Clinical trial results:
A Randomized, Open-Label, Multicenter, Phase 3 Trial Comparing Veliparib Plus Carboplatin and Paclitaxel Versus Investigator's Choice of Standard Chemotherapy in Subjects Receiving First Cytotoxic Chemotherapy for Metastatic or Advanced Non Squamous Non-Small Cell Lung Cancer (NSCLC) and Who Are Current or Former Smokers

Summary

EudraCT number	2014-002565-30
Trial protocol	FI CZ DE HU NL ES DK GB
Global end of trial date	21 February 2020

Results information

Result version number	v1 (current)
This version publication date	24 February 2021
First version publication date	24 February 2021

Trial information

Trial identification

Sponsor protocol code	M14-359

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02264990
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AbbVie
Sponsor organisation address	AbbVie House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire, United Kingdom, SL6-4UB
Public contact	Global Medical Services, AbbVie, 001 800-633-9110, abbvieclinicaltrials@abbvie.com
Scientific contact	Global Medical Services, AbbVie, 001 800-633-9110, abbvieclinicaltrials@abbvie.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	21 February 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 February 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to evaluate the safety and efficacy of veliparib plus carboplatin and paclitaxel versus the Investigator's choice of standard chemotherapy in adults with metastatic or advanced non-squamous non-small cell lung cancer.

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	30 September 2014
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	48 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 6
Country: Number of subjects enrolled	Australia: 19
Country: Number of subjects enrolled	Canada: 12
Country: Number of subjects enrolled	Czechia: 7
Country: Number of subjects enrolled	Denmark: 7
Country: Number of subjects enrolled	Finland: 3
Country: Number of subjects enrolled	Germany: 13
Country: Number of subjects enrolled	Hungary: 34
Country: Number of subjects enrolled	Israel: 14
Country: Number of subjects enrolled	Japan: 72
Country: Number of subjects enrolled	Korea, Republic of: 19
Country: Number of subjects enrolled	Netherlands: 31
Country: Number of subjects enrolled	New Zealand: 11
Country: Number of subjects enrolled	Russian Federation: 74
Country: Number of subjects enrolled	South Africa: 19
Country: Number of subjects enrolled	Taiwan: 14
Country: Number of subjects enrolled	Turkey: 27
Country: Number of subjects enrolled	United Kingdom: 62
Country: Number of subjects enrolled	United States: 97

Country: Number of subjects enrolled	Spain: 54
Worldwide total number of subjects	595
EEA total number of subjects	149

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)	316
From 65 to 84 years	278
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at 131 sites in 20 countries (Argentina, Australia, Canada, Czech Republic, Denmark, Finland, Germany, Hungary, Israel, Japan, South Korea, Netherlands, New Zealand, Russian Federation, South Africa, Spain, Taiwan, Turkey, United Kingdom, and United States).

Pre-assignment

Screening details:

Participants were randomized in a 1:1 ratio to veliparib plus carboplatin and paclitaxel (C/P) or investigator's choice of platinum doublet chemotherapy. Randomization was stratified by smoking status (current vs former), investigators' preferred doublet therapy (C/P vs cisplatin/pemetrexed vs carboplatin/pemetrexed), gender, and ECOG PS (0 vs 1).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Investigator's Choice Chemotherapy

Arm description:

Participants received Investigator's choice of standard doublet chemotherapy consisting of 1 of the following 3 options, administered on Day 1 of each 21-day cycle for a maximum of 6 cycles:
- Carboplatin at an area under the curve (AUC) of 6 mg/mL*min + paclitaxel 200 mg/m²
- Cisplatin 75 mg/m² + pemetrexed 500 mg/m²
- Carboplatin AUC 6 or AUC 5 mg/mL*min + pemetrexed 500 mg/m²

After completion of up to 6 cycles, optional maintenance pemetrexed was administered as 500 mg/m² on Day 1 of each 21-day cycle until toxicity required cessation of therapy, or radiographic progression occurred.

Arm type	Active comparator
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:

Administered at an AUC 6 mg/mL*min or AUC 5 mg/mL*min on Day 1 of each 21-day cycle.

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

Dosage and administration details:

Administered by intravenous infusion 200 mg/m² on Day 1 of each 21-day cycle.

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

Dosage and administration details:

Administered by intravenous infusion at 75 mg/m² on Day 1 of each 21-day cycle.

Investigational medicinal product name	Pemetrexed
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion, Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered by intravenous infusion at 500 mg/m² Day 1 of each 21-day cycle

Arm title	Veliparib + Carboplatin + Paclitaxel

Arm description:

Participants received 120 mg veliparib twice a day (BID) on Days -2 to 5 (7 days), carboplatin at an AUC of 6 mg/mL*min on Day 1 and paclitaxel 200 mg/m² on Day 1 of each 21-day cycle for a maximum of 6 cycles.
After completion of up to 6 cycles, optional maintenance pemetrexed was administered as 500 mg/m² on Day 1 of each 21-day cycle until toxicity required cessation of therapy, or radiographic progression occurred.

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

Dosage and administration details:

120 mg orally twice a day on Days -2 to 5 of each 21-day cycle.

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:

Administered at an AUC 6 mg/mL*min on Day 1 of each 21-day cycle.

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

Dosage and administration details:

Administered by intravenous infusion at 200 mg/m² on Day 1 of each 21-day cycle.

Number of subjects in period 1	Investigator's Choice Chemotherapy	Veliparib + Carboplatin + Paclitaxel
Started	297	298
Received Treatment	288	293
Received Maintenance Therapy	148	123
Completed	37	39
Not completed	260	259
Consent withdrawn by subject	4	5
Death	255	250
Other	-	1

Lost to follow-up	1	3

Baseline characteristics

Reporting groups

Reporting group title	Investigator's Choice Chemotherapy

Reporting group description:

Participants received Investigator's choice of standard doublet chemotherapy consisting of 1 of the following 3 options, administered on Day 1 of each 21-day cycle for a maximum of 6 cycles:
- Carboplatin at an area under the curve (AUC) of 6 mg/mL*min + paclitaxel 200 mg/m²
- Cisplatin 75 mg/m² + pemetrexed 500 mg/m²
- Carboplatin AUC 6 or AUC 5 mg/mL*min + pemetrexed 500 mg/m²

After completion of up to 6 cycles, optional maintenance pemetrexed was administered as 500 mg/m² on Day 1 of each 21-day cycle until toxicity required cessation of therapy, or radiographic progression occurred.

Reporting group title	Veliparib + Carboplatin + Paclitaxel

Reporting group description:

Participants received 120 mg veliparib twice a day (BID) on Days -2 to 5 (7 days), carboplatin at an AUC of 6 mg/mL*min on Day 1 and paclitaxel 200 mg/m² on Day 1 of each 21-day cycle for a maximum of 6 cycles.
After completion of up to 6 cycles, optional maintenance pemetrexed was administered as 500 mg/m² on Day 1 of each 21-day cycle until toxicity required cessation of therapy, or radiographic progression occurred.

Reporting group values	Investigator's Choice Chemotherapy	Veliparib + Carboplatin + Paclitaxel	Total
Number of subjects	297	298	595
Age categorical Units: Subjects			
< 65 years	153	163	316
≥ 65 years	144	135	279
Age continuous Units: years			
arithmetic mean	63.1	62.7	
standard deviation	± 8.99	± 9.02	-
Gender categorical Units: Subjects			
Female	90	92	182
Male	207	206	413
Race Units: Subjects			
White	233	229	462
Black	11	11	22
Asian	53	57	110
Other	0	1	1
Ethnicity Units: Subjects			
Hispanic or Latino	22	26	48
Not Hispanic or Latino	275	272	547
Region Units: Subjects			
US and Western EU and Australia and Canada	177	157	334
Eastern EU/Russia	68	88	156

Japan	37	35	72
Other Asia	15	18	33
Smoking Status Units: Subjects			
Current smoker	153	152	305
Past smoker	144	146	290
Investigators' Preferred Platinum Doublet Therapy			
The investigator's preferred choice of platinum doublet therapy prior to randomization, which was used as a stratification factor. Note that while the investigator's pre-randomization preferred choice for the doublet is summarized, all participants on the veliparib arm received carboplatin and paclitaxel as chemotherapy.			
Units: Subjects			
Carboplatin/paclitaxel	71	70	141
Cisplatin/pemetrexed	95	100	195
Carboplatin/pemetrexed	131	128	259
Eastern Cooperative Oncology Group (ECOG) Performance Status			
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; 1 = Restricted activity but ambulatory; 2 = Ambulatory but unable to carry out work activities; 3 = Limited Self-Care; 4 = Completely Disabled, No self-care			
Units: Subjects			
Grade 0 (Fully active)	113	116	229
Grade 1 (restricted but ambulatory)	184	182	366
Lung Subtype Panel (LSP) Assay Results			
LSP positive: Patients with tumors classified as positive for the gene expression-based lung subtype panel (LSP) biomarker LSP negative: Patients with tumors classified as negative for the gene expression-based lung subtype panel (LSP) biomarker			
Units: Subjects			
Not enough sample for LSP status evaluation	138	126	264
Sample QC failed	66	58	124
LSP positive	40	40	80
LSP negative	53	74	127

End points

End points reporting groups

Reporting group title	Investigator's Choice Chemotherapy

Reporting group description:

Participants received Investigator's choice of standard doublet chemotherapy consisting of 1 of the following 3 options, administered on Day 1 of each 21-day cycle for a maximum of 6 cycles:
- Carboplatin at an area under the curve (AUC) of 6 mg/mL*min + paclitaxel 200 mg/m²
- Cisplatin 75 mg/m² + pemetrexed 500 mg/m²
- Carboplatin AUC 6 or AUC 5 mg/mL*min + pemetrexed 500 mg/m²

After completion of up to 6 cycles, optional maintenance pemetrexed was administered as 500 mg/m² on Day 1 of each 21-day cycle until toxicity required cessation of therapy, or radiographic progression occurred.

Reporting group title	Veliparib + Carboplatin + Paclitaxel

Reporting group description:

Participants received 120 mg veliparib twice a day (BID) on Days -2 to 5 (7 days), carboplatin at an AUC of 6 mg/mL*min on Day 1 and paclitaxel 200 mg/m² on Day 1 of each 21-day cycle for a maximum of 6 cycles.
After completion of up to 6 cycles, optional maintenance pemetrexed was administered as 500 mg/m² on Day 1 of each 21-day cycle until toxicity required cessation of therapy, or radiographic progression occurred.

Primary: Overall Survival (OS) in the Lung Subtype Panel Positive Subgroup

End point title	Overall Survival (OS) in the Lung Subtype Panel Positive Subgroup

End point description:

Overall survival is defined as the time from the date that the participant was randomized to the date of the participant's death. OS was estimated using Kaplan-Meier methodology. Participants still alive at the data cut-off date were censored at the date they were last known to be alive.

End point type	Primary

End point timeframe:

From randomization up to the data cut-off date of 15 July 2019; the median follow-up time was 44.5 and 45.3 months in LSP+ participants for the investigator's choice chemotherapy and veliparib + C/P arms, respectively.

End point values	Investigator's Choice Chemotherapy	Veliparib + Carboplatin + Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40[1]	40[2]		
Units: months				
median (confidence interval 95%)	9.2 (5.1 to 11.7)	11.2 (7.5 to 15.8)		

Notes:

[1] - LSP-positive subgroup

[2] - LSP-positive subgroup

Statistical analyses

Statistical analysis title	Primary Analysis of OS in the LSP+ Subgroup
Comparison groups	Investigator's Choice Chemotherapy v Veliparib + Carboplatin + Paclitaxel

Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 0.113 [4]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.644
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.396
upper limit	1.048

Notes:

[3] - A fixed sequence testing procedure was used for analyses of the primary and secondary efficacy endpoints to control for the familywise error rate. If veliparib plus C/P treatment was not statistically significantly better compared to the investigators' choice of standard therapy for the primary efficacy endpoint of OS in LSP+ participants, then statistical significance would not be declared for any of the secondary efficacy endpoints.
[4] - Log rank test stratified by ECOG performance status, investigators' preferred platinum therapy, and gender.
Statistical significance was determined by a two-sided P value ≤ 0.05.

Secondary: Progression Free Survival (PFS) in the Lung Subtype Panel Positive Subgroup

End point title	Progression Free Survival (PFS) in the Lung Subtype Panel Positive Subgroup

End point description:

Progression-free survival is defined as the time from the date of randomization to the date of disease progression (PD) per Response Evaluation Criteria In Solid Tumors (RECIST) version 1.1 or death (all causes of mortality), whichever occurred first.
PD: At least a 20% increase in the size of target lesions, taking as reference the smallest size recorded since the treatment started (Baseline or after) with an absolute increase of at least 5 mm, the appearance of one or more new lesions, or unequivocal progression of existing non-target lesions.
PFS was estimated using Kaplan-Meier methodology. Participants who did not have an event of disease progression or had not died on or before the cut-off date were censored at the date of their last disease progression assessment on or before the cut-off date. Any PD and death occurring > 26 weeks and > 12 weeks after the previous assessment, respectively, were excluded and patients were censored at last assessment before PD or death.

End point type	Secondary

End point timeframe:

From randomization up to the data cut-off date of 15 July 2019; the median follow-up time was 44.5 and 45.3 months in LSP+ participants for the investigator's choice chemotherapy and veliparib + C/P arms, respectively.

End point values	Investigator's Choice Chemotherapy	Veliparib + Carboplatin + Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40[5]	40[6]		
Units: months				
median (confidence interval 95%)	5.2 (2.8 to 6.2)	6.3 (3.5 to 7.4)		

Notes:

[5] - Lung subtype panel positive subgroup

[6] - Lung subtype panel positive subgroup

Statistical analyses

Statistical analysis title	Analysis of PFS in LSP+ Subgroup
Comparison groups	Investigator's Choice Chemotherapy v Veliparib + Carboplatin + Paclitaxel
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	other[7]
P-value	= 0.26 [8]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.647
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.388
upper limit	1.08

Notes:

[7] - A fixed sequence testing procedure was used for analyses of the primary and secondary efficacy endpoints to control for the familywise error rate. If veliparib plus C/P treatment was not statistically significantly better than the investigators' choice of standard therapy for the primary efficacy endpoint of OS in LSP+ subjects, then statistical significance will not be declared for any of the secondary efficacy endpoints.
[8] - Log-rank test stratified by investigator's preferred platinum therapy, gender, and ECOG performance status.

Secondary: Objective Response Rate (ORR) in the Lung Subtype Panel Positive Subgroup

End point title	Objective Response Rate (ORR) in the Lung Subtype Panel Positive Subgroup

End point description:

Objective response rate is defined as the percentage of participants with a complete response (CR) or partial response (PR) per Response Evaluation Criteria In Solid Tumors (RECIST) version 1.1 criteria. Response must have been confirmed at a consecutive assessment 28 days or more after the assessment at which response was first observed.
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.
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:

Assessed on Day 1 of Cycles 3 and 5 then every 9 weeks for 1 year or until maintenance therapy was discontinued, then every 12 weeks until radiographic progression or death; median time on follow-up was 5.2 and 6.3 months in each group, respectively.

End point values	Investigator's Choice Chemotherapy	Veliparib + Carboplatin + Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40[9]	40[10]		
Units: percentage of participants				
number (confidence interval 95%)	30.0 (16.6 to 46.5)	22.5 (10.8 to 38.5)		

Notes:

[9] - Lung subtype panel positive subgroup

[10] - Lung subtype panel positive subgroup

Statistical analyses

Statistical analysis title	Analysis of ORR in LSP+ Subgroup
Comparison groups	Investigator's Choice Chemotherapy v Veliparib + Carboplatin + Paclitaxel
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.445 [11]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.23
upper limit	1.9

Notes:

[11] - Logistic regression adjusted for the covariates of ECOG performance status, investigators' preferred platinum therapy, and gender.

Secondary: Overall Survival in All Participants

End point title	Overall Survival in All Participants

End point description:

Overall survival is defined as the time from the date that the participant was randomized to the date of the participant's death. Overall survival was estimated using Kaplan-Meier methodology. Participants still alive at the data cut-off date were censored at the date they were last known to be alive.

End point type	Secondary

End point timeframe:

From randomization up to the data cut-off date of 15 July 2019; median follow-up time was 45.4 and 44.6 months in all participants for the investigator's choice chemotherapy and veliparib + C/P arms, respectively.

End point values	Investigator's Choice Chemotherapy	Veliparib + Carboplatin + Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	297[12]	298[13]		
Units: monthts				
median (confidence interval 95%)	12.1 (10.0 to 13.7)	12.1 (10.4 to 14.9)		

Notes:

[12] - Intention-to-treat population

[13] - Intention-to-treat population

Statistical analyses

Statistical analysis title	Analysis of Overall Survival in All Participants
Comparison groups	Investigator's Choice Chemotherapy v Veliparib + Carboplatin + Paclitaxel
Number of subjects included in analysis	595
Analysis specification	Pre-specified
Analysis type	other[14]
P-value	= 0.846
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.986
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.827
upper limit	1.176

Notes:

[14] - Log rank test stratified by LSP status, ECOG performance status, investigators' preferred platinum therapy, and gender.

Secondary: Progression-free Survival in All Participants

End point title	Progression-free Survival in All Participants

End point description:

Progression-free survival is defined as the time from the date of randomization to the date of disease progression (PD) per RECIST version 1.1 or death (all causes of mortality), whichever occurred first. PD: At least a 20% increase in the size of target lesions, taking as reference the smallest size recorded since the treatment started (Baseline or after) with an absolute increase of at least 5 mm, the appearance of one or more new lesions, or unequivocal progression of existing non-target lesions. PFS was estimated using Kaplan-Meier methodology. Participants who did not have an event of disease progression or had not died on or before the cut-off date were censored at the date of their last disease progression assessment on or before the cut-off date. Any PD and death occurring > 26 weeks and > 12 weeks after the previous assessment, respectively, were excluded and patients were censored at last assessment before PD or death.

End point type	Secondary

End point timeframe:

From randomization up to the data cut-off date of 15 July 2019; median follow-up time was 45.4 and 44.6 months in all participants for the investigator's choice chemotherapy and veliparib + C/P arms, respectively.

End point values	Investigator's Choice Chemotherapy	Veliparib + Carboplatin + Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	297[15]	298[16]		
Units: months				
median (confidence interval 95%)	6.7 (5.6 to 7.2)	5.9 (5.0 to 6.5)		

Notes:

[15] - Intention-to-treat population

[16] - Intention-to-treat population

Statistical analyses

Statistical analysis title	Analysis of PFS in All Participants
Comparison groups	Investigator's Choice Chemotherapy v Veliparib + Carboplatin + Paclitaxel
Number of subjects included in analysis	595
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.473 [17]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.035
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.867
upper limit	1.235

Notes:

[17] - Log rank test stratified by LSP status, ECOG performance status, investigators' preferred platinum therapy, and gender.

Secondary: Objective Response Rate in All Participants

End point title	Objective Response Rate in All Participants

End point description:

Objective response rate is defined as the percentage of participants with a complete response (CR) or partial response (PR) per Response Evaluation Criteria In Solid Tumors (RECIST) version 1.1 criteria. Response must have been confirmed at a consecutive assessment 28 days or more after the assessment at which response was first observed.
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.
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:

Assessed on Day 1 of Cycles 3 and 5 then every 9 weeks for 1 year or until maintenance therapy was discontinued, then every 12 weeks until radiographic progression or death; median time on follow-up was 6.7 and 5.9 months in each group, respectively.

End point values	Investigator's Choice Chemotherapy	Veliparib + Carboplatin + Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	297[18]	298[19]		
Units: percentage of participants				
number (confidence interval 95%)	29.0 (23.9 to 34.5)	26.2 (21.3 to 31.6)		

Notes:

[18] - Intention-to-treat population

[19] - Intention-to-treat population

Statistical analyses

Statistical analysis title	Analysis of ORR in All Participants
Comparison groups	Investigator's Choice Chemotherapy v Veliparib + Carboplatin + Paclitaxel

Number of subjects included in analysis	595
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.409 [20]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	1.24

Notes:

[20] - Logistic regression adjusted for the covariates of LSP status, ECOG performance status, investigators' preferred platinum therapy, and gender.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug until 30 days after last dose of study drug (veliparib or investigators' choice of standard chemotherapy); median duration of treatment ranged from 86 to 111 days for each treatment.

Adverse event reporting additional description:

The as-treated subjects population included all participants who received at least 1 dose of study drug (veliparib/investigator's choice of standard chemotherapy).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	Veliparib + Carboplatin + Paclitaxel

Reporting group description:

Participants received 120 mg veliparib twice a day (BID) on Days -2 to 5 (7 days), carboplatin at an AUC of 6 mg/mL*min on Day 1 and paclitaxel 200 mg/m² on Day 1 of each 21-day cycle for a maximum of 6 cycles.
After completion of up to 6 cycles, optional maintenance pemetrexed was administered as 500 mg/m² on Day 1 of each 21-day cycle until toxicity required cessation of therapy, or radiographic progression occurred.

Reporting group title	Investigator's Choice Chemotherapy

Reporting group description:

Participants received Investigator's choice of standard doublet chemotherapy consisting of 1 of the following 3 options, administered on Day 1 of each 21-day cycle for a maximum of 6 cycles:
- Carboplatin AUC 6 mg/mL*min + paclitaxel 200 mg/m²
- Cisplatin 75 mg/m² + pemetrexed 500 mg/m²
- Carboplatin AUC 6 or AUC 5 mg/mL*min + pemetrexed 500 mg/m² After completion of up to 6 cycles, optional maintenance pemetrexed was administered as 500 mg/m² on Day 1 of each 21-day cycle until toxicity required cessation of therapy, or radiographic progression occurred.

Serious adverse events	Veliparib + Carboplatin + Paclitaxel	Investigator's Choice Chemotherapy	
Total subjects affected by serious adverse events			
subjects affected / exposed	121 / 293 (41.30%)	98 / 288 (34.03%)	
number of deaths (all causes)	249	252	
number of deaths resulting from adverse events	24	22	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
CANCER PAIN			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTRIC CANCER			

subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MALIGNANT NEOPLASM PROGRESSION			
subjects affected / exposed	14 / 293 (4.78%)	10 / 288 (3.47%)	
occurrences causally related to treatment / all	0 / 19	0 / 12	
deaths causally related to treatment / all	0 / 8	0 / 4	
MALIGNANT PLEURAL EFFUSION			
subjects affected / exposed	0 / 293 (0.00%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
METASTASES TO BONE			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
METASTASES TO CENTRAL NERVOUS SYSTEM			
subjects affected / exposed	4 / 293 (1.37%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
METASTASES TO MENINGES			
subjects affected / exposed	0 / 293 (0.00%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERICARDIAL EFFUSION MALIGNANT			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
ANEURYSM			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
AXILLARY VEIN THROMBOSIS			

subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEEP VEIN THROMBOSIS			
subjects affected / exposed	0 / 293 (0.00%)	2 / 288 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOTENSION			
subjects affected / exposed	2 / 293 (0.68%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOVOLAEMIC SHOCK			
subjects affected / exposed	0 / 293 (0.00%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
ORTHOSTATIC HYPOTENSION			
subjects affected / exposed	0 / 293 (0.00%)	2 / 288 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
VENOUS THROMBOSIS			
subjects affected / exposed	0 / 293 (0.00%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	1 / 293 (0.34%)	2 / 288 (0.69%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
CATHETER SITE HAEMORRHAGE			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CHEST PAIN			

subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DISEASE PROGRESSION			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
FATIGUE			
subjects affected / exposed	0 / 293 (0.00%)	2 / 288 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
GENERAL PHYSICAL HEALTH DETERIORATION			
subjects affected / exposed	0 / 293 (0.00%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
MALAISE			
subjects affected / exposed	0 / 293 (0.00%)	3 / 288 (1.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
MULTIPLE ORGAN DYSFUNCTION SYNDROME			
subjects affected / exposed	0 / 293 (0.00%)	2 / 288 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	2 / 293 (0.68%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERIPHERAL SWELLING			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PYREXIA			

subjects affected / exposed	0 / 293 (0.00%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUDDEN DEATH			
subjects affected / exposed	2 / 293 (0.68%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	2 / 2	0 / 1	
deaths causally related to treatment / all	2 / 2	0 / 1	
SYSTEMIC INFLAMMATORY RESPONSE SYNDROME			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
ANAPHYLACTIC SHOCK			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (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 / 293 (1.02%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
ACUTE RESPIRATORY FAILURE			
subjects affected / exposed	2 / 293 (0.68%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	2 / 293 (0.68%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DYSPNOEA			

subjects affected / exposed	8 / 293 (2.73%)	7 / 288 (2.43%)	
occurrences causally related to treatment / all	0 / 8	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
DYSPNOEA EXERTIONAL			
subjects affected / exposed	0 / 293 (0.00%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HAEMOPTYSIS			
subjects affected / exposed	1 / 293 (0.34%)	3 / 288 (1.04%)	
occurrences causally related to treatment / all	1 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOXIA			
subjects affected / exposed	0 / 293 (0.00%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ORGANISING PNEUMONIA			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PLEURAL EFFUSION			
subjects affected / exposed	5 / 293 (1.71%)	6 / 288 (2.08%)	
occurrences causally related to treatment / all	0 / 7	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
PLEURITIC PAIN			
subjects affected / exposed	0 / 293 (0.00%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA ASPIRATION			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (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	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PRODUCTIVE COUGH			
subjects affected / exposed	0 / 293 (0.00%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PULMONARY EMBOLISM			
subjects affected / exposed	5 / 293 (1.71%)	6 / 288 (2.08%)	
occurrences causally related to treatment / all	2 / 5	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
PULMONARY HAEMORRHAGE			
subjects affected / exposed	0 / 293 (0.00%)	2 / 288 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
RESPIRATORY DISTRESS			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RESPIRATORY FAILURE			
subjects affected / exposed	2 / 293 (0.68%)	2 / 288 (0.69%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 2	
RHINORRHOEA			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
CONFUSIONAL STATE			
subjects affected / exposed	1 / 293 (0.34%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DELIRIUM			

subjects affected / exposed	2 / 293 (0.68%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEPRESSION			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DISORIENTATION			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
C-REACTIVE PROTEIN INCREASED			
subjects affected / exposed	0 / 293 (0.00%)	1 / 288 (0.35%)	
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 / 293 (0.34%)	1 / 288 (0.35%)	
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 / 293 (0.00%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEART INJURY			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
HIP FRACTURE			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

LUMBAR VERTEBRAL FRACTURE			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RADIATION OESOPHAGITIS			
subjects affected / exposed	0 / 293 (0.00%)	1 / 288 (0.35%)	
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 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
ARTERIOSPASM CORONARY			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (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	4 / 293 (1.37%)	2 / 288 (0.69%)	
occurrences causally related to treatment / all	1 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
ATRIAL FLUTTER			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIAC ARREST			
subjects affected / exposed	0 / 293 (0.00%)	2 / 288 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
CARDIAC FAILURE			
subjects affected / exposed	1 / 293 (0.34%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
CARDIAC FAILURE ACUTE			

subjects affected / exposed	0 / 293 (0.00%)	1 / 288 (0.35%)	
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 / 293 (0.34%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
CARDIOPULMONARY FAILURE			
subjects affected / exposed	2 / 293 (0.68%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
LEFT VENTRICULAR FAILURE			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERICARDIAL EFFUSION			
subjects affected / exposed	7 / 293 (2.39%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	1 / 7	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERICARDITIS			
subjects affected / exposed	0 / 293 (0.00%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUPRAVENTRICULAR TACHYCARDIA			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
CEREBRAL INFARCTION			
subjects affected / exposed	2 / 293 (0.68%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CEREBRAL ISCHAEMIA			

subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CEREBROVASCULAR ACCIDENT			
subjects affected / exposed	0 / 293 (0.00%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COGNITIVE DISORDER			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERIPHERAL SENSORY NEUROPATHY			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SPINAL CORD COMPRESSION			
subjects affected / exposed	1 / 293 (0.34%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	7 / 293 (2.39%)	15 / 288 (5.21%)	
occurrences causally related to treatment / all	2 / 8	0 / 17	
deaths causally related to treatment / all	0 / 0	0 / 0	
FEBRILE NEUTROPENIA			
subjects affected / exposed	13 / 293 (4.44%)	7 / 288 (2.43%)	
occurrences causally related to treatment / all	9 / 15	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
LEUKOPENIA			
subjects affected / exposed	2 / 293 (0.68%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LYMPHADENITIS			

subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEUTROPENIA			
subjects affected / exposed	6 / 293 (2.05%)	5 / 288 (1.74%)	
occurrences causally related to treatment / all	2 / 9	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
PANCYTOPENIA			
subjects affected / exposed	0 / 293 (0.00%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
THROMBOCYTOPENIA			
subjects affected / exposed	2 / 293 (0.68%)	6 / 288 (2.08%)	
occurrences causally related to treatment / all	1 / 2	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	2 / 293 (0.68%)	2 / 288 (0.69%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
APHTHOUS ULCER			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ASCITES			
subjects affected / exposed	0 / 293 (0.00%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COLITIS ISCHAEMIC			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
COLITIS ULCERATIVE			

subjects affected / exposed	0 / 293 (0.00%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CONSTIPATION			
subjects affected / exposed	2 / 293 (0.68%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	2 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIARRHOEA			
subjects affected / exposed	2 / 293 (0.68%)	2 / 288 (0.69%)	
occurrences causally related to treatment / all	1 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTRITIS			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (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 / 293 (0.00%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
INTESTINAL OBSTRUCTION			
subjects affected / exposed	0 / 293 (0.00%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
MESENTERIC VEIN THROMBOSIS			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (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	3 / 293 (1.02%)	3 / 288 (1.04%)	
occurrences causally related to treatment / all	2 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
OESOPHAGEAL STENOSIS			

subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
OESOPHAGITIS			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RECTAL HAEMORRHAGE			
subjects affected / exposed	0 / 293 (0.00%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
VOMITING			
subjects affected / exposed	6 / 293 (2.05%)	5 / 288 (1.74%)	
occurrences causally related to treatment / all	4 / 6	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
HEPATIC FUNCTION ABNORMAL			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
SUBCUTANEOUS EMPHYSEMA			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	1 / 293 (0.34%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
AZOTAEMIA			
subjects affected / exposed	0 / 293 (0.00%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

HAEMATURIA			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RENAL FAILURE			
subjects affected / exposed	0 / 293 (0.00%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RENAL IMPAIRMENT			
subjects affected / exposed	0 / 293 (0.00%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
URINARY RETENTION			
subjects affected / exposed	0 / 293 (0.00%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BACK PAIN			
subjects affected / exposed	3 / 293 (1.02%)	2 / 288 (0.69%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
BONE PAIN			
subjects affected / exposed	0 / 293 (0.00%)	1 / 288 (0.35%)	
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	1 / 293 (0.34%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

MUSCULOSKELETAL PAIN			
subjects affected / exposed	0 / 293 (0.00%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PAIN IN EXTREMITY			
subjects affected / exposed	1 / 293 (0.34%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
ABDOMINAL ABSCESS			
subjects affected / exposed	0 / 293 (0.00%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
APPENDICITIS PERFORATED			
subjects affected / exposed	0 / 293 (0.00%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
BACTERAEMIA			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BRONCHITIS			
subjects affected / exposed	1 / 293 (0.34%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CELLULITIS			
subjects affected / exposed	1 / 293 (0.34%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CLOSTRIDIUM DIFFICILE COLITIS			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEVICE RELATED INFECTION			

subjects affected / exposed	0 / 293 (0.00%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIARRHOEA INFECTIOUS			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
EMPYEMA			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROENTERITIS			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HERPES ZOSTER			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFECTION			
subjects affected / exposed	0 / 293 (0.00%)	2 / 288 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFLUENZA			
subjects affected / exposed	2 / 293 (0.68%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	4 / 293 (1.37%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	4 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
LUNG INFECTION			

subjects affected / exposed	2 / 293 (0.68%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LYMPHANGITIS			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEUTROPENIC SEPSIS			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERITONSILLAR ABSCESS			
subjects affected / exposed	0 / 293 (0.00%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA			
subjects affected / exposed	19 / 293 (6.48%)	8 / 288 (2.78%)	
occurrences causally related to treatment / all	4 / 26	0 / 9	
deaths causally related to treatment / all	0 / 3	0 / 0	
PNEUMONIA BACTERIAL			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA PSEUDOMONAL			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PSEUDOMONAL SEPSIS			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PULMONARY SEPSIS			

subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PYELONEPHRITIS			
subjects affected / exposed	0 / 293 (0.00%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 293 (0.34%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SEPSIS			
subjects affected / exposed	1 / 293 (0.34%)	4 / 288 (1.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 2	
SEPTIC SHOCK			
subjects affected / exposed	2 / 293 (0.68%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
URINARY TRACT INFECTION			
subjects affected / exposed	2 / 293 (0.68%)	2 / 288 (0.69%)	
occurrences causally related to treatment / all	1 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
VASCULAR DEVICE INFECTION			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VIRAL UPPER RESPIRATORY TRACT INFECTION			

subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	2 / 293 (0.68%)	2 / 288 (0.69%)	
occurrences causally related to treatment / all	1 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEHYDRATION			
subjects affected / exposed	0 / 293 (0.00%)	6 / 288 (2.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOCALCAEMIA			
subjects affected / exposed	0 / 293 (0.00%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOGLYCAEMIA			
subjects affected / exposed	1 / 293 (0.34%)	1 / 288 (0.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPONATRAEMIA			
subjects affected / exposed	1 / 293 (0.34%)	2 / 288 (0.69%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
TYPE 2 DIABETES MELLITUS			
subjects affected / exposed	1 / 293 (0.34%)	0 / 288 (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: 5 %

Non-serious adverse events	Veliparib + Carboplatin + Paclitaxel	Investigator's Choice Chemotherapy	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	275 / 293 (93.86%)	269 / 288 (93.40%)	
Investigations			
WEIGHT DECREASED			
subjects affected / exposed	14 / 293 (4.78%)	24 / 288 (8.33%)	
occurrences (all)	17	25	
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	17 / 293 (5.80%)	22 / 288 (7.64%)	
occurrences (all)	17	25	
DYSGEUSIA			
subjects affected / exposed	19 / 293 (6.48%)	29 / 288 (10.07%)	
occurrences (all)	20	33	
PERIPHERAL SENSORY NEUROPATHY			
subjects affected / exposed	131 / 293 (44.71%)	42 / 288 (14.58%)	
occurrences (all)	195	51	
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	112 / 293 (38.23%)	107 / 288 (37.15%)	
occurrences (all)	212	197	
LEUKOPENIA			
subjects affected / exposed	43 / 293 (14.68%)	40 / 288 (13.89%)	
occurrences (all)	77	77	
NEUTROPENIA			
subjects affected / exposed	104 / 293 (35.49%)	89 / 288 (30.90%)	
occurrences (all)	210	175	
THROMBOCYTOPENIA			
subjects affected / exposed	76 / 293 (25.94%)	54 / 288 (18.75%)	
occurrences (all)	155	102	
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	29 / 293 (9.90%)	30 / 288 (10.42%)	
occurrences (all)	58	50	
FATIGUE			

subjects affected / exposed	80 / 293 (27.30%)	89 / 288 (30.90%)	
occurrences (all)	108	117	
OEDEMA PERIPHERAL			
subjects affected / exposed	13 / 293 (4.44%)	24 / 288 (8.33%)	
occurrences (all)	16	36	
PYREXIA			
subjects affected / exposed	15 / 293 (5.12%)	16 / 288 (5.56%)	
occurrences (all)	17	21	
Gastrointestinal disorders			
CONSTIPATION			
subjects affected / exposed	69 / 293 (23.55%)	92 / 288 (31.94%)	
occurrences (all)	81	113	
DIARRHOEA			
subjects affected / exposed	51 / 293 (17.41%)	47 / 288 (16.32%)	
occurrences (all)	70	60	
NAUSEA			
subjects affected / exposed	86 / 293 (29.35%)	131 / 288 (45.49%)	
occurrences (all)	121	202	
STOMATITIS			
subjects affected / exposed	19 / 293 (6.48%)	30 / 288 (10.42%)	
occurrences (all)	24	32	
VOMITING			
subjects affected / exposed	39 / 293 (13.31%)	73 / 288 (25.35%)	
occurrences (all)	48	99	
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	27 / 293 (9.22%)	29 / 288 (10.07%)	
occurrences (all)	32	31	
DYSPNOEA			
subjects affected / exposed	42 / 293 (14.33%)	25 / 288 (8.68%)	
occurrences (all)	46	30	
HICCUPS			
subjects affected / exposed	17 / 293 (5.80%)	21 / 288 (7.29%)	
occurrences (all)	27	29	
OROPHARYNGEAL PAIN			

subjects affected / exposed	6 / 293 (2.05%)	15 / 288 (5.21%)	
occurrences (all)	8	16	
Skin and subcutaneous tissue disorders			
ALOPECIA			
subjects affected / exposed	137 / 293 (46.76%)	34 / 288 (11.81%)	
occurrences (all)	160	40	
RASH			
subjects affected / exposed	13 / 293 (4.44%)	25 / 288 (8.68%)	
occurrences (all)	16	29	
Psychiatric disorders			
INSOMNIA			
subjects affected / exposed	37 / 293 (12.63%)	30 / 288 (10.42%)	
occurrences (all)	39	30	
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	39 / 293 (13.31%)	26 / 288 (9.03%)	
occurrences (all)	45	35	
BACK PAIN			
subjects affected / exposed	17 / 293 (5.80%)	22 / 288 (7.64%)	
occurrences (all)	21	24	
BONE PAIN			
subjects affected / exposed	15 / 293 (5.12%)	9 / 288 (3.13%)	
occurrences (all)	21	13	
MYALGIA			
subjects affected / exposed	38 / 293 (12.97%)	17 / 288 (5.90%)	
occurrences (all)	50	22	
PAIN IN EXTREMITY			
subjects affected / exposed	15 / 293 (5.12%)	15 / 288 (5.21%)	
occurrences (all)	17	19	
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	63 / 293 (21.50%)	79 / 288 (27.43%)	
occurrences (all)	79	109	
HYPOMAGNESAEMIA			
subjects affected / exposed	21 / 293 (7.17%)	16 / 288 (5.56%)	
occurrences (all)	22	19	

HYPERGLYCAEMIA			
subjects affected / exposed	24 / 293 (8.19%)	11 / 288 (3.82%)	
occurrences (all)	24	15	
HYPONATRAEMIA			
subjects affected / exposed	16 / 293 (5.46%)	12 / 288 (4.17%)	
occurrences (all)	18	14	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 October 2014	Added language to include details on pregnancy testing and to clarify drug labeling
10 December 2014	Changed study phase from Phase 2 to Phase 3 throughout protocol to conform to request by US Food and Drug Administration (FDA); revised investigator's choice stratification factor to preferred platinum doublet chemotherapy to assure balance of subjects suitable for C/P across arms; revised eligibility criteria to reflect exclusion of subjects who have received prior cytotoxic chemotherapy chemoradiotherapy for NSCLC, except adjuvant or neoadjuvant therapy > 12 months prior to C1D-2 for clarification; expanded screening period from 21 to 28 days to reduce number of screen failures that may have occurred due to screening test delays; included Japan-specific protocol language requirements to include facilitation of Japanese sites.
17 July 2015	Clarified and changed the reference day defining baseline assessment windows throughout; added language regarding starting doses for subjects randomized to the investigator's choice arm; specified that 24 hour urine collection or radioisotope methods were allowed for creatinine clearance/glomerular filtration rate (GFR) measurement; specified washout periods for allowed prior NSCLC treatment in Exclusion Criterion 6; added Japan-specific requirements throughout.
09 May 2018	The patient population for the primary endpoint of OS was amended from current smokers to subjects who were positive for the LSP signature; subjects who were LSP positive were to also replace the current smoker population for other key efficacy analyses; updated number of subjects to be enrolled from approximately 525 to 595 subjects.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported