Clinical trial results:
A Phase 3 Randomized, Placebo-Controlled Trial of Carboplatin and Paclitaxel With or Without the PARP Inhibitor Veliparib (ABT-888) in HER2-Negative Metastatic or Locally Advanced Unresectable BRCA-Associated Breast Cancer

Summary

EudraCT number	2014-000345-70
Trial protocol	FI AT SE GB DK PT DE BE CZ NO HU IT NL LV ES FR LT EE PL
Global end of trial date	25 January 2024

Results information

Result version number	v1 (current)
This version publication date	01 February 2025
First version publication date	01 February 2025

Trial information

Trial identification

Sponsor protocol code	M12-914

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02163694
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AbbVie Deutschland GmbH & Co. KG
Sponsor organisation address	AbbVie House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire, United Kingdom, SL6 4UB, Berkshire, United Kingdom,
Public contact	Global Medical Services, AbbVie, Global Medical Services, AbbVie, 001 8006339110, abbvieclinicaltrials@abbvie.com
Scientific contact	Global Medical Services, AbbVie, 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	25 January 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 January 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to assess the progression-free survival (PFS) of veliparib in combination with carboplatin and paclitaxel (C/P) compared to placebo plus C/P in participants with a Breast Cancer Gene 1 or 2 (BRCA1; BRCA2) mutation in Human Epidermal Growth Factor Receptor 2 (HER2)-negative metastatic or locally advanced unresectable breast cancer. The secondary objectives of the study are to assess overall survival (OS), clinical benefit rate (CBR) through the end of Week 24, objective response rate (ORR) and PFS on subsequent therapy (PFS2) in participants treated with veliparib in combination with C/P versus placebo in combination with C/P.

Protection of trial subjects:

The investigator or his/her representative will explain the nature of the study to the subject, the benefits and risks anticipated from participation in the study, and answer all questions regarding this study. Prior to any study-related screening procedures being performed on the subject or any medications being discontinued by the subject in order to participate in this study, the informed consent statement will be reviewed, signed, and dated by the subject, the person who administered the informed consent, and any other signatories according to local requirements. A copy of the signed informed consent will be given to the subject and the original will be placed in the subject's medical record. An entry must also be made in the subject's dated source documents to confirm that informed consent was obtained prior to any study-related procedures and that the subject received a signed copy.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 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	Argentina: 2
Country: Number of subjects enrolled	Australia: 20
Country: Number of subjects enrolled	Austria: 9
Country: Number of subjects enrolled	Belarus: 9
Country: Number of subjects enrolled	Belgium: 23
Country: Number of subjects enrolled	Canada: 10
Country: Number of subjects enrolled	Chile: 15
Country: Number of subjects enrolled	Colombia: 3
Country: Number of subjects enrolled	Czechia: 21
Country: Number of subjects enrolled	Denmark: 14
Country: Number of subjects enrolled	Estonia: 2
Country: Number of subjects enrolled	Finland: 2

Country: Number of subjects enrolled	France: 41
Country: Number of subjects enrolled	Germany: 21
Country: Number of subjects enrolled	Hungary: 8
Country: Number of subjects enrolled	Israel: 23
Country: Number of subjects enrolled	Italy: 19
Country: Number of subjects enrolled	Korea, Republic of: 25
Country: Number of subjects enrolled	Latvia: 1
Country: Number of subjects enrolled	Lithuania: 5
Country: Number of subjects enrolled	Mexico: 4
Country: Number of subjects enrolled	Netherlands: 17
Country: Number of subjects enrolled	Norway: 1
Country: Number of subjects enrolled	Poland: 6
Country: Number of subjects enrolled	Portugal: 16
Country: Number of subjects enrolled	Romania: 11
Country: Number of subjects enrolled	Russian Federation: 14
Country: Number of subjects enrolled	Singapore: 3
Country: Number of subjects enrolled	South Africa: 13
Country: Number of subjects enrolled	Spain: 13
Country: Number of subjects enrolled	Sweden: 11
Country: Number of subjects enrolled	Taiwan: 1
Country: Number of subjects enrolled	Türkiye: 10
Country: Number of subjects enrolled	Ukraine: 33
Country: Number of subjects enrolled	United Kingdom: 13
Country: Number of subjects enrolled	United States: 74
Worldwide total number of subjects	513
EEA total number of subjects	241

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)	478
From 65 to 84 years	35
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 513 subjects enrolled in the study (N=174 to the placebo + C/P arm, and N=339 to the veliparib + C/P arm). Two subjects form each arm (N= 4) were determined not to have a suspected deleterious or deleterious
mutation in BRCA1/2 and were excluded from the ITT population

Pre-assignment

Screening details:

Subjects randomized to Pbo were eligible to crossover to unblinded veliparib monotherapy. Post Protocol Amend 5, investigators and subjects were unblinded,subjects randomized to Pbo discontinued from the study, subjects discontinuing therapy prior to progression no longer remained on study, and no new subjects initiated crossover unblinded therapy.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo + C/P

Arm description:

Placebo capsules for veliparib (120 mg) administered by mouth twice daily (BID) on Days -2 through 5 of a 21-day cycle. Carboplatin administered intravenously over approximately 15 to 30 minutes at AUC 6 mg/ml/min immediately following paclitaxel infusion on Day 1 of every cycle. Paclitaxel administered intravenously over approximately 1 hour at a dose of 80 mg/m² on Days 1, 8, and 15 of every cycle.

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

Dosage and administration details:

Supplied as 40 mg, 50 mg, or 100 mg capsules for oral administration twice daily (BID) on Days -2 through 5 of a 21-day cycle.

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously over approximately 15 to 30 minutes at an area under the curve (AUC) of 6 mg/mL/min immediately following paclitaxel infusion on Day 1 of every cycle. The duration of carboplatin infusion may be lengthened according to institutional guidelines.

Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered by intravenous infusion over approximately 1 hour at a dose of 80 mg/m² of body-surface area (BSA) on Days 1, 8, and 15 of each 21-day cycle. Paclitaxel is to be infused prior to carboplatin on Day 1. Dosing of veliparib/placebo is to be completed before the carboplatin or paclitaxel infusions.

Arm title	Veliparib + C/P

Arm description:

Veliparib capsules (120 mg) administered by mouth twice daily (BID) on Days -2 through 5 of a 21-day cycle. Carboplatin administered intravenously over approximately 15 to 30 minutes at AUC 6 mg/ml/min immediately following paclitaxel infusion on Day 1 of every cycle. Paclitaxel administered intravenously over approximately 1 hour at a dose of 80 mg/m² on Days 1, 8, and 15 of every cycle.

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

Dosage and administration details:

Supplied as 40 mg, 50 mg, or 100 mg capsules for oral administration twice daily (BID) on Days -2 through 5 of a 21-day cycle.

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously over approximately 15 to 30 minutes at an area under the curve (AUC) of 6 mg/mL/min immediately following paclitaxel infusion on Day 1 of every cycle. The duration of carboplatin infusion may be lengthened according to institutional guidelines.

Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered by intravenous infusion over approximately 1 hour at a dose of 80 mg/m² of body-surface area (BSA) on Days 1, 8, and 15 of each 21-day cycle. Paclitaxel is to be infused prior to carboplatin on Day 1. Dosing of veliparib/placebo is to be completed before the carboplatin or paclitaxel infusions.

Number of subjects in period 1[1]	Placebo + C/P	Veliparib + C/P
Started	172	337
Completed	0	0
Not completed	172	337
Adverse event- related to progression	4	10
Consent withdrawn by subject	13	28
Progressive disease per protocol	125	224

Adverse event- not related to progression	7	22
Other, not specified	17	22
Lost to follow-up	2	2
Sponsor discontinued study	3	29
Randomized but Not Treated	1	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: A total of 513 subjects were enrolled; 2 subjects were determined not to have a suspected deleterious or deleterious mutation in BRCA1/2 and were excluded from the ITT population. One (1) subject Age information missing; this subject has been categorized in the 18-64 or 65-84 Age Category.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo + C/P

Reporting group description:

Placebo capsules for veliparib (120 mg) administered by mouth twice daily (BID) on Days -2 through 5 of a 21-day cycle. Carboplatin administered intravenously over approximately 15 to 30 minutes at AUC 6 mg/ml/min immediately following paclitaxel infusion on Day 1 of every cycle. Paclitaxel administered intravenously over approximately 1 hour at a dose of 80 mg/m² on Days 1, 8, and 15 of every cycle.

Reporting group title	Veliparib + C/P

Reporting group description:

Veliparib capsules (120 mg) administered by mouth twice daily (BID) on Days -2 through 5 of a 21-day cycle. Carboplatin administered intravenously over approximately 15 to 30 minutes at AUC 6 mg/ml/min immediately following paclitaxel infusion on Day 1 of every cycle. Paclitaxel administered intravenously over approximately 1 hour at a dose of 80 mg/m² on Days 1, 8, and 15 of every cycle.

Reporting group values	Placebo + C/P	Veliparib + C/P	Total
Number of subjects	172	337	509
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	46.8	46.8	
standard deviation	± 10.81	± 10.73	-
Gender categorical Units: Subjects			
Female	169	333	502
Male	3	4	7

End points

End points reporting groups

Reporting group title	Placebo + C/P

Reporting group description:

Placebo capsules for veliparib (120 mg) administered by mouth twice daily (BID) on Days -2 through 5 of a 21-day cycle. Carboplatin administered intravenously over approximately 15 to 30 minutes at AUC 6 mg/ml/min immediately following paclitaxel infusion on Day 1 of every cycle. Paclitaxel administered intravenously over approximately 1 hour at a dose of 80 mg/m² on Days 1, 8, and 15 of every cycle.

Reporting group title	Veliparib + C/P

Reporting group description:

Veliparib capsules (120 mg) administered by mouth twice daily (BID) on Days -2 through 5 of a 21-day cycle. Carboplatin administered intravenously over approximately 15 to 30 minutes at AUC 6 mg/ml/ min immediately following paclitaxel infusion on Day 1 of every cycle. Paclitaxel administered intravenously over approximately 1 hour at a dose of 80 mg/m² on Days 1, 8, and 15 of every cycle.

Primary: Progression free survival (PFS)

End point title	Progression free survival (PFS)

End point description:

Number of days from the date the subject is randomized to the date the subject experiences a confirmed event of disease progression or to the date of death if disease progression is not reached

End point type	Primary

End point timeframe:

Measured up to 3 years after the last subject has enrolled in the study.

End point values	Placebo + C/P	Veliparib + C/P		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	172	337		
Units: month				
median (confidence interval 95%)	12.6 (10.6 to 14.4)	14.6 (12.5 to 17.7)		

Statistical analyses

Statistical analysis title	Placebo + C/P, Veliparib + C/P
Comparison groups	Placebo + C/P v Veliparib + C/P
Number of subjects included in analysis	509
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003
Method	Logrank

Statistical analysis title	Placebo + C/P, Veliparib + C/P
Comparison groups	Placebo + C/P v Veliparib + C/P
Number of subjects included in analysis	509
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003
Method	Stratified Cox proportional hazards
Parameter estimate	Stratified Cox proportional hazards
Point estimate	0.728
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	0.9

Secondary: Progression-free survival 2 (PFS2)

End point title	Progression-free survival 2 (PFS2)

End point description:

Days from randomization to the second objective radiographic progression or death of any cause after the first objective radiographic progression, whichever occurs first

End point type	Secondary

End point timeframe:

Measured up to 5 years after the last subject has enrolled in the study.

End point values	Placebo + C/P	Veliparib + C/P		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	172	337		
Units: month				
median (confidence interval 95%)	17.4 (16.0 to 20.7)	21.5 (19.9 to 25.3)		

Statistical analyses

Statistical analysis title	Placebo + C/P, Veliparib + C/P
Comparison groups	Placebo + C/P v Veliparib + C/P
Number of subjects included in analysis	509
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004
Method	Stratified Cox proportional hazards
Parameter estimate	Stratified Cox proportional hazards
Point estimate	0.737

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.597
upper limit	0.908

Secondary: Objective response rate (ORR)

End point title	Objective response rate (ORR)

End point description:

Proportion of subjects with a complete or partial objective response

End point type	Secondary

End point timeframe:

Measured up to 2 years after the last subject has enrolled in the study.

End point values	Placebo + C/P	Veliparib + C/P		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	172	337		
Units: percentage of participants				
number (confidence interval 95%)	93.2 (89.5 to 95.7)	90.7 (87.9 to 92.9)		

Statistical analyses

Statistical analysis title	Placebo + C/P, Veliparib + C/P
Comparison groups	Placebo + C/P v Veliparib + C/P
Number of subjects included in analysis	509
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.202 [1]
Method	Cochran-Mantel-Haenszel

Notes:

[1] - Nominal P value is from Cochran-Mantel-Haenszel test stratified by ER/PgR status and prior platinum therapy use.

Secondary: Overall survival (OS)

End point title	Overall survival (OS)

End point description:

Number of days from the day the subject is randomized to the date of the subject's death

End point type	Secondary

End point timeframe:

Measured up to 5 years after the last subject has enrolled in the study.

End point values	Placebo + C/P	Veliparib + C/P		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	172	337		
Units: month				
median (confidence interval 95%)	28.2 (24.7 to 32.8)	32.4 (27.4 to 38.1)		

Statistical analyses

Statistical analysis title	Placebo + C/P, Veliparib + C/P
Comparison groups	Veliparib + C/P v Placebo + C/P
Number of subjects included in analysis	509
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.41
Method	Stratified Cox proportional hazards
Parameter estimate	Stratified Cox proportional hazards
Point estimate	0.914
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.737
upper limit	1.333

Secondary: Clinical benefit rate (CBR)	
End point title	Clinical benefit rate (CBR)
End point description: Progression-free rate at 24 weeks from the Kaplan-Meier curve for time to progression	
End point type	Secondary
End point timeframe: Measured up to 5 years after the last subject has enrolled in the study.	

End point values	Placebo + C/P	Veliparib + C/P		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	172	337		
Units: percentage of participants				
number (confidence interval 95%)	93.2 (89.5 to 95.7)	90.7 (87.9 to 92.9)		

Statistical analyses

Statistical analysis title	Placebo + C/P, Veliparib + C/P
Comparison groups	Placebo + C/P v Veliparib + C/P
Number of subjects included in analysis	509
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.202 [2]
Method	Cochran-Mantel-Haenszel

Notes:

[2] - Nominal P value is from Cochran-Mantel-Haenszel test stratified by ER/PgR status and prior platinum therapy use.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-cause mortality were reported from enrollment to the end of study, median time on follow up was 84.5 and 81.8 months for Placebo + C/P and Veliparib + C/P, respectively.

Adverse event reporting additional description:

Treatment-emergent adverse events and serious adverse events were collected from first dose of study drug until 30 days after the last dose of study drug; mean duration on study drug was 115.0 and 117.5 days for Placebo + C/P and Veliparib + C/P, respectively.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	Veliparib_120_mg_BID_plus_Carboplatin_Paclitaxel
Reporting group description: -	
Reporting group title	Placebo_120_mg_BID_plus_Carboplatin_Paclitaxel

Reporting group description: -

Serious adverse events	Veliparib_120_mg_BID_plus_Carboplatin_Paclitaxel	Placebo_120_mg_BID_plus_Carboplatin_Paclitaxel	
Total subjects affected by serious adverse events			
subjects affected / exposed	135 / 339 (39.82%)	68 / 174 (39.08%)	
number of deaths (all causes)	244	129	
number of deaths resulting from adverse events	14	6	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
ACUTE MYELOID LEUKAEMIA			
subjects affected / exposed	4 / 339 (1.18%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	5 / 6	0 / 0	
deaths causally related to treatment / all	3 / 3	0 / 0	
BASAL CELL CARCINOMA			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (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	19 / 339 (5.60%)	11 / 174 (6.32%)	
occurrences causally related to treatment / all	0 / 26	0 / 12	
deaths causally related to treatment / all	0 / 7	0 / 3	
GASTRIC NEOPLASM			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COLON CANCER			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CANCER PAIN			
subjects affected / exposed	0 / 339 (0.00%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
MALIGNANT PLEURAL EFFUSION			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
METASTASES TO BONE			
subjects affected / exposed	0 / 339 (0.00%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
METASTASES TO BONE MARROW			
subjects affected / exposed	0 / 339 (0.00%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
METASTASES TO CENTRAL NERVOUS SYSTEM			
subjects affected / exposed	1 / 339 (0.29%)	4 / 174 (2.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
METASTASES TO LYMPH NODES			

subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
METASTASES TO MENINGES			
subjects affected / exposed	3 / 339 (0.88%)	2 / 174 (1.15%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
MYELODYSPLASTIC SYNDROME			
subjects affected / exposed	5 / 339 (1.47%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	7 / 7	0 / 1	
deaths causally related to treatment / all	1 / 1	0 / 0	
SECOND PRIMARY MALIGNANCY			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
TUMOUR PAIN			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
ILIAC ARTERY OCCLUSION			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
POOR VENOUS ACCESS			
subjects affected / exposed	0 / 339 (0.00%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEEP VEIN THROMBOSIS			
subjects affected / exposed	1 / 339 (0.29%)	3 / 174 (1.72%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
AORTIC STENOSIS			

subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
ABORTION INDUCED			
subjects affected / exposed	0 / 339 (0.00%)	1 / 174 (0.57%)	
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			
HYPERTHERMIA			
subjects affected / exposed	0 / 339 (0.00%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
GENERAL PHYSICAL HEALTH DETERIORATION			
subjects affected / exposed	0 / 339 (0.00%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
FATIGUE			
subjects affected / exposed	2 / 339 (0.59%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	4 / 4	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DISEASE PROGRESSION			
subjects affected / exposed	0 / 339 (0.00%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CHEST PAIN			
subjects affected / exposed	3 / 339 (0.88%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	1 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
MALAISE			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

NON-CARDIAC CHEST PAIN			
subjects affected / exposed	1 / 339 (0.29%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PYREXIA			
subjects affected / exposed	9 / 339 (2.65%)	4 / 174 (2.30%)	
occurrences causally related to treatment / all	3 / 12	2 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
PAIN			
subjects affected / exposed	1 / 339 (0.29%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
ANAPHYLACTIC REACTION			
subjects affected / exposed	2 / 339 (0.59%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CONTRAST MEDIA ALLERGY			
subjects affected / exposed	0 / 339 (0.00%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERSENSITIVITY			
subjects affected / exposed	0 / 339 (0.00%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HAEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DRUG HYPERSENSITIVITY			
subjects affected / exposed	1 / 339 (0.29%)	3 / 174 (1.72%)	
occurrences causally related to treatment / all	1 / 1	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

Reproductive system and breast disorders			
PELVIC PAIN			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
ATELECTASIS			
subjects affected / exposed	0 / 339 (0.00%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
LARYNGEAL OEDEMA			
subjects affected / exposed	0 / 339 (0.00%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
EPISTAXIS			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DYSPNOEA			
subjects affected / exposed	2 / 339 (0.59%)	2 / 174 (1.15%)	
occurrences causally related to treatment / all	0 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMOMEDIASTINUM			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PLEURITIC PAIN			
subjects affected / exposed	0 / 339 (0.00%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PLEURAL EFFUSION			

subjects affected / exposed	1 / 339 (0.29%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PULMONARY ARTERY THROMBOSIS			
subjects affected / exposed	0 / 339 (0.00%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
PULMONARY EMBOLISM			
subjects affected / exposed	5 / 339 (1.47%)	2 / 174 (1.15%)	
occurrences causally related to treatment / all	1 / 6	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
PNEUMOTHORAX			
subjects affected / exposed	2 / 339 (0.59%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RESPIRATORY FAILURE			
subjects affected / exposed	0 / 339 (0.00%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Psychiatric disorders			
MANIA			
subjects affected / exposed	0 / 339 (0.00%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ANXIETY			
subjects affected / exposed	1 / 339 (0.29%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PSYCHOTIC DISORDER			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			

DEVICE BREAKAGE			
subjects affected / exposed	0 / 339 (0.00%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
BLOOD CREATININE INCREASED			
subjects affected / exposed	0 / 339 (0.00%)	1 / 174 (0.57%)	
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			
FEMORAL NECK FRACTURE			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (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	0 / 339 (0.00%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PROCEDURAL PAIN			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
PERICARDITIS			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	4 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIOPULMONARY FAILURE			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIO-RESPIRATORY ARREST			

subjects affected / exposed	0 / 339 (0.00%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
APHASIA			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CERVICAL CORD COMPRESSION			
subjects affected / exposed	0 / 339 (0.00%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CEREBRAL INFARCTION			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BRAIN OEDEMA			
subjects affected / exposed	2 / 339 (0.59%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
LETHARGY			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DYSARTHRIA			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYDROCEPHALUS			
subjects affected / exposed	0 / 339 (0.00%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEADACHE			

subjects affected / exposed	0 / 339 (0.00%)	2 / 174 (1.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIZZINESS			
subjects affected / exposed	2 / 339 (0.59%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
INTRACRANIAL PRESSURE INCREASED			
subjects affected / exposed	0 / 339 (0.00%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
MENINGEAL DISORDER			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
VASCULAR ENCEPHALOPATHY			
subjects affected / exposed	0 / 339 (0.00%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SYNCOPE			
subjects affected / exposed	0 / 339 (0.00%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SEIZURE			
subjects affected / exposed	4 / 339 (1.18%)	2 / 174 (1.15%)	
occurrences causally related to treatment / all	2 / 4	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
SCIATICA			
subjects affected / exposed	1 / 339 (0.29%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PRESYNCOPE			

subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PARTIAL SEIZURES			
subjects affected / exposed	0 / 339 (0.00%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
HAEMORRHAGIC DISORDER			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LEUKOPENIA			
subjects affected / exposed	2 / 339 (0.59%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	4 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ANAEMIA			
subjects affected / exposed	16 / 339 (4.72%)	5 / 174 (2.87%)	
occurrences causally related to treatment / all	21 / 21	8 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
FEBRILE NEUTROPENIA			
subjects affected / exposed	11 / 339 (3.24%)	3 / 174 (1.72%)	
occurrences causally related to treatment / all	11 / 11	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEUTROPENIA			
subjects affected / exposed	8 / 339 (2.36%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	11 / 11	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
THROMBOCYTOPENIA			
subjects affected / exposed	14 / 339 (4.13%)	5 / 174 (2.87%)	
occurrences causally related to treatment / all	20 / 21	4 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			

VERTIGO			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
DIPLOPIA			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RETINAL ARTERY OCCLUSION			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
COLITIS MICROSCOPIC			
subjects affected / exposed	0 / 339 (0.00%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ABDOMINAL PAIN UPPER			
subjects affected / exposed	0 / 339 (0.00%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ABDOMINAL PAIN LOWER			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ABDOMINAL PAIN			
subjects affected / exposed	1 / 339 (0.29%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ABDOMINAL HERNIA			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

ILEUS			
subjects affected / exposed	0 / 339 (0.00%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTRITIS			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
FAECALOMA			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIARRHOEA			
subjects affected / exposed	2 / 339 (0.59%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CONSTIPATION			
subjects affected / exposed	2 / 339 (0.59%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	2 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INTESTINAL OBSTRUCTION			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SMALL INTESTINAL OBSTRUCTION			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PANCREATITIS ACUTE			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
NONINFECTIVE SIALOADENITIS			

subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (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	6 / 339 (1.77%)	2 / 174 (1.15%)	
occurrences causally related to treatment / all	6 / 9	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
TOOTHACHE			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VOMITING			
subjects affected / exposed	6 / 339 (1.77%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	6 / 8	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
CHOLELITHIASIS			
subjects affected / exposed	2 / 339 (0.59%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CHOLECYSTITIS			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
ANGIOEDEMA			
subjects affected / exposed	0 / 339 (0.00%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
HAEMATURIA			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

CHRONIC KIDNEY DISEASE			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ACUTE KIDNEY INJURY			
subjects affected / exposed	0 / 339 (0.00%)	1 / 174 (0.57%)	
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			
BACK PAIN			
subjects affected / exposed	4 / 339 (1.18%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	1 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MUSCULAR WEAKNESS			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
JOINT LOCK			
subjects affected / exposed	0 / 339 (0.00%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
INTERVERTEBRAL DISC PROTRUSION			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MUSCULOSKELETAL CHEST PAIN			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SPINAL STENOSIS			
subjects affected / exposed	0 / 339 (0.00%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

OSTEONECROSIS OF JAW			
subjects affected / exposed	0 / 339 (0.00%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
OSTEOARTHRITIS			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
NECK PAIN			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
BREAST CELLULITIS			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
APPENDICITIS			
subjects affected / exposed	2 / 339 (0.59%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ABSCESS JAW			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFECTED DERMAL CYST			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROENTERITIS VIRAL			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ERYSIPELAS			

subjects affected / exposed	2 / 339 (0.59%)	2 / 174 (1.15%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
CELLULITIS			
subjects affected / exposed	4 / 339 (1.18%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	4 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BRONCHITIS MORAXELLA			
subjects affected / exposed	0 / 339 (0.00%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFECTED LYMPHOCELE			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BRONCHITIS			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFLUENZA			
subjects affected / exposed	3 / 339 (0.88%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	1 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MENINGITIS			
subjects affected / exposed	0 / 339 (0.00%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFECTION			

subjects affected / exposed	0 / 339 (0.00%)	2 / 174 (1.15%)	
occurrences causally related to treatment / all	0 / 0	2 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
MYELITIS			
subjects affected / exposed	0 / 339 (0.00%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
NASOPHARYNGITIS			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
OPHTHALMIC HERPES ZOSTER			
subjects affected / exposed	0 / 339 (0.00%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEUTROPENIC SEPSIS			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEUTROPENIC INFECTION			
subjects affected / exposed	2 / 339 (0.59%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PAROTID ABSCESS			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 339 (0.00%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA			

subjects affected / exposed	7 / 339 (2.06%)	2 / 174 (1.15%)	
occurrences causally related to treatment / all	4 / 8	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMOCYSTIS JIROVECII PNEUMONIA			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RESPIRATORY TRACT INFECTION VIRAL			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SEPSIS			
subjects affected / exposed	4 / 339 (1.18%)	4 / 174 (2.30%)	
occurrences causally related to treatment / all	1 / 4	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 0	
STAPHYLOCOCCAL SKIN INFECTION			
subjects affected / exposed	0 / 339 (0.00%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SINUSITIS			
subjects affected / exposed	3 / 339 (0.88%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SEPTIC SHOCK			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	2 / 339 (0.59%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VIRAL INFECTION			

subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
UROSEPSIS			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
URINARY TRACT INFECTION			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEVICE RELATED INFECTION			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEVICE RELATED SEPSIS			
subjects affected / exposed	1 / 339 (0.29%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VASCULAR DEVICE INFECTION			
subjects affected / exposed	5 / 339 (1.47%)	2 / 174 (1.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
DIABETES MELLITUS			
subjects affected / exposed	0 / 339 (0.00%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEHYDRATION			
subjects affected / exposed	2 / 339 (0.59%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ELECTROLYTE IMBALANCE			

subjects affected / exposed	0 / 339 (0.00%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
GOUT			
subjects affected / exposed	0 / 339 (0.00%)	1 / 174 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOKALAEMIA			
subjects affected / exposed	2 / 339 (0.59%)	0 / 174 (0.00%)	
occurrences causally related to treatment / all	2 / 2	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_120_mg_BID_plus_Carboplatin_Paclitaxel	Placebo_120_mg_BID_plus_Carboplatin_Paclitaxel	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	332 / 339 (97.94%)	169 / 174 (97.13%)	
Vascular disorders			
HOT FLUSH			
subjects affected / exposed	41 / 339 (12.09%)	13 / 174 (7.47%)	
occurrences (all)	52	16	
HYPERTENSION			
subjects affected / exposed	25 / 339 (7.37%)	12 / 174 (6.90%)	
occurrences (all)	40	14	
LYMPHOEDEMA			
subjects affected / exposed	20 / 339 (5.90%)	11 / 174 (6.32%)	
occurrences (all)	20	15	
General disorders and administration site conditions			
CHEST PAIN			
subjects affected / exposed	19 / 339 (5.60%)	14 / 174 (8.05%)	
occurrences (all)	29	15	
ASTHENIA			
subjects affected / exposed	85 / 339 (25.07%)	45 / 174 (25.86%)	
occurrences (all)	346	141	

FATIGUE			
subjects affected / exposed	168 / 339 (49.56%)	90 / 174 (51.72%)	
occurrences (all)	383	218	
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	27 / 339 (7.96%)	15 / 174 (8.62%)	
occurrences (all)	50	26	
MUCOSAL INFLAMMATION			
subjects affected / exposed	30 / 339 (8.85%)	7 / 174 (4.02%)	
occurrences (all)	37	7	
PYREXIA			
subjects affected / exposed	59 / 339 (17.40%)	35 / 174 (20.11%)	
occurrences (all)	83	45	
PERIPHERAL SWELLING			
subjects affected / exposed	18 / 339 (5.31%)	9 / 174 (5.17%)	
occurrences (all)	21	10	
PAIN			
subjects affected / exposed	20 / 339 (5.90%)	11 / 174 (6.32%)	
occurrences (all)	22	11	
OEDEMA PERIPHERAL			
subjects affected / exposed	69 / 339 (20.35%)	20 / 174 (11.49%)	
occurrences (all)	96	25	
Immune system disorders			
DRUG HYPERSENSITIVITY			
subjects affected / exposed	58 / 339 (17.11%)	32 / 174 (18.39%)	
occurrences (all)	91	66	
Reproductive system and breast disorders			
BREAST PAIN			
subjects affected / exposed	19 / 339 (5.60%)	10 / 174 (5.75%)	
occurrences (all)	25	13	
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	77 / 339 (22.71%)	34 / 174 (19.54%)	
occurrences (all)	126	48	
DYSPNOEA			
subjects affected / exposed	71 / 339 (20.94%)	34 / 174 (19.54%)	
occurrences (all)	105	43	

DYSPNOEA EXERTIONAL			
subjects affected / exposed	24 / 339 (7.08%)	7 / 174 (4.02%)	
occurrences (all)	32	18	
EPISTAXIS			
subjects affected / exposed	62 / 339 (18.29%)	29 / 174 (16.67%)	
occurrences (all)	87	37	
OROPHARYNGEAL PAIN			
subjects affected / exposed	31 / 339 (9.14%)	14 / 174 (8.05%)	
occurrences (all)	44	16	
PRODUCTIVE COUGH			
subjects affected / exposed	18 / 339 (5.31%)	9 / 174 (5.17%)	
occurrences (all)	23	14	
RHINORRHOEA			
subjects affected / exposed	21 / 339 (6.19%)	4 / 174 (2.30%)	
occurrences (all)	29	5	
Psychiatric disorders			
INSOMNIA			
subjects affected / exposed	63 / 339 (18.58%)	33 / 174 (18.97%)	
occurrences (all)	84	47	
DEPRESSION			
subjects affected / exposed	30 / 339 (8.85%)	10 / 174 (5.75%)	
occurrences (all)	36	12	
ANXIETY			
subjects affected / exposed	40 / 339 (11.80%)	13 / 174 (7.47%)	
occurrences (all)	48	17	
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	59 / 339 (17.40%)	25 / 174 (14.37%)	
occurrences (all)	151	61	
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	50 / 339 (14.75%)	23 / 174 (13.22%)	
occurrences (all)	115	62	
BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	26 / 339 (7.67%)	9 / 174 (5.17%)	
occurrences (all)	48	18	

WEIGHT INCREASED			
subjects affected / exposed	19 / 339 (5.60%)	5 / 174 (2.87%)	
occurrences (all)	40	13	
Cardiac disorders			
PALPITATIONS			
subjects affected / exposed	20 / 339 (5.90%)	4 / 174 (2.30%)	
occurrences (all)	28	4	
TACHYCARDIA			
subjects affected / exposed	14 / 339 (4.13%)	11 / 174 (6.32%)	
occurrences (all)	20	16	
Nervous system disorders			
PERIPHERAL SENSORY NEUROPATHY			
subjects affected / exposed	158 / 339 (46.61%)	89 / 174 (51.15%)	
occurrences (all)	347	185	
PARAESTHESIA			
subjects affected / exposed	33 / 339 (9.73%)	16 / 174 (9.20%)	
occurrences (all)	40	30	
NEUROPATHY PERIPHERAL			
subjects affected / exposed	22 / 339 (6.49%)	15 / 174 (8.62%)	
occurrences (all)	27	19	
HEADACHE			
subjects affected / exposed	124 / 339 (36.58%)	67 / 174 (38.51%)	
occurrences (all)	217	113	
DYSGEUSIA			
subjects affected / exposed	48 / 339 (14.16%)	19 / 174 (10.92%)	
occurrences (all)	61	27	
DIZZINESS			
subjects affected / exposed	68 / 339 (20.06%)	34 / 174 (19.54%)	
occurrences (all)	114	53	
TASTE DISORDER			
subjects affected / exposed	19 / 339 (5.60%)	13 / 174 (7.47%)	
occurrences (all)	39	19	
Blood and lymphatic system disorders			
LEUKOPENIA			
subjects affected / exposed	133 / 339 (39.23%)	65 / 174 (37.36%)	
occurrences (all)	700	319	
ANAEMIA			

subjects affected / exposed	256 / 339 (75.52%)	117 / 174 (67.24%)	
occurrences (all)	1147	501	
LYMPHOPENIA			
subjects affected / exposed	43 / 339 (12.68%)	14 / 174 (8.05%)	
occurrences (all)	139	33	
NEUTROPENIA			
subjects affected / exposed	292 / 339 (86.14%)	156 / 174 (89.66%)	
occurrences (all)	2450	1286	
THROMBOCYTOPENIA			
subjects affected / exposed	257 / 339 (75.81%)	118 / 174 (67.82%)	
occurrences (all)	1659	581	
Ear and labyrinth disorders			
TINNITUS			
subjects affected / exposed	21 / 339 (6.19%)	8 / 174 (4.60%)	
occurrences (all)	43	8	
VERTIGO			
subjects affected / exposed	24 / 339 (7.08%)	14 / 174 (8.05%)	
occurrences (all)	38	20	
Eye disorders			
DRY EYE			
subjects affected / exposed	24 / 339 (7.08%)	10 / 174 (5.75%)	
occurrences (all)	26	11	
VISION BLURRED			
subjects affected / exposed	10 / 339 (2.95%)	9 / 174 (5.17%)	
occurrences (all)	13	10	
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	52 / 339 (15.34%)	24 / 174 (13.79%)	
occurrences (all)	81	30	
ABDOMINAL DISTENSION			
subjects affected / exposed	18 / 339 (5.31%)	7 / 174 (4.02%)	
occurrences (all)	19	10	
DYSPEPSIA			
subjects affected / exposed	61 / 339 (17.99%)	20 / 174 (11.49%)	
occurrences (all)	88	24	
DRY MOUTH			

subjects affected / exposed	34 / 339 (10.03%)	17 / 174 (9.77%)	
occurrences (all)	42	17	
DIARRHOEA			
subjects affected / exposed	151 / 339 (44.54%)	69 / 174 (39.66%)	
occurrences (all)	337	141	
CONSTIPATION			
subjects affected / exposed	117 / 339 (34.51%)	59 / 174 (33.91%)	
occurrences (all)	183	87	
ABDOMINAL PAIN UPPER			
subjects affected / exposed	56 / 339 (16.52%)	23 / 174 (13.22%)	
occurrences (all)	90	33	
GASTRITIS			
subjects affected / exposed	4 / 339 (1.18%)	10 / 174 (5.75%)	
occurrences (all)	5	10	
VOMITING			
subjects affected / exposed	118 / 339 (34.81%)	72 / 174 (41.38%)	
occurrences (all)	280	160	
TOOTHACHE			
subjects affected / exposed	26 / 339 (7.67%)	11 / 174 (6.32%)	
occurrences (all)	30	12	
STOMATITIS			
subjects affected / exposed	46 / 339 (13.57%)	24 / 174 (13.79%)	
occurrences (all)	74	32	
NAUSEA			
subjects affected / exposed	240 / 339 (70.80%)	118 / 174 (67.82%)	
occurrences (all)	772	328	
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	18 / 339 (5.31%)	8 / 174 (4.60%)	
occurrences (all)	20	8	
Skin and subcutaneous tissue disorders			
RASH			
subjects affected / exposed	43 / 339 (12.68%)	22 / 174 (12.64%)	
occurrences (all)	58	28	
PRURITUS			

subjects affected / exposed	32 / 339 (9.44%)	8 / 174 (4.60%)	
occurrences (all)	45	12	
ALOPECIA			
subjects affected / exposed	182 / 339 (53.69%)	87 / 174 (50.00%)	
occurrences (all)	254	113	
DRY SKIN			
subjects affected / exposed	27 / 339 (7.96%)	6 / 174 (3.45%)	
occurrences (all)	29	7	
ERYTHEMA			
subjects affected / exposed	18 / 339 (5.31%)	9 / 174 (5.17%)	
occurrences (all)	20	18	
Musculoskeletal and connective tissue disorders			
BONE PAIN			
subjects affected / exposed	41 / 339 (12.09%)	23 / 174 (13.22%)	
occurrences (all)	54	39	
BACK PAIN			
subjects affected / exposed	66 / 339 (19.47%)	42 / 174 (24.14%)	
occurrences (all)	105	62	
ARTHRALGIA			
subjects affected / exposed	77 / 339 (22.71%)	58 / 174 (33.33%)	
occurrences (all)	133	98	
MYALGIA			
subjects affected / exposed	60 / 339 (17.70%)	26 / 174 (14.94%)	
occurrences (all)	88	39	
MUSCLE SPASMS			
subjects affected / exposed	20 / 339 (5.90%)	9 / 174 (5.17%)	
occurrences (all)	25	13	
MUSCULOSKELETAL CHEST PAIN			
subjects affected / exposed	25 / 339 (7.37%)	9 / 174 (5.17%)	
occurrences (all)	29	9	
PAIN IN EXTREMITY			
subjects affected / exposed	71 / 339 (20.94%)	40 / 174 (22.99%)	
occurrences (all)	119	53	
NECK PAIN			

subjects affected / exposed	17 / 339 (5.01%)	8 / 174 (4.60%)	
occurrences (all)	23	11	
Infections and infestations			
INFLUENZA			
subjects affected / exposed	19 / 339 (5.60%)	7 / 174 (4.02%)	
occurrences (all)	26	7	
BRONCHITIS			
subjects affected / exposed	21 / 339 (6.19%)	5 / 174 (2.87%)	
occurrences (all)	27	6	
NASOPHARYNGITIS			
subjects affected / exposed	60 / 339 (17.70%)	27 / 174 (15.52%)	
occurrences (all)	89	42	
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	17 / 339 (5.01%)	4 / 174 (2.30%)	
occurrences (all)	26	5	
RESPIRATORY TRACT INFECTION VIRAL			
subjects affected / exposed	15 / 339 (4.42%)	10 / 174 (5.75%)	
occurrences (all)	33	16	
RHINITIS			
subjects affected / exposed	20 / 339 (5.90%)	4 / 174 (2.30%)	
occurrences (all)	24	5	
SINUSITIS			
subjects affected / exposed	29 / 339 (8.55%)	9 / 174 (5.17%)	
occurrences (all)	34	12	
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	52 / 339 (15.34%)	19 / 174 (10.92%)	
occurrences (all)	86	27	
URINARY TRACT INFECTION			
subjects affected / exposed	41 / 339 (12.09%)	17 / 174 (9.77%)	
occurrences (all)	77	43	
Metabolism and nutrition disorders			
DEHYDRATION			
subjects affected / exposed	17 / 339 (5.01%)	4 / 174 (2.30%)	
occurrences (all)	23	4	
HYPERGLYCAEMIA			

subjects affected / exposed	22 / 339 (6.49%)	9 / 174 (5.17%)	
occurrences (all)	65	19	
DECREASED APPETITE			
subjects affected / exposed	81 / 339 (23.89%)	56 / 174 (32.18%)	
occurrences (all)	106	71	
HYPOPHOSPHATAEMIA			
subjects affected / exposed	26 / 339 (7.67%)	9 / 174 (5.17%)	
occurrences (all)	51	28	
HYPONATRAEMIA			
subjects affected / exposed	18 / 339 (5.31%)	5 / 174 (2.87%)	
occurrences (all)	24	5	
HYPOKALAEMIA			
subjects affected / exposed	44 / 339 (12.98%)	19 / 174 (10.92%)	
occurrences (all)	95	47	
HYPOCALCAEMIA			
subjects affected / exposed	29 / 339 (8.55%)	14 / 174 (8.05%)	
occurrences (all)	55	21	
HYPOMAGNESAEMIA			
subjects affected / exposed	83 / 339 (24.48%)	39 / 174 (22.41%)	
occurrences (all)	196	108	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 June 2014	Amendment 1 – Updated to require contraception use for 6 months following completion of therapy in male and female subjects and to clarify that abstinence is an approved method of birth control; updated exclusion criteria to include hypersensitivity to Tartrazine, Orange Yellow-S or other constituents; updated to clarify definition of uncontrolled hypertension.
11 February 2015	Amendment 2 – Updated to change the primary efficacy endpoint of PFS as determined by a BICR to PFS as determined by the investigator, with BICR as supportive of the investigator's assessment; to clarify that bone-only disease and/or hormone receptor-positive disease are eligible for the study; that post-baseline CNS imaging is not required in subjects without evidence of CNS metastases at Screening; updated dose modification language; added unblinded team to manage subjects who enter crossover therapy upon confirmed disease progression (no subjects entered crossover prior to Amendment 2).
17 June 2016	Amendment 3 – Updated to increase the number of subjects based upon data from Phase 2 Study M12-895, including revising protocol assumptions and adjusting the sample size based on pre-planned adaptation; to clarify clinical data to be collected and submitted for central review to support progression; to clarify blinding information; to clarify veliparib/placebo administration after discontinuation of chemotherapy; to clarify screening and randomization pregnancy testing and prior anticancer requirements; to add a post-treatment phase schedule of assessments; included updated NCCN criteria for BRCA testing.
23 July 2020	Amendment 4 – Updated to add benefits and risks evaluation information and updated study procedures in the context of the COVID-19 pandemic, introduced the option of off-site phone visits every other cycle for subjects who have been receiving single-agent veliparib/placebo at a stable dose without adjustment for multiple cycles without uncontrolled adverse events, and to add table of assessments for these visits, removed references to Blinded/Unblinded TA MD and study teams throughout protocol, included language to indicate that AbbVie may remove the requirements for sites to send clinical laboratory samples to the central laboratory and radiology scans to the central reviewer, or discontinue the requirements for central review at any time during the course of the study, updated tumor assessment schedule from every 9 weeks to allow every 12 weeks (or at longer intervals not to exceed 24 weeks per the investigator's discretion) from the prior scan, update IDMC review language, update the guidelines on when chemotherapy can begin based on hematologic blood counts, added language on the reporting of myelodysplastic syndrome, acute myeloid leukemia, or any secondary primary malignancy, modify the Table of Study Procedures for Post Treatment Phase and for patients that are considered on study, off drug, clarify the timing/conduct of additional OS analyses before the final OS analysis, if needed, changed DOR from secondary to tertiary endpoint, include updates from Administrative Changes 3 and 4 throughout the protocol, updated contacts for safety reporting related questions or concerns and protocol deviations, and corrected grammatical errors and inconsistencies throughout the protocol.

06 August 2022	Amendment 5 – Updated on the protocol-specified PFS and OS analyses, added actions to be taken with subjects on treatment after final OS analysis, indicated unblinding to treatment assignments, specified no new starts of crossover open-label monotherapy after progression for subjects randomized to placebo, indicated subjects receiving placebo must be discontinued from the study, modified study procedures for subjects continuing on study treatment, increased interval between required on-site visits for subjects on veliparib monotherapy, removed use of central laboratory for clinical laboratory tests, central review of tumor assessment scans, included details on how to perform specific activities/procedures that may be impacted by changes in global/local regulations due to the pandemic and/or the geopolitical conflict in Ukraine and surrounding impacted regions.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

None reported

Notes: