Clinical trial results:
A Phase I/II randomised, double-blind, multi-centre study to assess the efficacy of AZD2281 when given in combination with paclitaxel in the 1st or 2nd line treatment of patients with metastatic Triple Negative Breast Cancer

Summary

EudraCT number	2008-002608-25
Trial protocol	AT BE CZ DK
Global end of trial date	09 November 2009

Results information

Result version number	v1 (current)
This version publication date	22 February 2019
First version publication date	22 February 2019

Trial information

Trial identification

Sponsor protocol code	D0810C00011

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,, Södertälje, Sweden,
Public contact	Clinical Trial Transparency Team, AstraZeneca, ClinicalTrialTransparency@astrazeneca.com
Scientific contact	Clinical Trial Transparency Team, AstraZeneca, 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	09 November 2009
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 November 2009
Global end of trial reached?	Yes
Global end of trial date	09 November 2009
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the Phase I part of this study was:
· To establish the appropriate doses of paclitaxel and AZD2281 in combination, based on safety and tolerability (for use in the randomised Phase II part of the study).

The primary objective of the Phase II part of this study was:
· To determine the efficacy (assessed by Progression Free Survival [PFS]) of AZD2281 in combination with paclitaxel compared to paclitaxel alone in this patient population.

Protection of trial subjects:

This study was performed in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with International Council on Harmonisation/Good Clinical Practice, applicable regulatory requirements and the AstraZeneca policy on Bioethics and Human Biological Samples.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 September 2008
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 3
Country: Number of subjects enrolled	Australia: 12
Country: Number of subjects enrolled	Austria: 1
Country: Number of subjects enrolled	Belgium: 3
Worldwide total number of subjects	19
EEA total number of subjects	4

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	17
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

In the Phase 1 part of this study, 24 patients were enrolled at 6 centres in 4 countries: Australia (3), Austria (1), Belgium (1) and Canada (1). Protocol Amendment 1 was implemented before recruitment of Cohort 2, which introduced the use of a G-CSF for initial management of neutropenia.

Pre-assignment

Screening details:

In this trial, there was a screening period of 28 days prior to first dose of study treatment. There were 5 patients who were in the pre-assignment period but were not subsequently assigned treatment. This was due to Progression (1), Incorrect enrolment (3) and Voluntary withdrawal (1).

Pre-assignment period milestones

Number of subjects started	24[1]
Number of subjects completed	19

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Consent withdrawn by subject: 1
Reason: Number of subjects	Incorrect enrolment: 3
Reason: Number of subjects	Lack of efficacy: 1

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: There were 5 patients who were in the pre-assignment period but were not subsequently assigned treatment. This was due to Progression (1), Incorrect enrolment (3) and Voluntary withdrawal (1).

Period 1

Period 1 title	Phase I - Safety Run-In (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

The Phase I part of this study is open-label.

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1

Arm description: -

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 through a 28 day cycle

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

Dosage and administration details:

90 mg/m2 IV for 6 to 10 cycles

Arm title	Cohort 2

Arm description:

Both arms have the same allocated treatment, however Cohort 2 allowed the use of a granulocyte colony stimulating factor (G-CSF; filgrastim) for initial management of neutropenia

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 through a 28 day cycle

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

Dosage and administration details:

90 mg/m2 IV for 6 to 10 cycles

Number of subjects in period 1	Cohort 1	Cohort 2
Started	9	10
Completed	1	3
Not completed	8	7
Consent withdrawn by subject	1	-
Lack of efficacy	7	7

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1
Reporting group description: -	
Reporting group title	Cohort 2
Reporting group description:	
Both arms have the same allocated treatment, however Cohort 2 allowed the use of a granulocyte colony stimulating factor (G-CSF; filgrastim) for initial management of neutropenia	

Reporting group values	Cohort 1	Cohort 2	Total
Number of subjects	9	10	19
Age Categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	8	9	17
From 65-84 years	1	1	2
85 years and over	0	0	0
Age Continuous			
Units: years			
arithmetic mean	50.0	50.7	
standard deviation	± 11.5	± 8.2	-
Gender Categorical			
Units: Subjects			
Female	9	10	19
Male	0	0	0
Race			
Units: Subjects			
White	9	10	19
Age			
Units: years			
median	49.0	49.5	
full range (min-max)	36 to 71	38 to 67	-

Subject analysis sets	
Subject analysis set title	FAS
Subject analysis set type	Full analysis
Subject analysis set description:	
Includes all patients eligible to be dosed	

Reporting group values	FAS		
Number of subjects	19		
Age Categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	17		
From 65-84 years	2		
85 years and over	0		
Age Continuous Units: years			
arithmetic mean	50.4		
standard deviation	± 9.6		
Gender Categorical Units: Subjects			
Female	19		
Male	0		
Race Units: Subjects			
White	19		
Age Units: years			
median	49.0		
full range (min-max)	36 to 71		

End points

End points reporting groups

Reporting group title	Cohort 1
Reporting group description: -	
Reporting group title	Cohort 2
Reporting group description:	
Both arms have the same allocated treatment, however Cohort 2 allowed the use of a granulocyte colony stimulating factor (G-CSF; filgrastim) for initial management of neutropenia	
Subject analysis set title	FAS
Subject analysis set type	Full analysis
Subject analysis set description:	
Includes all patients eligible to be dosed	

Primary: Patients with At Least One Adverse Event

End point title	Patients with At Least One Adverse Event[1]
End point description:	
End point type	Primary
End point timeframe:	
From signing of ICF throughout treatment period up to and including 30-day follow-up period.	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This study was terminated prematurely and therefore there was no formal statistical analysis of safety and tolerability data

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	10		
Units: Subjects				
Number of Patients	9	10		
Percentage	100	100		

Statistical analyses

No statistical analyses for this end point

Primary: Patients with At Least One Adverse Event Causally Related to Olaparib

End point title	Patients with At Least One Adverse Event Causally Related to Olaparib[2]
End point description:	
End point type	Primary
End point timeframe:	
From signing of ICF throughout treatment period up to and including 30-day follow-up period.	

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This study was terminated prematurely and therefore there was no formal statistical analysis of safety and tolerability data

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	10		
Units: Subjects				
Number of Patients	7	9		

Statistical analyses

No statistical analyses for this end point

Primary: Patients with At Least One Adverse Event Causally Related to Paclitaxel

End point title	Patients with At Least One Adverse Event Causally Related to Paclitaxel[3]

End point description:

End point type	Primary

End point timeframe:

From signing of ICF throughout treatment period up to and including 30-day follow-up period.

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This study was terminated prematurely and therefore there was no formal statistical analysis of safety and tolerability data

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	10		
Units: Subjects	9	10		

Statistical analyses

No statistical analyses for this end point

Primary: Patients with At Least One Adverse Event of CTCAE Grade 3 or Higher

End point title	Patients with At Least One Adverse Event of CTCAE Grade 3 or Higher[4]

End point description:

End point type	Primary

End point timeframe:

From signing of ICF throughout treatment period up to and including 30-day follow-up period.

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This study was terminated prematurely and therefore there was no formal statistical analysis of safety and tolerability data

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	10		
Units: Subjects	8	5		

Statistical analyses

No statistical analyses for this end point

Primary: Patients with At Least One Adverse Event with Outcome Death

End point title	Patients with At Least One Adverse Event with Outcome

End point description:

End point type	Primary

End point timeframe:

From signing of ICF throughout treatment period up to and including 30-day follow-up period.

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This study was terminated prematurely and therefore there was no formal statistical analysis of safety and tolerability data

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	10		
Units: Subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Patients with At Least One Serious Adverse Event

End point title	Patients with At Least One Serious Adverse Event[6]

End point description:

End point type	Primary

End point timeframe:

From signing of ICF throughout treatment period up to and including 30-day follow-up period.

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This study was terminated prematurely and therefore there was no formal statistical analysis of safety and tolerability data

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	10		
Units: Subjects	2	4		

Statistical analyses

No statistical analyses for this end point

Primary: Patients with At Least One Adverse Event Leading to Discontinuation of IP

End point title	Patients with At Least One Adverse Event Leading to Discontinuation of IP[7]

End point description:

End point type	Primary

End point timeframe:

From signing of ICF throughout treatment period up to and including 30-day follow-up period.

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This study was terminated prematurely and therefore there was no formal statistical analysis of safety and tolerability data

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	10		
Units: Subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of patients with ≥2 CTC grade changes from baseline for haematology parameters

End point title	Number of patients with ≥2 CTC grade changes from baseline for haematology parameters[8]

End point description:

Baseline is defined as the last result obtained prior to the start of study treatment.

End point type	Primary

End point timeframe:

Derived from lab assessments between the start of treatment and 30 days following the date of last dose of study medication.

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This study was terminated prematurely and therefore there was no formal statistical analysis of safety and tolerability data

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	10		
Units: Subjects				
Leucocytes	9	6		
Neutrophils	7	6		
Lymphocytes	4	4		
Platelets	1	1		
aPTT	2	1		

Statistical analyses

No statistical analyses for this end point

Primary: Number of patients with CTC grade changes to 3 or 4 from baseline for haematology parameters

End point title	Number of patients with CTC grade changes to 3 or 4 from baseline for haematology parameters[9]

End point description:

End point type	Primary

End point timeframe:

Derived from lab assessments between the start of treatment and 30 days following the date of last dose of study
medication.
Baseline is defined as the last result obtained prior to the start of study treatment.

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This study was terminated prematurely and therefore there was no formal statistical analysis of safety and tolerability data

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	10		
Units: Subjects				
Leucocytes	3	3		
Neutrophils	2	3		
Lymphocytes	4	3		
Platelets	1	0		
aPTT	1	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of patients with ≥2 CTC grade changes from baseline for clinical chemistry parameters

End point title	Number of patients with ≥2 CTC grade changes from baseline for clinical chemistry parameters[10]

End point description:

End point type	Primary

End point timeframe:

Derived from lab assessments between the start of treatment and 30 days following the date of last dose of study medication.
Baseline is defined as the last result obtained prior to the start of study treatment.

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This study was terminated prematurely and therefore there was no formal statistical analysis of safety and tolerability data

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	10		
Units: Subjects				
ALT	0	1		
AST	0	0		
γ-GT	3	1		
Total bilirubin	0	1		
ALP	0	0		
Albumin	0	1		
Amylase	0	0		
Lipase	0	3		
Creatinine	1	0		
Glucose (low)	0	0		
Glucose (high)	4	1		
Calcium (low)	0	0		
Calcium (high)	0	0		
Magnesium (low)	0	0		
Magnesium (high)	0	0		
Potassium (low)	0	0		
Potassium (high)	2	0		
Sodium (low)	2	2		
Sodium (high)	0	1		

Statistical analyses

No statistical analyses for this end point

Primary: Number of patients with CTC grade changes to 3 or 4 from baseline for clinical chemistry parameters

End point title	Number of patients with CTC grade changes to 3 or 4 from baseline for clinical chemistry parameters[11]

End point description:

End point type	Primary

End point timeframe:

Derived from lab assessments between the start of treatment and 30 days following the date of last dose of study
medication.
Baseline is defined as the last result obtained prior to the start of study treatment.

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This study was terminated prematurely and therefore there was no formal statistical analysis of safety and tolerability data

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9[12]	10[13]		
Units: Subjects				
ALT	0	2		
AST	0	2		
γ-GT	1	3		
Total bilirubin	0	1		
ALP	0	1		
Albumin	0	0		
Amylase	0	1		
Lipase	0	1		
Creatinine	0	0		
Glucose (low)	0	0		
Glucose (high)	3	1		
Calcium (low)	0	0		
Calcium (high)	0	0		
Magnesium (low)	0	0		
Magnesium (high)	0	0		
Potassium (low)	0	0		
Potassium (high)	1	0		
Sodium (low)	2	2		
Sodium (high)	0	1		

Notes:

[12] - 1 patient had a Grade 4 CTC elevation in γ-GT at baseline with no change to max severity is excluded
[13] - 1 patient had a Grade 4 CTC elevation in γ-GT at baseline with no change to max severity is excluded

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug until last study visit

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13.0

Reporting groups

Reporting group title	200mg bd - Cohort 2
Reporting group description: -	
Reporting group title	200mg bd - Cohort 1

Reporting group description: -

Serious adverse events	200mg bd - Cohort 2	200mg bd - Cohort 1	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 10 (40.00%)	2 / 9 (22.22%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	0	
Vascular disorders			
DEEP VEIN THROMBOSIS			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HAEMODYNAMIC INSTABILITY			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
APHASIA			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
FEBRILE NEUTROPENIA			

subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
PYREXIA			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
CELLULITIS			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEVICE RELATED INFECTION			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFECTION			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	200mg bd - Cohort 2	200mg bd - Cohort 1	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 10 (100.00%)	9 / 9 (100.00%)	
Vascular disorders			
DEEP VEIN THROMBOSIS			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
HOT FLUSH			
subjects affected / exposed	1 / 10 (10.00%)	2 / 9 (22.22%)	
occurrences (all)	1	2	

HYPERTENSION			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
HYPOTENSION			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
LYMPHOEDEMA			
subjects affected / exposed	1 / 10 (10.00%)	1 / 9 (11.11%)	
occurrences (all)	2	1	
THROMBOPHLEBITIS SUPERFICIAL			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
CHILLS			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
FATIGUE			
subjects affected / exposed	4 / 10 (40.00%)	7 / 9 (77.78%)	
occurrences (all)	4	9	
FEELING COLD			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
MALAISE			
subjects affected / exposed	0 / 10 (0.00%)	2 / 9 (22.22%)	
occurrences (all)	0	2	
OEDEMA			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
OEDEMA PERIPHERAL			

subjects affected / exposed	2 / 10 (20.00%)	1 / 9 (11.11%)	
occurrences (all)	2	1	
PYREXIA			
subjects affected / exposed	0 / 10 (0.00%)	2 / 9 (22.22%)	
occurrences (all)	0	2	
THROMBOSIS IN DEVICE			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
BREAST PAIN			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
VULVOVAGINAL DISCOMFORT			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	0 / 10 (0.00%)	3 / 9 (33.33%)	
occurrences (all)	0	3	
DYSPHONIA			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
DYSPNOEA			
subjects affected / exposed	3 / 10 (30.00%)	3 / 9 (33.33%)	
occurrences (all)	3	4	
EPISTAXIS			
subjects affected / exposed	3 / 10 (30.00%)	2 / 9 (22.22%)	
occurrences (all)	4	2	
OROPHARYNGEAL PAIN			
subjects affected / exposed	2 / 10 (20.00%)	2 / 9 (22.22%)	
occurrences (all)	3	2	
PLEURAL EFFUSION			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
PRODUCTIVE COUGH			

subjects affected / exposed	0 / 10 (0.00%)	2 / 9 (22.22%)	
occurrences (all)	0	2	
RHINORRHOEA			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	1 / 10 (10.00%)	3 / 9 (33.33%)	
occurrences (all)	1	3	
CONFUSIONAL STATE			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
DEPRESSION			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
INSOMNIA			
subjects affected / exposed	2 / 10 (20.00%)	1 / 9 (11.11%)	
occurrences (all)	2	1	
MOOD ALTERED			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
BLOOD LACTATE DEHYDROGENASE			

ABNORMAL			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
GAMMA-GLUTAMYLTRANSFERASE ABNORMAL			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
WEIGHT INCREASED			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Cardiac disorders			
PALPITATIONS			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
TACHYCARDIA			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Nervous system disorders			
APHONIA			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
ATAXIA			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
COGNITIVE DISORDER			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
DIZZINESS			
subjects affected / exposed	0 / 10 (0.00%)	3 / 9 (33.33%)	
occurrences (all)	0	3	
DYSGEUSIA			
subjects affected / exposed	3 / 10 (30.00%)	2 / 9 (22.22%)	
occurrences (all)	3	2	
HEADACHE			
subjects affected / exposed	2 / 10 (20.00%)	3 / 9 (33.33%)	
occurrences (all)	2	4	
HYPOAESTHESIA			

subjects affected / exposed	2 / 10 (20.00%)	0 / 9 (0.00%)	
occurrences (all)	2	0	
LETHARGY			
subjects affected / exposed	3 / 10 (30.00%)	2 / 9 (22.22%)	
occurrences (all)	3	2	
MIGRAINE			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
NEUROPATHY PERIPHERAL			
subjects affected / exposed	3 / 10 (30.00%)	3 / 9 (33.33%)	
occurrences (all)	3	3	
PARAESTHESIA			
subjects affected / exposed	0 / 10 (0.00%)	3 / 9 (33.33%)	
occurrences (all)	0	3	
PERIPHERAL SENSORY NEUROPATHY			
subjects affected / exposed	2 / 10 (20.00%)	2 / 9 (22.22%)	
occurrences (all)	2	2	
SENSORY LOSS			
subjects affected / exposed	1 / 10 (10.00%)	1 / 9 (11.11%)	
occurrences (all)	1	1	
SYNCOPE			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
TREMOR			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	1 / 10 (10.00%)	5 / 9 (55.56%)	
occurrences (all)	1	11	
LEUKOPENIA			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	4	
LYMPH NODE PAIN			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	

NEUTROPENIA			
subjects affected / exposed	4 / 10 (40.00%)	7 / 9 (77.78%)	
occurrences (all)	9	22	
Ear and labyrinth disorders			
TINNITUS			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
VERTIGO			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Eye disorders			
DARK CIRCLES UNDER EYES			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
DRY EYE			
subjects affected / exposed	1 / 10 (10.00%)	1 / 9 (11.11%)	
occurrences (all)	1	1	
EYE PAIN			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
EYE SWELLING			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
LACRIMATION INCREASED			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
VISION BLURRED			
subjects affected / exposed	1 / 10 (10.00%)	2 / 9 (22.22%)	
occurrences (all)	1	2	
Gastrointestinal disorders			
ABDOMINAL DISCOMFORT			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
ABDOMINAL PAIN			
subjects affected / exposed	1 / 10 (10.00%)	3 / 9 (33.33%)	
occurrences (all)	1	3	
ABDOMINAL DISTENSION			

subjects affected / exposed	0 / 10 (0.00%)	2 / 9 (22.22%)		
occurrences (all)	0	2		
ABDOMINAL PAIN UPPER				
subjects affected / exposed	1 / 10 (10.00%)	4 / 9 (44.44%)		
occurrences (all)	1	5		
ABDOMINAL WALL HAEMATOMA				
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)		
occurrences (all)	0	1		
CONSTIPATION				
subjects affected / exposed	2 / 10 (20.00%)	4 / 9 (44.44%)		
occurrences (all)	2	5		
DENTAL CARIES				
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)		
occurrences (all)	0	1		
DIARRHOEA				
subjects affected / exposed	6 / 10 (60.00%)	6 / 9 (66.67%)		
occurrences (all)	6	7		
DRY MOUTH				
subjects affected / exposed	1 / 10 (10.00%)	1 / 9 (11.11%)		
occurrences (all)	1	1		
DYSPEPSIA				
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)		
occurrences (all)	0	1		
GASTRITIS				
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)		
occurrences (all)	1	0		
GASTROOESOPHAGEAL REFLUX DISEASE				
subjects affected / exposed	2 / 10 (20.00%)	1 / 9 (11.11%)		
occurrences (all)	3	1		
HAEMORRHOIDS				
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)		
occurrences (all)	0	1		
MOUTH ULCERATION				
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)		
occurrences (all)	1	0		

NAUSEA			
subjects affected / exposed	6 / 10 (60.00%)	6 / 9 (66.67%)	
occurrences (all)	7	11	
STOMATITIS			
subjects affected / exposed	1 / 10 (10.00%)	2 / 9 (22.22%)	
occurrences (all)	2	4	
VOMITING			
subjects affected / exposed	3 / 10 (30.00%)	3 / 9 (33.33%)	
occurrences (all)	4	5	
Hepatobiliary disorders			
HEPATIC PAIN			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
ACNE			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
ALOPECIA			
subjects affected / exposed	4 / 10 (40.00%)	7 / 9 (77.78%)	
occurrences (all)	4	9	
DERMATITIS ACNEIFORM			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
ERYTHEMA			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
HYPERHIDROSIS			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
NAIL DISORDER			
subjects affected / exposed	1 / 10 (10.00%)	2 / 9 (22.22%)	
occurrences (all)	1	2	
NIGHT SWEATS			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
PRURITUS			

subjects affected / exposed	2 / 10 (20.00%)	2 / 9 (22.22%)	
occurrences (all)	2	2	
RASH			
subjects affected / exposed	5 / 10 (50.00%)	1 / 9 (11.11%)	
occurrences (all)	8	1	
SKIN DISORDER			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Renal and urinary disorders			
ANURIA			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
DYSURIA			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
HAEMATURIA			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
POLLAKIURIA			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
RENAL FAILURE			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
STRESS URINARY INCONTINENCE			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
URINARY RETENTION			
subjects affected / exposed	1 / 10 (10.00%)	1 / 9 (11.11%)	
occurrences (all)	1	1	
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	2 / 10 (20.00%)	2 / 9 (22.22%)	
occurrences (all)	2	4	
ARTHRITIS			

subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
BACK PAIN			
subjects affected / exposed	4 / 10 (40.00%)	2 / 9 (22.22%)	
occurrences (all)	4	2	
BONE PAIN			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	2	
MUSCLE SPASMS			
subjects affected / exposed	0 / 10 (0.00%)	2 / 9 (22.22%)	
occurrences (all)	0	2	
MUSCLE TIGHTNESS			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
MUSCULAR WEAKNESS			
subjects affected / exposed	0 / 10 (0.00%)	2 / 9 (22.22%)	
occurrences (all)	0	2	
MUSCULOSKELETAL CHEST PAIN			
subjects affected / exposed	1 / 10 (10.00%)	2 / 9 (22.22%)	
occurrences (all)	1	3	
MUSCULOSKELETAL PAIN			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
MUSCULOSKELETAL STIFFNESS			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
MYALGIA			
subjects affected / exposed	2 / 10 (20.00%)	4 / 9 (44.44%)	
occurrences (all)	2	4	
NECK PAIN			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
PAIN IN EXTREMITY			
subjects affected / exposed	1 / 10 (10.00%)	2 / 9 (22.22%)	
occurrences (all)	1	2	
Infections and infestations			

CYSTITIS			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
DEVICE RELATED INFECTION			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
HERPES ZOSTER			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	
occurrences (all)	2	0	
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	2 / 10 (20.00%)	0 / 9 (0.00%)	
occurrences (all)	2	0	
NASOPHARYNGITIS			
subjects affected / exposed	1 / 10 (10.00%)	2 / 9 (22.22%)	
occurrences (all)	1	3	
SINUSITIS			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
SKIN INFECTION			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	3 / 10 (30.00%)	2 / 9 (22.22%)	
occurrences (all)	5	4	
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
VIRAL PHARYNGITIS			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
ACIDOSIS			
subjects affected / exposed	0 / 10 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
DECREASED APPETITE			

subjects affected / exposed	2 / 10 (20.00%)	2 / 9 (22.22%)	
occurrences (all)	2	3	
DEHYDRATION			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
HYPERGLYCAEMIA			
subjects affected / exposed	1 / 10 (10.00%)	1 / 9 (11.11%)	
occurrences (all)	1	1	
HYPOKALAEMIA			
subjects affected / exposed	1 / 10 (10.00%)	0 / 9 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 January 2009	Addresses dose modifications, introducing in a step-wise approach the addition of granulocyte-colony stimulating factor (G-CSF) support (Cohort 2)
17 March 2009	Changes to Phase II part of the trial: Giving patients the possibility to receive maximum tolerated dose of Olaparib on monotherapy, removing requirement for BRCA testing and incorporating a single interim analysis of progression free survival
04 August 2009	Addresses the study closure, the management of Phase I patients currently receiving study treatment, and the definition of end of study given the decision not to proceed to Phase II.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported