjects affected / exposed	12 / 186 (6.45%)	8 / 195 (4.10%)	
occurrences (all)	35	22	
Hypoalbuminaemia			
subjects affected / exposed	10 / 186 (5.38%)	7 / 195 (3.59%)	
occurrences (all)	18	21	

Hypokalaemia subjects affected / exposed occurrences (all)	5 / 186 (2.69%) 7	13 / 195 (6.67%) 16	
Hyponatraemia subjects affected / exposed occurrences (all)	9 / 186 (4.84%) 10	10 / 195 (5.13%) 18	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 October 2011	- Changed a co-primary objective to the following: "Evaluate PFS in patients with KRAS mutated NSCLC." Co-primary endpoint - changed to PFS in the mKRAS pop. - Disease control rate (DCR) replaced clinical benefit rate (CBR) in the associated secondary objectives - Changed interval since diagnosis of advanced disease changed from "≤12 vs. >12 mo to ≤6 vs. >6 mo (prospective stratification factor)
05 March 2012	Administrative changes. No changes to primary or secondary endpoints.
14 May 2012	- Restricted study enrollment to patients with adenocarcinoma NSCLC; stopped enrollment of non-adenocarcinoma patients. Nonadenocarcinoma patients already on-study were to discontinue treatment with ganetespib. Investigators could continue treatment of these patients with docetaxel alone, per standard of care. - Limited analysis of primary and secondary endpoints to patients with adenocarcinoma NSCLC. - Increased overall sample size from 240 to 300 patients - Changed co-primary endpoint to PFS in patients with eLDH - Added a secondary objective for mKRAS: "Compare the 2 treatments in patients with mutated KRAS (mKRAS) with respect to the following: ORR, DCR, tumor size change, 1-year OS rate, OS"
24 August 2012	- Increased overall sample size to 340 adenocarcinoma patients - Remove cap on patients with normal LDH
19 August 2013	End of study after Stage 1 was formalized in this Amendment. Included the additional potential risk of intestinal perforation with ganetespib.

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.

Study was terminated after stage 1. Stage 2 (the Phase 3 portion of the study) was never implemented as a part of this study. The Phase 3 study, Protocol 9090-14 was initiated instead.

Notes: