Clinical trial results:
A Randomized, Placebo-Controlled, Double-Blind, Phase 3 Study Evaluating Safety and Efficacy of the Addition of Veliparib Plus Carboplatin Versus the Addition of Carboplatin to Standard Neoadjuvant Chemotherapy Versus Standard Neoadjuvant Chemotherapy in Subjects With Early Stage Triple Negative Breast Cancer (TNBC)

Summary

EudraCT number	2013-002377-21
Trial protocol	BE DE CZ HU GB ES IT PL FR
Global end of trial date	12 November 2020

Results information

Result version number	v1 (current)
This version publication date	29 October 2021
First version publication date	29 October 2021

Trial information

Trial identification

Sponsor protocol code	M14-011

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02032277
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 8006339110, abbvieclinicaltrials@abbvie.com
Scientific contact	Global Medical Services, AbbVie, 001 8006339110, 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	12 November 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	12 November 2020
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 the rate of pathologic complete response (pCR) in breast and any resected lymph node tissue after treatment with neoadjuvant veliparib in combination with carboplatin and paclitaxel followed by doxorubicin + cyclophosphamide compared to two neoadjuvant chemotherapy regimens (carboplatin + paclitaxel followed by doxorubicin + cyclophosphamide or paclitaxel alone followed by doxorubicin + cyclophosphamide) in participants with early stage TNBC.

Protection of trial subjects:

Subject and/or legal guardian read and understood the information provided about the study and gave written permission.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 April 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 19
Country: Number of subjects enrolled	Belgium: 25
Country: Number of subjects enrolled	Canada: 10
Country: Number of subjects enrolled	Czechia: 20
Country: Number of subjects enrolled	France: 36
Country: Number of subjects enrolled	Germany: 55
Country: Number of subjects enrolled	Hungary: 20
Country: Number of subjects enrolled	Italy: 13
Country: Number of subjects enrolled	Korea, Republic of: 73
Country: Number of subjects enrolled	Netherlands: 3
Country: Number of subjects enrolled	Russian Federation: 23
Country: Number of subjects enrolled	Spain: 39
Country: Number of subjects enrolled	Taiwan: 8
Country: Number of subjects enrolled	United Kingdom: 8
Country: Number of subjects enrolled	United States: 282
Worldwide total number of subjects	634
EEA total number of subjects	211

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)	555
From 65 to 84 years	79
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Screening procedures and baseline tumor assessments were performed within 28 days prior to the first dose of study drug (except the baseline mammogram, which could be up to 56 days prior to the start of study treatment).

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, Data analyst, Carer

Blinding implementation details:

AbbVie, the Investigator, the study site personnel, and subject remained blinded to each subject's treatment with veliparib/placebo. AbbVie, the Investigator, the study site personnel other than pharmacy personnel, and the subject remained blinded to each subject's treatment with carboplatin/placebo throughout the course of the study.

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC

Arm description:

veliparib (50 mg oral [PO] twice daily [BID]) + carboplatin (area under the curve [AUC] 6 mg/mL/min) + paclitaxel (80 mg/m^2) followed by doxorubicin/cyclophosphamide (AC)

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:

50 mg veliparib for 12 weeks (or up to a maximum of 16 weeks) during Chemotherapy Segment 1

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 (AUC 6 mg/mL/min) on Day 1 of four 21-day cycles via infusion during Chemotherapy Segment 1

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:

paclitaxel (80 mg/m^2) on Day 1 of 12 weekly cycles via infusion during Chemotherapy Segment 1

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

Dosage and administration details:

doxorubicin (60 mg/m^2) on Day 1 of four 14-day cycles or four 21-day cycles beginning with Chemotherapy Segment 2

Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

cyclophosphamide (600 mg/m^2) on Day 1 of four 14-day cycles or four 21-day cycles beginning with Chemotherapy Segment 2

Arm title	Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC

Arm description:

placebo + carboplatin (AUC 6 mg/mL/min) + paclitaxel (80 mg/m^2) followed by AC

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

Dosage and administration details:

placebo for veliparib for 12 weeks (or up to a maximum of 16 weeks) during Chemotherapy Segment 1

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 (AUC 6 mg/mL/min) on Day 1 of four 21-day cycles via infusion during Chemotherapy Segment 1

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:

paclitaxel (80 mg/m^2) on Day 1 of 12 weekly cycles via infusion during Chemotherapy Segment 1

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

Dosage and administration details:

doxorubicin (60 mg/m^2) on Day 1 of four 14-day cycles or four 21-day cycles beginning with Chemotherapy Segment 2

Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

cyclophosphamide (600 mg/m^2) on Day 1 of four 14-day cycles or four 21-day cycles beginning with Chemotherapy Segment 2

Arm title	Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo

Arm description:

placebo + placebo + paclitaxel (80 mg/m^2) followed by AC

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

Dosage and administration details:

placebo for veliparib for 12 weeks (or up to a maximum of 16 weeks) during Chemotherapy Segment 1

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

Dosage and administration details:

placebo for carboplatin via infusion during Chemotherapy Segment 1

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:

paclitaxel (80 mg/m^2) on Day 1 of 12 weekly cycles via infusion during Chemotherapy Segment 1

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

Dosage and administration details:

doxorubicin (60 mg/m^2) on Day 1 of four 14-day cycles or four 21-day cycles beginning with Chemotherapy Segment 2

Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

cyclophosphamide (600 mg/m^2) on Day 1 of four 14-day cycles or four 21-day cycles beginning with Chemotherapy Segment 2

Number of subjects in period 1	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC	Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC	Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo
Started	316	160	158
Completed	248	123	115
Not completed	68	37	43
Consent withdrawn by subject	13	8	10
Death	38	16	24
Lost to follow-up	16	10	8
Other, Not Specified	1	3	1

Baseline characteristics

Reporting groups	
Reporting group title	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC
Reporting group description:	
veliparib (50 mg oral [PO] twice daily [BID]) + carboplatin (area under the curve [AUC] 6 mg/mL/min) + paclitaxel (80 mg/m^2) followed by doxorubicin/cyclophosphamide (AC)	
Reporting group title	Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC
Reporting group description:	
placebo + carboplatin (AUC 6 mg/mL/min) + paclitaxel (80 mg/m^2) followed by AC	
Reporting group title	Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo
Reporting group description:	
placebo + placebo + paclitaxel (80 mg/m^2) followed by AC	

Reporting group values	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC	Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC	Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo
Number of subjects	316	160	158
Age categorical Units: Subjects			
<= 50 years	151	87	81
> 50 years	165	73	77
Gender categorical Units: Subjects			
Female	316	160	158
Male	0	0	0
Ethnicity Units: Subjects			
Hispanic or Latino	48	19	21
Not Hispanic or Latino	268	140	136
Unknown or Not Reported	0	1	1
Race Units: Subjects			
Asian	51	23	18
Native Hawaiian or Other Pacific Islander	0	2	0
Black or African American	33	7	15
White	232	127	124
More than one race	0	0	1
Unknown or Not Reported	0	1	0

Reporting group values	Total		
Number of subjects	634		
Age categorical Units: Subjects			
<= 50 years	319		
> 50 years	315		

Gender categorical Units: Subjects			
Female	634		
Male	0		
Ethnicity Units: Subjects			
Hispanic or Latino	88		
Not Hispanic or Latino	544		
Unknown or Not Reported	2		
Race Units: Subjects			
Asian	92		
Native Hawaiian or Other Pacific Islander	2		
Black or African American	55		
White	483		
More than one race	1		
Unknown or Not Reported	1		

End points

End points reporting groups

Reporting group title	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC
Reporting group description: veliparib (50 mg oral [PO] twice daily [BID]) + carboplatin (area under the curve [AUC] 6 mg/mL/min) + paclitaxel (80 mg/m^2) followed by doxorubicin/cyclophosphamide (AC)	
Reporting group title	Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC
Reporting group description: placebo + carboplatin (AUC 6 mg/mL/min) + paclitaxel (80 mg/m^2) followed by AC	
Reporting group title	Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo
Reporting group description: placebo + placebo + paclitaxel (80 mg/m^2) followed by AC	

Primary: Percentage of Participants With Pathological Complete Response (pCR)

End point title	Percentage of Participants With Pathological Complete Response (pCR)
End point description: pCR in the breast tissue and the lymph node tissue was assessed upon completion of pre-operative systemic therapy and definitive surgery. pCR was defined by the absence of any residual invasive cancer on hematoxylin and eosin evaluation of the resected breast specimen and any resected lymph node tissue following completion of neoadjuvant systemic therapy.	
End point type	Primary
End point timeframe: At the time of definitive surgery (approximately 24-36 weeks from first dose of study drug)	

End point values	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC	Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC	Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	316	160	158	
Units: percentage of participants				
number (confidence interval 95%)	53.2 (47.7 to 58.7)	57.5 (49.8 to 65.2)	31.0 (23.8 to 38.2)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: Unstratified analysis	
Comparison groups	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC

Number of subjects included in analysis	476
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	1.2

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Unstratified analysis	
Comparison groups	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC
Number of subjects included in analysis	476
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference
Point estimate	-4.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.8
upper limit	5.1

Statistical analysis title	Statistical Analysis 3
Statistical analysis description:	
Stratified analysis: all calculations were stratified by breast cancer gene (BRCA) status, lymph node stage, and dose density. OR was by Mantel-Haenszel method; confidence intervals were based on the normal approximation.	
Comparison groups	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC
Number of subjects included in analysis	476
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.357
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	1.2

Statistical analysis title	Statistical Analysis 4
Statistical analysis description: Stratified analysis: all calculations were stratified by breast cancer gene (BRCA) status, lymph node stage, and dose density. Difference was by Mantel-Haenszel method; confidence intervals were based on the normal approximation.	
Comparison groups	Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC v Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC
Number of subjects included in analysis	476
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference
Point estimate	-4.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.8
upper limit	4.9

Statistical analysis title	Statistical Analysis 5
Statistical analysis description: Unstratified analysis	
Comparison groups	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo
Number of subjects included in analysis	474
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	2.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.7
upper limit	3.8

Statistical analysis title	Statistical Analysis 6
Statistical analysis description: Unstratified analysis	
Comparison groups	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo

Number of subjects included in analysis	474
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference
Point estimate	22.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.1
upper limit	31.2

Statistical analysis title	Statistical Analysis 7

Statistical analysis description:

Stratified analysis: all calculations were stratified by breast cancer gene (BRCA) status, lymph node stage, and dose density. OR was by Mantel-Haenszel method; confidence intervals were based on the normal approximation.

Comparison groups	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo
Number of subjects included in analysis	474
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	2.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.7
upper limit	3.9

Statistical analysis title	Statistical Analysis 8

Statistical analysis description:

Stratified analysis: all calculations were stratified by breast cancer gene (BRCA) status, lymph node stage, and dose density. Difference was by Mantel-Haenszel method; confidence intervals were based on the normal approximation.

Comparison groups	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo
Number of subjects included in analysis	474
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference
Point estimate	22.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.2
upper limit	31.2

Secondary: Percentage of Participants With Events of Disease Progression or Death

End point title	Percentage of Participants With Events of Disease Progression or Death

End point description:

Event free survival (EFS) was secondary endpoint, defined as the time from random assignment to documentation of the first of the following events: discontinuation of study therapy due to protocol-defined progression prior to surgery; local, regional, or distant invasive recurrence of breast cancer following curative surgery; a new breast cancer; a new onset malignancy; or death as a result of any cause.

Due to low event rates, the median EFS could not be estimated for any of the treatment arms. Therefore, the data table presents the percentage of participants with any of the above events within the given time frame. If a participant had not experienced any of the above events, that participant was censored at date of last available disease assessment.

End point type	Secondary

End point timeframe:

Up to 4 years from the date of definitive surgery (i.e., approximately 24-36 weeks from first dose of study drug)

End point values	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC	Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC	Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	316	160	158	
Units: percentage of participants				
number (not applicable)	20.6	18.8	29.7	

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Unstratified analysis

Comparison groups	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC
Number of subjects included in analysis	476
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.69
Method	Logrank

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Unstratified analysis

Comparison groups	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC
Number of subjects included in analysis	476
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.778
Method	Wilcoxon p-value

Statistical analysis title	Statistical Analysis 3
Comparison groups	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC
Number of subjects included in analysis	476
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.69
Method	Cox proportional hazard model
Parameter estimate	Hazard ratio (HR)
Point estimate	1.092
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.709
upper limit	1.683

Statistical analysis title	Statistical Analysis 4
Statistical analysis description: Stratified analysis: all calculations were stratified by breast cancer gene (BRCA) status, lymph node stage, and dose density.	
Comparison groups	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC
Number of subjects included in analysis	476
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.62
Method	Logrank

Statistical analysis title	Statistical Analysis 5
Statistical analysis description: Stratified analysis: all calculations were stratified by breast cancer gene (BRCA) status, lymph node stage, and dose density.	
Comparison groups	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC

Number of subjects included in analysis	476
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.627
Method	Wilcoxon p-value

Statistical analysis title	Statistical Analysis 6
Statistical analysis description:	
Stratified analysis: all calculations were stratified by breast cancer gene (BRCA) status, lymph node stage, and dose density.	
Comparison groups	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC
Number of subjects included in analysis	476
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.62
Method	Cox proportional hazard model
Parameter estimate	Hazard ratio (HR)
Point estimate	1.116
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.724
upper limit	1.721

Statistical analysis title	Statistical Analysis 8
Statistical analysis description:	
Unstratified analysis	
Comparison groups	Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo v Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC
Number of subjects included in analysis	474
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.013
Method	Wilcoxon p-value

Statistical analysis title	Statistical Analysis 9
Statistical analysis description:	
Unstratified analysis	
Comparison groups	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo

Number of subjects included in analysis	474
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.021
Method	Cox proportional hazard model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.643
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.442
upper limit	0.935

Statistical analysis title	Statistical Analysis 10
Statistical analysis description:	
Stratified analysis: all calculations were stratified by breast cancer gene (BRCA) status, lymph node stage, and dose density.	
Comparison groups	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo
Number of subjects included in analysis	474
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.015
Method	Logrank

Statistical analysis title	Statistical Analysis 11
Statistical analysis description:	
Stratified analysis: all calculations were stratified by breast cancer gene (BRCA) status, lymph node stage, and dose density.	
Comparison groups	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo
Number of subjects included in analysis	474
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.04
Method	Wilcoxon p-value

Statistical analysis title	Statistical Analysis 12
Statistical analysis description:	
Stratified analysis: all calculations were stratified by breast cancer gene (BRCA) status, lymph node stage, and dose density.	
Comparison groups	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo

Number of subjects included in analysis	474
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.016
Method	Cox proportional hazard model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.432
upper limit	0.917

Statistical analysis title	Statistical Analysis 7
Statistical analysis description:	
Unstratified analysis	
Comparison groups	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo
Number of subjects included in analysis	474
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.02
Method	Logrank

Secondary: Percentage of Participants With an Event of Death

End point title	Percentage of Participants With an Event of Death

End point description:

Overall survival (OS) was secondary endpoint, defined as the number of days from the day the participant was randomized to the date of the participant's 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.
Due to low event rates, the median EFS could not be estimated for any of the treatment arms. Therefore, the data table presents the percentage of participants with any of the above events within the given time frame. If a participant had not died, then the data was censored at the date when the participant was last known to be alive.

End point type	Secondary

End point timeframe:

Up to 4 years from the date of definitive surgery (i.e., approximately 24-36 weeks from first dose of study drug)

End point values	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC	Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC	Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	316	160	158	
Units: percentage of participants				
number (not applicable)	12.0	10.0	13.9	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: Unstratified analysis	
Comparison groups	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC
Number of subjects included in analysis	476
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.536
Method	Logrank

Statistical analysis title	Statistical Analysis 2
Comparison groups	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC
Number of subjects included in analysis	476
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.642
Method	Wilcoxon p-value

Statistical analysis title	Statistical Analysis 3
Statistical analysis description: Unstratified analysis	
Comparison groups	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC
Number of subjects included in analysis	476
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.536
Method	Cox proportional hazard model
Parameter estimate	Hazard ratio (HR)
Point estimate	1.202

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	2.156

Statistical analysis title	Statistical Analysis 4
Statistical analysis description:	
Stratified analysis: all calculations were stratified by breast cancer gene (BRCA) status, lymph node stage, and dose density.	
Comparison groups	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC
Number of subjects included in analysis	476
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.454
Method	Logrank

Statistical analysis title	Statistical Analysis 5
Statistical analysis description:	
Stratified analysis: all calculations were stratified by breast cancer gene (BRCA) status, lymph node stage, and dose density.	
Comparison groups	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC
Number of subjects included in analysis	476
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.404
Method	Wilcoxon p-value

Statistical analysis title	Statistical Analysis 6
Statistical analysis description:	
Stratified analysis: all calculations were stratified by breast cancer gene (BRCA) status, lymph node stage, and dose density.	
Comparison groups	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC
Number of subjects included in analysis	476
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.455
Method	Cox proportional hazard model
Parameter estimate	Hazard ratio (HR)
Point estimate	1.25

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.696
upper limit	2.242

Statistical analysis title	Statistical Analysis 7
Statistical analysis description: Unstratified analysis	
Comparison groups	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo
Number of subjects included in analysis	474
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.431
Method	Logrank

Statistical analysis title	Statistical Analysis 8
Statistical analysis description: Unstratified analysis	
Comparison groups	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo
Number of subjects included in analysis	474
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.426
Method	Wilcoxon p-value

Statistical analysis title	Statistical Analysis 9
Statistical analysis description: Unstratified analysis	
Comparison groups	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo
Number of subjects included in analysis	474
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.432
Method	Cox proportional hazard model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.479
upper limit	1.37

Statistical analysis title	Statistical Analysis 10
Statistical analysis description: Stratified analysis: all calculations were stratified by breast cancer gene (BRCA) status, lymph node stage, and dose density.	
Comparison groups	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo
Number of subjects included in analysis	474
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.454
Method	Logrank

Statistical analysis title	Statistical Analysis 11
Statistical analysis description: Stratified analysis: all calculations were stratified by breast cancer gene (BRCA) status, lymph node stage, and dose density.	
Comparison groups	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo
Number of subjects included in analysis	474
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.837
Method	Wilcoxon p-value

Statistical analysis title	Statistical Analysis 12
Statistical analysis description: Stratified analysis: all calculations were stratified by breast cancer gene (BRCA) status, lymph node stage, and dose density.	
Comparison groups	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo
Number of subjects included in analysis	474
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.452
Method	Cox proportional hazard model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.817
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.483
upper limit	1.383

Secondary: Percentage of Participants Eligible for Breast Conservation After Therapy

End point title	Percentage of Participants Eligible for Breast Conservation After Therapy

End point description:

Whether a participant was eligible for breast conserving surgery for whom mastectomy was planned at diagnosis was determined by the participant's surgeon prior to chemotherapy and after completion of chemotherapy. The breast conservation rate (BCR) was defined as the rate at which participants are eligible for breast conservation after neoadjuvant therapy among participants for whom mastectomy was planned at diagnosis, and is presented as the percentage of participants eligible for breast conservation after therapy among participants who were deemed ineligible for breast conservation surgery at screening.

Randomized participants who were deemed ineligible for breast conservation surgery at screening. Only participants with evaluations at both screening and pre-op visits were included.

End point type	Secondary

End point timeframe:

At the time of definitive surgery (approximately 24-36 weeks from first dose of study drug)

End point values	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC	Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC	Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	73	34	34	
Units: percentage of particiants				
number (confidence interval 95%)	61.6 (50.5 to 72.8)	44.1 (27.4 to 60.8)	44.1 (27.4 to 60.8)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Unstratified analysis	
Comparison groups	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	2.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	4.6

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: Unstratified analysis	
Comparison groups	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference
Point estimate	17.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	37.6

Statistical analysis title	Statistical Analysis 3
Statistical analysis description: Stratified analysis: all calculations were stratified by breast cancer gene (BRCA) status, lymph node stage, and dose density. OR was by Mantel-Haenszel method; confidence intervals were based on the normal approximation.	
Comparison groups	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	4.5

Statistical analysis title	Statistical Analysis 4
Statistical analysis description: Stratified analysis: all calculations were stratified by breast cancer gene (BRCA) status, lymph node stage, and dose density. Difference was by Mantel-Haenszel method; confidence intervals were based on the normal approximation.	
Comparison groups	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC

Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.132
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference
Point estimate	15.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.3
upper limit	35.9

Statistical analysis title	Statistical Analysis 5
Statistical analysis description:	
Unstratified analysis	
Comparison groups	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	2.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	4.6

Statistical analysis title	Statistical Analysis 6
Statistical analysis description:	
Unstratified analysis	
Comparison groups	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference
Point estimate	17.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	37.6

Statistical analysis title	Statistical Analysis 7

Statistical analysis description:

Stratified analysis: all calculations were stratified by breast cancer gene (BRCA) status, lymph node stage, and dose density. OR was by Mantel-Haenszel method; confidence intervals were based on the normal approximation.

Comparison groups	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	1.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	4.5

Statistical analysis title	Statistical Analysis 8

Statistical analysis description:

Stratified analysis: all calculations were stratified by breast cancer gene (BRCA) status, lymph node stage, and dose density. Difference was by Mantel-Haenszel method; confidence intervals were based on the normal approximation.

Comparison groups	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC v Arm C: Placebo + Placebo + Paclitaxel, Followed by AC placebo
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.139
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference
Point estimate	15.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.6
upper limit	36.3

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug through 30 days following discontinuation of study drug administration; up to a maximum of 150 days.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC

Reporting group description:

veliparib (50 mg PO BID) + carboplatin (AUC 6 mg/mL/min) + paclitaxel (80 mg/m^2) followed by AC

Reporting group title	Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC

Reporting group description:

placebo + carboplatin (AUC 6 mg/mL/min) + paclitaxel (80 mg/m^2) followed by AC

Reporting group title	Arm C: Placebo + Placebo + Paclitaxel, Followed by AC

Reporting group description:

placebo + placebo + paclitaxel (80 mg/m^2) followed by AC

Serious adverse events	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC	Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC	Arm C: Placebo + Placebo + Paclitaxel, Followed by AC
Total subjects affected by serious adverse events			
subjects affected / exposed	95 / 313 (30.35%)	22 / 157 (14.01%)	42 / 158 (26.58%)
number of deaths (all causes)	38	22	16
number of deaths resulting from adverse events	1	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
METASTASES TO MENINGES			
subjects affected / exposed	0 / 313 (0.00%)	0 / 157 (0.00%)	1 / 158 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
DEEP VEIN THROMBOSIS			
subjects affected / exposed	1 / 313 (0.32%)	1 / 157 (0.64%)	1 / 158 (0.63%)
occurrences causally related to treatment / all	0 / 1	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EMBOLISM			

subjects affected / exposed	0 / 313 (0.00%)	1 / 157 (0.64%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERTENSION			
subjects affected / exposed	1 / 313 (0.32%)	0 / 157 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
DEATH			
subjects affected / exposed	1 / 313 (0.32%)	0 / 157 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
FATIGUE			
subjects affected / exposed	1 / 313 (0.32%)	0 / 157 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MALAISE			
subjects affected / exposed	1 / 313 (0.32%)	0 / 157 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	0 / 313 (0.00%)	0 / 157 (0.00%)	1 / 158 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYREXIA			
subjects affected / exposed	4 / 313 (1.28%)	1 / 157 (0.64%)	2 / 158 (1.27%)
occurrences causally related to treatment / all	1 / 5	0 / 1	1 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
DYSPNOEA			
subjects affected / exposed	2 / 313 (0.64%)	2 / 157 (1.27%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

HYPOXIA			
subjects affected / exposed	1 / 313 (0.32%)	0 / 157 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PAINFUL RESPIRATION			
subjects affected / exposed	0 / 313 (0.00%)	1 / 157 (0.64%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONITIS			
subjects affected / exposed	0 / 313 (0.00%)	1 / 157 (0.64%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PULMONARY EMBOLISM			
subjects affected / exposed	6 / 313 (1.92%)	3 / 157 (1.91%)	2 / 158 (1.27%)
occurrences causally related to treatment / all	2 / 6	2 / 3	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
ADJUSTMENT DISORDER WITH DEPRESSED MOOD			
subjects affected / exposed	1 / 313 (0.32%)	0 / 157 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANXIETY			
subjects affected / exposed	1 / 313 (0.32%)	0 / 157 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MENTAL STATUS CHANGES			
subjects affected / exposed	1 / 313 (0.32%)	0 / 157 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PSYCHOGENIC SEIZURE			
subjects affected / exposed	1 / 313 (0.32%)	0 / 157 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Investigations			
ELECTROCARDIOGRAM QT PROLONGED			
subjects affected / exposed	0 / 313 (0.00%)	0 / 157 (0.00%)	1 / 158 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
ANKLE FRACTURE			
subjects affected / exposed	1 / 313 (0.32%)	0 / 157 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FEMORAL NECK FRACTURE			
subjects affected / exposed	1 / 313 (0.32%)	0 / 157 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFUSION RELATED REACTION			
subjects affected / exposed	1 / 313 (0.32%)	0 / 157 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RIB FRACTURE			
subjects affected / exposed	1 / 313 (0.32%)	0 / 157 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
WOUND SECRETION			
subjects affected / exposed	1 / 313 (0.32%)	0 / 157 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
WRIST FRACTURE			
subjects affected / exposed	0 / 313 (0.00%)	1 / 157 (0.64%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
ATRIAL FIBRILLATION			

subjects affected / exposed	0 / 313 (0.00%)	1 / 157 (0.64%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ATRIAL FLUTTER			
subjects affected / exposed	0 / 313 (0.00%)	1 / 157 (0.64%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MYOCARDIAL ISCHAEMIA			
subjects affected / exposed	0 / 313 (0.00%)	0 / 157 (0.00%)	1 / 158 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SINUS TACHYCARDIA			
subjects affected / exposed	0 / 313 (0.00%)	0 / 157 (0.00%)	1 / 158 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUPRAVENTRICULAR EXTRASYSTOLES			
subjects affected / exposed	0 / 313 (0.00%)	0 / 157 (0.00%)	1 / 158 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUPRAVENTRICULAR TACHYCARDIA			
subjects affected / exposed	0 / 313 (0.00%)	0 / 157 (0.00%)	1 / 158 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TACHYCARDIA			
subjects affected / exposed	1 / 313 (0.32%)	0 / 157 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VENTRICULAR EXTRASYSTOLES			
subjects affected / exposed	0 / 313 (0.00%)	0 / 157 (0.00%)	1 / 158 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
CEREBROVASCULAR ACCIDENT			

subjects affected / exposed	1 / 313 (0.32%)	0 / 157 (0.00%)	1 / 158 (0.63%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIZZINESS			
subjects affected / exposed	0 / 313 (0.00%)	1 / 157 (0.64%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEADACHE			
subjects affected / exposed	0 / 313 (0.00%)	0 / 157 (0.00%)	1 / 158 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MIGRAINE WITH AURA			
subjects affected / exposed	0 / 313 (0.00%)	0 / 157 (0.00%)	1 / 158 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PARTIAL SEIZURES			
subjects affected / exposed	0 / 313 (0.00%)	0 / 157 (0.00%)	1 / 158 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEIZURE			
subjects affected / exposed	0 / 313 (0.00%)	1 / 157 (0.64%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SYNCOPE			
subjects affected / exposed	3 / 313 (0.96%)	0 / 157 (0.00%)	1 / 158 (0.63%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	11 / 313 (3.51%)	3 / 157 (1.91%)	6 / 158 (3.80%)
occurrences causally related to treatment / all	3 / 14	0 / 3	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FEBRILE NEUTROPENIA			

subjects affected / exposed	51 / 313 (16.29%)	6 / 157 (3.82%)	23 / 158 (14.56%)
occurrences causally related to treatment / all	5 / 55	0 / 6	1 / 26
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LEUKOPENIA			
subjects affected / exposed	0 / 313 (0.00%)	2 / 157 (1.27%)	1 / 158 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUTROPENIA			
subjects affected / exposed	4 / 313 (1.28%)	1 / 157 (0.64%)	1 / 158 (0.63%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCYTOPENIA			
subjects affected / exposed	1 / 313 (0.32%)	0 / 157 (0.00%)	1 / 158 (0.63%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
THROMBOCYTOPENIA			
subjects affected / exposed	4 / 313 (1.28%)	0 / 157 (0.00%)	2 / 158 (1.27%)
occurrences causally related to treatment / all	1 / 4	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	2 / 313 (0.64%)	1 / 157 (0.64%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ABDOMINAL PAIN UPPER			
subjects affected / exposed	1 / 313 (0.32%)	0 / 157 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIARRHOEA			
subjects affected / exposed	1 / 313 (0.32%)	0 / 157 (0.00%)	1 / 158 (0.63%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENTEROCOLITIS			

subjects affected / exposed	0 / 313 (0.00%)	0 / 157 (0.00%)	1 / 158 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMORRHOIDAL HAEMORRHAGE			
subjects affected / exposed	1 / 313 (0.32%)	0 / 157 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MALLORY-WEISS SYNDROME			
subjects affected / exposed	1 / 313 (0.32%)	0 / 157 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NAUSEA			
subjects affected / exposed	6 / 313 (1.92%)	2 / 157 (1.27%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 6	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUTROPENIC COLITIS			
subjects affected / exposed	0 / 313 (0.00%)	0 / 157 (0.00%)	1 / 158 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PROCTALGIA			
subjects affected / exposed	1 / 313 (0.32%)	0 / 157 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RECTAL HAEMORRHAGE			
subjects affected / exposed	1 / 313 (0.32%)	0 / 157 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	3 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
STOMATITIS			
subjects affected / exposed	0 / 313 (0.00%)	1 / 157 (0.64%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VOMITING			

subjects affected / exposed	3 / 313 (0.96%)	2 / 157 (1.27%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	1 / 5	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
HEPATITIS			
subjects affected / exposed	0 / 313 (0.00%)	0 / 157 (0.00%)	1 / 158 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
HIDRADENITIS			
subjects affected / exposed	1 / 313 (0.32%)	0 / 157 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	0 / 313 (0.00%)	1 / 157 (0.64%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	1 / 313 (0.32%)	0 / 157 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MUSCULAR WEAKNESS			
subjects affected / exposed	0 / 313 (0.00%)	0 / 157 (0.00%)	1 / 158 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
ATYPICAL PNEUMONIA			
subjects affected / exposed	1 / 313 (0.32%)	0 / 157 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BACTERAEMIA			

subjects affected / exposed	0 / 313 (0.00%)	0 / 157 (0.00%)	2 / 158 (1.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRONCHITIS			
subjects affected / exposed	2 / 313 (0.64%)	0 / 157 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CELLULITIS			
subjects affected / exposed	0 / 313 (0.00%)	0 / 157 (0.00%)	1 / 158 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CLOSTRIDIUM DIFFICILE COLITIS			
subjects affected / exposed	1 / 313 (0.32%)	0 / 157 (0.00%)	1 / 158 (0.63%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CLOSTRIDIUM DIFFICILE INFECTION			
subjects affected / exposed	1 / 313 (0.32%)	0 / 157 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CYSTITIS			
subjects affected / exposed	0 / 313 (0.00%)	0 / 157 (0.00%)	1 / 158 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEVICE RELATED SEPSIS			
subjects affected / exposed	0 / 313 (0.00%)	0 / 157 (0.00%)	1 / 158 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENTEROCOLITIS INFECTIOUS			
subjects affected / exposed	0 / 313 (0.00%)	0 / 157 (0.00%)	2 / 158 (1.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENTEROCOLITIS VIRAL			

subjects affected / exposed	0 / 313 (0.00%)	0 / 157 (0.00%)	1 / 158 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HERPES SIMPLEX MENINGITIS			
subjects affected / exposed	0 / 313 (0.00%)	0 / 157 (0.00%)	1 / 158 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFLUENZA			
subjects affected / exposed	1 / 313 (0.32%)	1 / 157 (0.64%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 313 (0.00%)	1 / 157 (0.64%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OESOPHAGEAL CANDIDIASIS			
subjects affected / exposed	1 / 313 (0.32%)	0 / 157 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMOCYSTIS JIROVECII PNEUMONIA			
subjects affected / exposed	0 / 313 (0.00%)	1 / 157 (0.64%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA			
subjects affected / exposed	4 / 313 (1.28%)	0 / 157 (0.00%)	1 / 158 (0.63%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYELONEPHRITIS			
subjects affected / exposed	1 / 313 (0.32%)	0 / 157 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEPSIS			

subjects affected / exposed	1 / 313 (0.32%)	0 / 157 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SINUSITIS			
subjects affected / exposed	1 / 313 (0.32%)	0 / 157 (0.00%)	1 / 158 (0.63%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TONSILLITIS			
subjects affected / exposed	1 / 313 (0.32%)	0 / 157 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TOOTH ABSCESS			
subjects affected / exposed	2 / 313 (0.64%)	0 / 157 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 313 (0.00%)	0 / 157 (0.00%)	1 / 158 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY TRACT INFECTION			
subjects affected / exposed	1 / 313 (0.32%)	0 / 157 (0.00%)	3 / 158 (1.90%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VASCULAR DEVICE INFECTION			
subjects affected / exposed	1 / 313 (0.32%)	0 / 157 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VIRAL INFECTION			
subjects affected / exposed	0 / 313 (0.00%)	1 / 157 (0.64%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VULVAL ABSCESS			

subjects affected / exposed	1 / 313 (0.32%)	0 / 157 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
WOUND INFECTION			
subjects affected / exposed	1 / 313 (0.32%)	0 / 157 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
DEHYDRATION			
subjects affected / exposed	0 / 313 (0.00%)	1 / 157 (0.64%)	1 / 158 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOKALAEMIA			
subjects affected / exposed	0 / 313 (0.00%)	0 / 157 (0.00%)	1 / 158 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPONATRAEMIA			
subjects affected / exposed	1 / 313 (0.32%)	0 / 157 (0.00%)	0 / 158 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Arm A: Veliparib + Carboplatin + Paclitaxel, Followed by AC	Arm B: Placebo + Carboplatin + Paclitaxel, Followed by AC	Arm C: Placebo + Placebo + Paclitaxel, Followed by AC
Total subjects affected by non-serious adverse events			
subjects affected / exposed	312 / 313 (99.68%)	157 / 157 (100.00%)	158 / 158 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
CANCER PAIN			
subjects affected / exposed	3 / 313 (0.96%)	8 / 157 (5.10%)	0 / 158 (0.00%)
occurrences (all)	3	8	0
Vascular disorders			

FLUSHING			
subjects affected / exposed	11 / 313 (3.51%)	9 / 157 (5.73%)	7 / 158 (4.43%)
occurrences (all)	14	10	7
HOT FLUSH			
subjects affected / exposed	51 / 313 (16.29%)	22 / 157 (14.01%)	28 / 158 (17.72%)
occurrences (all)	63	27	34
HYPERTENSION			
subjects affected / exposed	17 / 313 (5.43%)	6 / 157 (3.82%)	3 / 158 (1.90%)
occurrences (all)	27	7	3
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	51 / 313 (16.29%)	20 / 157 (12.74%)	25 / 158 (15.82%)
occurrences (all)	134	43	64
FATIGUE			
subjects affected / exposed	183 / 313 (58.47%)	89 / 157 (56.69%)	92 / 158 (58.23%)
occurrences (all)	339	158	169
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	17 / 313 (5.43%)	4 / 157 (2.55%)	2 / 158 (1.27%)
occurrences (all)	18	8	2
OEDEMA PERIPHERAL			
subjects affected / exposed	29 / 313 (9.27%)	16 / 157 (10.19%)	15 / 158 (9.49%)
occurrences (all)	32	19	18
PAIN			
subjects affected / exposed	17 / 313 (5.43%)	8 / 157 (5.10%)	9 / 158 (5.70%)
occurrences (all)	22	9	10
PYREXIA			
subjects affected / exposed	39 / 313 (12.46%)	16 / 157 (10.19%)	15 / 158 (9.49%)
occurrences (all)	49	22	17
Immune system disorders			
DRUG HYPERSENSITIVITY			
subjects affected / exposed	12 / 313 (3.83%)	2 / 157 (1.27%)	9 / 158 (5.70%)
occurrences (all)	14	2	10
Reproductive system and breast disorders			
BREAST PAIN			
subjects affected / exposed	7 / 313 (2.24%)	13 / 157 (8.28%)	3 / 158 (1.90%)
occurrences (all)	7	14	6

Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	64 / 313 (20.45%)	24 / 157 (15.29%)	25 / 158 (15.82%)
occurrences (all)	77	31	30
DYSPNOEA			
subjects affected / exposed	55 / 313 (17.57%)	21 / 157 (13.38%)	31 / 158 (19.62%)
occurrences (all)	73	26	44
EPISTAXIS			
subjects affected / exposed	46 / 313 (14.70%)	27 / 157 (17.20%)	21 / 158 (13.29%)
occurrences (all)	52	31	22
NASAL CONGESTION			
subjects affected / exposed	13 / 313 (4.15%)	11 / 157 (7.01%)	6 / 158 (3.80%)
occurrences (all)	15	13	6
OROPHARYNGEAL PAIN			
subjects affected / exposed	26 / 313 (8.31%)	8 / 157 (5.10%)	16 / 158 (10.13%)
occurrences (all)	28	9	16
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	24 / 313 (7.67%)	18 / 157 (11.46%)	15 / 158 (9.49%)
occurrences (all)	27	18	17
INSOMNIA			
subjects affected / exposed	71 / 313 (22.68%)	31 / 157 (19.75%)	37 / 158 (23.42%)
occurrences (all)	75	36	43
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	32 / 313 (10.22%)	10 / 157 (6.37%)	18 / 158 (11.39%)
occurrences (all)	51	15	27
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	26 / 313 (8.31%)	6 / 157 (3.82%)	16 / 158 (10.13%)
occurrences (all)	40	6	24
WEIGHT DECREASED			
subjects affected / exposed	9 / 313 (2.88%)	3 / 157 (1.91%)	8 / 158 (5.06%)
occurrences (all)	11	4	10
Nervous system disorders			

DIZZINESS			
subjects affected / exposed	55 / 313 (17.57%)	20 / 157 (12.74%)	24 / 158 (15.19%)
occurrences (all)	64	22	34
DYSGEUSIA			
subjects affected / exposed	75 / 313 (23.96%)	29 / 157 (18.47%)	39 / 158 (24.68%)
occurrences (all)	82	32	40
HEADACHE			
subjects affected / exposed	88 / 313 (28.12%)	46 / 157 (29.30%)	40 / 158 (25.32%)
occurrences (all)	109	63	53
PARAESTHESIA			
subjects affected / exposed	31 / 313 (9.90%)	12 / 157 (7.64%)	17 / 158 (10.76%)
occurrences (all)	41	21	19
PERIPHERAL SENSORY NEUROPATHY			
subjects affected / exposed	135 / 313 (43.13%)	77 / 157 (49.04%)	70 / 158 (44.30%)
occurrences (all)	190	121	93
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	212 / 313 (67.73%)	37 / 157 (23.57%)	105 / 158 (66.46%)
occurrences (all)	632	59	281
LEUKOPENIA			
subjects affected / exposed	62 / 313 (19.81%)	21 / 157 (13.38%)	43 / 158 (27.22%)
occurrences (all)	138	33	102
NEUTROPENIA			
subjects affected / exposed	237 / 313 (75.72%)	45 / 157 (28.66%)	115 / 158 (72.78%)
occurrences (all)	836	96	406
THROMBOCYTOPENIA			
subjects affected / exposed	169 / 313 (53.99%)	4 / 157 (2.55%)	67 / 158 (42.41%)
occurrences (all)	460	6	147
Eye disorders			
DRY EYE			
subjects affected / exposed	14 / 313 (4.47%)	9 / 157 (5.73%)	5 / 158 (3.16%)
occurrences (all)	14	10	5
VISION BLURRED			
subjects affected / exposed	11 / 313 (3.51%)	8 / 157 (5.10%)	4 / 158 (2.53%)
occurrences (all)	11	9	4
Gastrointestinal disorders			

ABDOMINAL PAIN			
subjects affected / exposed	37 / 313 (11.82%)	13 / 157 (8.28%)	21 / 158 (13.29%)
occurrences (all)	45	19	27
ABDOMINAL PAIN UPPER			
subjects affected / exposed	25 / 313 (7.99%)	9 / 157 (5.73%)	6 / 158 (3.80%)
occurrences (all)	37	11	9
CONSTIPATION			
subjects affected / exposed	135 / 313 (43.13%)	71 / 157 (45.22%)	62 / 158 (39.24%)
occurrences (all)	168	102	77
DIARRHOEA			
subjects affected / exposed	120 / 313 (38.34%)	58 / 157 (36.94%)	50 / 158 (31.65%)
occurrences (all)	184	78	68
DRY MOUTH			
subjects affected / exposed	24 / 313 (7.67%)	9 / 157 (5.73%)	3 / 158 (1.90%)
occurrences (all)	26	9	3
DYSPEPSIA			
subjects affected / exposed	46 / 313 (14.70%)	29 / 157 (18.47%)	32 / 158 (20.25%)
occurrences (all)	60	43	38
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	30 / 313 (9.58%)	13 / 157 (8.28%)	9 / 158 (5.70%)
occurrences (all)	36	18	9
NAUSEA			
subjects affected / exposed	225 / 313 (71.88%)	98 / 157 (62.42%)	119 / 158 (75.32%)
occurrences (all)	450	169	256
STOMATITIS			
subjects affected / exposed	121 / 313 (38.66%)	41 / 157 (26.11%)	48 / 158 (30.38%)
occurrences (all)	162	49	67
VOMITING			
subjects affected / exposed	90 / 313 (28.75%)	26 / 157 (16.56%)	58 / 158 (36.71%)
occurrences (all)	130	38	93
Skin and subcutaneous tissue disorders			
ALOPECIA			
subjects affected / exposed	190 / 313 (60.70%)	102 / 157 (64.97%)	95 / 158 (60.13%)
occurrences (all)	231	120	119
DERMATITIS ACNEIFORM			

subjects affected / exposed	25 / 313 (7.99%)	16 / 157 (10.19%)	10 / 158 (6.33%)
occurrences (all)	29	18	13
DRY SKIN			
subjects affected / exposed	9 / 313 (2.88%)	8 / 157 (5.10%)	5 / 158 (3.16%)
occurrences (all)	9	8	5
ERYTHEMA			
subjects affected / exposed	4 / 313 (1.28%)	10 / 157 (6.37%)	4 / 158 (2.53%)
occurrences (all)	5	10	5
NAIL DISCOLOURATION			
subjects affected / exposed	20 / 313 (6.39%)	10 / 157 (6.37%)	7 / 158 (4.43%)
occurrences (all)	20	10	7
NAIL DISORDER			
subjects affected / exposed	12 / 313 (3.83%)	9 / 157 (5.73%)	7 / 158 (4.43%)
occurrences (all)	12	10	7
ONYCHOLYSIS			
subjects affected / exposed	2 / 313 (0.64%)	8 / 157 (5.10%)	7 / 158 (4.43%)
occurrences (all)	2	9	8
PRURITUS			
subjects affected / exposed	21 / 313 (6.71%)	12 / 157 (7.64%)	14 / 158 (8.86%)
occurrences (all)	25	15	14
RASH			
subjects affected / exposed	25 / 313 (7.99%)	9 / 157 (5.73%)	13 / 158 (8.23%)
occurrences (all)	26	10	16
RASH MACULO-PAPULAR			
subjects affected / exposed	17 / 313 (5.43%)	8 / 157 (5.10%)	4 / 158 (2.53%)
occurrences (all)	27	13	5
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	37 / 313 (11.82%)	37 / 157 (23.57%)	25 / 158 (15.82%)
occurrences (all)	52	41	35
BACK PAIN			
subjects affected / exposed	34 / 313 (10.86%)	13 / 157 (8.28%)	14 / 158 (8.86%)
occurrences (all)	40	13	14
BONE PAIN			

subjects affected / exposed	43 / 313 (13.74%)	11 / 157 (7.01%)	18 / 158 (11.39%)
occurrences (all)	49	12	23
MUSCLE SPASMS			
subjects affected / exposed	16 / 313 (5.11%)	3 / 157 (1.91%)	6 / 158 (3.80%)
occurrences (all)	19	3	6
MUSCULAR WEAKNESS			
subjects affected / exposed	16 / 313 (5.11%)	4 / 157 (2.55%)	3 / 158 (1.90%)
occurrences (all)	18	4	4
MYALGIA			
subjects affected / exposed	67 / 313 (21.41%)	37 / 157 (23.57%)	31 / 158 (19.62%)
occurrences (all)	96	48	45
PAIN IN EXTREMITY			
subjects affected / exposed	20 / 313 (6.39%)	8 / 157 (5.10%)	15 / 158 (9.49%)
occurrences (all)	23	8	18
Infections and infestations			
FOLLICULITIS			
subjects affected / exposed	7 / 313 (2.24%)	10 / 157 (6.37%)	7 / 158 (4.43%)
occurrences (all)	9	12	7
NASOPHARYNGITIS			
subjects affected / exposed	23 / 313 (7.35%)	10 / 157 (6.37%)	10 / 158 (6.33%)
occurrences (all)	28	12	12
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	27 / 313 (8.63%)	13 / 157 (8.28%)	10 / 158 (6.33%)
occurrences (all)	35	14	13
URINARY TRACT INFECTION			
subjects affected / exposed	22 / 313 (7.03%)	12 / 157 (7.64%)	12 / 158 (7.59%)
occurrences (all)	27	14	14
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	74 / 313 (23.64%)	28 / 157 (17.83%)	39 / 158 (24.68%)
occurrences (all)	96	44	57
DEHYDRATION			
subjects affected / exposed	25 / 313 (7.99%)	8 / 157 (5.10%)	15 / 158 (9.49%)
occurrences (all)	52	19	27
HYPERGLYCAEMIA			

subjects affected / exposed	12 / 313 (3.83%)	5 / 157 (3.18%)	10 / 158 (6.33%)
occurrences (all)	16	8	16
HYPOKALAEMIA			
subjects affected / exposed	36 / 313 (11.50%)	11 / 157 (7.01%)	16 / 158 (10.13%)
occurrences (all)	56	14	29
HYPOMAGNESAEMIA			
subjects affected / exposed	23 / 313 (7.35%)	2 / 157 (1.27%)	10 / 158 (6.33%)
occurrences (all)	34	2	12

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 November 2013	• Update Residual Cancer Burden (RCB) to a tertiary endpoint and clarify that RCB information will not be collected from all sites. • Revise pregnancy testing requirements; Remove 3 hour PK sample at paclitaxel (P)1 visit and request PK samples at P1 visit only if feasible. • Updated the blood samples for Pharmacogenetic analysis to include the collection of an additional (optional) 4mL whole blood sample (for a total of 2 samples) at P1. • Clarify plan for tumor biopsy collection and remove biopsy collection at AC1; Add Quality of Life Questionnaire (QLQ)-C30 questionnaire in the study procedures, remove Quality of Life Questionnaire Chemotherapy-Induced Peripheral Neuropathy (QLQ CIPN20) questionnaire and revise the frequency and duration of collection. • Update survival data collection frequency to every 6 months and clarify which data points will be collected in the survival portion of the study.
01 April 2014	• Update Inclusion Criterion 7 to require the use of contraception for 6 months following completion of therapy. • Add Inclusion Criterion 9 to ensure subjects are capable of taking oral medication. • Add requirement for pregnancy testing at P4, P7, P10 and AC1 visits. • Add requirement for urine testing at AC2 and AC4 visits.
22 July 2014	• Increase approximate number of participating sites to 250. • Update clinical stage in Inclusion Criterion 2 to T2-3 N0-2 or T1 N1-2. • Allow for subjects with Stage III disease to undergo alternate imaging per local standards.
25 November 2014	• Update Study Procedures, Medical History and Oncology History to collect menses history and family history of breast and ovarian cancer to evaluate (post-study analysis) for chemotherapy induced amenorrhea and to generate hypotheses around benefits of investigational therapy in subjects with or without a family history of breast and/or ovarian cancer. • Update PK methods to include additional timepoints to collect a sample for analysis to coincide with the time of relapse; increase the sample volume for plasma markers to ensure sufficient plasma is available for testing using the current methods; include circulating nucleic acid sample collection for additional sequencing studies. • Correct the duration for avoiding pregnancy from 90 days to 6 months to align with Inclusion Criterion.
31 August 2016	• Update appropriate sections to move Event Free Survival (EFS) and Overall Survival (OS) from Tertiary Efficacy Endpoints to Secondary Efficacy Endpoints • Change primary contact for protocol deviations.
25 October 2018	• Revise the duration subjects will be evaluated for disease recurrent during the Post-Surgery Follow-Up period for the secondary endpoint of event-free survival (EFS). • Update primary study contacts for protocol deviations.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported