Clinical trial results:
A Phase 3 Placebo-Controlled Study of Carboplatin/Paclitaxel With or Without Concurrent and Continuation Maintenance Veliparib (PARP Inhibitor) in Subjects With Previously Untreated Stages III or IV High-Grade Serous Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer

Summary

EudraCT number	2014-005070-11
Trial protocol	DK ES PL
Global end of trial date	05 October 2023
Results information	
Result version number	v1 (current)
This version publication date	18 October 2024
First version publication date	18 October 2024

Trial information

Trial identification	
Sponsor protocol code	M13-694
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02470585
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
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	05 October 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 October 2023
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 evaluate whether progression-free survival (PFS) was prolonged with the addition of veliparib to standard platinum-based chemotherapy (carboplatin/paclitaxel [C/P]) and continued as maintenance therapy compared with chemotherapy alone.

The study was terminated early (business decision not related to patient safety).

Protection of trial subjects:

Subjects signed and dated an informed consent, approved by an independent ethics committee (IEC)/institutional review board (IRB), prior to the initiation of any screening or study-specific procedures.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 July 2015
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: 75
Country: Number of subjects enrolled	Brazil: 11
Country: Number of subjects enrolled	Denmark: 5
Country: Number of subjects enrolled	Israel: 33
Country: Number of subjects enrolled	Japan: 78
Country: Number of subjects enrolled	Korea, Republic of: 70
Country: Number of subjects enrolled	Poland: 2
Country: Number of subjects enrolled	Spain: 46
Country: Number of subjects enrolled	United Kingdom: 27
Country: Number of subjects enrolled	United States: 793
Worldwide total number of subjects	1140
EEA total number of subjects	53

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)	686
From 65 to 84 years	448
85 years and over	6

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants were randomized in a 1:1:1 ratio to one of three treatment groups. Randomization was stratified according to the timing of surgery and residual disease after primary surgery or interval surgery, the paclitaxel schedule, stage of disease, geographic region, and germline breast cancer susceptibility gene (BRCA) mutation status.

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 + Carboplatin + Paclitaxel -> Placebo

Arm description:

Participants received placebo to veliparib orally twice a day in combination with carboplatin given at an area under the curve [AUC] of 6 mg per milliliter per minute (mg/mL/min), every 3 weeks, and paclitaxel 175 mg per square meter (mg/m²) of body-surface area (BSA), administered every 3 weeks, or 80 mg/m² administered weekly, for six 21-day cycles.

Participants who completed chemotherapy without disease progression received matching placebo twice daily for an additional thirty 21-day cycles of maintenance therapy.

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

Dosage and administration details:

Administered by intravenous infusion, either 80 mg/m² of body-surface area (BSA) on Days 1, 8, and 15 of each 21-day cycle (weekly dosing), or 175 mg/m² of BSA on Day 1 of each 21-day cycle (3-week dosing).

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

Dosage and administration details:

Administered by intravenous infusion at an area under the curve (AUC) of 6 mg/mL/min every 3 weeks.

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

Dosage and administration details:

Capsules for oral administration

Arm title	Veliparib + Carboplatin + Paclitaxel -> Placebo

Arm description:

Participants received 150 mg veliparib orally twice a day in combination with carboplatin given at an AUC of 6 mg/mL/min every 3 weeks, and paclitaxel 175 mg/m² of BSA administered every 3 weeks, or 80 mg/m² administered weekly, for six 21-day cycles.

Participants who completed chemotherapy without disease progression received matching placebo twice daily for an additional thirty 21-day cycles of maintenance therapy.

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

Dosage and administration details:

Capsules for oral administration

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

Dosage and administration details:

Administered by intravenous infusion at an area under the curve (AUC) of 6 mg/mL/min every 3 weeks.

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

Dosage and administration details:

Administered by intravenous infusion, either 80 mg/m² of body-surface area (BSA) on Days 1, 8, and 15 of each 21-day cycle (weekly dosing), or 175 mg/m² of BSA on Day 1 of each 21-day cycle (3-week dosing).

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

Dosage and administration details:

Capsules for oral administration

Arm title	Veliparib + Carboplatin + Paclitaxel -> Veliparib

Arm description:

Participants received 150 mg veliparib orally twice a day in combination with carboplatin given at an AUC of 6 mg/mL/min every 3 weeks, and paclitaxel 175 mg/m² of BSA administered every 3 weeks, or 80 mg/m² administered weekly, for six 21-day cycles.

Participants who completed chemotherapy without disease progression received single-agent veliparib at

a dose of 300 mg twice daily for 2 weeks (transition period) and then 400 mg veliparib twice daily if the dose in the transition period was not associated with limiting side effects for an additional thirty 21-day cycles of maintenance therapy.

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

Dosage and administration details:

Capsules for oral administration

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

Dosage and administration details:

Administered by intravenous infusion at an area under the curve (AUC) of 6 mg/mL/min every 3 weeks.

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

Dosage and administration details:

Administered by intravenous infusion, either 80 mg/m² of body-surface area (BSA) on Days 1, 8, and 15 of each 21-day cycle (weekly dosing), or 175 mg/m² of BSA on Day 1 of each 21-day cycle (3-week dosing).

Number of subjects in period 1	Placebo + Carboplatin + Paclitaxel -> Placebo	Veliparib + Carboplatin + Paclitaxel -> Placebo	Veliparib + Carboplatin + Paclitaxel -> Veliparib
Started	375	383	382
Completed	0	0	0
Not completed	375	383	382
Death	224	227	199
Other, not specified	5	7	14
Missing due to site non-compliance	-	2	3
Lost to follow-up	8	15	13
Withdrew consent	21	22	31
Sponsor discontinued study	117	110	122

Baseline characteristics

Reporting groups

Reporting group title	Placebo + Carboplatin + Paclitaxel -> Placebo

Reporting group description:

Participants received placebo to veliparib orally twice a day in combination with carboplatin given at an area under the curve [AUC] of 6 mg per milliliter per minute (mg/mL/min), every 3 weeks, and paclitaxel 175 mg per square meter (mg/m²) of body-surface area (BSA), administered every 3 weeks, or 80 mg/m² administered weekly, for six 21-day cycles.

Participants who completed chemotherapy without disease progression received matching placebo twice daily for an additional thirty 21-day cycles of maintenance therapy.

Reporting group title	Veliparib + Carboplatin + Paclitaxel -> Placebo

Reporting group description:

Participants received 150 mg veliparib orally twice a day in combination with carboplatin given at an AUC of 6 mg/mL/min every 3 weeks, and paclitaxel 175 mg/m² of BSA administered every 3 weeks, or 80 mg/m² administered weekly, for six 21-day cycles.

Participants who completed chemotherapy without disease progression received matching placebo twice daily for an additional thirty 21-day cycles of maintenance therapy.

Reporting group title	Veliparib + Carboplatin + Paclitaxel -> Veliparib

Reporting group description:

Participants received 150 mg veliparib orally twice a day in combination with carboplatin given at an AUC of 6 mg/mL/min every 3 weeks, and paclitaxel 175 mg/m² of BSA administered every 3 weeks, or 80 mg/m² administered weekly, for six 21-day cycles.

Participants who completed chemotherapy without disease progression received single-agent veliparib at a dose of 300 mg twice daily for 2 weeks (transition period) and then 400 mg veliparib twice daily if the dose in the transition period was not associated with limiting side effects for an additional thirty 21-day cycles of maintenance therapy.

Reporting group values	Placebo + Carboplatin + Paclitaxel -> Placebo	Veliparib + Carboplatin + Paclitaxel -> Placebo	Veliparib + Carboplatin + Paclitaxel -> Veliparib
Number of subjects	375	383	382
Age categorical Units: Subjects			
< 65 years	233	226	228
≥ 65 years	142	157	154
Age continuous Units: years			
median	62.0	62.0	62.0
full range (min-max)	33.0 to 86.0	22.0 to 88.0	30.0 to 85.0
Gender categorical Units: Subjects			
Female	375	383	382
Male	0	0	0
Ethnicity Units: Subjects			
Hispanic or Latino	28	27	26
Not Hispanic or Latino	347	356	356
Unknown or Not Reported	0	0	0

Race/Ethnicity Units: Subjects			
White	299	297	300
Black or African American	10	13	20
Asian	59	69	56
American Indian or Alaska Native	1	1	1
Native Hawaiian or other Pacific Islander	1	0	2
Multi-race	3	0	0
Missing	2	3	3
Geographic Region Units: Subjects			
North America	266	261	267
Japan	23	30	25
Rest of World	86	92	90
BRCA-Deficient Status			
The BRCA-mutation cohort was defined as participants who had deleterious or suspected deleterious germline (gBRCA) or tissue-based (tBRCA) mutations as determined by the Myriad BRACAnalysis® companion diagnostic (CDx) or myChoice® HRD CDx assay, respectively, in BRCA1 or BRCA2.			
Units: Subjects			
Germline or tissue BRCA1/2 mutation	92	98	108
Germline or tissue BRCA1/2 wildtype	254	243	245
Missing	29	42	29
Homologous Recombination Deficiency (HRD) Status			
The HRD cohort consisted of participants who had tumors that were BRCA-mutated or had HRD according to the Myriad myChoice® assay, on which a score of ≥33 was considered to indicate HRD status, and a score of < 33 was considered to indicate non-HRD status.			
Units: Subjects			
HRD	207	206	214
Non-HRD	124	123	125
Missing	44	54	43
Stage of Disease			
Staging of primary ovarian carcinomas according to the International Federation of Gynecology and Obstetrics (FIGO) criteria, based on clinical examination, surgical exploration, histologic characteristics and cytologic testing. STAGE III: Tumor involves 1 or both ovaries with cytologically or histologically confirmed spread to the peritoneum outside the pelvis and/or metastases to the retroperitoneal lymph nodes. STAGE IV: Distant metastases excluding peritoneal metastases			
Units: Subjects			
Stage III	292	288	295
Stage IV	82	94	87
Missing	1	1	0
Type of Surgery Received			
Cytoreductive surgery could be performed before randomization and the initiation of study treatment (primary) or after 3 cycles of study treatment (interval), determined at the discretion of the investigator.			
Units: Subjects			
Primary	250	253	261

Interval	107	114	99
No surgery received	18	16	22
Residual Disease After Primary Surgery			
Data were collected after interval surgery after cycle 3.			
Units: Subjects			
No residual disease	116	118	124
Microscopic residual disease only	58	46	54
Any macroscopic residual disease	76	89	83
Did not undergo primary surgery	125	130	121
Residual Disease After Interval Surgery Units: Subjects			
No residual disease	50	46	45
Microscopic residual disease only	22	30	24
Any macroscopic residual disease	31	34	27
Missing	4	4	3
Did not undergo interval surgery	268	269	283
Paclitaxel Dosing Regimen Units: Subjects			
Weekly	193	203	190
Every 3 weeks	179	178	189
Missing	3	2	3
Germline BRCA Status Units: Subjects			
Germline BRCA1/2 mutation	63	71	80
Germline BRCA1/2 wildtype	305	305	298
Missing	7	7	4

Reporting group values	Total		
Number of subjects	1140		
Age categorical Units: Subjects			
< 65 years	687		
≥ 65 years	453		
Age continuous Units: years median full range (min-max)	- -		
Gender categorical Units: Subjects			
Female	1140		
Male	0		
Ethnicity Units: Subjects			
Hispanic or Latino	81		
Not Hispanic or Latino	1059		
Unknown or Not Reported	0		
Race/Ethnicity Units: Subjects			
White	896		
Black or African American	43		

Asian	184		
American Indian or Alaska Native	3		
Native Hawaiian or other Pacific Islander	3		
Multi-race	3		
Missing	8		
Geographic Region			
Units: Subjects			
North America	794		
Japan	78		
Rest of World	268		
BRCA-Deficient Status			
The BRCA-mutation cohort was defined as participants who had deleterious or suspected deleterious germline (gBRCA) or tissue-based (tBRCA) mutations as determined by the Myriad BRACAnalysis® companion diagnostic (CDx) or myChoice® HRD CDx assay, respectively, in BRCA1 or BRCA2.			
Units: Subjects			
Germline or tissue BRCA1/2 mutation	298		
Germline or tissue BRCA1/2 wildtype	742		
Missing	100		
Homologous Recombination Deficiency (HRD) Status			
The HRD cohort consisted of participants who had tumors that were BRCA-mutated or had HRD according to the Myriad myChoice® assay, on which a score of ≥33 was considered to indicate HRD status, and a score of < 33 was considered to indicate non-HRD status.			
Units: Subjects			
HRD	627		
Non-HRD	372		
Missing	141		
Stage of Disease			
Staging of primary ovarian carcinomas according to the International Federation of Gynecology and Obstetrics (FIGO) criteria, based on clinical examination, surgical exploration, histologic characteristics and cytologic testing. STAGE III: Tumor involves 1 or both ovaries with cytologically or histologically confirmed spread to the peritoneum outside the pelvis and/or metastases to the retroperitoneal lymph nodes. STAGE IV: Distant metastases excluding peritoneal metastases			
Units: Subjects			
Stage III	875		
Stage IV	263		
Missing	2		
Type of Surgery Received			
Cytoreductive surgery could be performed before randomization and the initiation of study treatment (primary) or after 3 cycles of study treatment (interval), determined at the discretion of the investigator.			
Units: Subjects			
Primary	764		
Interval	320		
No surgery received	56		
Residual Disease After Primary Surgery			
Data were collected after interval surgery after cycle 3.			

Units: Subjects			
No residual disease	358		
Microscopic residual disease only	158		
Any macroscopic residual disease	248		
Did not undergo primary surgery	376		
Residual Disease After Interval Surgery Units: Subjects			
No residual disease	141		
Microscopic residual disease only	76		
Any macroscopic residual disease	92		
Missing	11		
Did not undergo interval surgery	820		
Paclitaxel Dosing Regimen Units: Subjects			
Weekly	586		
Every 3 weeks	546		
Missing	8		
Germline BRCA Status Units: Subjects			
Germline BRCA1/2 mutation	214		
Germline BRCA1/2 wildtype	908		
Missing	18		

End points

End points reporting groups

Reporting group title	Placebo + Carboplatin + Paclitaxel -> Placebo

Reporting group description:

Participants received placebo to veliparib orally twice a day in combination with carboplatin given at an area under the curve [AUC] of 6 mg per milliliter per minute (mg/mL/min), every 3 weeks, and paclitaxel 175 mg per square meter (mg/m²) of body-surface area (BSA), administered every 3 weeks, or 80 mg/m² administered weekly, for six 21-day cycles.

Participants who completed chemotherapy without disease progression received matching placebo twice daily for an additional thirty 21-day cycles of maintenance therapy.

Reporting group title	Veliparib + Carboplatin + Paclitaxel -> Placebo

Reporting group description:

Participants received 150 mg veliparib orally twice a day in combination with carboplatin given at an AUC of 6 mg/mL/min every 3 weeks, and paclitaxel 175 mg/m² of BSA administered every 3 weeks, or 80 mg/m² administered weekly, for six 21-day cycles.

Participants who completed chemotherapy without disease progression received matching placebo twice daily for an additional thirty 21-day cycles of maintenance therapy.

Reporting group title	Veliparib + Carboplatin + Paclitaxel -> Veliparib

Reporting group description:

Participants received 150 mg veliparib orally twice a day in combination with carboplatin given at an AUC of 6 mg/mL/min every 3 weeks, and paclitaxel 175 mg/m² of BSA administered every 3 weeks, or 80 mg/m² administered weekly, for six 21-day cycles.

Participants who completed chemotherapy without disease progression received single-agent veliparib at a dose of 300 mg twice daily for 2 weeks (transition period) and then 400 mg veliparib twice daily if the dose in the transition period was not associated with limiting side effects for an additional thirty 21-day cycles of maintenance therapy.

Primary: Progression-Free Survival (PFS) in the BRCA-deficient Population (Arm 3 vs Arm 1)

End point title	Progression-Free Survival (PFS) in the BRCA-deficient Population (Arm 3 vs Arm 1)

End point description:

PFS: time from date subject was randomized to date subject experienced an event of disease progression, per Response Evaluation Criteria In Solid Tumors (RECIST) criteria v 1.1 (as determined by investigator) or to date of death if disease progression wasn’t reached. If subject didn’t have an event of disease progression/death prior to analysis cut-off date, their data were censored at date of last evaluable disease assessment. PFS was estimated using the Kaplan–Meier method, when protocol-specified number of PFS events was reached.

Progressive Disease (PD): At least a 20% increase in size of target lesions, compared with smallest size recorded since Tx began, and an absolute increase of ≥5 mm, or unequivocal progression of existing non-target lesions or the appearance of new lesions.

Analysis Population: subjects with either a gBRCA and/or tBRCA deleterious or suspected deleterious mutation in BRCA1 or BRCA2

99999 in table below = can't be estimated due to low no. of events

End point type	Primary

End point timeframe:

From randomization until the primary analysis data cut-off date of 03 May 2019, the median duration of follow-up was 28 months.

End point values	Placebo + Carboplatin + Paclitaxel -> Placebo	Veliparib + Carboplatin + Paclitaxel -> Placebo	Veliparib + Carboplatin + Paclitaxel -> Veliparib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	92	98	108	
Units: months				
median (confidence interval 95%)	22.0 (17.8 to 29.1)	21.1 (17.0 to 25.5)	34.7 (31.8 to 99999)	

Statistical analyses

Statistical analysis title	Arm 3 versus Arm 1

Statistical analysis description:

Analysis for Veliparib + Carboplatin + Paclitaxel -> Veliparib vs. Placebo + Carboplatin + Paclitaxel -> Placebo was stratified by residual disease status and disease stage. Multiplicity considerations included 3 treatment arms, (2 pairwise comparisons), 3 sequentially inclusive populations (BRCA-deficient population, HRD population, and ITT population), and multiple endpoints.

Comparison groups	Placebo + Carboplatin + Paclitaxel -> Placebo v Veliparib + Carboplatin + Paclitaxel -> Veliparib
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [1]
Method	Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.435
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.277
upper limit	0.683

Notes:

[1] - A fixed-sequence testing procedure was used to control the Type I error rate at 0.05 from the primary endpoints sequentially through the secondary endpoints. A 2-sided p-value of ≤0.05 was considered statistically significant.

Primary: Progression-Free Survival (PFS) in the Homologous Recombination Deficiency Cohort (Arm 3 vs Arm 1)

End point title	Progression-Free Survival (PFS) in the Homologous Recombination Deficiency Cohort (Arm 3 vs Arm 1)

End point description:

PFS: time from date subject was randomized to date subject experienced an event of disease progression, per Response Evaluation Criteria In Solid Tumors (RECIST) criteria v 1.1 (as determined by investigator) or to date of death if disease progression wasn't reached. If subject didn't have an event of disease progression/death prior to analysis cut-off date, their data were censored at date of last evaluable disease assessment. PFS was estimated using the Kaplan–Meier method, when protocol-specified number of PFS events was reached.

Progressive Disease (PD): At least a 20% increase in size of target lesions, compared with smallest size recorded since Tx began, and an absolute increase of ≥5 mm, or unequivocal progression of existing

non-target lesions or the appearance of new lesions.

Analysis Population: HRD cohort including those in the BRCA-mutation cohort and those with HRD tumors

End point type	Primary

End point timeframe:

From randomization until the primary analysis data cut-off date of 03 May 2019, the median duration of follow-up was 28 months.

End point values	Placebo + Carboplatin + Paclitaxel -> Placebo	Veliparib + Carboplatin + Paclitaxel -> Placebo	Veliparib + Carboplatin + Paclitaxel -> Veliparib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	207	206	214	
Units: months				
median (confidence interval 95%)	20.5 (17.8 to 22.8)	18.1 (16.4 to 22.7)	31.9 (25.8 to 38.0)	

Statistical analyses

Statistical analysis title	Arm 3 versus Arm 1

Statistical analysis description:

Analysis for Veliparib + Carboplatin + Paclitaxel -> Veliparib vs. Placebo + Carboplatin + Paclitaxel -> Placebo was stratified by residual disease status and disease stage. Multiplicity considerations included 3 treatment arms, (2 pairwise comparisons), 3 sequentially inclusive populations (BRCA-deficient population, HRD population, and ITT population), and multiple endpoints.

Comparison groups	Placebo + Carboplatin + Paclitaxel -> Placebo v Veliparib + Carboplatin + Paclitaxel -> Veliparib
Number of subjects included in analysis	421
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [2]
Method	Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.572
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.433
upper limit	0.756

Notes:

[2] - A fixed-sequence testing procedure was used to control the Type I error rate at 0.05 from the primary endpoints sequentially through the secondary endpoints. A 2-sided p-value of ≤0.05 was considered statistically significant.

Primary: Progression-Free Survival (PFS) in the Intention-to-treat Population (Arm 3 vs Arm 1)

End point title	Progression-Free Survival (PFS) in the Intention-to-treat Population (Arm 3 vs Arm 1)

End point description:

PFS: time from date subject was randomized to date subject experienced an event of disease progression, per Response Evaluation Criteria In Solid Tumors (RECIST) criteria v 1.1 (as determined by investigator) or to date of death if disease progression wasn't reached. If subject didn't have an event of disease progression/death prior to analysis cut-off date, their data were censored at date of last evaluable disease assessment. PFS was estimated using the Kaplan–Meier method, when protocol-specified number of PFS events was reached.

Progressive Disease (PD): At least a 20% increase in size of target lesions, compared with smallest size recorded since Tx began, and an absolute increase of ≥5 mm, or unequivocal progression of existing non-target lesions or the appearance of new lesions.

Analysis Population: ITT population (all randomized subjects)

End point type	Primary

End point timeframe:

From randomization until the primary analysis data cut-off date of 03 May 2019, the median duration of follow-up was 28 months.

End point values	Placebo + Carboplatin + Paclitaxel -> Placebo	Veliparib + Carboplatin + Paclitaxel -> Placebo	Veliparib + Carboplatin + Paclitaxel -> Veliparib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	375	383	382	
Units: months				
median (confidence interval 95%)	17.3 (15.1 to 19.1)	15.2 (14.1 to 17.3)	23.5 (19.3 to 26.3)	

Statistical analyses

Statistical analysis title	Arm 3 versus Arm 1

Statistical analysis description:

Analysis for Veliparib + Carboplatin + Paclitaxel -> Veliparib vs. Placebo + Carboplatin + Paclitaxel -> Placebo was stratified by residual disease status, disease stage, paclitaxel dosing regimen, and BRCA-mutation status. Multiplicity considerations included 3 treatment arms, (2 pairwise comparisons), 3 sequentially inclusive populations (BRCA-deficient population, HRD population, and ITT populations), and multiple endpoints.

Comparison groups	Veliparib + Carboplatin + Paclitaxel -> Veliparib v Placebo + Carboplatin + Paclitaxel -> Placebo
Number of subjects included in analysis	757
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [3]
Method	Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.683

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.562
upper limit	0.831

Notes:

[3] - A fixed-sequence testing procedure was used to control the Type I error rate at 0.05 from the primary endpoints sequentially through the secondary endpoints. A 2-sided p-value of ≤0.05 was considered statistically significant.

Secondary: Overall Survival (OS) in the BRCA-deficient Population

End point title	Overall Survival (OS) in the BRCA-deficient Population

End point description:

OS is defined as the time from the day the participant was randomized to the date of death, and was calculated using Kaplan-Meier methods. All events of death will be included, regardless of whether the event occurs while the participant is still taking study drug, or after discontinuation of study drug. If a participant has not died, then the data will be censored at the date the participant is last known to be alive.

Analysis population: BRCA-Deficient population: All randomized participants with germline and/or tissue deleterious/suspected deleterious BRCA1/2 mutation

-99999 and 99999 in the table below indicates could not be estimated due to the low number of events.

End point type	Secondary

End point timeframe:

From the time of randomization to the end of the study, up to 98 months

End point values	Placebo + Carboplatin + Paclitaxel -> Placebo	Veliparib + Carboplatin + Paclitaxel -> Placebo	Veliparib + Carboplatin + Paclitaxel -> Veliparib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	92	98	108	
Units: months				
median (confidence interval 95%)	89.5 (83.3 to 99999)	99999 (69.3 to 99999)	99999 (-99999 to 99999)	

Statistical analyses

Statistical analysis title	Arm 3 versus Arm 1

Statistical analysis description:

Analysis for Veliparib + Carboplatin + Paclitaxel -> Veliparib vs. Placebo + Carboplatin + Paclitaxel -> Placebo was stratified by residual disease status and disease stage. Multiplicity considerations included 3 treatment arms, (2 pairwise comparisons), 3 sequentially inclusive populations (BRCA-deficient population, HRD population, and ITT population), and multiple endpoints.

Comparison groups	Placebo + Carboplatin + Paclitaxel -> Placebo v Veliparib +

	Carboplatin + Paclitaxel -> Veliparib
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.328 [4]
Method	Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.567
upper limit	1.429

Notes:

[4] - A fixed-sequence testing procedure was used to control the Type I error rate at 0.05 from the primary endpoints sequentially through the secondary endpoints.

Statistical analysis title	Arm 2 versus Arm 1

Statistical analysis description:

Analysis for Veliparib + Carboplatin + Paclitaxel -> Placebo vs. Placebo + Carboplatin + Paclitaxel -> Placebo was stratified by residual disease status and disease stage. Multiplicity considerations included 3 treatment arms, (2 pairwise comparisons), 3 sequentially inclusive populations (BRCA-deficient population, HRD population, and ITT population), and multiple endpoints.

Comparison groups	Veliparib + Carboplatin + Paclitaxel -> Placebo v Placebo + Carboplatin + Paclitaxel -> Placebo
Number of subjects included in analysis	190
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.808 [5]
Method	Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.218
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.78
upper limit	1.903

Notes:

[5] - A fixed-sequence testing procedure was used to control the Type I error rate at 0.05 from the primary endpoints sequentially through the secondary endpoints.

Secondary: Overall Survival (OS) in the Homologous Recombination Deficiency Population

End point title	Overall Survival (OS) in the Homologous Recombination Deficiency Population

End point description:

OS is defined as the time from the day the participant was randomized to the date of death, and was calculated using Kaplan-Meier methods. All events of death will be included, regardless of whether the event occurs while the participant is still taking study drug, or after discontinuation of study drug. If a participant has not died, then the data will be censored at the date the participant is last known to be alive.

Analysis population: All randomized participants considered BRCA-Deficient and those determined to have HRD tumors based on HRD score

99999 in the table below indicates could not be estimated due to the low number of events.

End point type	Secondary

End point timeframe:

From the time of randomization to the end of the study, up to 98 months

End point values	Placebo + Carboplatin + Paclitaxel -> Placebo	Veliparib + Carboplatin + Paclitaxel -> Placebo	Veliparib + Carboplatin + Paclitaxel -> Veliparib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	207	206	214	
Units: months				
median (confidence interval 95%)	71.5 (59.6 to 87.6)	74.4 (65.4 to 99999)	99999 (73.8 to 99999)	

Statistical analyses

Statistical analysis title	Arm 3 versus Arm 1

Statistical analysis description:

Analysis for Veliparib + Carboplatin + Paclitaxel -> Veliparib vs. Placebo + Carboplatin + Paclitaxel -> Placebo was stratified by residual disease status and disease stage. Multiplicity considerations included 3 treatment arms, (2 pairwise comparisons), 3 sequentially inclusive populations (BRCA-deficient population, HRD population, and ITT population), and multiple endpoints.

Comparison groups	Placebo + Carboplatin + Paclitaxel -> Placebo v Veliparib + Carboplatin + Paclitaxel -> Veliparib
Number of subjects included in analysis	421
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.116 [6]
Method	Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.844
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	1.114

Notes:

[6] - A fixed-sequence testing procedure was used to control the Type I error rate at 0.05 from the primary endpoints sequentially through the secondary endpoints.

Statistical analysis title	Arm 2 versus Arm 1

Statistical analysis description:

Analysis for Veliparib + Carboplatin + Paclitaxel -> Placebo vs. Placebo + Carboplatin + Paclitaxel -> Placebo was stratified by residual disease status and disease stage. Multiplicity considerations included 3 treatment arms, (2 pairwise comparisons), 3 sequentially inclusive populations (BRCA-deficient population, HRD population, and ITT population), and multiple endpoints.

Comparison groups	Placebo + Carboplatin + Paclitaxel -> Placebo v Veliparib + Carboplatin + Paclitaxel -> Placebo
Number of subjects included in analysis	413
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.352 [7]
Method	Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.949
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.726
upper limit	1.242

Notes:

[7] - A fixed-sequence testing procedure was used to control the Type I error rate at 0.05 from the primary endpoints sequentially through the secondary endpoints.

Secondary: Overall Survival (OS) in the Whole Population

End point title	Overall Survival (OS) in the Whole Population

End point description:

OS is defined as the time from the day the participant was randomized to the date of death, and was calculated using Kaplan-Meier methods. All events of death will be included, regardless of whether the event occurs while the participant is still taking study drug, or after discontinuation of study drug. If a participant has not died, then the data will be censored at the date the participant is last known to be alive.

Analysis population: All randomized participants

End point type	Secondary

End point timeframe:

From the time of randomization to the end of the study, up to 98 months

End point values	Placebo + Carboplatin + Paclitaxel -> Placebo	Veliparib + Carboplatin + Paclitaxel -> Placebo	Veliparib + Carboplatin + Paclitaxel -> Veliparib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	375	383	382	
Units: months				
median (confidence interval 95%)	57.8 (52.3 to 63.8)	58.0 (50.6 to 64.1)	59.2 (52.1 to 68.2)	

Statistical analyses

Statistical analysis title	Arm 3 versus Arm 1

Statistical analysis description:

Analysis for Veliparib + Carboplatin + Paclitaxel -> Veliparib vs. Placebo + Carboplatin + Paclitaxel -> Placebo was stratified by residual disease status, disease stage, choice of paclitaxel dosing regimen, and BRCA-mutation status. Multiplicity considerations included 3 treatment arms, (2 pairwise comparisons),

3 sequentially inclusive populations (BRCA-deficient, HRD, and ITT populations), and multiple endpoints.

Comparison groups	Placebo + Carboplatin + Paclitaxel -> Placebo v Veliparib + Carboplatin + Paclitaxel -> Veliparib
Number of subjects included in analysis	757
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.283 [8]
Method	Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.946
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.782
upper limit	1.144

Notes:

[8] - A fixed-sequence testing procedure was used to control the Type I error rate at 0.05 from the primary efficacy endpoints sequentially through the secondary efficacy endpoints.

Statistical analysis title	Arm 2 versus Arm 1

Statistical analysis description:

Analysis for Veliparib + Carboplatin + Paclitaxel -> Placebo vs. Placebo + Carboplatin + Paclitaxel -> Placebo was stratified by residual disease status, disease stage, choice of paclitaxel dosing regimen, and BRCA-mutation status. Multiplicity considerations included 3 treatment arms, (2 pairwise comparisons), 3 sequentially inclusive populations (BRCA-deficient, HRD, and ITT populations), and multiple endpoints.

Comparison groups	Placebo + Carboplatin + Paclitaxel -> Placebo v Veliparib + Carboplatin + Paclitaxel -> Placebo
Number of subjects included in analysis	758
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.638 [9]
Method	Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.034
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.859
upper limit	1.244

Notes:

[9] - A fixed-sequence testing procedure was used to control the Type I error rate at 0.05 from the primary efficacy endpoints sequentially through the secondary efficacy endpoints.

Secondary: Change From Baseline in Disease Related Symptom (DRS) Score in the BRCA-mutation Population

End point title	Change From Baseline in Disease Related Symptom (DRS) Score in the BRCA-mutation Population

End point description:

The Disease Related Symptom score is a subset of the National Comprehensive Cancer Network Functional Assessment of Cancer Therapy Ovarian Symptom Index–18 (NFOSI-18), which evaluates nine symptoms related to ovarian cancer. The NFOSI-18 DRS score ranges from 0 to 36, with higher scores indicating a lower burden of symptoms and a score of 0 being severely symptomatic. A 3-point difference was defined as clinically meaningful. A positive change from Baseline indicates improvement.

Change from Baseline was calculated using a used a mixed-model for repeated measures (MMRM) with

treatment, stratification factors of residual disease and stage of disease, time point and treatment-by-time point interaction as fixed effect factors, and Baseline DRS score as a covariate.

DRS was not included in the fixed-sequence testing procedure.

Analysis population: BRCA-mutation population, participants with available data at each time point

End point type	Secondary

End point timeframe:

Baseline and Day 1 of Cycles 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, and 35

End point values	Placebo + Carboplatin + Paclitaxel -> Placebo	Veliparib + Carboplatin + Paclitaxel -> Placebo	Veliparib + Carboplatin + Paclitaxel -> Veliparib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	92	98	108	
Units: score on a scale				
least squares mean (standard error)				
Cycle 3 (n=87, 84, 92)	1.8 (± 0.52)	0.5 (± 0.53)	0.9 (± 0.51)	
Cycle 5 (n=81, 80, 84)	1.7 (± 0.57)	0.7 (± 0.58)	0.3 (± 0.56)	
Cycle 7 (n=78, 84, 83)	2.6 (± 0.55)	1.8 (± 0.54)	1.8 (± 0.54)	
Cycle 9 (n=79, 80, 80)	3.3 (± 0.60)	3.3 (± 0.60)	2.4 (± 0.59)	
Cycle 11 (n=73, 81, 82)	3.2 (± 0.56)	3.6 (± 0.55)	2.9 (± 0.54)	
Cycle 13 (n=74, 80, 70)	3.6 (± 0.57)	3.8 (± 0.57)	3.0 (± 0.57)	
Cycle 15 (n=69, 63, 69)	4.3 (± 0.53)	4.0 (± 0.54)	3.4 (± 0.52)	
Cycle 17 (n=64, 66, 70)	3.8 (± 0.56)	4.0 (± 0.57)	3.2 (± 0.55)	
Cycle 19 (n=58, 53, 66)	4.0 (± 0.62)	4.0 (± 0.63)	2.7 (± 0.59)	
Cycle 21 (n=55, 56, 72)	4.6 (± 0.59)	3.9 (± 0.59)	3.2 (± 0.55)	
Cycle 23 (n=48, 47, 59)	4.2 (± 0.55)	4.0 (± 0.56)	2.8 (± 0.52)	
Cycle 25 (n=48, 45, 58)	4.0 (± 0.58)	5.0 (± 0.60)	3.5 (± 0.55)	
Cycle 27 (n=41, 42, 53)	4.5 (± 0.56)	4.8 (± 0.56)	3.0 (± 0.52)	
Cycle 29 (n=41, 39, 60)	4.0 (± 0.66)	5.3 (± 0.66)	2.9 (± 0.59)	
Cycle 31 (n=36, 36, 51)	4.8 (± 0.57)	4.8 (± 0.58)	2.9 (± 0.52)	
Cycle 33 (n=38, 38, 58)	3.9 (± 0.66)	5.1 (± 0.67)	3.9 (± 0.59)	
Cycle 35 (n=37, 37, 52)	4.5 (± 0.61)	5.0 (± 0.62)	3.2 (± 0.56)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Disease Related Symptom (DRS) Score in the HRD Population

End point title	Change From Baseline in Disease Related Symptom (DRS) Score in the HRD Population

End point description:

The Disease Related Symptom score is a subset of the National Comprehensive Cancer Network Functional Assessment of Cancer Therapy Ovarian Symptom Index–18 (NFOSI-18), which evaluates nine symptoms related to ovarian cancer. The NFOSI-18 DRS score ranges from 0 to 36, with higher

scores indicating a lower burden of symptoms and a score of 0 being severely symptomatic. A 3-point difference was defined as clinically meaningful. A positive change from Baseline indicates improvement.

Change from Baseline was calculated using a used a mixed-model for repeated measures (MMRM) with treatment, stratification factors of residual disease and stage of disease, time point and treatment-by-time point interaction as fixed effect factors, and Baseline DRS score as a covariate.

DRS was not included in the fixed-sequence testing procedure.

Analysis population: HRD population, participants with available data at each time point

End point type	Secondary
End point timeframe:	
Baseline and Day 1 of Cycles 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, and 35	

End point values	Placebo + Carboplatin + Paclitaxel -> Placebo	Veliparib + Carboplatin + Paclitaxel -> Placebo	Veliparib + Carboplatin + Paclitaxel -> Veliparib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	207	206	214	
Units: score on a scale				
least squares mean (standard error)				
Cycle 3 (n=187, 179, 186)	1.5 (± 0.35)	0.5 (± 0.36)	0.9 (± 0.35)	
Cycle 5 (n=178, 169, 172)	1.7 (± 0.37)	1.1 (± 0.37)	0.8 (± 0.37)	
Cycle 7 (n=172, 168, 170)	2.4 (± 0.35)	1.8 (± 0.36)	2.2 (± 0.35)	
Cycle 9 (n=173, 165, 165)	3.3 (± 0.37)	3.6 (± 0.38)	2.3 (± 0.38)	
Cycle 11 (n=162, 161, 159)	3.5 (± 0.36)	3.5 (± 0.36)	2.7 (± 0.36)	
Cycle 13 (n=160, 159, 134)	3.6 (± 0.37)	3.8 (± 0.38)	2.7 (± 0.39)	
Cycle 15 (n=149, 138, 130)	4.2 (± 0.35)	3.9 (± 0.36)	3.3 (± 0.37)	
Cycle 17 (n=139, 129, 124)	3.9 (± 0.39)	3.4 (± 0.40)	3.0 (± 0.40)	
Cycle 19 (n=120, 107, 119)	4.2 (± 0.40)	3.7 (± 0.42)	2.7 (± 0.41)	
Cycle 21 (n=115, 110, 118)	4.6 (± 0.40)	3.6 (± 0.41)	3.0 (± 0.40)	
Cycle 23 (n=105, 95, 103)	4.1 (± 0.38)	3.6 (± 0.39)	3.1 (± 0.38)	
Cycle 25 (n=99, 86, 96)	4.1 (± 0.40)	4.4 (± 0.41)	3.5 (± 0.40)	
Cycle 27 (n=88, 81, 87)	4.4 (± 0.39)	4.4 (± 0.40)	3.0 (± 0.38)	
Cycle 29 (n=86, 76, 96)	4.2 (± 0.43)	4.7 (± 0.44)	3.2 (± 0.41)	
Cycle 31 (n=78, 73, 82)	3.9 (± 0.41)	4.3 (± 0.42)	3.3 (± 0.40)	
Cycle 33 (n=73, 74, 89)	4.2 (± 0.45)	4.7 (± 0.45)	3.9 (± 0.42)	
Cycle 35 (n=68, 69, 78)	4.1 (± 0.44)	4.6 (± 0.45)	3.4 (± 0.43)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Disease Related Symptom (DRS) Score in the Whole Population

End point title	Change From Baseline in Disease Related Symptom (DRS) Score in the Whole Population

End point description:

The Disease Related Symptom score is a subset of the National Comprehensive Cancer Network Functional Assessment of Cancer Therapy Ovarian Symptom Index–18 (NFOSI-18), which evaluates nine symptoms related to ovarian cancer. The NFOSI-18 DRS score ranges from 0 to 36, with higher scores indicating a lower burden of symptoms and a score of 0 being severely symptomatic. A 3-point difference was defined as clinically meaningful. A positive change from Baseline indicates improvement.

Change from Baseline was calculated using a used a mixed-model for repeated measures (MMRM) with treatment, stratification factors of residual disease, stage of disease, choice of paclitaxel dosing regimen and BRCA-deficient status, time point and treatment-by-time point interaction as fixed effect factors, and Baseline DRS score as a covariate.

DRS was not included in the fixed-sequence testing procedure.

Analysis population: All randomized participants with available data at each time point

End point type	Secondary

End point timeframe:

Baseline and Day 1 of Cycles 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, and 35

End point values	Placebo + Carboplatin + Paclitaxel -> Placebo	Veliparib + Carboplatin + Paclitaxel -> Placebo	Veliparib + Carboplatin + Paclitaxel -> Veliparib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	375	383	382	
Units: score on a scale				
least squares mean (standard error)				
Cycle 3 (n=333, 332, 320)	1.5 (± 0.28)	0.4 (± 0.28)	0.9 (± 0.28)	
Cycle 5 (n=310, 312, 301)	1.6 (± 0.29)	0.9 (± 0.29)	0.8 (± 0.29)	
Cycle 7 (n=300, 301, 287)	2.3 (± 0.29)	1.8 (± 0.29)	2.1 (± 0.29)	
Cycle 9 (n=291, 290, 277)	3.3 (± 0.29)	3.8 (± 0.29)	2.4 (± 0.29)	
Cycle 11 (n=270, 267, 249)	3.5 (± 0.29)	4.0 (± 0.28)	3.0 (± 0.29)	
Cycle 13 (n=254, 254, 225)	3.8 (± 0.30)	4.0 (± 0.30)	3.2 (± 0.30)	
Cycle 15 (n=224, 226, 207)	4.2 (± 0.30)	3.8 (± 0.30)	3.3 (± 0.30)	
Cycle 17 (n=204, 203, 202)	4.1 (± 0.32)	3.7 (± 0.32)	3.4 (± 0.32)	
Cycle 19 (n=177, 171, 178)	4.4 (± 0.32)	4.0 (± 0.32)	3.1 (± 0.32)	
Cycle 21 (n=170, 160, 174)	4.3 (± 0.34)	3.6 (± 0.34)	3.3 (± 0.33)	
Cycle 23 (n=151, 139, 154)	4.0 (± 0.33)	3.9 (± 0.33)	3.3 (± 0.32)	
Cycle 25 (n=145, 127, 145)	4.0 (± 0.34)	4.1 (± 0.35)	3.5 (± 0.33)	
Cycle 27 (n=129, 120, 130)	4.4 (± 0.33)	4.2 (± 0.34)	3.5 (± 0.32)	
Cycle 29 (n=123, 114, 136)	4.4 (± 0.34)	4.4 (± 0.35)	3.4 (± 0.33)	
Cycle 31 (n=112, 109, 120)	4.0 (± 0.36)	4.2 (± 0.37)	3.3 (± 0.35)	
Cycle 33 (n=106, 105, 123)	4.1 (± 0.38)	4.4 (± 0.38)	3.7 (± 0.36)	
Cycle 35 (n=99, 100, 111)	4.4 (± 0.37)	4.2 (± 0.37)	3.7 (± 0.35)	

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (PFS) in the BRCA-deficient Population (Arm 2 vs Arm 1)

End point title	Progression-Free Survival (PFS) in the BRCA-deficient Population (Arm 2 vs Arm 1)

End point description:

PFS: time from date subject was randomized to date subject experienced an event of disease progression, per Response Evaluation Criteria In Solid Tumors (RECIST) criteria v 1.1 (as determined by investigator) or to date of death if disease progression wasn't reached. If subject didn't have an event of disease progression/death prior to analysis cut-off date, their data were censored at date of last evaluable disease assessment. PFS was estimated using the Kaplan–Meier method, when protocol specified number of PFS events was reached.

Progressive Disease (PD): At least a 20% increase in size of target lesions, compared with smallest size recorded since Tx began, and an absolute increase of ≥5 mm, or unequivocal progression of existing non-target lesions or the appearance of new lesions.

Analysis Population: subjects with either a gBRCA and/or tBRCA deleterious or suspected deleterious mutation in BRCA1 or BRCA2

99999 in table below = can't be estimated due to low no. of events

End point type	Secondary

End point timeframe:

From randomization until the primary analysis data cut-off date of 03 May 2019, the median duration of follow-up was 28 months.

End point values	Placebo + Carboplatin + Paclitaxel -> Placebo	Veliparib + Carboplatin + Paclitaxel -> Placebo	Veliparib + Carboplatin + Paclitaxel -> Veliparib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	92	98	108	
Units: months				
median (confidence interval 95%)	22.0 (17.8 to 29.1)	21.1 (17.0 to 25.5)	34.7 (31.8 to 99999)	

Statistical analyses

Statistical analysis title	Arm 2 versus Arm 1

Statistical analysis description:

Analysis for Veliparib + Carboplatin + Paclitaxel -> Placebo vs. Placebo + Carboplatin + Paclitaxel -> Placebo was stratified by residual disease status and disease stage. Multiplicity considerations included 3 treatment arms, (2 pairwise comparisons), 3 sequentially inclusive populations (BRCA-deficient population, HRD population, and ITT population), and multiple endpoints.

Comparison groups	Placebo + Carboplatin + Paclitaxel -> Placebo v Veliparib + Carboplatin + Paclitaxel -> Placebo
Number of subjects included in analysis	190
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.335 [10]
Method	Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.215

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.821
upper limit	1.799

Notes:

[10] - A fixed-sequence testing procedure was used to control the Type I error rate at 0.05 from the primary endpoints sequentially through the secondary endpoints.

Secondary: Progression-Free Survival (PFS) in the Homologous Recombination Deficiency Cohort (Arm 2 vs Arm 1)

End point title	Progression-Free Survival (PFS) in the Homologous Recombination Deficiency Cohort (Arm 2 vs Arm 1)

End point description:

PFS: time from date subject was randomized to date subject experienced an event of disease progression, per Response Evaluation Criteria In Solid Tumors (RECIST) criteria v 1.1 (as determined by investigator) or to date of death if disease progression wasn't reached. If subject didn't have an event of disease progression/death prior to analysis cut-off date, their data were censored at date of last evaluable disease assessment. PFS was estimated using the Kaplan–Meier method, when protocol-specified number of PFS events was reached.

Progressive Disease (PD): At least a 20% increase in size of target lesions, compared with smallest size recorded since Tx began, and an absolute increase of ≥5 mm, or unequivocal progression of existing non-target lesions or the appearance of new lesions.

Analysis Population: HRD cohort including those in the BRCA-mutation cohort and those with HRD tumors

End point type	Secondary

End point timeframe:

From randomization until the primary analysis data cut-off date of 03 May 2019, the median duration of follow-up was 28 months.

End point values	Placebo + Carboplatin + Paclitaxel -> Placebo	Veliparib + Carboplatin + Paclitaxel -> Placebo	Veliparib + Carboplatin + Paclitaxel -> Veliparib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	207	206	214	
Units: months				
median (confidence interval 95%)	20.5 (17.8 to 22.8)	18.1 (16.4 to 22.7)	31.9 (25.8 to 38.0)	

Statistical analyses

Statistical analysis title	Arm 2 versus Arm 1

Statistical analysis description:

Analysis for Veliparib + Carboplatin + Paclitaxel -> Placebo vs. Placebo + Carboplatin + Paclitaxel -> Placebo was stratified by residual disease status and disease stage. Multiplicity considerations included 3 treatment arms, (2 pairwise comparisons), 3 sequentially inclusive populations (BRCA-deficient population, HRD population, and ITT population), and multiple endpoints.

Comparison groups	Placebo + Carboplatin + Paclitaxel -> Placebo v Veliparib +

	Carboplatin + Paclitaxel -> Placebo
Number of subjects included in analysis	413
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.462 [11]
Method	Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.855
upper limit	1.414

Notes:

[11] - A fixed-sequence testing procedure was used to control the Type I error rate at 0.05 from the primary endpoints sequentially through the secondary endpoints.

Secondary: Progression-Free Survival (PFS) in the Intention-to-treat Population (Arm 2 vs Arm 1)

End point title	Progression-Free Survival (PFS) in the Intention-to-treat Population (Arm 2 vs Arm 1)

End point description:

PFS: time from date subject was randomized to date subject experienced an event of disease progression, per Response Evaluation Criteria In Solid Tumors (RECIST) criteria v 1.1 (as determined by investigator) or to date of death if disease progression wasn't reached. If subject didn't have an event of disease progression/death prior to analysis cut-off date, their data were censored at date of last evaluable disease assessment. PFS was estimated using the Kaplan–Meier method, when protocol-specified number of PFS events was reached.

Progressive Disease (PD): At least a 20% increase in size of target lesions, compared with smallest size recorded since Tx began, and an absolute increase of ≥5 mm, or unequivocal progression of existing non-target lesions or the appearance of new lesions.

Analysis Population: ITT population (all randomized subjects)

End point type	Secondary

End point timeframe:

From randomization until the primary analysis data cut-off date of 03 May 2019, the median duration of follow-up was 28 months.

End point values	Placebo + Carboplatin + Paclitaxel -> Placebo	Veliparib + Carboplatin + Paclitaxel -> Placebo	Veliparib + Carboplatin + Paclitaxel -> Veliparib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	375	383	382	
Units: months				
median (confidence interval 95%)	17.3 (15.1 to 19.1)	15.2 (14.1 to 17.3)	23.5 (19.3 to 26.3)	

Statistical analyses

Statistical analysis title	Arm 2 versus Arm 1

Statistical analysis description:

Analysis for Veliparib + Carboplatin + Paclitaxel -> Placebo vs. Placebo + Carboplatin + Paclitaxel -> Placebo was stratified by residual disease status, disease stage, paclitaxel dosing regimen, and BRCA-mutation status. Multiplicity considerations included 3 treatment arms, (2 pairwise comparisons), 3 sequentially inclusive populations (BRCA-deficient population, HRD population, and ITT populations), and multiple endpoints.

Comparison groups	Placebo + Carboplatin + Paclitaxel -> Placebo v Veliparib + Carboplatin + Paclitaxel -> Placebo
Number of subjects included in analysis	758
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.45 [12]
Method	Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.073
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.895
upper limit	1.287

Notes:

[12] - A fixed-sequence testing procedure was used to control the Type I error rate at 0.05 from the primary endpoints sequentially through the secondary endpoints.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-cause mortality and adverse events were collected from the time informed consent was signed through the end of the study.

Adverse event reporting additional description:

Median time on follow-up was 81.7 months for the Placebo + Carboplatin + Paclitaxel -> Placebo group, 81.2 months for the Veliparib + Carboplatin + Paclitaxel -> Placebo group, and 81.1 months for the Veliparib + Carboplatin + Paclitaxel -> Veliparib group.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	Placebo + Carboplatin + Paclitaxel -> Placebo

Reporting group description:

Participants received placebo to veliparib orally twice a day in combination with carboplatin given at an area under the curve (AUC) of 6 milligrams per milliliter per minute (mg/mL/min) every 3 weeks, and paclitaxel 175 mg per square meter (mg/m²) of body-surface area (BSA), administered every 3 weeks, or 80 mg/m² administered weekly, for six 21-day cycles.

Participants who completed chemotherapy without disease progression received matching placebo twice daily for an additional thirty 21-day cycles of maintenance therapy.

Reporting group title	Veliparib + Carboplatin + Paclitaxel -> Veliparib

Reporting group description:

Participants received 150 mg veliparib orally twice a day in combination with carboplatin given at an AUC of 6 mg/mL/min every 3 weeks, and paclitaxel 175 mg/m² of BSA administered every 3 weeks, or 80 mg/m² administered weekly, for six 21-day cycles.

Participants who completed chemotherapy without disease progression received single-agent\ veliparib at a dose of 300 mg twice daily for 2 weeks (transition period) and then 400 mg veliparib twice daily if the dose in the transition period was not associated with limiting side effects for an additional thirty 21-day cycles of maintenance therapy.

Reporting group title	Veliparib + Carboplatin + Paclitaxel -> Placebo

Reporting group description:

Participants received 150 mg veliparib orally twice a day in combination with carboplatin given at an AUC of 6 mg/mL/min every 3 weeks, and paclitaxel 175 mg/m² of BSA administered every 3 weeks, or 80 mg/m² administered weekly, for six 21-day cycles.

Participants who completed chemotherapy without disease progression received matching placebo twice daily for an additional thirty 21-day cycles of maintenance therapy.

Serious adverse events	Placebo + Carboplatin + Paclitaxel -> Placebo	Veliparib + Carboplatin + Paclitaxel -> Veliparib	Veliparib + Carboplatin + Paclitaxel -> Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	143 / 375 (38.13%)	146 / 382 (38.22%)	130 / 383 (33.94%)
number of deaths (all causes)	228	209	234
number of deaths resulting from adverse events	6	11	9

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
ACUTE MYELOID LEUKAEMIA			
subjects affected / exposed	0 / 375 (0.00%)	2 / 382 (0.52%)	0 / 383 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
MALIGNANT NEOPLASM PROGRESSION			
subjects affected / exposed	14 / 375 (3.73%)	5 / 382 (1.31%)	11 / 383 (2.87%)
occurrences causally related to treatment / all	0 / 14	0 / 6	0 / 13
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 4
MALIGNANT PLEURAL EFFUSION			
subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	2 / 383 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
METASTASES TO CENTRAL NERVOUS SYSTEM			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MYELODYSPLASTIC SYNDROME			
subjects affected / exposed	0 / 375 (0.00%)	2 / 382 (0.52%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	2 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEOPLASM MALIGNANT			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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
OVARIAN CANCER			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Vascular disorders			
THROMBOPHLEBITIS			

subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VENOUS THROMBOSIS			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
SUBCLAVIAN VEIN THROMBOSIS			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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
DEEP VEIN THROMBOSIS			
subjects affected / exposed	2 / 375 (0.53%)	4 / 382 (1.05%)	2 / 383 (0.52%)
occurrences causally related to treatment / all	1 / 2	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EMBOLISM			
subjects affected / exposed	1 / 375 (0.27%)	1 / 382 (0.26%)	0 / 383 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERTENSION			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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
HYPOTENSION			
subjects affected / exposed	1 / 375 (0.27%)	1 / 382 (0.26%)	2 / 383 (0.52%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
JUGULAR VEIN THROMBOSIS			
subjects affected / exposed	2 / 375 (0.53%)	2 / 382 (0.52%)	0 / 383 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LYMPHOCELE			

subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PHLEBITIS			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
General disorders and administration site conditions			
CHEST PAIN			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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
ASTHENIA			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
CHEST DISCOMFORT			
subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
IMPLANT SITE EXTRAVASATION			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
INCARCERATED HERNIA			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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	1 / 375 (0.27%)	4 / 382 (1.05%)	0 / 383 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PAIN			

subjects affected / exposed	1 / 375 (0.27%)	1 / 382 (0.26%)	0 / 383 (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
PELVIC MASS			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
PYREXIA			
subjects affected / exposed	6 / 375 (1.60%)	9 / 382 (2.36%)	3 / 383 (0.78%)
occurrences causally related to treatment / all	0 / 6	2 / 9	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HERNIA			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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
CHILLS			
subjects affected / exposed	0 / 375 (0.00%)	2 / 382 (0.52%)	0 / 383 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DISEASE PROGRESSION			
subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
FATIGUE			
subjects affected / exposed	0 / 375 (0.00%)	2 / 382 (0.52%)	0 / 383 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GENERAL PHYSICAL HEALTH DETERIORATION			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Immune system disorders			
ANAPHYLACTIC REACTION			

subjects affected / exposed	1 / 375 (0.27%)	1 / 382 (0.26%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DRUG HYPERSENSITIVITY			
subjects affected / exposed	1 / 375 (0.27%)	2 / 382 (0.52%)	2 / 383 (0.52%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
FEMALE GENITAL TRACT FISTULA			
subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VAGINAL HAEMORRHAGE			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
Respiratory, thoracic and mediastinal disorders			
PNEUMONITIS ASPIRATION			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
PLEURAL EFFUSION			
subjects affected / exposed	4 / 375 (1.07%)	0 / 382 (0.00%)	7 / 383 (1.83%)
occurrences causally related to treatment / all	0 / 4	0 / 0	1 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMOPTYSIS			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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
DYSPNOEA EXERTIONAL			
subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

DYSPNOEA AT REST			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
DYSPNOEA			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	2 / 383 (0.52%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COUGH			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ACUTE RESPIRATORY FAILURE			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ACUTE RESPIRATORY DISTRESS SYNDROME			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
PNEUMOTHORAX SPONTANEOUS			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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
PNEUMOTHORAX			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	2 / 383 (0.52%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PULMONARY THROMBOSIS			

subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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
PULMONARY EMBOLISM			
subjects affected / exposed	10 / 375 (2.67%)	12 / 382 (3.14%)	10 / 383 (2.61%)
occurrences causally related to treatment / all	2 / 10	3 / 13	0 / 11
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
RESPIRATORY FAILURE			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
RESPIRATORY TRACT CONGESTION			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
Psychiatric disorders			
SUICIDE ATTEMPT			
subjects affected / exposed	1 / 375 (0.27%)	1 / 382 (0.26%)	0 / 383 (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
MENTAL STATUS CHANGES			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
DEPRESSION			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CONFUSIONAL STATE			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
Product issues			
DEVICE BREAKAGE			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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
DEVICE DISLOCATION			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
Investigations			
INTERNATIONAL NORMALISED RATIO INCREASED			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
SOLUBLE FIBRIN MONOMER COMPLEX INCREASED			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
Injury, poisoning and procedural complications			
ANASTOMOTIC LEAK			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ACETABULUM FRACTURE			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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
ANKLE FRACTURE			

subjects affected / exposed	2 / 375 (0.53%)	0 / 382 (0.00%)	0 / 383 (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
CONCUSSION			
subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FALL			
subjects affected / exposed	7 / 375 (1.87%)	0 / 382 (0.00%)	0 / 383 (0.00%)
occurrences causally related to treatment / all	1 / 7	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FEMUR FRACTURE			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FRACTURED SACRUM			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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
GASTROINTESTINAL STOMA COMPLICATION			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
POST PROCEDURAL HAEMORRHAGE			
subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INCISIONAL HERNIA			
subjects affected / exposed	1 / 375 (0.27%)	1 / 382 (0.26%)	0 / 383 (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
INTESTINAL ANASTOMOSIS COMPLICATION			

subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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
JOINT DISLOCATION			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
LUMBAR VERTEBRAL FRACTURE			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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
MULTIPLE INJURIES			
subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PELVIC FRACTURE			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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
HEAT ILLNESS			
subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PROCEDURAL COMPLICATION			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
SKELETAL INJURY			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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
SPINAL COMPRESSION FRACTURE			

subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
SPINAL FRACTURE			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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
THORACIC VERTEBRAL FRACTURE			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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
VAGINAL CUFF DEHISCENCE			
subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
WOUND COMPLICATION			
subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
WOUND DECOMPOSITION			
subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
WOUND DEHISCENCE			
subjects affected / exposed	1 / 375 (0.27%)	1 / 382 (0.26%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RIB FRACTURE			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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
Cardiac disorders			
ACUTE CORONARY SYNDROME			

subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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
ATRIAL FIBRILLATION			
subjects affected / exposed	3 / 375 (0.80%)	1 / 382 (0.26%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	1 / 3	1 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MYOCARDIAL INFARCTION			
subjects affected / exposed	1 / 375 (0.27%)	1 / 382 (0.26%)	0 / 383 (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
STRESS CARDIOMYOPATHY			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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
SUPRAVENTRICULAR TACHYCARDIA			
subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TACHYCARDIA			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
VENTRICULAR EXTRASYSTOLES			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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
PALPITATIONS			
subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	2 / 383 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
MIGRAINE			

subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
LOSS OF CONSCIOUSNESS			
subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TRANSIENT ISCHAEMIC ATTACK			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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
SYNCOPE			
subjects affected / exposed	6 / 375 (1.60%)	6 / 382 (1.57%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	2 / 6	0 / 6	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEURALGIA			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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
MIGRAINE WITH AURA			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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
CEREBELLAR INFARCTION			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
CEREBRAL ARTERY EMBOLISM			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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
CEREBRAL VENOUS SINUS THROMBOSIS			

subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
CEREBROVASCULAR ACCIDENT			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEADACHE			
subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERSOMNIA			
subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	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	4 / 375 (1.07%)	14 / 382 (3.66%)	13 / 383 (3.39%)
occurrences causally related to treatment / all	3 / 4	15 / 18	10 / 14
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
APLASTIC ANAEMIA			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
NEUTROPENIA			
subjects affected / exposed	6 / 375 (1.60%)	12 / 382 (3.14%)	16 / 383 (4.18%)
occurrences causally related to treatment / all	0 / 9	10 / 16	6 / 22
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FEBRILE NEUTROPENIA			
subjects affected / exposed	9 / 375 (2.40%)	15 / 382 (3.93%)	19 / 383 (4.96%)
occurrences causally related to treatment / all	2 / 10	9 / 17	9 / 20
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LEUKOPENIA			

subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BONE MARROW FAILURE			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
THROMBOCYTOPENIA			
subjects affected / exposed	3 / 375 (0.80%)	10 / 382 (2.62%)	9 / 383 (2.35%)
occurrences causally related to treatment / all	3 / 3	14 / 20	8 / 12
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
VISION BLURRED			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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
Gastrointestinal disorders			
ABDOMINAL ADHESIONS			
subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ABDOMINAL HERNIA			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ABDOMINAL INCARCERATED HERNIA			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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
ABDOMINAL PAIN			
subjects affected / exposed	5 / 375 (1.33%)	9 / 382 (2.36%)	9 / 383 (2.35%)
occurrences causally related to treatment / all	2 / 5	1 / 10	0 / 10
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENTEROCOLITIS			

subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ASCITES			
subjects affected / exposed	7 / 375 (1.87%)	2 / 382 (0.52%)	3 / 383 (0.78%)
occurrences causally related to treatment / all	1 / 9	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COLITIS			
subjects affected / exposed	1 / 375 (0.27%)	1 / 382 (0.26%)	3 / 383 (0.78%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COLITIS ULCERATIVE			
subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CONSTIPATION			
subjects affected / exposed	3 / 375 (0.80%)	2 / 382 (0.52%)	5 / 383 (1.31%)
occurrences causally related to treatment / all	0 / 3	0 / 2	1 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIARRHOEA			
subjects affected / exposed	3 / 375 (0.80%)	2 / 382 (0.52%)	4 / 383 (1.04%)
occurrences causally related to treatment / all	3 / 3	2 / 2	1 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIVERTICULAR PERFORATION			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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
ABDOMINAL PAIN UPPER			
subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EPIPLOIC APPENDAGITIS			

subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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
MECHANICAL ILEUS			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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
GASTRIC VOLVULUS			
subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMATEMESIS			
subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMOPERITONEUM			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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
HIATUS HERNIA			
subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ILEAL PERFORATION			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
ILEUS			
subjects affected / exposed	2 / 375 (0.53%)	3 / 382 (0.79%)	7 / 383 (1.83%)
occurrences causally related to treatment / all	0 / 2	0 / 4	1 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTESTINAL OBSTRUCTION			

subjects affected / exposed	2 / 375 (0.53%)	6 / 382 (1.57%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 4	0 / 7	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
INTESTINAL PERFORATION			
subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTESTINAL PSEUDO-OBSTRUCTION			
subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTRA-ABDOMINAL FLUID COLLECTION			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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
LARGE INTESTINAL OBSTRUCTION			
subjects affected / exposed	1 / 375 (0.27%)	1 / 382 (0.26%)	2 / 383 (0.52%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LARGE INTESTINE PERFORATION			
subjects affected / exposed	2 / 375 (0.53%)	0 / 382 (0.00%)	0 / 383 (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
GASTRIC ULCER			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
NAUSEA			
subjects affected / exposed	4 / 375 (1.07%)	13 / 382 (3.40%)	11 / 383 (2.87%)
occurrences causally related to treatment / all	2 / 5	14 / 16	7 / 11
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OESOPHAGITIS ULCERATIVE			

subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCREATITIS			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
PANCREATITIS ACUTE			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
PNEUMOPERITONEUM			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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	3 / 375 (0.80%)	0 / 382 (0.00%)	0 / 383 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SMALL INTESTINAL PERFORATION			
subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
SPIGELIAN HERNIA			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
UPPER GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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	5 / 375 (1.33%)	12 / 382 (3.14%)	10 / 383 (2.61%)
occurrences causally related to treatment / all	3 / 5	13 / 16	6 / 10
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SMALL INTESTINAL OBSTRUCTION			
subjects affected / exposed	19 / 375 (5.07%)	11 / 382 (2.88%)	13 / 383 (3.39%)
occurrences causally related to treatment / all	0 / 22	0 / 14	0 / 17
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Hepatobiliary disorders			
CHOLECYSTITIS			
subjects affected / exposed	1 / 375 (0.27%)	1 / 382 (0.26%)	0 / 383 (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
CHOLECYSTITIS ACUTE			
subjects affected / exposed	0 / 375 (0.00%)	2 / 382 (0.52%)	0 / 383 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BILE DUCT STONE			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
Skin and subcutaneous tissue disorders			
SKIN ULCER			
subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
NEPHROLITHIASIS			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
URETEROLITHIASIS			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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

HYDRONEPHROSIS			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
URINARY RETENTION			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
HAEMATURIA			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ACUTE KIDNEY INJURY			
subjects affected / exposed	2 / 375 (0.53%)	2 / 382 (0.52%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RENAL VEIN THROMBOSIS			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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
RENAL INFARCT			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
Endocrine disorders			
ADRENAL INSUFFICIENCY			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
HYPERTHYROIDISM			
subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue			

disorders			
FLANK PAIN			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
INTERVERTEBRAL DISC PROTRUSION			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
MUSCULAR WEAKNESS			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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
OSTEOARTHRITIS			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
Infections and infestations			
ABDOMINAL ABSCESS			
subjects affected / exposed	1 / 375 (0.27%)	1 / 382 (0.26%)	3 / 383 (0.78%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ATYPICAL MYCOBACTERIAL INFECTION			
subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BACTERAEMIA			
subjects affected / exposed	1 / 375 (0.27%)	1 / 382 (0.26%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BACTEROIDES BACTERAEMIA			

subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
BRONCHITIS			
subjects affected / exposed	1 / 375 (0.27%)	1 / 382 (0.26%)	0 / 383 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CATHETER SITE INFECTION			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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
CELLULITIS			
subjects affected / exposed	1 / 375 (0.27%)	1 / 382 (0.26%)	2 / 383 (0.52%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CLOSTRIDIUM DIFFICILE COLITIS			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CLOSTRIDIUM DIFFICILE INFECTION			
subjects affected / exposed	3 / 375 (0.80%)	1 / 382 (0.26%)	2 / 383 (0.52%)
occurrences causally related to treatment / all	1 / 4	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COLONIC ABSCESS			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
DIVERTICULITIS			

subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EMPYEMA			
subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENDOCARDITIS			
subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENTEROBACTER INFECTION			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
ENTEROCOCCAL BACTERAEMIA			
subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
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 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ERYSIPELAS			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
ESCHERICHIA INFECTION			
subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
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	0 / 375 (0.00%)	3 / 382 (0.79%)	3 / 383 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROENTERITIS			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
GASTROENTERITIS VIRAL			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
GROIN ABSCESS			
subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
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 ZOSTER			
subjects affected / exposed	2 / 375 (0.53%)	0 / 382 (0.00%)	0 / 383 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
IMPLANT SITE INFECTION			
subjects affected / exposed	2 / 375 (0.53%)	0 / 382 (0.00%)	0 / 383 (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
INFECTED LYMPHOCELE			
subjects affected / exposed	0 / 375 (0.00%)	2 / 382 (0.52%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ESCHERICHIA URINARY TRACT INFECTION			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
INTERVERTEBRAL DISCITIS			

subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
KIDNEY INFECTION			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LARGE INTESTINE INFECTION			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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
LYMPHANGITIS			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MENINGITIS CRYPTOCOCCAL			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
PELVIC INFECTION			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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
NASOPHARYNGITIS			
subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUTROPENIC SEPSIS			

subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OPHTHALMIC HERPES ZOSTER			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OSTEOMYELITIS			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OTITIS MEDIA			
subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PELVIC ABSCESS			
subjects affected / exposed	1 / 375 (0.27%)	1 / 382 (0.26%)	2 / 383 (0.52%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NAIL INFECTION			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
SEPSIS			
subjects affected / exposed	7 / 375 (1.87%)	5 / 382 (1.31%)	3 / 383 (0.78%)
occurrences causally related to treatment / all	0 / 7	0 / 6	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
SEPTIC EMBOLUS			
subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERIORBITAL CELLULITIS			

subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERITONEAL ABSCESS			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERITONITIS			
subjects affected / exposed	2 / 375 (0.53%)	0 / 382 (0.00%)	0 / 383 (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
PHARYNGITIS STREPTOCOCCAL			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
PNEUMONIA			
subjects affected / exposed	6 / 375 (1.60%)	4 / 382 (1.05%)	5 / 383 (1.31%)
occurrences causally related to treatment / all	1 / 7	0 / 5	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA ASPIRATION			
subjects affected / exposed	2 / 375 (0.53%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
POST PROCEDURAL INFECTION			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
POSTOPERATIVE ABSCESS			

subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
POSTOPERATIVE WOUND INFECTION			
subjects affected / exposed	1 / 375 (0.27%)	1 / 382 (0.26%)	2 / 383 (0.52%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYELONEPHRITIS ACUTE			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
PHLEBITIS INFECTIVE			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
SEPTIC SHOCK			
subjects affected / exposed	5 / 375 (1.33%)	4 / 382 (1.05%)	3 / 383 (0.78%)
occurrences causally related to treatment / all	0 / 6	0 / 5	1 / 3
deaths causally related to treatment / all	0 / 3	0 / 2	1 / 1
SPONTANEOUS BACTERIAL PERITONITIS			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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
STAPHYLOCOCCAL INFECTION			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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
STAPHYLOCOCCAL SEPSIS			
subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUBCUTANEOUS ABSCESS			

subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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
SUBDIAPHRAGMATIC ABSCESS			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 375 (0.00%)	2 / 382 (0.52%)	2 / 383 (0.52%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY TRACT INFECTION			
subjects affected / exposed	4 / 375 (1.07%)	7 / 382 (1.83%)	6 / 383 (1.57%)
occurrences causally related to treatment / all	0 / 5	0 / 7	1 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UROSEPSIS			
subjects affected / exposed	1 / 375 (0.27%)	1 / 382 (0.26%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VIRAL INFECTION			
subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
WOUND INFECTION			
subjects affected / exposed	2 / 375 (0.53%)	0 / 382 (0.00%)	3 / 383 (0.78%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SYSTEMIC CANDIDA			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	0 / 383 (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
DEVICE RELATED INFECTION			

subjects affected / exposed	2 / 375 (0.53%)	0 / 382 (0.00%)	0 / 383 (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
Metabolism and nutrition disorders			
DIABETES MELLITUS			
subjects affected / exposed	0 / 375 (0.00%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DECREASED APPETITE			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
DEHYDRATION			
subjects affected / exposed	6 / 375 (1.60%)	6 / 382 (1.57%)	0 / 383 (0.00%)
occurrences causally related to treatment / all	1 / 6	2 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERKALAEMIA			
subjects affected / exposed	1 / 375 (0.27%)	0 / 382 (0.00%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOALBUMINAEMIA			
subjects affected / exposed	1 / 375 (0.27%)	1 / 382 (0.26%)	0 / 383 (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
HYPOCALCAEMIA			
subjects affected / exposed	0 / 375 (0.00%)	1 / 382 (0.26%)	0 / 383 (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
HYPOKALAEMIA			
subjects affected / exposed	0 / 375 (0.00%)	3 / 382 (0.79%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	0 / 0	0 / 3	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPONATRAEMIA			

subjects affected / exposed	2 / 375 (0.53%)	6 / 382 (1.57%)	1 / 383 (0.26%)
occurrences causally related to treatment / all	1 / 2	4 / 7	0 / 1
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	Placebo + Carboplatin + Paclitaxel -> Placebo	Veliparib + Carboplatin + Paclitaxel -> Veliparib	Veliparib + Carboplatin + Paclitaxel -> Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	369 / 375 (98.40%)	376 / 382 (98.43%)	375 / 383 (97.91%)
Vascular disorders			
HOT FLUSH			
subjects affected / exposed	49 / 375 (13.07%)	43 / 382 (11.26%)	44 / 383 (11.49%)
occurrences (all)	53	50	48
HYPERTENSION			
subjects affected / exposed	38 / 375 (10.13%)	32 / 382 (8.38%)	38 / 383 (9.92%)
occurrences (all)	66	60	60
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	28 / 375 (7.47%)	41 / 382 (10.73%)	36 / 383 (9.40%)
occurrences (all)	58	64	56
FATIGUE			
subjects affected / exposed	221 / 375 (58.93%)	257 / 382 (67.28%)	235 / 383 (61.36%)
occurrences (all)	353	456	407
MALAISE			
subjects affected / exposed	21 / 375 (5.60%)	31 / 382 (8.12%)	22 / 383 (5.74%)
occurrences (all)	34	37	31
MUCOSAL INFLAMMATION			
subjects affected / exposed	19 / 375 (5.07%)	18 / 382 (4.71%)	16 / 383 (4.18%)
occurrences (all)	21	21	18
OEDEMA PERIPHERAL			
subjects affected / exposed	73 / 375 (19.47%)	56 / 382 (14.66%)	58 / 383 (15.14%)
occurrences (all)	84	77	62
PAIN			

subjects affected / exposed	22 / 375 (5.87%)	21 / 382 (5.50%)	22 / 383 (5.74%)
occurrences (all)	25	23	31
PYREXIA			
subjects affected / exposed	25 / 375 (6.67%)	23 / 382 (6.02%)	33 / 383 (8.62%)
occurrences (all)	28	30	38
Immune system disorders			
DRUG HYPERSENSITIVITY			
subjects affected / exposed	63 / 375 (16.80%)	51 / 382 (13.35%)	48 / 383 (12.53%)
occurrences (all)	84	56	63
Respiratory, thoracic and mediastinal disorders			
OROPHARYNGEAL PAIN			
subjects affected / exposed	39 / 375 (10.40%)	27 / 382 (7.07%)	24 / 383 (6.27%)
occurrences (all)	46	33	27
NASAL CONGESTION			
subjects affected / exposed	26 / 375 (6.93%)	18 / 382 (4.71%)	6 / 383 (1.57%)
occurrences (all)	29	22	6
COUGH			
subjects affected / exposed	58 / 375 (15.47%)	59 / 382 (15.45%)	57 / 383 (14.88%)
occurrences (all)	70	70	63
DYSPNOEA			
subjects affected / exposed	76 / 375 (20.27%)	84 / 382 (21.99%)	91 / 383 (23.76%)
occurrences (all)	106	111	112
EPISTAXIS			
subjects affected / exposed	59 / 375 (15.73%)	56 / 382 (14.66%)	61 / 383 (15.93%)
occurrences (all)	70	61	66
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	58 / 375 (15.47%)	59 / 382 (15.45%)	61 / 383 (15.93%)
occurrences (all)	72	70	74
DEPRESSION			
subjects affected / exposed	39 / 375 (10.40%)	34 / 382 (8.90%)	46 / 383 (12.01%)
occurrences (all)	46	43	58
INSOMNIA			
subjects affected / exposed	89 / 375 (23.73%)	109 / 382 (28.53%)	120 / 383 (31.33%)
occurrences (all)	105	134	141
Investigations			

ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	41 / 375 (10.93%)	40 / 382 (10.47%)	31 / 383 (8.09%)
occurrences (all)	64	52	55
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	31 / 375 (8.27%)	31 / 382 (8.12%)	22 / 383 (5.74%)
occurrences (all)	46	35	41
BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	19 / 375 (5.07%)	16 / 382 (4.19%)	10 / 383 (2.61%)
occurrences (all)	26	21	13
WEIGHT DECREASED			
subjects affected / exposed	32 / 375 (8.53%)	54 / 382 (14.14%)	41 / 383 (10.70%)
occurrences (all)	45	71	52
WEIGHT INCREASED			
subjects affected / exposed	35 / 375 (9.33%)	36 / 382 (9.42%)	26 / 383 (6.79%)
occurrences (all)	49	52	34
Injury, poisoning and procedural complications			
CONTUSION			
subjects affected / exposed	13 / 375 (3.47%)	20 / 382 (5.24%)	17 / 383 (4.44%)
occurrences (all)	13	28	21
FALL			
subjects affected / exposed	19 / 375 (5.07%)	18 / 382 (4.71%)	15 / 383 (3.92%)
occurrences (all)	20	23	16
PROCEDURAL PAIN			
subjects affected / exposed	37 / 375 (9.87%)	25 / 382 (6.54%)	18 / 383 (4.70%)
occurrences (all)	46	25	19
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	90 / 375 (24.00%)	100 / 382 (26.18%)	83 / 383 (21.67%)
occurrences (all)	121	126	105
DYSGEUSIA			
subjects affected / exposed	57 / 375 (15.20%)	73 / 382 (19.11%)	47 / 383 (12.27%)
occurrences (all)	70	80	54
HEADACHE			

subjects affected / exposed	97 / 375 (25.87%)	98 / 382 (25.65%)	90 / 383 (23.50%)
occurrences (all)	136	143	124
PERIPHERAL SENSORY NEUROPATHY			
subjects affected / exposed	256 / 375 (68.27%)	242 / 382 (63.35%)	235 / 383 (61.36%)
occurrences (all)	415	373	346
TREMOR			
subjects affected / exposed	9 / 375 (2.40%)	23 / 382 (6.02%)	6 / 383 (1.57%)
occurrences (all)	11	26	6
Blood and lymphatic system disorders			
NEUTROPENIA			
subjects affected / exposed	247 / 375 (65.87%)	273 / 382 (71.47%)	266 / 383 (69.45%)
occurrences (all)	673	848	881
LYMPHOPENIA			
subjects affected / exposed	15 / 375 (4.00%)	26 / 382 (6.81%)	15 / 383 (3.92%)
occurrences (all)	28	57	20
LEUKOPENIA			
subjects affected / exposed	89 / 375 (23.73%)	114 / 382 (29.84%)	87 / 383 (22.72%)
occurrences (all)	223	333	261
ANAEMIA			
subjects affected / exposed	191 / 375 (50.93%)	226 / 382 (59.16%)	232 / 383 (60.57%)
occurrences (all)	514	672	603
THROMBOCYTOPENIA			
subjects affected / exposed	119 / 375 (31.73%)	209 / 382 (54.71%)	216 / 383 (56.40%)
occurrences (all)	266	735	630
Eye disorders			
VISION BLURRED			
subjects affected / exposed	32 / 375 (8.53%)	27 / 382 (7.07%)	19 / 383 (4.96%)
occurrences (all)	33	27	22
Gastrointestinal disorders			
DYSPEPSIA			
subjects affected / exposed	41 / 375 (10.93%)	36 / 382 (9.42%)	45 / 383 (11.75%)
occurrences (all)	53	42	55
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	22 / 375 (5.87%)	34 / 382 (8.90%)	28 / 383 (7.31%)
occurrences (all)	23	46	30
NAUSEA			

subjects affected / exposed	246 / 375 (65.60%)	289 / 382 (75.65%)	259 / 383 (67.62%)
occurrences (all)	425	578	433
STOMATITIS			
subjects affected / exposed	52 / 375 (13.87%)	59 / 382 (15.45%)	47 / 383 (12.27%)
occurrences (all)	67	67	52
VOMITING			
subjects affected / exposed	128 / 375 (34.13%)	174 / 382 (45.55%)	123 / 383 (32.11%)
occurrences (all)	211	309	170
DIARRHOEA			
subjects affected / exposed	149 / 375 (39.73%)	164 / 382 (42.93%)	137 / 383 (35.77%)
occurrences (all)	248	255	228
CONSTIPATION			
subjects affected / exposed	157 / 375 (41.87%)	165 / 382 (43.19%)	177 / 383 (46.21%)
occurrences (all)	203	228	241
ABDOMINAL PAIN UPPER			
subjects affected / exposed	29 / 375 (7.73%)	29 / 382 (7.59%)	18 / 383 (4.70%)
occurrences (all)	38	37	24
ABDOMINAL PAIN			
subjects affected / exposed	114 / 375 (30.40%)	118 / 382 (30.89%)	105 / 383 (27.42%)
occurrences (all)	163	162	143
ABDOMINAL DISTENSION			
subjects affected / exposed	45 / 375 (12.00%)	34 / 382 (8.90%)	48 / 383 (12.53%)
occurrences (all)	55	39	54
DRY MOUTH			
subjects affected / exposed	19 / 375 (5.07%)	22 / 382 (5.76%)	10 / 383 (2.61%)
occurrences (all)	20	23	12
Skin and subcutaneous tissue disorders			
NAIL DISCOLOURATION			
subjects affected / exposed	21 / 375 (5.60%)	9 / 382 (2.36%)	10 / 383 (2.61%)
occurrences (all)	21	9	10
ALOPECIA			
subjects affected / exposed	214 / 375 (57.07%)	197 / 382 (51.57%)	216 / 383 (56.40%)
occurrences (all)	271	256	271
RASH MACULO-PAPULAR			
subjects affected / exposed	30 / 375 (8.00%)	22 / 382 (5.76%)	11 / 383 (2.87%)
occurrences (all)	35	31	15

RASH			
subjects affected / exposed	56 / 375 (14.93%)	48 / 382 (12.57%)	54 / 383 (14.10%)
occurrences (all)	68	53	64
PRURITUS			
subjects affected / exposed	40 / 375 (10.67%)	28 / 382 (7.33%)	35 / 383 (9.14%)
occurrences (all)	49	33	41
Renal and urinary disorders			
DYSURIA			
subjects affected / exposed	22 / 375 (5.87%)	16 / 382 (4.19%)	17 / 383 (4.44%)
occurrences (all)	24	17	18
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	136 / 375 (36.27%)	114 / 382 (29.84%)	112 / 383 (29.24%)
occurrences (all)	217	166	152
BACK PAIN			
subjects affected / exposed	66 / 375 (17.60%)	67 / 382 (17.54%)	66 / 383 (17.23%)
occurrences (all)	87	88	75
BONE PAIN			
subjects affected / exposed	27 / 375 (7.20%)	33 / 382 (8.64%)	25 / 383 (6.53%)
occurrences (all)	46	37	36
MUSCULAR WEAKNESS			
subjects affected / exposed	23 / 375 (6.13%)	23 / 382 (6.02%)	24 / 383 (6.27%)
occurrences (all)	28	33	34
MYALGIA			
subjects affected / exposed	75 / 375 (20.00%)	71 / 382 (18.59%)	59 / 383 (15.40%)
occurrences (all)	106	96	80
PAIN IN EXTREMITY			
subjects affected / exposed	55 / 375 (14.67%)	51 / 382 (13.35%)	46 / 383 (12.01%)
occurrences (all)	70	64	56
Infections and infestations			
NASOPHARYNGITIS			
subjects affected / exposed	21 / 375 (5.60%)	26 / 382 (6.81%)	19 / 383 (4.96%)
occurrences (all)	26	32	22
SINUSITIS			
subjects affected / exposed	18 / 375 (4.80%)	21 / 382 (5.50%)	18 / 383 (4.70%)
occurrences (all)	27	22	20

UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	43 / 375 (11.47%)	34 / 382 (8.90%)	28 / 383 (7.31%)
occurrences (all)	52	44	36
URINARY TRACT INFECTION			
subjects affected / exposed	67 / 375 (17.87%)	70 / 382 (18.32%)	64 / 383 (16.71%)
occurrences (all)	104	91	91
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	85 / 375 (22.67%)	110 / 382 (28.80%)	82 / 383 (21.41%)
occurrences (all)	101	143	106
DEHYDRATION			
subjects affected / exposed	20 / 375 (5.33%)	30 / 382 (7.85%)	32 / 383 (8.36%)
occurrences (all)	21	37	48
HYPERGLYCAEMIA			
subjects affected / exposed	18 / 375 (4.80%)	27 / 382 (7.07%)	18 / 383 (4.70%)
occurrences (all)	35	50	26
HYPOALBUMINAEMIA			
subjects affected / exposed	19 / 375 (5.07%)	16 / 382 (4.19%)	12 / 383 (3.13%)
occurrences (all)	31	31	17
HYPOKALAEMIA			
subjects affected / exposed	69 / 375 (18.40%)	59 / 382 (15.45%)	68 / 383 (17.75%)
occurrences (all)	107	94	113
HYPOMAGNESAEMIA			
subjects affected / exposed	98 / 375 (26.13%)	85 / 382 (22.25%)	96 / 383 (25.07%)
occurrences (all)	199	143	142
HYPONATRAEMIA			
subjects affected / exposed	25 / 375 (6.67%)	25 / 382 (6.54%)	21 / 383 (5.48%)
occurrences (all)	33	35	24
HYPOPHOSPHATAEMIA			
subjects affected / exposed	21 / 375 (5.60%)	11 / 382 (2.88%)	14 / 383 (3.66%)
occurrences (all)	31	14	18

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 May 2016	Amendment 1 Modified the starting dose of maintenance therapy of veliparib/placebo to 300 mg BID and established process for site-level unblinding after disease progression.
21 September 2016	Amendment 2 Adjusted stratification factors to include gBRCA mutation status (positive vs. negative or Unknown) as per IDMC recommendation.
14 November 2016	Amendment 3 Clarified the use of growth factors and modified the neutrophil and PLT count threshold for starting cycles in maintenance phase.
24 March 2017	Amendment 4 Clarified dose modification guidance and provided guidance for starting and stopping veliparib/placebo for surgical procedures and management of subjects with IV contrast allergies.
10 December 2018	Amendment 5 Expanded planned analyses to investigate whether the addition of veliparib in combination with chemotherapy and in maintenance would improve outcomes in the HRD population.
24 April 2019	Amendment 6 Provided estimated number of events needed in treatment Arm 1 and Arm 3 to trigger the primary analyses of PFS in the BRCA-deficient, HRD, and whole populations.
01 May 2020	Amendment 7 Added benefits and risks evaluation information and updated study procedures in the context of the ongoing COVID-19 pandemic.
08 March 2021	Amendment 8 A final OS analyses occurred when required OS events accrued in all populations. Benefits and risks evaluation information added in the context of the ongoing COVID-19 pandemic.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported