Clinical trial results:
A Phase II Open-Label, Randomised, Comparative, International Multicentre Study to Compare the Safety and Efficacy of Two Different Doses of AZD2281 Given Orally Twice Daily Versus Intravenous Liposomal Doxorubicin Given Monthly in Patients With Advanced BRCA1- or BRCA2-Associated Ovarian Cancer Who Have Failed Previous Platinum-Based Chemotherapy

Summary

EudraCT number	2007-007622-22
Trial protocol	GB SE BE DE ES
Global end of trial date	30 April 2010

Results information

Result version number	v1 (current)
This version publication date	05 October 2019
First version publication date	05 October 2019

Trial information

Trial identification

Sponsor protocol code	D0810C00012

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	AstraZeneca
Sponsor organisation address	151 85, Sodertalje, Sweden,
Public contact	Paula del Rosario, AstraZeneca, +44 7884 735492, ClinicalTrialTransparency@astrazeneca.com
Scientific contact	Paula del Rosario, AstraZeneca, +44 7884 735492, ClinicalTrialTransparency@astrazeneca.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	13 December 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 April 2010
Global end of trial reached?	Yes
Global end of trial date	30 April 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the efficacy of 2 different dose levels of olaparib with liposomal doxorubicin in patients with advanced BRCA1- or BRCA2- associated ovarian cancer. This was assessed by the following:

Primary variable
• Progression-free survival (PFS)

Secondary variables
• Objective response rate (complete response (CR) and partial response (PR)) at various timepoints and overall
• Overall duration of response
• Tumour size
• CA-125 levels
• Overall survival

Protection of trial subjects:

The Patient Informed Consent Document will incorporate wording that complies with relevant data protection and privacy legislation. Pursuant to this wording, patients will authorise the collection, use and disclosure of their study data by the Investigator and by those persons who need that information for the purposes of the study.

The Sponsor reserves the right to stop the study at any time on the basis of new information regarding safety or efficacy, or if study progress is unsatisfactory, or for other valid administrative reasons. After such a decision is made, the Investigator must inform all screened patients within 1 week.

If any pregnancy occurs in the course of the study, then investigators or other site personnel must inform appropriate AstraZeneca representatives immediately but no later than the end of the next business day of when he or she becomes aware of it. The designated AstraZeneca representative works with the investigator to ensure that all relevant information is provided to the appropriate AstraZeneca Patient Safety data entry site within 30 calendar days.

Any crossover patients must be followed for full safety assessments for 57 days.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 July 2008
Long term follow-up planned	Yes
Long term follow-up rationale	Regulatory reason, Safety
Long term follow-up duration	1 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 6
Country: Number of subjects enrolled	Belgium: 4
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Israel: 24
Country: Number of subjects enrolled	Poland: 14
Country: Number of subjects enrolled	Spain: 2
Country: Number of subjects enrolled	Sweden: 2
Country: Number of subjects enrolled	United Kingdom: 18
Country: Number of subjects enrolled	United States: 26
Worldwide total number of subjects	97
EEA total number of subjects	41

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)	84
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

First patient enrolled on 30 July 2008 and last patient on 3 March 2009 at 25 centres in 9 countries

Pre-assignment

Screening details:

97 of 125 screened women with advanced BRCA 1/2 ovarian cancer who had chemotherapy were randomized

Period 1

Period 1 title	Randomised part
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Olaparib 200 mg bd

Arm description:

Olaparib (AZD2281) 200 mg oral capsules twice daily

Arm type	Experimental
Investigational medicinal product name	AZD2281
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

200 mg bd orally

Arm title	Olaparib 400 mg bd

Arm description:

Olaparib (AZD2281) 400 mg oral capsules twice daily

Arm type	Experimental
Investigational medicinal product name	AZD2281
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

400 mg bd orally

Arm title	Liposomal doxorubicin

Arm description:

Liposomal doxorubicin 50 mg/m2 intravenously every 4 weeks

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

Dosage and administration details:
50 mg/m2 i.v.

Number of subjects in period 1	Olaparib 200 mg bd	Olaparib 400 mg bd	Liposomal doxorubicin
Started	32	32	33
Completed	32	32	32
Not completed	0	0	1
Consent withdrawn by subject	-	-	1

Period 2

Period 2 title	Ongoing Initial Study Treatment at DCO
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Olaparib 200 mg bd

Arm description:
Olaparib (AZD2281) 200 mg oral capsules twice daily

Arm type	Experimental
Investigational medicinal product name	AZD2281
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:
200 mg bd orally

Arm title	Olaparib 400 mg bd

Arm description:
Olaparib (AZD2281) 400 mg oral capsules twice daily

Arm type	Experimental
Investigational medicinal product name	AZD2281
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:
400 mg bd orally

Arm title	Liposomal doxorubicin

Arm description:

Liposomal doxorubicin 50 mg/m2 iv every 4 weeks

Arm type	Experimental
Investigational medicinal product name	Doxil
Investigational medicinal product code	
Other name	Caelyx
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

50 mg/m2 i.v.

Number of subjects in period 2	Olaparib 200 mg bd	Olaparib 400 mg bd	Liposomal doxorubicin
Started	32	32	32
Discontinued initial study treatment	22	20	25
Completed	10	12	7
Not completed	22	20	25
Consent withdrawn by subject	1	2	1
Adverse event, non-fatal	1	2	3
Condition under investigation worsened	19	15	13
Unknown	1	-	2
Other reason	-	1	6

Baseline characteristics

Reporting groups	
Reporting group title	Olaparib 200 mg bd
Reporting group description:	
Olaparib (AZD2281) 200 mg oral capsules twice daily	
Reporting group title	Olaparib 400 mg bd
Reporting group description:	
Olaparib (AZD2281) 400 mg oral capsules twice daily	
Reporting group title	Liposomal doxorubicin
Reporting group description:	
Liposomal doxorubicin 50 mg/m2 intravenously every 4 weeks	

Reporting group values	Olaparib 200 mg bd	Olaparib 400 mg bd	Liposomal doxorubicin
Number of subjects	32	32	33
Age categorical Units: Subjects			
Adults (<50 years)	7	10	12
From >=50 to <65 years	20	18	17
65 years and over	5	4	4
Age Continuous Units: Years			
arithmetic mean	57.2	53.8	54.3
standard deviation	± 8.53	± 8.77	± 9.32
Sex: Female, Male Units: Subjects			
Female	32	32	33
Male	0	0	0
BRCA status Units: Subjects			
Deleterious BRCA1 mutation	26	28	27
Deleterious BRCA2 mutation	6	4	6
Race/Ethnicity, Customized			
Race/Ethnicity (Jewish ethnicity)			
Units: Subjects			
African-Caribbean	0	0	1
Ashkenazi Jewish	8	10	11
Sephardic Jewish	0	0	2
Not applicable	20	21	19
Other	4	1	0

Reporting group values	Total		
Number of subjects	97		
Age categorical Units: Subjects			
Adults (<50 years)	29		
From >=50 to <65 years	55		
65 years and over	13		

Age Continuous Units: Years arithmetic mean standard deviation	- 		
Sex: Female, Male Units: Subjects			
Female Male	97 0		
BRCA status Units: Subjects			
Deleterious BRCA1 mutation Deleterious BRCA2 mutation	81 16		
Race/Ethnicity, Customized			
Race/Ethnicity (Jewish ethnicity)			
Units: Subjects			
African-Caribbean Ashkenazi Jewish Sephardic Jewish Not applicable Other	1 29 2 60 5		

Subject analysis sets

Subject analysis set title	Full analysis set
Subject analysis set type	Full analysis

Subject analysis set description:
All randomised patients

Reporting group values	Full analysis set		
Number of subjects	97		
Age categorical Units: Subjects			
Adults (<50 years) From >=50 to <65 years 65 years and over	29 55 13		
Age Continuous Units: Years arithmetic mean standard deviation	 55.1 ± 8.92		
Sex: Female, Male Units: Subjects			
Female Male	97 0		
BRCA status Units: Subjects			
Deleterious BRCA1 mutation Deleterious BRCA2 mutation	81 16		
Race/Ethnicity, Customized			
Race/Ethnicity (Jewish ethnicity)			
Units: Subjects			
African-Caribbean	1		

Ashkenazi Jewish	29		
Sephardic Jewish	2		
Not applicable	60		
Other	5		

End points

End points reporting groups

Reporting group title	Olaparib 200 mg bd
Reporting group description:	
Olaparib (AZD2281) 200 mg oral capsules twice daily	
Reporting group title	Olaparib 400 mg bd
Reporting group description:	
Olaparib (AZD2281) 400 mg oral capsules twice daily	
Reporting group title	Liposomal doxorubicin
Reporting group description:	
Liposomal doxorubicin 50 mg/m2 intravenously every 4 weeks	
Reporting group title	Olaparib 200 mg bd
Reporting group description:	
Olaparib (AZD2281) 200 mg oral capsules twice daily	
Reporting group title	Olaparib 400 mg bd
Reporting group description:	
Olaparib (AZD2281) 400 mg oral capsules twice daily	
Reporting group title	Liposomal doxorubicin
Reporting group description:	
Liposomal doxorubicin 50 mg/m2 iv every 4 weeks	
Subject analysis set title	Full analysis set
Subject analysis set type	Full analysis
Subject analysis set description:	
All randomised patients	

Primary: Progression free survival (PFS)

End point title	Progression free survival (PFS)
End point description:	
PFS was defined as the time to progression from the date of randomisation until the date of radiological assessment of progression per RECIST criteria or death (by any cause in the absence of progression)	
End point type	Primary
End point timeframe:	
Tumour assessment was to be assessed at screening, every 8 weeks during the study and at the withdrawal visit, up to 56 weeks. (Data cut-off for primary analysis of PFS: 15 September 2009)	

End point values	Olaparib 200 mg bd	Olaparib 400 mg bd	Liposomal doxorubicin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	32	32	33	
Units: Number of patients that progressed				
number (not applicable)				
Number of patients that progressed	19	20	20	
Percentage of patients that progressed	59.4	62.5	60.6	
Median PFS	6.5	8.8	7.1	
Lower 95% Limit for Median PFS	5.5	5.4	3.7	
Upper 95% Limit for Median PFS	10.1	9.2	10.7	

Statistical analyses

Statistical analysis title	Analysis of progression free survival

Statistical analysis description:

Analysis of olaparib 200 or 400 mg bd (n=64) versus liposomal doxorubicin (n=33). A hazard ratio < 1 favours olaparib.

Comparison groups	Olaparib 200 mg bd v Olaparib 400 mg bd v Liposomal doxorubicin
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.6604 [1]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.51
upper limit	1.56

Notes:

[1] - If the observed p-value for the combined olaparib groups is <0.025 (1-sided) then the result will be regarded as statistically significant.

Statistical analysis title	Analysis of progression free survival

Statistical analysis description:

Analysis of olaparib 200 (n=32) versus liposomal doxorubicin (n=33). A hazard ratio < 1 favours olaparib.

Comparison groups	Olaparib 200 mg bd v Liposomal doxorubicin
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.7794 [2]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.48
upper limit	1.74

Notes:

[2] - An observed p-value of <0.005 (1-sided) will be regarded as statistically significant for a given pairwise comparison.

Statistical analysis title	Analysis of progression-free survival

Statistical analysis description:

Analysis of olaparib 400 (n=32) versus liposomal doxorubicin (n=33). A hazard ratio < 1 favours olaparib.

Comparison groups	Olaparib 400 mg bd v Liposomal doxorubicin
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.6604 [3]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.45
upper limit	1.62

Notes:

[3] - An observed p-value of <0.005 (1-sided) will be regarded as statistically significant for a given pairwise comparison.

Secondary: Objective response rate (ORR)

End point title	Objective response rate (ORR)

End point description:

ORR was defined according to RECIST. Complete response (CR) or partial response - (PR)- 30% decrease Patients with a best RECIST response of CR or PR had to have a confirmed response at least 28 days later.

End point type	Secondary

End point timeframe:

At the time that 57 PFS events had occurred (Data cut-off for primary analysis of PFS: 15 September 2009)

End point values	Olaparib 200 mg bd	Olaparib 400 mg bd	Liposomal doxorubicin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	32	32	33	
Units: Number of responders				
number (not applicable)				
Complete response	0	0	0	
Number of Partial responders	8	10	6	
% of Partial responders	25.0	31.3	18.2	

Statistical analyses

Statistical analysis title	Analysis of objective response rate

Statistical analysis description:

Analysis of olaparib 200 or 400 (n=64) versus liposomal doxorubicin (n=33).

Comparison groups	Olaparib 200 mg bd v Olaparib 400 mg bd v Liposomal doxorubicin

Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1291 [4]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	7.32

Notes:

[4] - 2-sided p-value

Statistical analysis title	Analysis of objective response rate
Statistical analysis description:	
Analysis of olaparib 200 (n=32) versus liposomal doxorubicin (n=33).	
Comparison groups	Olaparib 200 mg bd v Liposomal doxorubicin
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3131 [5]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	7.01

Notes:

[5] - 2-sided p-value

Statistical analysis title	Analysis of objective response rate
Statistical analysis description:	
Analysis of olaparib 400 (n=32) versus liposomal doxorubicin (n=33).	
Comparison groups	Olaparib 400 mg bd v Liposomal doxorubicin
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1079
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	9.76

Secondary: Disease control rate

End point title	Disease control rate

End point description:

The number of patients with confirmed CR (disappearance of all target lesions) or PR (30% decrease in the sum of the longest diameter of target lesions) or SD (small changes) >4 months, divided by the number of randomised patients

End point type	Secondary

End point timeframe:

At the time that 57 PFS events had occurred (Data cut-off for primary analysis of PFS: 15 September 2009)

End point values	Olaparib 200 mg bd	Olaparib 400 mg bd	Liposomal doxorubicin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	32	32	33	
Units: Number (%) of responders				
number (not applicable)				
Number of Participants	21	21	19	
% Participants	65.6	65.6	57.6	

Statistical analyses

No statistical analyses for this end point

Secondary: Overall duration of response

End point title	Overall duration of response

End point description:

The duration of response was defined as time (months) from initial assessment of PR/CR until earliest date of objective progression or death. (Values may be underestimated as some patients had not progressed at final analysis so true duration is likely to be greater than that in database.)

End point type	Secondary

End point timeframe:

At the time that 57 PFS events had occurred (Data cut-off for primary analysis of PFS: 15 September 2009)

End point values	Olaparib 200 mg bd	Olaparib 400 mg bd	Liposomal doxorubicin	Full analysis set
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	8[6]	10	6	18
Units: Months				
median (confidence interval 95%)	5.95 (3.71 to 999999999)	6.80 (5.52 to 7.39)	5.49 (4.67 to 9.13)	6.24 (5.52 to 7.39)

Notes:

[6] - The upper limit for the 95% CI for median was not reached.

Statistical analyses

No statistical analyses for this end point

Secondary: Best percentage change in tumour size

End point title	Best percentage change in tumour size

End point description:

The percentage change (reduction) from baseline in the sum of the lengths of the longest diameter (LD) of the RECIST target lesions were objectively documented, regardless of whether the patient was still taking study medication

End point type	Secondary

End point timeframe:

At the time that 57 PFS events had occurred (Data cut-off for primary analysis of PFS: 15 September 2009)

End point values	Olaparib 200 mg bd	Olaparib 400 mg bd	Liposomal doxorubicin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	32	32	33	
Units: Percent change				
median (full range (min-max))	-15.90 (-75.30 to 31.48)	-24.60 (-100.00 to 51.10)	-14.3 (-87.5 to 32.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Best percentage change from baseline in CA-125 levels

End point title	Best percentage change from baseline in CA-125 levels

End point description:

Best percentage change in cancer antigen 125 (CA-125) levels

End point type	Secondary

End point timeframe:

At the time that 57 PFS events had occurred (Data cut-off for primary analysis of PFS: 15 September 2009)

End point values	Olaparib 200 mg bd	Olaparib 400 mg bd	Liposomal doxorubicin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	30	31	33	
Units: Percent change				
median (full range (min-max))	-37.42 (-98.77 to 327.76)	-71.19 (-96.88 to 70.56)	-55.8 (-99.5 to 192.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Confirmed RECIST response and/or CA-125 response

End point title	Confirmed RECIST response and/or CA-125 response

End point description:

The percentage of patients reporting a RECIST confirmed response and/or a CA-125 response (in the absence of progression). A CA-125 response was defined as a confirmed greater or equal to 50% reduction in CA-125.

End point type	Secondary

End point timeframe:

At the time that 57 PFS events had occurred (Data cut-off for primary analysis of PFS: 15 September 2009)

End point values	Olaparib 200 mg bd	Olaparib 400 mg bd	Liposomal doxorubicin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	32	32	33	
Units: Percentage of participants				
number (not applicable)	37.5	59.4	39.4	

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival (OS)

End point title	Overall survival (OS)

End point description:

OS was defined as time from randomisation to date of death from any cause. Patients who had not died at time of analysis were censored at last date they were known to be alive. Median OS was not calculable for olaparib groups due to an insufficient number of deaths so the percentage of participants who died are shown along with 95% confidence intervals

End point type	Secondary

End point timeframe:

At the time of the cut-off for the final analysis of overall survival (30 April 2010)

End point values	Olaparib 200 mg bd	Olaparib 400 mg bd	Liposomal doxorubicin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	32	32	33	
Units: Number of deaths				
number (not applicable)				
Number of deaths	9	11	13	
% of deaths	28.1	34.4	39.4	

Statistical analyses

Statistical analysis title	Analysis of overall survival
Statistical analysis description:	
Analysis of olaparib 200 or 400 (n=64) versus liposomal doxorubicin (n=33).	
Comparison groups	Olaparib 200 mg bd v Olaparib 400 mg bd v Liposomal doxorubicin
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.5781 [7]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.41
upper limit	1.7

Notes:

[7] - 2-sided p-value

Statistical analysis title	Analysis of overall survival
Statistical analysis description:	
Analysis of olaparib 200 (n=32) versus liposomal doxorubicin (n=33).	
Comparison groups	Olaparib 200 mg bd v Liposomal doxorubicin
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3417 [8]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.66

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.27
upper limit	1.55

Notes:

[8] - 2-sided p-value

Statistical analysis title	Analysis of overall survival

Statistical analysis description:

Analysis of olaparib 400 (n=32) versus liposomal doxorubicin (n=33).

Comparison groups	Olaparib 400 mg bd v Liposomal doxorubicin
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9877 [9]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.44
upper limit	2.27

Notes:

[9] - 2-sided p-value

Secondary: Best quality of life (QoL) response for Trial Outcome Index (TOI)

End point title	Best quality of life (QoL) response for Trial Outcome Index (TOI)

End point description:

Best HRQoL response using the TOI endpoint. Improvement was defined as a change from baseline of greater than or equal to +7. The TOI score ranges from 0-100.

End point type	Secondary

End point timeframe:

At the time that 57 PFS events had occurred (Data cut-off for primary analysis of PFS: 15 September 2009)

End point values	Olaparib 200 mg bd	Olaparib 400 mg bd	Liposomal doxorubicin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	25	29	27	
Units: Number of patients				
number (not applicable)				
Number Improved	7	5	3	
% Improved	21.9	15.6	9.1	
Number No change	10	10	11	
% No change	31.3	31.3	33.3	
Number Worsened	3	7	6	

% Worsened	9.4	21.9	18.2	
Number Non-evaluable	5	7	7	
% Non-evaluable	15.6	21.9	21.2	

Statistical analyses

No statistical analyses for this end point

Secondary: Best QoL response for total Functional Analysis of Cancer Therapy - Ovarian (FACT-O)

End point title	Best QoL response for total Functional Analysis of Cancer Therapy - Ovarian (FACT-O)

End point description:

Best HRQoL response using the total FACT-O endpoint. Improvement was defined as a change from baseline of greater than or equal to +9.

End point type	Secondary

End point timeframe:

At the time that 57 PFS events had occurred (Data cut-off for primary analysis of PFS: 15 September 2009)

End point values	Olaparib 200 mg bd	Olaparib 400 mg bd	Liposomal doxorubicin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	25	29	27	
Units: Number of patients				
number (not applicable)				
Number Improved	3	6	1	
% Improved	9.4	18.8	3.0	
Number No Change	14	11	11	
% No Change	43.8	34.4	33.3	
Number Worsened	3	5	7	
% Worsened	9.4	15.6	21.2	
Number Non-evaluable	5	7	8	
% Non-evaluable	15.6	21.9	24.2	

Statistical analyses

No statistical analyses for this end point

Secondary: Best QoL response for FACT-O symptom index (FOSI)

End point title	Best QoL response for FACT-O symptom index (FOSI)

End point description:

Best HRQoL response using the FOSI endpoint. Improvement was defined as a change from baseline of greater than or equal to +3.

End point type	Secondary

End point timeframe:

At the time that 57 PFS events had occurred (Data cut-off for primary analysis of PFS: 15 September 2009)

End point values	Olaparib 200 mg bd	Olaparib 400 mg bd	Liposomal doxorubicin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	25	29	27	
Units: Number of patients				
number (not applicable)				
Number Improved	5	4	3	
% Improved	15.6	12.5	9.1	
Number No change	14	9	10	
% No change	43.8	28.1	30.3	
Number Worsened	1	9	7	
% Worsened	3.1	28.1	21.2	
Number Non-evaluable	5	7	7	
% Non-evaluable	15.6	21.9	21.2	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: AEs with onset between first dose and last dose+30 days or AEs for ongoing patients at PFS DCO	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	13.0

Reporting groups	
Reporting group title	Olaparib 200 mg bd
Reporting group description: -	
Reporting group title	Liposomal Doxorubicin
Reporting group description: -	
Reporting group title	Olaparib 400 mg bd
Reporting group description: -	

Serious adverse events	Olaparib 200 mg bd	Liposomal Doxorubicin	Olaparib 400 mg bd
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 32 (15.63%)	5 / 32 (15.63%)	6 / 32 (18.75%)
number of deaths (all causes)	9	13	11
number of deaths resulting from adverse events	2	0	0
Investigations			
HAEMOGLOBIN DECREASED			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
MYELODYSPLASTIC SYNDROME			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Vascular disorders			
DEEP VEIN THROMBOSIS			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (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
Nervous system disorders			

CEREBROVASCULAR ACCIDENT			
subjects affected / exposed	2 / 32 (6.25%)	0 / 32 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
SYNCOPE			
subjects affected / exposed	1 / 32 (3.13%)	1 / 32 (3.13%)	0 / 32 (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
General disorders and administration site conditions			
FATIGUE			
subjects affected / exposed	1 / 32 (3.13%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYREXIA			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
ABDOMINAL PAIN LOWER			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (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
CONSTIPATION			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 32 (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
INTESTINAL OBSTRUCTION			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NAUSEA			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (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

SMALL INTESTINAL OBSTRUCTION			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUBILEUS			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VOMITING			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (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			
DYSPNOEA			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (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
Hepatobiliary disorders			
CHOLELITHIASIS			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
INTERVERTEBRAL DISC DEGENERATION			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
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 CHEST PAIN			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 32 (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
Infections and infestations			
BACTERAEMIA			

subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Olaparib 200 mg bd	Liposomal Doxorubicin	Olaparib 400 mg bd
Total subjects affected by non-serious adverse events			
subjects affected / exposed	32 / 32 (100.00%)	31 / 32 (96.88%)	32 / 32 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
CANCER PAIN			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
LIP NEOPLASM BENIGN			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
PARANEOPLASTIC DERMATOMYOSITIS			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
FLUSHING			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
HOT FLUSH			
subjects affected / exposed	4 / 32 (12.50%)	1 / 32 (3.13%)	1 / 32 (3.13%)
occurrences (all)	5	1	1
HYPERTENSION			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	7 / 32 (21.88%)
occurrences (all)	0	2	7
HYPOTENSION			
subjects affected / exposed	2 / 32 (6.25%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	2	1	0
LYMPHOEDEMA			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1

THROMBOPHLEBITIS			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	2
THROMBOSIS			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
VASCULITIS			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
VENA CAVA THROMBOSIS			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
VENOUS THROMBOSIS			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	1 / 32 (3.13%)
occurrences (all)	0	1	1
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	6 / 32 (18.75%)	4 / 32 (12.50%)	11 / 32 (34.38%)
occurrences (all)	8	4	20
CATHETER SITE HAEMATOMA			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
CATHETER SITE PAIN			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
CHEST DISCOMFORT			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
CHEST PAIN			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
CHILLS			
subjects affected / exposed	0 / 32 (0.00%)	3 / 32 (9.38%)	1 / 32 (3.13%)
occurrences (all)	0	3	1
DISCOMFORT			

subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
FATIGUE			
subjects affected / exposed	12 / 32 (37.50%)	14 / 32 (43.75%)	21 / 32 (65.63%)
occurrences (all)	16	20	29
LOCAL SWELLING			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
MUCOSAL INFLAMMATION			
subjects affected / exposed	0 / 32 (0.00%)	7 / 32 (21.88%)	0 / 32 (0.00%)
occurrences (all)	0	12	0
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
OEDEMA PERIPHERAL			
subjects affected / exposed	2 / 32 (6.25%)	2 / 32 (6.25%)	3 / 32 (9.38%)
occurrences (all)	2	2	3
PAIN			
subjects affected / exposed	0 / 32 (0.00%)	2 / 32 (6.25%)	1 / 32 (3.13%)
occurrences (all)	0	2	2
PYREXIA			
subjects affected / exposed	1 / 32 (3.13%)	4 / 32 (12.50%)	4 / 32 (12.50%)
occurrences (all)	1	4	4
SUPRAPUBIC PAIN			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
Immune system disorders			
CONTRAST MEDIA ALLERGY			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	1	0	1
DRUG HYPERSENSITIVITY			
subjects affected / exposed	0 / 32 (0.00%)	2 / 32 (6.25%)	0 / 32 (0.00%)
occurrences (all)	0	2	0
HYPERSENSITIVITY			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0

Reproductive system and breast disorders			
ATROPHIC VULVOVAGINITIS			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
BREAST PAIN			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
PELVIC PAIN			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
VAGINAL DISCHARGE			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
VAGINAL HAEMORRHAGE			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
VAGINAL LESION			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
VULVAL ULCERATION			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
VULVOVAGINAL DRYNESS			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
VULVOVAGINAL PRURITUS			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	6 / 32 (18.75%)	5 / 32 (15.63%)	6 / 32 (18.75%)
occurrences (all)	8	6	6
DYSPHONIA			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
DYSPNOEA			

subjects affected / exposed	2 / 32 (6.25%)	4 / 32 (12.50%)	2 / 32 (6.25%)
occurrences (all)	2	10	2
DYSPNOEA EXERTIONAL			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	2
NASAL CONGESTION			
subjects affected / exposed	1 / 32 (3.13%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	1	1	0
NASAL DRYNESS			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
NASAL MUCOSAL DISORDER			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
NASAL ULCER			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
OROPHARYNGEAL PAIN			
subjects affected / exposed	4 / 32 (12.50%)	2 / 32 (6.25%)	1 / 32 (3.13%)
occurrences (all)	4	2	1
PLEURITIC PAIN			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	2	0
PRODUCTIVE COUGH			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	2
RHINITIS ALLERGIC			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
RHINORRHOEA			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
SPUTUM DISCOLOURED			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
THROAT IRRITATION			

subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	2	0	1
WHEEZING			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	1 / 32 (3.13%)
occurrences (all)	0	1	1
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	2 / 32 (6.25%)	2 / 32 (6.25%)	1 / 32 (3.13%)
occurrences (all)	2	2	2
DEPRESSED MOOD			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
DEPRESSION			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	1	0	1
INSOMNIA			
subjects affected / exposed	3 / 32 (9.38%)	2 / 32 (6.25%)	4 / 32 (12.50%)
occurrences (all)	5	3	4
STRESS			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
BLOOD CREATININE INCREASED			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	2
BLOOD MAGNESIUM DECREASED			
subjects affected / exposed	1 / 32 (3.13%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	1	1	0
BODY TEMPERATURE INCREASED			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	3 / 32 (9.38%)
occurrences (all)	2	0	4
ELECTROCARDIOGRAM QT PROLONGED			

subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
HAEMOGLOBIN DECREASED			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	2
INTERNATIONAL NORMALISED RATIO INCREASED			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
OCCULT BLOOD POSITIVE			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
WEIGHT DECREASED			
subjects affected / exposed	2 / 32 (6.25%)	2 / 32 (6.25%)	2 / 32 (6.25%)
occurrences (all)	2	2	2
Injury, poisoning and procedural complications			
CONTRAST MEDIA REACTION			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
CONTUSION			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
INCISIONAL HERNIA			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
JOINT INJURY			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
JOINT SPRAIN			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
MUSCLE STRAIN			

subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
PROCEDURAL PAIN			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
WOUND			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
CARDIAC DISORDER			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
LEFT VENTRICULAR HYPERTROPHY			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
PALPITATIONS			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	2 / 32 (6.25%)
occurrences (all)	0	1	2
TACHYCARDIA			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
TRICUSPID VALVE INCOMPETENCE			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	2 / 32 (6.25%)	3 / 32 (9.38%)	7 / 32 (21.88%)
occurrences (all)	2	3	9
DYSGEUSIA			
subjects affected / exposed	5 / 32 (15.63%)	0 / 32 (0.00%)	5 / 32 (15.63%)
occurrences (all)	5	0	5
FORMICATION			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
HEADACHE			

subjects affected / exposed	8 / 32 (25.00%)	8 / 32 (25.00%)	9 / 32 (28.13%)
occurrences (all)	10	11	11
MEMORY IMPAIRMENT			
subjects affected / exposed	2 / 32 (6.25%)	1 / 32 (3.13%)	1 / 32 (3.13%)
occurrences (all)	2	1	1
NEUROPATHY PERIPHERAL			
subjects affected / exposed	2 / 32 (6.25%)	2 / 32 (6.25%)	3 / 32 (9.38%)
occurrences (all)	4	2	3
NEUROTOXICITY			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	1	0	1
PARAESTHESIA			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
PAROSMIA			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	1	0	1
PERIPHERAL SENSORY NEUROPATHY			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
POOR QUALITY SLEEP			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
PRESYNCOPE			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	1	0	1
RESTLESS LEGS SYNDROME			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
SINUS HEADACHE			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	4 / 32 (12.50%)	2 / 32 (6.25%)	11 / 32 (34.38%)
occurrences (all)	4	2	15

ANAEMIA MACROCYTIC			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
LEUKOPENIA			
subjects affected / exposed	5 / 32 (15.63%)	1 / 32 (3.13%)	2 / 32 (6.25%)
occurrences (all)	6	1	2
LYMPHOPENIA			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
NEUTROPENIA			
subjects affected / exposed	2 / 32 (6.25%)	6 / 32 (18.75%)	3 / 32 (9.38%)
occurrences (all)	2	9	5
THROMBOCYTOPENIA			
subjects affected / exposed	2 / 32 (6.25%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	2	1	0
Ear and labyrinth disorders			
DEAFNESS			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
VERTIGO			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	1	0	1
Eye disorders			
BLEPHAROSPASM			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
CONJUNCTIVITIS			
subjects affected / exposed	1 / 32 (3.13%)	1 / 32 (3.13%)	1 / 32 (3.13%)
occurrences (all)	1	1	1
CORNEAL DEPOSITS			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
DRY EYE			
subjects affected / exposed	0 / 32 (0.00%)	2 / 32 (6.25%)	0 / 32 (0.00%)
occurrences (all)	0	2	0
EYE INFLAMMATION			

subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
EYELID OEDEMA			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
EYELIDS PRURITUS			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
KERATOCONJUNCTIVITIS SICCA			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
LACRIMATION INCREASED			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
PHOTOPHOBIA			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
VISION BLURRED			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
VISUAL IMPAIRMENT			
subjects affected / exposed	1 / 32 (3.13%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	1	1	0
Gastrointestinal disorders			
ABDOMINAL DISCOMFORT			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	2
ABDOMINAL DISTENSION			
subjects affected / exposed	3 / 32 (9.38%)	5 / 32 (15.63%)	3 / 32 (9.38%)
occurrences (all)	3	5	4
ABDOMINAL PAIN			
subjects affected / exposed	12 / 32 (37.50%)	12 / 32 (37.50%)	8 / 32 (25.00%)
occurrences (all)	18	23	18
ABDOMINAL PAIN LOWER			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	1 / 32 (3.13%)
occurrences (all)	0	1	1

ABDOMINAL PAIN UPPER			
subjects affected / exposed	1 / 32 (3.13%)	2 / 32 (6.25%)	2 / 32 (6.25%)
occurrences (all)	1	2	2
ANAL FISSURE			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
ANAL SPHINCTER ATONY			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
ANORECTAL VARICES HAEMORRHAGE			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
ASCITES			
subjects affected / exposed	2 / 32 (6.25%)	0 / 32 (0.00%)	0 / 32 (0.00%)
occurrences (all)	10	0	0
CONSTIPATION			
subjects affected / exposed	9 / 32 (28.13%)	12 / 32 (37.50%)	6 / 32 (18.75%)
occurrences (all)	11	14	7
DIARRHOEA			
subjects affected / exposed	8 / 32 (25.00%)	10 / 32 (31.25%)	12 / 32 (37.50%)
occurrences (all)	11	14	16
DRY MOUTH			
subjects affected / exposed	0 / 32 (0.00%)	3 / 32 (9.38%)	4 / 32 (12.50%)
occurrences (all)	0	3	5
DYSPEPSIA			
subjects affected / exposed	5 / 32 (15.63%)	7 / 32 (21.88%)	7 / 32 (21.88%)
occurrences (all)	7	7	10
DYSPHAGIA			
subjects affected / exposed	0 / 32 (0.00%)	2 / 32 (6.25%)	1 / 32 (3.13%)
occurrences (all)	0	2	1
EPIGASTRIC DISCOMFORT			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
FAECAL INCONTINENCE			

subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
FLATULENCE			
subjects affected / exposed	2 / 32 (6.25%)	2 / 32 (6.25%)	4 / 32 (12.50%)
occurrences (all)	2	2	4
GASTRITIS			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	2
GASTROINTESTINAL DISORDER			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
GASTROINTESTINAL SOUNDS ABNORMAL			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	1 / 32 (3.13%)	2 / 32 (6.25%)	3 / 32 (9.38%)
occurrences (all)	1	2	3
GINGIVAL BLEEDING			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
GLOSSODYNIA			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
HAEMORRHOIDS			
subjects affected / exposed	1 / 32 (3.13%)	3 / 32 (9.38%)	1 / 32 (3.13%)
occurrences (all)	1	3	1
INTESTINAL OBSTRUCTION			
subjects affected / exposed	0 / 32 (0.00%)	2 / 32 (6.25%)	0 / 32 (0.00%)
occurrences (all)	0	2	0
MOUTH ULCERATION			
subjects affected / exposed	0 / 32 (0.00%)	2 / 32 (6.25%)	0 / 32 (0.00%)
occurrences (all)	0	2	0
NAUSEA			

subjects affected / exposed	19 / 32 (59.38%)	18 / 32 (56.25%)	25 / 32 (78.13%)
occurrences (all)	24	35	44
ODYNOPHAGIA			
subjects affected / exposed	1 / 32 (3.13%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	1	1	0
ORAL PAIN			
subjects affected / exposed	1 / 32 (3.13%)	2 / 32 (6.25%)	0 / 32 (0.00%)
occurrences (all)	1	2	0
PROCTALGIA			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
RECTAL HAEMORRHAGE			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	1 / 32 (3.13%)
occurrences (all)	0	1	1
RETCHING			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
SALIVARY HYPERSECRETION			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	2
SENSITIVITY OF TEETH			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
SMALL INTESTINAL OBSTRUCTION			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
STOMATITIS			
subjects affected / exposed	0 / 32 (0.00%)	19 / 32 (59.38%)	1 / 32 (3.13%)
occurrences (all)	0	32	1
TOOTH DISCOLOURATION			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
TOOTHACHE			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
VOMITING			

subjects affected / exposed	11 / 32 (34.38%)	10 / 32 (31.25%)	16 / 32 (50.00%)
occurrences (all)	17	16	31
Hepatobiliary disorders			
LIVER INJURY			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	1 / 32 (3.13%)
occurrences (all)	0	1	1
Skin and subcutaneous tissue disorders			
ACNE			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	2	0
ALOPECIA			
subjects affected / exposed	3 / 32 (9.38%)	7 / 32 (21.88%)	4 / 32 (12.50%)
occurrences (all)	3	7	4
BLISTER			
subjects affected / exposed	0 / 32 (0.00%)	4 / 32 (12.50%)	0 / 32 (0.00%)
occurrences (all)	0	5	0
DERMATITIS ACNEIFORM			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
DRY SKIN			
subjects affected / exposed	1 / 32 (3.13%)	4 / 32 (12.50%)	0 / 32 (0.00%)
occurrences (all)	1	4	0
ERYTHEMA			
subjects affected / exposed	0 / 32 (0.00%)	6 / 32 (18.75%)	0 / 32 (0.00%)
occurrences (all)	0	8	0
EXFOLIATIVE RASH			
subjects affected / exposed	0 / 32 (0.00%)	2 / 32 (6.25%)	0 / 32 (0.00%)
occurrences (all)	0	2	0
HYPERHIDROSIS			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
NAIL DISORDER			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	1 / 32 (3.13%)
occurrences (all)	0	1	1
NIGHT SWEATS			

subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	1 / 32 (3.13%)
occurrences (all)	0	1	2
ONYCHOCLASIS			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
ONYCHOMADESIS			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
PALMAR ERYTHEMA			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
PALMAR-PLANTAR ERYTHRODYSAESTHESIA SYNDROME			
subjects affected / exposed	0 / 32 (0.00%)	20 / 32 (62.50%)	0 / 32 (0.00%)
occurrences (all)	0	33	0
PETECHIAE			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
PHOTOSENSITIVITY REACTION			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	2	0
PIGMENTATION DISORDER			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
PRURITUS			
subjects affected / exposed	0 / 32 (0.00%)	5 / 32 (15.63%)	0 / 32 (0.00%)
occurrences (all)	0	5	0
RASH			
subjects affected / exposed	3 / 32 (9.38%)	14 / 32 (43.75%)	3 / 32 (9.38%)
occurrences (all)	4	24	4
RASH GENERALISED			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
RASH MACULAR			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0

RASH MACULO-PAPULAR			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
SKIN BURNING SENSATION			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
SKIN EROSION			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
SKIN EXFOLIATION			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
SKIN HYPERPIGMENTATION			
subjects affected / exposed	0 / 32 (0.00%)	3 / 32 (9.38%)	0 / 32 (0.00%)
occurrences (all)	0	3	0
SKIN LESION			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
SKIN ULCER			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
URTICARIA			
subjects affected / exposed	1 / 32 (3.13%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	1	1	0
XERODERMA			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
BLADDER SPASM			
subjects affected / exposed	1 / 32 (3.13%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	1	1	0
DYSURIA			
subjects affected / exposed	1 / 32 (3.13%)	1 / 32 (3.13%)	1 / 32 (3.13%)
occurrences (all)	1	1	1
HAEMATURIA			

subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
POLLAKIURIA			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	2 / 32 (6.25%)
occurrences (all)	1	0	2
RENAL IMPAIRMENT			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
URETHRAL PAIN			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
URINARY RETENTION			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	3 / 32 (9.38%)	2 / 32 (6.25%)	0 / 32 (0.00%)
occurrences (all)	4	4	0
BACK PAIN			
subjects affected / exposed	3 / 32 (9.38%)	5 / 32 (15.63%)	6 / 32 (18.75%)
occurrences (all)	3	6	6
BONE PAIN			
subjects affected / exposed	1 / 32 (3.13%)	1 / 32 (3.13%)	1 / 32 (3.13%)
occurrences (all)	1	1	1
CHONDROPATHY			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
FLANK PAIN			
subjects affected / exposed	2 / 32 (6.25%)	0 / 32 (0.00%)	0 / 32 (0.00%)
occurrences (all)	2	0	0
GROIN PAIN			
subjects affected / exposed	1 / 32 (3.13%)	2 / 32 (6.25%)	0 / 32 (0.00%)
occurrences (all)	1	2	0
JOINT STIFFNESS			

subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
MUSCLE SPASMS			
subjects affected / exposed	2 / 32 (6.25%)	0 / 32 (0.00%)	2 / 32 (6.25%)
occurrences (all)	2	0	4
MUSCULOSKELETAL CHEST PAIN			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	1 / 32 (3.13%)
occurrences (all)	0	1	1
MUSCULOSKELETAL DISCOMFORT			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
MUSCULOSKELETAL PAIN			
subjects affected / exposed	2 / 32 (6.25%)	2 / 32 (6.25%)	1 / 32 (3.13%)
occurrences (all)	3	2	1
MUSCULOSKELETAL STIFFNESS			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
MYALGIA			
subjects affected / exposed	2 / 32 (6.25%)	1 / 32 (3.13%)	2 / 32 (6.25%)
occurrences (all)	2	1	2
NECK PAIN			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
PAIN IN EXTREMITY			
subjects affected / exposed	1 / 32 (3.13%)	3 / 32 (9.38%)	3 / 32 (9.38%)
occurrences (all)	1	3	3
PAIN IN JAW			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	1 / 32 (3.13%)	1 / 32 (3.13%)	1 / 32 (3.13%)
occurrences (all)	2	1	1
CANDIDIASIS			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0

CELLULITIS			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
EAR INFECTION			
subjects affected / exposed	1 / 32 (3.13%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	1	1	0
ECZEMA INFECTED			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
FOLLICULITIS			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
FUNGAL INFECTION			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
FURUNCLE			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
GASTROENTERITIS			
subjects affected / exposed	0 / 32 (0.00%)	2 / 32 (6.25%)	0 / 32 (0.00%)
occurrences (all)	0	2	0
GASTROINTESTINAL INFECTION			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
GENITAL HERPES			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
GINGIVAL INFECTION			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
HERPES ZOSTER			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
INCISION SITE ABSCESS			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0

INFECTED SEBACEOUS CYST			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
INFLUENZA			
subjects affected / exposed	3 / 32 (9.38%)	1 / 32 (3.13%)	2 / 32 (6.25%)
occurrences (all)	4	1	3
INTERTRIGO CANDIDA			
subjects affected / exposed	0 / 32 (0.00%)	2 / 32 (6.25%)	0 / 32 (0.00%)
occurrences (all)	0	3	0
LOCALISED INFECTION			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	1	0	1
NAIL INFECTION			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
NASOPHARYNGITIS			
subjects affected / exposed	2 / 32 (6.25%)	3 / 32 (9.38%)	2 / 32 (6.25%)
occurrences (all)	2	3	4
ORAL CANDIDIASIS			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	2	0
ORAL HERPES			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
ORAL INFECTION			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
PHARYNGITIS			
subjects affected / exposed	1 / 32 (3.13%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	1	1	0
POSTOPERATIVE WOUND INFECTION			

subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
PULPITIS DENTAL			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
RHINITIS			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	2
SINUSITIS			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
TINEA PEDIS			
subjects affected / exposed	0 / 32 (0.00%)	2 / 32 (6.25%)	0 / 32 (0.00%)
occurrences (all)	0	2	0
TONSILLITIS			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	2
TOOTH ABSCESS			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	5 / 32 (15.63%)	2 / 32 (6.25%)	2 / 32 (6.25%)
occurrences (all)	6	2	2
URINARY TRACT INFECTION			
subjects affected / exposed	5 / 32 (15.63%)	4 / 32 (12.50%)	11 / 32 (34.38%)
occurrences (all)	5	7	20
VIRAL INFECTION			
subjects affected / exposed	2 / 32 (6.25%)	1 / 32 (3.13%)	2 / 32 (6.25%)
occurrences (all)	3	1	5
VIRAL UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 32 (3.13%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	1	1	0
VULVOVAGINAL CANDIDIASIS			

subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	1	0	1
Metabolism and nutrition disorders			
CACHEXIA			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
DECREASED APPETITE			
subjects affected / exposed	5 / 32 (15.63%)	8 / 32 (25.00%)	5 / 32 (15.63%)
occurrences (all)	5	10	8
DEHYDRATION			
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
HYPERCALCAEMIA			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
HYPERGLYCAEMIA			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	1	0	1
HYPOKALAEMIA			
subjects affected / exposed	1 / 32 (3.13%)	1 / 32 (3.13%)	1 / 32 (3.13%)
occurrences (all)	1	1	1
HYPOMAGNESAEMIA			
subjects affected / exposed	2 / 32 (6.25%)	1 / 32 (3.13%)	1 / 32 (3.13%)
occurrences (all)	2	2	1
HYPOPROTEINAEMIA			
subjects affected / exposed	0 / 32 (0.00%)	0 / 32 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
INCREASED APPETITE			
subjects affected / exposed	1 / 32 (3.13%)	0 / 32 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 March 2008	Clarification that withdrawal was from study treatment rather than from study (Section 3.2.1, Section 3.2.2, Section 3.3.2, Section 3.5.2.1, Section 4.5.1, Section 4.5.1.1, Section 5.3.2, and Section 5.3.3. For any patient with a treatment-free interval of more than 12 months, then re-treatment with platinum should be the first option. However a patient may be considered for this study if there is a medical contra-indication to further platinum chemotherapy. This must be discussed both with the patient and with AstraZeneca prior to consent and any screening procedures (Section 4.3). Collection of demography data and extra data for cardiac monitoring (ECG and MUGA scans) and safety haematology and biochemistry (e.g. mean cell volume, amylase and lipase assessments) (Section 5.2.2, Section 5.2.9, Section 5.2.10, Section 3.3.3.5, Section 5.2.12.1)
20 May 2008	Change to number of doses of olaparib to be studied (Study title, Section 1.6, Section 3.2.1) Collection of OS as secondary objective, changes to statistical methods as a result of change in number in olaparib dose groups, clarification of patient management (Section 2.1, Section 2.2, Section 4.3, Section 5.2.14, Section 7.2, Section 7.4.1, Section 7.4.1.5, Section 7.5.1) Changes to management of toxicity based on the new dose group of 200 mg bd (Section 3.3.2) Inclusion criteria (Section 4.1) Exclusion criteria (Section 4.2) Clarification of safety assessments (Section 5.3.2)

13 November 2008	Synopsis, Target patient population Text changes to Synopsis, Key Procedures, Overall Survival (Section 7.4.1.5), Determination of sample size (Section 7.5), Adverse event reporting period Section 6.6) to account for overall survival as secondary endpoint. Inclusion Criteria (Section 4.1, criterion 7) Exclusion Criteria (Section 4.2, criterion 2) Exclusion Criteria (Section 4.2 previously criterion 5, now criterion 6) Assignment of patient E-code number and stratification (Section 4.3) Discontinuation from study treatment and (Section 4.5.1.2) and CT or MRI scans (Section 5.2.14) Treatment period(s) and assessments text (Section 5.3.2) Withdrawal visit text (Section 5.3.3) Crossover from liposomal doxorubicin text (Section 5.3.4) Patient management Post-Primary Analysis (new section) (Section 5.3.6)
05 April 2010	Key procedures and statistical summary (Synopsis), Table 5, crossover from liposomal doxorubicin text (Section 5.3.4), Table 6, Final follow-up visit text (Section 5.3.5), Patient management post primary analysis (Section 5.3.6), Figure 2, patient management post data cut-off text (Section 5.3.7, new text), Adverse event reporting period text (Section 6.6), Overall survival text (Section 7.4.1.5), Determination of sample size text (Section 7.5), Study timetable text (Section 11) Clinical experience text (Section 1.5) Management of olaparib toxicity text (Section 3.3.2) Exclusion criteria (Section 4.2; criterion 15) Discontinuation from study treatment text (Section 4.5.1.2), Crossover from liposomal doxorubicin text (Section 5.3.4) Table 7 (New table of study schedule for patients crossing over from liposomal doxorubicin to olaparib following approval of protocol amendment 4) Patient management post primary analysis (Section 5.3.6) Figure 2 Reporting of AE and SAE text (Section 6.2)

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

The AEs reported include all events up to the OS data cut-off. After the PFS data cut-off, AEs were only collected for the olaparib and cross-over groups. The safety profile of these 2 groups at OS was consistent with that at the time of PFS.

Notes: