



## Clinical trial results:

### Randomized, Double-Blind, Multicenter, Phase 3 Study Comparing Veliparib Plus Carboplatin and Paclitaxel Versus Placebo Plus Carboplatin and Paclitaxel in Previously Untreated Advanced or Metastatic Squamous Non-Small Cell Lung Cancer (NSCLC)

#### Summary

EudraCT number	2013-005020-42
Trial protocol	SK FI LT CZ PT HU NO SE DE AT IT IE DK NL ES GR LV PL FR
Global end of trial date	20 November 2019

#### Results information

Result version number	v1 (current)
This version publication date	03 December 2020
First version publication date	03 December 2020

#### Trial information

##### Trial identification

Sponsor protocol code	M11-089
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02106546
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	Abbvie Deutschland GmbH & Co.KG
Sponsor organisation address	AbbVie House, Vanwall Business Park, Maidenhead, Berkshire, United Kingdom, SL6-4UB
Public contact	Global Medical Services, AbbVie, 001 800-633-9110, <a href="mailto:abbvieclinicaltrials@abbvie.com">abbvieclinicaltrials@abbvie.com</a>
Scientific contact	Global Medical Services, AbbVie, 001 800-633-9110, <a href="mailto:abbvieclinicaltrials@abbvie.com">abbvieclinicaltrials@abbvie.com</a>

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	20 November 2019
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	20 November 2019
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of the study was to assess whether the addition of oral veliparib to carboplatin and paclitaxel (C/P) would improve overall survival (OS) compared to the addition of placebo to C/P in current smokers with previously untreated locally advanced and metastatic squamous NSCLC.

Protection of trial subjects:

Subject read and understood the information provided about the study and gave written permission.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 April 2014
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	4 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 16
Country: Number of subjects enrolled	Austria: 5
Country: Number of subjects enrolled	Belarus: 45
Country: Number of subjects enrolled	Brazil: 28
Country: Number of subjects enrolled	Canada: 27
Country: Number of subjects enrolled	Croatia: 15
Country: Number of subjects enrolled	Czech Republic: 30
Country: Number of subjects enrolled	Denmark: 8
Country: Number of subjects enrolled	Egypt: 17
Country: Number of subjects enrolled	Estonia: 5
Country: Number of subjects enrolled	Finland: 6
Country: Number of subjects enrolled	France: 47
Country: Number of subjects enrolled	Germany: 10
Country: Number of subjects enrolled	Greece: 27
Country: Number of subjects enrolled	Hungary: 79
Country: Number of subjects enrolled	Ireland: 12
Country: Number of subjects enrolled	Israel: 13
Country: Number of subjects enrolled	Italy: 19
Country: Number of subjects enrolled	Latvia: 19

Country: Number of subjects enrolled	Lithuania: 9
Country: Number of subjects enrolled	Mexico: 7
Country: Number of subjects enrolled	Netherlands: 23
Country: Number of subjects enrolled	New Zealand: 2
Country: Number of subjects enrolled	Norway: 10
Country: Number of subjects enrolled	Poland: 17
Country: Number of subjects enrolled	Portugal: 19
Country: Number of subjects enrolled	Puerto Rico: 1
Country: Number of subjects enrolled	Russian Federation: 90
Country: Number of subjects enrolled	Serbia: 23
Country: Number of subjects enrolled	Slovakia: 11
Country: Number of subjects enrolled	South Africa: 18
Country: Number of subjects enrolled	Spain: 37
Country: Number of subjects enrolled	Sweden: 8
Country: Number of subjects enrolled	Switzerland: 12
Country: Number of subjects enrolled	Turkey: 43
Country: Number of subjects enrolled	Ukraine: 73
Country: Number of subjects enrolled	United Kingdom: 44
Country: Number of subjects enrolled	United States: 95
Worldwide total number of subjects	970
EEA total number of subjects	460

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)	517
From 65 to 84 years	453
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

A total of 218 sites in 37 countries enrolled participants with previously untreated advanced or metastatic squamous non-small cell lung cancer (NSCLC).

### Pre-assignment

Screening details:

Participants were randomized 1:1 to 1 of 2 groups. Randomization was stratified by tumor stage (locally advanced vs metastatic), Eastern Cooperative Oncology Group performance score (0 vs 1), geographic region (Western Europe/Australia/Americas vs Eastern Europe/Russia), and smoking history (current smoker vs never smoked vs past smoker).

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Placebo + Carboplatin + Paclitaxel

Arm description:

Participants received placebo orally twice a day (BID) on Days -2 to 5 (7 consecutive days) of each 21-day cycle and carboplatin at an area under the concentration-time curve (AUC) 6 mg/mL/min and paclitaxel 200 mg/m<sup>2</sup> by intravenous (IV) infusion on Day 1 of each 21-day cycle for up to a maximum 6 cycles of treatment, until treatment toxicity which, in the Investigator's opinion, prohibited further therapy, or until radiographic progression.

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

Dosage and administration details:

Capsules taken orally twice a day, 12 hours apart.

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Carboplatin administered intravenously over approximately 15 to 30 minutes at (AUC 6 mg/mL/min) immediately following paclitaxel infusion.

Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Paclitaxel administered intravenously over 3 hours at a dose of 200 mg/m<sup>2</sup>.

<b>Arm title</b>	Veliparib + Carboplatin + Paclitaxel
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**Arm description:**

Participants received veliparib 120 mg orally twice daily (BID) on Days -2 to 5 (7 consecutive days) of each 21-day cycle and carboplatin at an AUC 6 mg/mL/min and paclitaxel 200 mg/m<sup>2</sup> by intravenous (IV) infusion on Day 1 of each 21-day cycle for up to a maximum 6 cycles of treatment, until treatment toxicity which, in the Investigator's opinion, prohibited further therapy, or until radiographic progression.

Arm type	Experimental
Investigational medicinal product name	Veliparib
Investigational medicinal product code	
Other name	ABT-888
Pharmaceutical forms	Capsule
Routes of administration	Oral use

**Dosage and administration details:**

Capsules taken orally twice a day, 12 hours apart.

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

**Dosage and administration details:**

Carboplatin administered intravenously over approximately 15 to 30 minutes at (AUC 6 mg/mL/min) immediately following paclitaxel infusion.

Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

**Dosage and administration details:**

Paclitaxel administered intravenously over 3 hours at a dose of 200 mg/m<sup>2</sup>.

<b>Number of subjects in period 1</b>	<b>Placebo + Carboplatin + Paclitaxel</b>	<b>Veliparib + Carboplatin + Paclitaxel</b>
Started	484	486
Received Treatment	482	485
Completed	268	288
Not completed	216	198
Adverse Event Related to Progression	25	17
Consent withdrawn by subject	17	16
Other	9	7
Progressive Disease	81	78
Adverse Event Not Related to Progression	82	80
Lost to follow-up	2	-

## Baseline characteristics

### Reporting groups

Reporting group title	Placebo + Carboplatin + Paclitaxel
Reporting group description:	
Participants received placebo orally twice a day (BID) on Days -2 to 5 (7 consecutive days) of each 21-day cycle and carboplatin at an area under the concentration-time curve (AUC) 6 mg/mL/min and paclitaxel 200 mg/m <sup>2</sup> by intravenous (IV) infusion on Day 1 of each 21-day cycle for up to a maximum 6 cycles of treatment, until treatment toxicity which, in the Investigator's opinion, prohibited further therapy, or until radiographic progression.	
Reporting group title	Veliparib + Carboplatin + Paclitaxel
Reporting group description:	
Participants received veliparib 120 mg orally twice daily (BID) on Days -2 to 5 (7 consecutive days) of each 21-day cycle and carboplatin at an AUC 6 mg/mL/min and paclitaxel 200 mg/m <sup>2</sup> by intravenous (IV) infusion on Day 1 of each 21-day cycle for up to a maximum 6 cycles of treatment, until treatment toxicity which, in the Investigator's opinion, prohibited further therapy, or until radiographic progression.	

Reporting group values	Placebo + Carboplatin + Paclitaxel	Veliparib + Carboplatin + Paclitaxel	Total
Number of subjects	484	486	970
Age categorical			
Units: Subjects			
< 65 years	256	261	517
≥ 65 years	228	225	453
Age continuous			
Units: years			
median	64.0	64.0	
full range (min-max)	33 to 84	36 to 83	-
Gender categorical			
Units: Subjects			
Female	100	75	175
Male	384	411	795
Race			
Units: Subjects			
White	477	471	948
Black	5	9	14
Asian	0	5	5
Other	2	1	3
Geographic Region			
Units: Subjects			
Western Europe/Australia/Americas	239	242	481
Eastern Europe/Russia	245	244	489
Eastern Cooperative Oncology Group (ECOG) Performance Status (PS)			
ECOG performance status is used by doctors and researchers to assess how a participant's disease is progressing, assess how the disease affects the daily living activities of the participant and determine appropriate treatment and prognosis. 0 = Fully Active (Most Favorable Activity); 1 = Restricted activity but ambulatory; 2 = Ambulatory but unable to carry out work activities; 3 = Limited Self-Care; 4 = Completely Disabled, No self-care (Least Favorable Activity)			
Units: Subjects			

Grade 0 (fully active)	165	166	331
Grade 1 (restricted but ambulatory)	319	320	639
Smoking Status Units: Subjects			
Current smoker	276	276	552
Past smoker	181	181	362
Never smoked	27	29	56
Tumor Stage Units: Subjects			
Locally advanced	112	114	226
Metastatic	372	372	744

## End points

### End points reporting groups

Reporting group title	Placebo + Carboplatin + Paclitaxel
Reporting group description:	
Participants received placebo orally twice a day (BID) on Days -2 to 5 (7 consecutive days) of each 21-day cycle and carboplatin at an area under the concentration-time curve (AUC) 6 mg/mL/min and paclitaxel 200 mg/m <sup>2</sup> by intravenous (IV) infusion on Day 1 of each 21-day cycle for up to a maximum 6 cycles of treatment, until treatment toxicity which, in the Investigator's opinion, prohibited further therapy, or until radiographic progression.	
Reporting group title	Veliparib + Carboplatin + Paclitaxel
Reporting group description:	
Participants received veliparib 120 mg orally twice daily (BID) on Days -2 to 5 (7 consecutive days) of each 21-day cycle and carboplatin at an AUC 6 mg/mL/min and paclitaxel 200 mg/m <sup>2</sup> by intravenous (IV) infusion on Day 1 of each 21-day cycle for up to a maximum 6 cycles of treatment, until treatment toxicity which, in the Investigator's opinion, prohibited further therapy, or until radiographic progression.	

### Primary: Overall Survival in Current Smokers

End point title	Overall Survival in Current Smokers
End point description:	
Overall survival (OS) was calculated as the time from the date that the participant was randomized to the date of death. All events of death were included, regardless of whether the event occurred while the participant was still taking study drug, or after the participant discontinued study drug. Participants who had not died prior to the analysis cut-off date were censored at the date they were last known to be alive, or on the cut-off date if survival data were known after the cut-off date. The distributions of OS on the two treatment arms were estimated using the Kaplan-Meier method. The data cut-off date for the analyses of primary and secondary efficacy endpoints was pre-specified as the date of the 400th death in current smokers and 667 events in the total ITT population. OS was analysed in the intent-to-treat (ITT) population (all randomized participants) who were current smokers	
End point type	Primary
End point timeframe:	
From randomization to the primary analysis data cut-off date in 2017.	

End point values	Placebo + Carboplatin + Paclitaxel	Veliparib + Carboplatin + Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	276 <sup>[1]</sup>	276 <sup>[2]</sup>		
Units: months				
median (confidence interval 95%)	11.1 (9.6 to 12.6)	11.9 (10.5 to 13.5)		

Notes:

[1] - Current smokers

[2] - Current smokers

### Statistical analyses

Statistical analysis title	Primary Analysis of OS in Current Smokers
Comparison groups	Placebo + Carboplatin + Paclitaxel v Veliparib + Carboplatin + Paclitaxel



Number of subjects included in analysis	552
Analysis specification	Pre-specified
Analysis type	superiority <sup>[3]</sup>
P-value	= 0.266 <sup>[4]</sup>
Method	Stratified Log-rank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.905
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.744
upper limit	1.101

Notes:

[3] - Statistical significance was determined by a two-sided P-value  $\leq 0.05$ . If the primary endpoint was not met, all analyses of secondary and other efficacy endpoints were to be performed in a descriptive manner and treated as exploratory, with P-values interpreted as nominal.

[4] - Log-rank test stratified by tumor staging (locally advanced vs metastatic) and ECOG performance status (0 vs 1).

### Secondary: Overall Survival in All Participants - Primary Analysis

End point title	Overall Survival in All Participants - Primary Analysis
End point description:	Overall survival was calculated as the time from the date that the participant was randomized to the date of death. All events of death were included, regardless of whether the event occurred while the participant was still taking study drug, or after the participant discontinued study drug. Participants who had not died prior to the analysis cut-off date were censored at the date they were last known to be alive, or on the cut-off date if survival data were known after the cut-off date. The distributions of OS on the two treatment arms were estimated using the Kaplan-Meier method. The data cut-off date for the analyses of primary and secondary efficacy endpoints was pre-specified as the date of the 400th death in current smokers and 667 events in the total ITT population.
End point type	Secondary
End point timeframe:	From randomization to the primary analysis data cut-off date in 2017.

End point values	Placebo + Carboplatin + Paclitaxel	Veliparib + Carboplatin + Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	484 <sup>[5]</sup>	486 <sup>[6]</sup>		
Units: months				
median (confidence interval 95%)	11.2 (10.1 to 12.6)	12.2 (10.9 to 13.5)		

Notes:

[5] - Intent-to-treat population

[6] - Intent-to-treat population

### Statistical analyses

Statistical analysis title	Primary Analysis of OS in All Participants
Comparison groups	Placebo + Carboplatin + Paclitaxel v Veliparib + Carboplatin + Paclitaxel

Number of subjects included in analysis	970
Analysis specification	Pre-specified
Analysis type	other <sup>[7]</sup>
P-value	= 0.098 <sup>[8]</sup>
Method	Stratified Log-rank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.889
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.767
upper limit	1.031

Notes:

[7] - If the primary endpoint was not met, all analyses of secondary and other efficacy endpoints were to be performed in a descriptive manner and treated as exploratory, with P-values interpreted as nominal.

[8] - Stratified by tumor staging (locally advanced vs metastatic), smoking status (current smokers vs past vs never smokers), and ECOG PS (0 vs 1).

### Secondary: Progression-Free Survival in Current Smokers

End point title	Progression-Free Survival in Current Smokers
End point description:	Progression-free survival (PFS) was calculated using Kaplan-Meier methods as the time from the date that the participant was randomized to the date the participant experienced an event of disease progression or to the date of death (all causes of mortality) if disease progression was not reached. Participants who did not have an event of progression or death prior to the analysis cut-off date were censored at the date of the last disease assessment before the cut-off date, or at the date of randomization if they did not have a post-baseline assessment. Disease progression was defined according to Response Evaluation Criteria in Solid Tumors (RECIST), version 1.1: At least a 20% increase in the sum of the longest diameter (LD) of target lesions, taking as reference the smallest sum LD recorded since the treatment started (baseline or after) with an absolute increase of at least 5 mm, unequivocal progression of existing non-target lesions, or the appearance of any new lesions.
End point type	Secondary
End point timeframe:	From randomization to the primary analysis data cut-off date in 2017

End point values	Placebo + Carboplatin + Paclitaxel	Veliparib + Carboplatin + Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	276 <sup>[9]</sup>	276 <sup>[10]</sup>		
Units: months				
median (confidence interval 95%)	5.6 (5.4 to 5.7)	5.6 (5.5 to 5.8)		

Notes:

[9] - Current smokers

[10] - Current smokers

### Statistical analyses

Statistical analysis title	Analysis of PFS in Current Smokers
Comparison groups	Placebo + Carboplatin + Paclitaxel v Veliparib + Carboplatin + Paclitaxel

Number of subjects included in analysis	552
Analysis specification	Pre-specified
Analysis type	other <sup>[11]</sup>
P-value	= 0.376 <sup>[12]</sup>
Method	Stratified Log-rank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.918
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.763
upper limit	1.105

Notes:

[11] - If the primary endpoint was not met, all analyses of secondary and other efficacy endpoints were to be performed in a descriptive manner and treated as exploratory, with P-values interpreted as nominal.

[12] - Log-rank test stratified by tumor staging (locally advanced vs metastatic) and ECOG performance status (0 vs 1).

### Secondary: Progression-Free Survival in All Participants - Primary Analysis

End point title	Progression-Free Survival in All Participants - Primary Analysis
End point description:	Progression-free survival (PFS) was calculated using Kaplan-Meier methods as the time from the date that the participant was randomized to the date the participant experienced an event of disease progression or to the date of death (all causes of mortality) if disease progression was not reached. Participants who did not have an event of progression or death prior to the analysis cut-off date were censored at the date of the last disease assessment before the cut-off date, or at the date of randomization if they did not have a post-baseline assessment. Disease progression was defined according to Response Evaluation Criteria in Solid Tumors (RECIST), version 1.1: At least a 20% increase in the sum of the longest diameter (LD) of target lesions, taking as reference the smallest sum LD recorded since the treatment started (baseline or after) with an absolute increase of at least 5 mm, unequivocal progression of existing non-target lesions, or the appearance of any new lesions.
End point type	Secondary
End point timeframe:	From randomization to the primary analysis data cut-off date in 2017.

End point values	Placebo + Carboplatin + Paclitaxel	Veliparib + Carboplatin + Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	484 <sup>[13]</sup>	486 <sup>[14]</sup>		
Units: months				
median (confidence interval 95%)	5.6 (5.5 to 5.7)	5.6 (5.6 to 5.8)		

Notes:

[13] - Intent-to-treat population

[14] - Intent-to-treat population

### Statistical analyses

Statistical analysis title	Primary Analysis of PFS in All Participants
Comparison groups	Placebo + Carboplatin + Paclitaxel v Veliparib + Carboplatin + Paclitaxel

Number of subjects included in analysis	970
Analysis specification	Pre-specified
Analysis type	other <sup>[15]</sup>
P-value	= 0.132 <sup>[16]</sup>
Method	Stratified Log-rank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.895
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.778
upper limit	1.031

Notes:

[15] - If the primary endpoint was not met, all analyses of secondary and other efficacy endpoints were to be performed in a descriptive manner and treated as exploratory, with P-values interpreted as nominal.

[16] - Stratified by tumor staging (locally advanced vs metastatic), smoking status (current smokers vs past vs never smokers), and ECOG PS (0 vs 1).

### Secondary: Objective Response Rate in Current Smokers

End point title	Objective Response Rate in Current Smokers
End point description:	
Disease assessments were made using computed tomography (CT) scans of the full chest and abdomen and assessed by the investigator according to the Response Evaluation Criteria in Solid Tumors (RECIST) v1.1.	
Objective response rate (ORR) is defined as the percentage of participants a with complete or partial response, confirmed 4 weeks after the first documentation.	
Complete Response (CR): The disappearance of all target and non-target lesions, and no new lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to < 10 mm.	
Partial Response (PR): At least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters, persistence of one or more non-target lesion(s) and/or maintenance of tumor marker level above the normal limits, or any new lesions.	
End point type	Secondary
End point timeframe:	
Tumor assessments were performed on Day 1 of Cycle 3 and Cycle 5, every 6 weeks until 1 year after starting treatment, and then every 12 weeks until radiographic progression, additional cancer treatment, or death; median time on follow-up was 20 months.	

End point values	Placebo + Carboplatin + Paclitaxel	Veliparib + Carboplatin + Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	276 <sup>[17]</sup>	276 <sup>[18]</sup>		
Units: percentage of participants				
number (confidence interval 95%)	34.8 (29.2 to 40.7)	34.4 (28.8 to 40.4)		

Notes:

[17] - Current smokers

[18] - Current smokers

### Statistical analyses

<b>Statistical analysis title</b>	Analysis of ORR in Current Smokers
Comparison groups	Placebo + Carboplatin + Paclitaxel v Veliparib + Carboplatin + Paclitaxel
Number of subjects included in analysis	552
Analysis specification	Pre-specified
Analysis type	other <sup>[19]</sup>
P-value	= 0.92 <sup>[20]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[19] - If the primary endpoint was not met, all analyses of secondary and other efficacy endpoints were to be performed in a descriptive manner and treated as exploratory, with P-values interpreted as nominal.

[20] - Cochran-Mantel-Haenszel (CMH) test stratified by tumor staging (locally advanced versus metastatic) and ECOG performance status (0 versus 1).

## Secondary: Objective Response Rate in All Participants - Primary Analysis

End point title	Objective Response Rate in All Participants - Primary Analysis
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End point description:

Disease assessments were made using computed tomography (CT) scans of the full chest and abdomen and assessed by the investigator according to RECIST v1.1.

Objective response rate (ORR) is defined as the percentage of participants with a complete or partial response that was confirmed 4 weeks after the first documentation.

Complete Response (CR): The disappearance of all target and non-target lesions, and no new lesions.

Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to < 10 mm.

Partial Response (PR): At least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters, persistence of one or more non-target lesion(s) and/or maintenance of tumor marker level above the normal limits, or any new lesions.

End point type	Secondary
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End point timeframe:

Tumor assessments were performed on Day 1 of Cycle 3 and Cycle 5, every 6 weeks until 1 year after starting treatment, and then every 12 weeks until radiographic progression, additional cancer treatment, or death; median time on follow-up was 20 months.

End point values	Placebo + Carboplatin + Paclitaxel	Veliparib + Carboplatin + Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	484 <sup>[21]</sup>	486 <sup>[22]</sup>		
Units: percentage of participants				
number (confidence interval 95%)	37.2 (32.9 to 41.7)	37.0 (32.7 to 41.5)		

Notes:

[21] - Intent-to-treat population

[22] - Intent-to-treat population

## Statistical analyses

<b>Statistical analysis title</b>	Analysis of ORR in All Participants
Comparison groups	Placebo + Carboplatin + Paclitaxel v Veliparib + Carboplatin + Paclitaxel

Number of subjects included in analysis	970
Analysis specification	Pre-specified
Analysis type	other <sup>[23]</sup>
P-value	= 0.963 <sup>[24]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[23] - If the primary endpoint was not met, all analyses of secondary and other efficacy endpoints were to be performed in a descriptive manner and treated as exploratory, with P-values interpreted as nominal.

[24] - Stratified by tumor stage (locally advanced vs metastatic), smoking status (current smokers vs past smokers vs never smoked), and ECOG PS (0 vs 1).

## Secondary: Overall Survival in All Participants - Final Analysis

End point title	Overall Survival in All Participants - Final Analysis
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End point description:

Overall survival was calculated as the time from the date that the participant was randomized to the date of death. All events of death were included, regardless of whether the event occurred while the participant was still taking study drug, or after the participant discontinued study drug. Participants who had not died prior to the analysis cut-off date were censored at the date they were last known to be alive. The distributions of OS on the two treatment arms were estimated using the Kaplan-Meier method.

End point type	Secondary
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End point timeframe:

From randomization to the end of study

End point values	Placebo + Carboplatin + Paclitaxel	Veliparib + Carboplatin + Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	484 <sup>[25]</sup>	486 <sup>[26]</sup>		
Units: months				
median (confidence interval 95%)	11.2 (10.1 to 12.6)	12.2 (10.9 to 13.5)		

Notes:

[25] - Intent-to-treat population

[26] - Intent-to-treat population

## Statistical analyses

<b>Statistical analysis title</b>	Final Analysis of OS in All Participants
Comparison groups	Placebo + Carboplatin + Paclitaxel v Veliparib + Carboplatin + Paclitaxel
Number of subjects included in analysis	970
Analysis specification	Pre-specified
Analysis type	other <sup>[27]</sup>
P-value	= 0.032 <sup>[28]</sup>
Method	Stratified Log-rank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.853

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.747
upper limit	0.974

Notes:

[27] - If the primary endpoint was not met, all analyses of secondary and other efficacy endpoints were to be performed in a descriptive manner and treated as exploratory, with P-values interpreted as nominal.

[28] - Stratified by tumor staging (locally advanced vs metastatic), smoking status (current smokers vs past vs never smokers), and ECOG PS (0 vs 1).

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Deaths are reported from randomization until the end of follow-up; median time on study was 49.8 and 47.1 months in the placebo and veliparib arms respectively.

AEs are reported from first dose of study drug until 30 days after last dose; max 181 days

Adverse event reporting additional description:

Adverse event data are reported for all participants who received at least 1 dose of study drug (veliparib/placebo).

One participant randomized to each arm who did not receive treatment and are not included in the safety analysis set died in addition to those in the table below.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

### Reporting groups

Reporting group title	Veliparib + Carboplatin + Paclitaxel
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Reporting group description:

Participants received veliparib 120 mg orally BID on Days -2 to 5 (7 consecutive days) of each 21-day cycle and carboplatin at an AUC 6 mg/mL/min and paclitaxel 200 mg/m<sup>2</sup> by IV infusion on Day 1 of each 21-day cycle for up to a maximum 6 cycles of treatment, until treatment toxicity which, in the Investigator's opinion, prohibited further therapy, or until radiographic progression.

Reporting group title	Placebo + Carboplatin + Paclitaxel
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Reporting group description:

Participants received placebo orally BID on Days -2 to 5 (7 consecutive days) of each 21-day cycle and carboplatin at an AUC 6 mg/mL/min and paclitaxel 200 mg/m<sup>2</sup> by IV infusion on Day 1 of each 21-day cycle for up to a maximum 6 cycles of treatment, until treatment toxicity which, in the Investigator's opinion, prohibited further therapy, or until radiographic progression.

Serious adverse events	Veliparib + Carboplatin + Paclitaxel	Placebo + Carboplatin + Paclitaxel	
Total subjects affected by serious adverse events			
subjects affected / exposed	155 / 485 (31.96%)	164 / 482 (34.02%)	
number of deaths (all causes)	435	443	
number of deaths resulting from adverse events	38	44	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
MALIGNANT NEOPLASM PROGRESSION			
subjects affected / exposed	8 / 485 (1.65%)	13 / 482 (2.70%)	
occurrences causally related to treatment / all	1 / 8	0 / 13	
deaths causally related to treatment / all	0 / 6	0 / 9	
METASTASES TO CENTRAL NERVOUS SYSTEM			



subjects affected / exposed	0 / 485 (0.00%)	2 / 482 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
<b>METASTASES TO HEART</b>			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
<b>METASTASES TO SPINE</b>			
subjects affected / exposed	1 / 485 (0.21%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>NON-SMALL CELL LUNG CANCER</b>			
subjects affected / exposed	1 / 485 (0.21%)	3 / 482 (0.62%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 3	
<b>TUMOUR COMPRESSION</b>			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>TUMOUR PAIN</b>			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Vascular disorders</b>			
<b>AORTIC THROMBOSIS</b>			
subjects affected / exposed	1 / 485 (0.21%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>EMBOLISM</b>			
subjects affected / exposed	1 / 485 (0.21%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
<b>HYPOTENSION</b>			

subjects affected / exposed	2 / 485 (0.41%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ORTHOSTATIC HYPOTENSION			
subjects affected / exposed	1 / 485 (0.21%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUPERIOR VENA CAVA SYNDROME			
subjects affected / exposed	2 / 485 (0.41%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
ADVERSE DRUG REACTION			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CHEST PAIN			
subjects affected / exposed	4 / 485 (0.82%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEATH			
subjects affected / exposed	4 / 485 (0.82%)	3 / 482 (0.62%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 4	0 / 3	
DISEASE PROGRESSION			
subjects affected / exposed	1 / 485 (0.21%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	1 / 1	0 / 1	
FATIGUE			
subjects affected / exposed	1 / 485 (0.21%)	3 / 482 (0.62%)	
occurrences causally related to treatment / all	1 / 1	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
GENERAL PHYSICAL HEALTH DETERIORATION			

subjects affected / exposed	1 / 485 (0.21%)	3 / 482 (0.62%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
MULTIPLE ORGAN DYSFUNCTION SYNDROME			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
PAIN			
subjects affected / exposed	0 / 485 (0.00%)	2 / 482 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERFORMANCE STATUS DECREASED			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PYREXIA			
subjects affected / exposed	2 / 485 (0.41%)	3 / 482 (0.62%)	
occurrences causally related to treatment / all	0 / 2	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
ANAPHYLACTIC REACTION			
subjects affected / exposed	1 / 485 (0.21%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DRUG HYPERSENSITIVITY			
subjects affected / exposed	3 / 485 (0.62%)	7 / 482 (1.45%)	
occurrences causally related to treatment / all	0 / 3	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
OVARIAN MASS			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

PROSTATITIS			
subjects affected / exposed	1 / 485 (0.21%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
TESTICULAR CYST			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
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 / 485 (0.00%)	3 / 482 (0.62%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 3	
ALVEOLITIS			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ASPIRATION			
subjects affected / exposed	1 / 485 (0.21%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
ATELECTASIS			
subjects affected / exposed	2 / 485 (0.41%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BRONCHIAL OBSTRUCTION			
subjects affected / exposed	1 / 485 (0.21%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	1 / 485 (0.21%)	2 / 482 (0.41%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

DYSпноEA			
subjects affected / exposed	4 / 485 (0.82%)	6 / 482 (1.24%)	
occurrences causally related to treatment / all	0 / 4	0 / 6	
deaths causally related to treatment / all	0 / 1	0 / 1	
HAEMOPTYSIS			
subjects affected / exposed	7 / 485 (1.44%)	3 / 482 (0.62%)	
occurrences causally related to treatment / all	0 / 7	1 / 3	
deaths causally related to treatment / all	0 / 3	1 / 1	
HYPOXIA			
subjects affected / exposed	1 / 485 (0.21%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
LUNG INFILTRATION			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PLEURAL EFFUSION			
subjects affected / exposed	8 / 485 (1.65%)	4 / 482 (0.83%)	
occurrences causally related to treatment / all	1 / 8	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 0	
PNEUMONIA ASPIRATION			
subjects affected / exposed	1 / 485 (0.21%)	0 / 482 (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	1 / 485 (0.21%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMOTHORAX			
subjects affected / exposed	2 / 485 (0.41%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMOTHORAX SPONTANEOUS			

subjects affected / exposed	1 / 485 (0.21%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>PULMONARY EMBOLISM</b>			
subjects affected / exposed	5 / 485 (1.03%)	6 / 482 (1.24%)	
occurrences causally related to treatment / all	2 / 5	1 / 6	
deaths causally related to treatment / all	0 / 1	0 / 1	
<b>PULMONARY HAEMORRHAGE</b>			
subjects affected / exposed	2 / 485 (0.41%)	3 / 482 (0.62%)	
occurrences causally related to treatment / all	0 / 2	1 / 3	
deaths causally related to treatment / all	0 / 2	1 / 2	
<b>PULMONARY OEDEMA</b>			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>RESPIRATORY DISORDER</b>			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>RESPIRATORY DISTRESS</b>			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
<b>RESPIRATORY FAILURE</b>			
subjects affected / exposed	2 / 485 (0.41%)	3 / 482 (0.62%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 2	
<b>Psychiatric disorders</b>			
<b>INSOMNIA</b>			
subjects affected / exposed	1 / 485 (0.21%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Investigations</b>			

BLOOD CREATININE INCREASED			
subjects affected / exposed	1 / 485 (0.21%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
GENERAL PHYSICAL CONDITION ABNORMAL			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
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			
FALL			
subjects affected / exposed	1 / 485 (0.21%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
FEMORAL NECK FRACTURE			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PROCEDURAL PAIN			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SPINAL COMPRESSION FRACTURE			
subjects affected / exposed	1 / 485 (0.21%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
TOXICITY TO VARIOUS AGENTS			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ULNA FRACTURE			
subjects affected / exposed	1 / 485 (0.21%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiac disorders			
ACUTE CORONARY SYNDROME			
subjects affected / exposed	0 / 485 (0.00%)	2 / 482 (0.41%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
ACUTE MYOCARDIAL INFARCTION			
subjects affected / exposed	3 / 485 (0.62%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	2 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ANGINA PECTORIS			
subjects affected / exposed	1 / 485 (0.21%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ARRHYTHMIA			
subjects affected / exposed	1 / 485 (0.21%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ATRIAL FIBRILLATION			
subjects affected / exposed	3 / 485 (0.62%)	7 / 482 (1.45%)	
occurrences causally related to treatment / all	0 / 3	3 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
ATRIAL FLUTTER			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIAC ARREST			
subjects affected / exposed	2 / 485 (0.41%)	2 / 482 (0.41%)	
occurrences causally related to treatment / all	0 / 2	1 / 2	
deaths causally related to treatment / all	0 / 2	1 / 2	
CARDIAC FAILURE			
subjects affected / exposed	1 / 485 (0.21%)	2 / 482 (0.41%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 2	
CARDIAC FAILURE ACUTE			



subjects affected / exposed	0 / 485 (0.00%)	2 / 482 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
CARDIAC FAILURE CONGESTIVE			
subjects affected / exposed	1 / 485 (0.21%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIOVASCULAR INSUFFICIENCY			
subjects affected / exposed	1 / 485 (0.21%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	1 / 1	0 / 1	
INTRACARDIAC MASS			
subjects affected / exposed	1 / 485 (0.21%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MYOCARDIAL INFARCTION			
subjects affected / exposed	1 / 485 (0.21%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERICARDIAL EFFUSION			
subjects affected / exposed	1 / 485 (0.21%)	2 / 482 (0.41%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
SINUS TACHYCARDIA			
subjects affected / exposed	1 / 485 (0.21%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
TACHYCARDIA			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
CEREBRAL HAEMORRHAGE			

subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
CEREBROVASCULAR ACCIDENT			
subjects affected / exposed	3 / 485 (0.62%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
COGNITIVE DISORDER			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIZZINESS			
subjects affected / exposed	1 / 485 (0.21%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEMIPARESIS			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEUROPATHY PERIPHERAL			
subjects affected / exposed	1 / 485 (0.21%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PARTIAL SEIZURES			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERIPHERAL SENSORY NEUROPATHY			
subjects affected / exposed	1 / 485 (0.21%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PRESYNCOPE			

subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SEIZURE			
subjects affected / exposed	1 / 485 (0.21%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SYNCOPE			
subjects affected / exposed	2 / 485 (0.41%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
TRANSIENT ISCHAEMIC ATTACK			
subjects affected / exposed	2 / 485 (0.41%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	12 / 485 (2.47%)	21 / 482 (4.36%)	
occurrences causally related to treatment / all	5 / 18	7 / 24	
deaths causally related to treatment / all	0 / 0	0 / 1	
FEBRILE NEUTROPENIA			
subjects affected / exposed	17 / 485 (3.51%)	20 / 482 (4.15%)	
occurrences causally related to treatment / all	10 / 18	12 / 21	
deaths causally related to treatment / all	0 / 1	0 / 0	
LEUKOPENIA			
subjects affected / exposed	2 / 485 (0.41%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEUTROPENIA			
subjects affected / exposed	8 / 485 (1.65%)	12 / 482 (2.49%)	
occurrences causally related to treatment / all	2 / 8	3 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
PANCYTOPENIA			

subjects affected / exposed	3 / 485 (0.62%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
THROMBOCYTOPENIA			
subjects affected / exposed	3 / 485 (0.62%)	4 / 482 (0.83%)	
occurrences causally related to treatment / all	3 / 5	2 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
VERTIGO			
subjects affected / exposed	1 / 485 (0.21%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	1 / 485 (0.21%)	2 / 482 (0.41%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
ABDOMINAL PAIN UPPER			
subjects affected / exposed	1 / 485 (0.21%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ASCITES			
subjects affected / exposed	0 / 485 (0.00%)	2 / 482 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
CONSTIPATION			
subjects affected / exposed	1 / 485 (0.21%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIARRHOEA			
subjects affected / exposed	2 / 485 (0.41%)	5 / 482 (1.04%)	
occurrences causally related to treatment / all	2 / 2	3 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIVERTICULAR PERFORATION			

subjects affected / exposed	1 / 485 (0.21%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DUODENAL ULCER			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DUODENAL ULCER PERFORATION			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DYSPHAGIA			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ENTERITIS			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
FAECES DISCOLOURED			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTRIC HAEMORRHAGE			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTRIC ULCER			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
GASTRITIS			

subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>GASTRITIS EROSIVE</b>			
subjects affected / exposed	1 / 485 (0.21%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>GASTROINTESTINAL HAEMORRHAGE</b>			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
<b>GASTROINTESTINAL PERFORATION</b>			
subjects affected / exposed	1 / 485 (0.21%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>NAUSEA</b>			
subjects affected / exposed	0 / 485 (0.00%)	4 / 482 (0.83%)	
occurrences causally related to treatment / all	0 / 0	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>OESOPHAGEAL STENOSIS</b>			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>SMALL INTESTINAL OBSTRUCTION</b>			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>TONGUE OEDEMA</b>			
subjects affected / exposed	1 / 485 (0.21%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>VOMITING</b>			

subjects affected / exposed	0 / 485 (0.00%)	3 / 482 (0.62%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Hepatobiliary disorders</b>			
<b>HEPATITIS ACUTE</b>			
subjects affected / exposed	1 / 485 (0.21%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>PORTAL VEIN THROMBOSIS</b>			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Renal and urinary disorders</b>			
<b>ACUTE KIDNEY INJURY</b>			
subjects affected / exposed	2 / 485 (0.41%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>AZOTAEMIA</b>			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
<b>NEPHROLITHIASIS</b>			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>RENAL COLIC</b>			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>RENAL IMPAIRMENT</b>			
subjects affected / exposed	1 / 485 (0.21%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>URINARY RETENTION</b>			

subjects affected / exposed	1 / 485 (0.21%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Musculoskeletal and connective tissue disorders</b>			
<b>ARTHRALGIA</b>			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>BACK PAIN</b>			
subjects affected / exposed	2 / 485 (0.41%)	3 / 482 (0.62%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>BONE PAIN</b>			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>FLANK PAIN</b>			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>INTERVERTEBRAL DISC PROTRUSION</b>			
subjects affected / exposed	1 / 485 (0.21%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>MUSCULAR WEAKNESS</b>			
subjects affected / exposed	0 / 485 (0.00%)	2 / 482 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>MUSCULOSKELETAL CHEST PAIN</b>			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>PAIN IN EXTREMITY</b>			



subjects affected / exposed	1 / 485 (0.21%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>PATHOLOGICAL FRACTURE</b>			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Infections and infestations</b>			
<b>ANAL ABSCESS</b>			
subjects affected / exposed	1 / 485 (0.21%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>BACTERAEMIA</b>			
subjects affected / exposed	1 / 485 (0.21%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>BRONCHITIS</b>			
subjects affected / exposed	2 / 485 (0.41%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>CLOSTRIDIUM DIFFICILE COLITIS</b>			
subjects affected / exposed	1 / 485 (0.21%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>DIVERTICULITIS</b>			
subjects affected / exposed	1 / 485 (0.21%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>EMPYEMA</b>			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>ENTEROCOLITIS INFECTIOUS</b>			

subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>GASTROENTERITIS</b>			
subjects affected / exposed	2 / 485 (0.41%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
<b>INFECTION</b>			
subjects affected / exposed	0 / 485 (0.00%)	2 / 482 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>LOWER RESPIRATORY TRACT INFECTION</b>			
subjects affected / exposed	3 / 485 (0.62%)	7 / 482 (1.45%)	
occurrences causally related to treatment / all	1 / 3	1 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>LUNG ABSCESS</b>			
subjects affected / exposed	0 / 485 (0.00%)	2 / 482 (0.41%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>LUNG INFECTION</b>			
subjects affected / exposed	3 / 485 (0.62%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>MESENTERIC ABSCESS</b>			
subjects affected / exposed	1 / 485 (0.21%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>NEUTROPENIC SEPSIS</b>			
subjects affected / exposed	0 / 485 (0.00%)	2 / 482 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
<b>ORAL CANDIDIASIS</b>			

subjects affected / exposed	1 / 485 (0.21%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
OSTEOMYELITIS			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA			
subjects affected / exposed	23 / 485 (4.74%)	19 / 482 (3.94%)	
occurrences causally related to treatment / all	4 / 24	4 / 21	
deaths causally related to treatment / all	0 / 3	1 / 2	
PNEUMONIA BACTERIAL			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA KLEBSIELLA			
subjects affected / exposed	1 / 485 (0.21%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA STAPHYLOCOCCAL			
subjects affected / exposed	1 / 485 (0.21%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
PULMONARY SEPSIS			
subjects affected / exposed	1 / 485 (0.21%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
PYELONEPHRITIS			
subjects affected / exposed	1 / 485 (0.21%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RESPIRATORY TRACT INFECTION			

subjects affected / exposed	4 / 485 (0.82%)	5 / 482 (1.04%)	
occurrences causally related to treatment / all	1 / 4	1 / 5	
deaths causally related to treatment / all	0 / 0	1 / 1	
SEPSIS			
subjects affected / exposed	4 / 485 (0.82%)	2 / 482 (0.41%)	
occurrences causally related to treatment / all	2 / 4	0 / 2	
deaths causally related to treatment / all	1 / 1	0 / 0	
SEPTIC EMBOLUS			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
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	4 / 485 (0.82%)	2 / 482 (0.41%)	
occurrences causally related to treatment / all	0 / 4	1 / 2	
deaths causally related to treatment / all	0 / 2	1 / 1	
SINUSITIS			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUBCUTANEOUS ABSCESS			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
URINARY TRACT INFECTION			
subjects affected / exposed	1 / 485 (0.21%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
URINARY TRACT INFECTION ENTEROCOCCAL			

subjects affected / exposed	0 / 485 (0.00%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	1 / 485 (0.21%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEHYDRATION			
subjects affected / exposed	3 / 485 (0.62%)	2 / 482 (0.41%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
ELECTROLYTE IMBALANCE			
subjects affected / exposed	1 / 485 (0.21%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERCALCAEMIA			
subjects affected / exposed	1 / 485 (0.21%)	3 / 482 (0.62%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERGLYCAEMIA			
subjects affected / exposed	2 / 485 (0.41%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERURICAEMIA			
subjects affected / exposed	1 / 485 (0.21%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOGLYCAEMIA			
subjects affected / exposed	1 / 485 (0.21%)	0 / 482 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOKALAEMIA			

subjects affected / exposed	1 / 485 (0.21%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>HYPONATRAEMIA</b>			
subjects affected / exposed	1 / 485 (0.21%)	1 / 482 (0.21%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

<b>Non-serious adverse events</b>	<b>Veliparib + Carboplatin + Paclitaxel</b>	<b>Placebo + Carboplatin + Paclitaxel</b>	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	441 / 485 (90.93%)	438 / 482 (90.87%)	
<b>Investigations</b>			
<b>WEIGHT DECREASED</b>			
subjects affected / exposed	26 / 485 (5.36%)	36 / 482 (7.47%)	
occurrences (all)	29	42	
<b>Nervous system disorders</b>			
<b>DIZZINESS</b>			
subjects affected / exposed	26 / 485 (5.36%)	24 / 482 (4.98%)	
occurrences (all)	30	26	
<b>DYSGEUSIA</b>			
subjects affected / exposed	22 / 485 (4.54%)	26 / 482 (5.39%)	
occurrences (all)	22	29	
<b>NEUROPATHY PERIPHERAL</b>			
subjects affected / exposed	43 / 485 (8.87%)	43 / 482 (8.92%)	
occurrences (all)	57	58	
<b>PARAESTHESIA</b>			
subjects affected / exposed	27 / 485 (5.57%)	43 / 482 (8.92%)	
occurrences (all)	29	57	
<b>PERIPHERAL SENSORY NEUROPATHY</b>			
subjects affected / exposed	153 / 485 (31.55%)	148 / 482 (30.71%)	
occurrences (all)	217	220	
<b>Blood and lymphatic system disorders</b>			

ANAEMIA			
subjects affected / exposed	157 / 485 (32.37%)	146 / 482 (30.29%)	
occurrences (all)	254	232	
LEUKOPENIA			
subjects affected / exposed	53 / 485 (10.93%)	34 / 482 (7.05%)	
occurrences (all)	86	46	
LYMPHOPENIA			
subjects affected / exposed	25 / 485 (5.15%)	18 / 482 (3.73%)	
occurrences (all)	37	22	
NEUTROPENIA			
subjects affected / exposed	152 / 485 (31.34%)	133 / 482 (27.59%)	
occurrences (all)	259	227	
THROMBOCYTOPENIA			
subjects affected / exposed	92 / 485 (18.97%)	98 / 482 (20.33%)	
occurrences (all)	173	185	
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	71 / 485 (14.64%)	72 / 482 (14.94%)	
occurrences (all)	114	118	
FATIGUE			
subjects affected / exposed	100 / 485 (20.62%)	105 / 482 (21.78%)	
occurrences (all)	134	143	
OEDEMA PERIPHERAL			
subjects affected / exposed	25 / 485 (5.15%)	23 / 482 (4.77%)	
occurrences (all)	30	24	
PYREXIA			
subjects affected / exposed	32 / 485 (6.60%)	34 / 482 (7.05%)	
occurrences (all)	37	44	
Gastrointestinal disorders			
CONSTIPATION			
subjects affected / exposed	74 / 485 (15.26%)	84 / 482 (17.43%)	
occurrences (all)	90	98	
DIARRHOEA			
subjects affected / exposed	83 / 485 (17.11%)	76 / 482 (15.77%)	
occurrences (all)	110	91	
NAUSEA			

subjects affected / exposed	116 / 485 (23.92%)	112 / 482 (23.24%)	
occurrences (all)	142	146	
VOMITING			
subjects affected / exposed	44 / 485 (9.07%)	51 / 482 (10.58%)	
occurrences (all)	61	65	
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	62 / 485 (12.78%)	69 / 482 (14.32%)	
occurrences (all)	71	73	
DYSPNOEA			
subjects affected / exposed	70 / 485 (14.43%)	55 / 482 (11.41%)	
occurrences (all)	77	61	
Skin and subcutaneous tissue disorders			
ALOPECIA			
subjects affected / exposed	232 / 485 (47.84%)	220 / 482 (45.64%)	
occurrences (all)	268	245	
RASH			
subjects affected / exposed	12 / 485 (2.47%)	25 / 482 (5.19%)	
occurrences (all)	13	32	
Psychiatric disorders			
INSOMNIA			
subjects affected / exposed	32 / 485 (6.60%)	38 / 482 (7.88%)	
occurrences (all)	36	40	
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	65 / 485 (13.40%)	66 / 482 (13.69%)	
occurrences (all)	77	97	
MYALGIA			
subjects affected / exposed	56 / 485 (11.55%)	43 / 482 (8.92%)	
occurrences (all)	83	59	
PAIN IN EXTREMITY			
subjects affected / exposed	46 / 485 (9.48%)	40 / 482 (8.30%)	
occurrences (all)	58	45	
Metabolism and nutrition disorders			
DECREASED APPETITE			



subjects affected / exposed	68 / 485 (14.02%)	77 / 482 (15.98%)	
occurrences (all)	84	88	
HYPERGLYCAEMIA			
subjects affected / exposed	33 / 485 (6.80%)	36 / 482 (7.47%)	
occurrences (all)	49	61	
HYPOKALAEMIA			
subjects affected / exposed	19 / 485 (3.92%)	27 / 482 (5.60%)	
occurrences (all)	21	34	
HYPOMAGNESAEMIA			
subjects affected / exposed	33 / 485 (6.80%)	29 / 482 (6.02%)	
occurrences (all)	48	35	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 May 2014	Updated inclusion/exclusion criteria and updated requirements for physical examination to include neurological evaluation and hearing assessment at Screening and C2D1 – C6D1, in agreement with regulatory feedback.
10 July 2014	Updated inclusion/exclusion criteria, moved duration of response (DOR) from a secondary endpoint to a tertiary endpoint, and clarified that confirmed response was required as part of ORR analysis in agreement with regulatory feedback.
02 February 2016	The primary endpoint was amended to OS in current smokers with OS of all subjects as a secondary endpoint (as Phase 2 data suggested that veliparib benefit may be most evident in smokers). Corresponding changes were also made to the sample size calculation and timing of efficacy and futility interim analysis to align with primary endpoint change.

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported