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Clinical Trial Summary Report

STOMP: Small cell lung cancer Trial of Olaparib (AZD2281) as Maintenance Programme: a randomised, double blind, multicentre phase II trial

Version 1.0, 09-Dec-2021

Sponsor:	Sheffield Teaching Hospitals NHS Foundation Trust
Sponsor reference number:	STH15845
CRCTU reference number:	LU2006
EudraCT number:	2010-021165-76
IRAS number:	56786

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Sheffield Teaching Hospitals NHS
NHS Foundation Trust

CLINICAL TRIAL SUMMARY REPORT

Acronym:	STOMP
Title:	Small cell lung cancer Trial of Olaparib (AZD2281) as Maintenance Programme: a randomised, double blind, multicentre phase II trial
Sponsor:	Sheffield Teaching Hospitals NHS Foundation Trust
Sponsor Reference Number:	STH15845
EudraCT Number:	2010-021165-76
REC Reference Number:	11/YH/0290
Details of Investigational Medicinal Product(s):	Name: Olaparib, supplied by AstraZeneca Mode of action: olaparib inhibits the activity of polyadenosine 5'diphosphoribose polymerase (PARP), an enzyme involved in DNA transcription, repair and cell cycle regulation. This action has been shown to inhibit the growth of some tumour types. Therapeutic class: PARP inhibitor
Details of Trial Arms:	Patients were randomised in a 2:1:2:1 ratio to the following treatments: - Olaparib 300mg BD - Placebo 300mg BD - Olaparib 200mg TDS - Placebo 200mg TDS Treatment was given continuously until death, disease progression, unacceptable toxicities or withdrawal of patient consent up to a maximum of 2 years.
Start Date: *Date trial opened to recruitment*	21-Nov-2013
End of Trial: *Date of declaration of the end of the trial*	11-Dec-2020

This report was prepared by the Chief Investigator and the Cancer Research UK Clinical Trials Unit (CRCTU) on behalf of the Sponsor.

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SIGNATORY:

Name:	Professor Penella J Woll	Function:	Chief Investigator
Signature:	Obtained via email (see below)	Date:	

From: Penella Woll
To: Rebecca Keogh (Cancer Clinical Trials Unit)
Cc: STOMP (at) trials.bham.ac.uk
Subject: RE: STOMP Clinical Trial Summary Report - Please review and approve
Date: 10 December 2021 16:22:32

Hi Becky

I have now read the report.

I'm happy to approve this version.

Best wishes

Penella

Sent from Mail for Windows

From: Rebecca Keogh
Sent: 09 December 2021 16:06
To: 'Penella Woll'
Cc: STOMP (at) trials.bham.ac.uk
Subject: STOMP Clinical Trial Summary Report - Please review and approve
Importance: High

Hi Penella,

Please see attached the Clinical Trial Summary Report for STOMP. Please can you review the document and if you are happy with this then respond to this email to confirm your review and approval.

DOCUMENT DETAILS:		
Document name	**Document version number**	**Document version date**
STOMP Clinical Trial Summary Report	v1.0	09-Dec-2021

DISTRIBUTION LIST		
Name	**Role within trial**	**Role in review***
Penella J Woll	Chief Investigator	reviewer, approver

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GENERAL INFORMATION

ABBREVIATIONS

Abbreviation	Explanation
AE	Adverse Event
AML	Acute Myeloid Leukaemia
ANC	Absolute neutrophil count
AR	Adverse Reaction
BER	Base Excision Repair
BD	Twice a Day
CR	Complete Response
CRF	Case Report Form
CRCTU	Cancer Research UK Clinical Trials Unit
CT	Computerised Tomography
CTC	Circulating Tumour Cells
CTCAE	Common Terminology Criteria for Adverse Events
DMC	Data Monitoring Committee
DNA	Deoxyribonucleic Acid
DSB	Double Strand Break
ECOG	Eastern Co-operative Oncology Group
GCP	Good Clinical Practice
IMP	Investigational Medicinal Product
ISF	Investigator Site File
IWRS	Interactive Web Response System
MDS	Myelodysplastic Syndrome
MHRA	Medicines and Healthcare products Regulatory Agency
PARP	Polyadenosine 5'-diphosphoribose polymerisation
PD	Progressive Disease
PFS	Progression Free Survival
PO	Administered Orally
PR	Partial Response
REC	Research Ethics Committee
RECIST	Response Evaluation Criteria in Solid Tumours
SAE	Serious Adverse Event
SAR	Serious Adverse Reaction
SCLC	Small Cell Lung Cancer
SD	Stable Disease
SUSAR	Suspected Unexpected Serious Adverse Reaction
TDS	Three Times a Day
TMG	Trial Management Group
U&E	Urine and Electrolytes
ULN	Upper Limit of Normal

TRIAL DESIGN

STOMP was designed as a multicentre, prospective, double-blind, randomised, phase II trial of olaparib vs placebo, 300mg po BD or 200mg po TDS, taken continuously starting no more than 42 days after day 1 of the most recent chemotherapy cycle, or 21 days after the end of the most recent dose of radiotherapy, in patients with small cell lung cancer (SCLC).

For patients who received chemotherapy followed by radiotherapy, the radiotherapy must had begun within 35 days from the start of the last chemotherapy cycle. Those patients that fulfilled the eligibility criteria were stratified by disease extent (M0 vs M1a/b with any T or N stage, according to the American Joint Committee on Cancer (AJCC) TNM staging for lung cancer) and prior radiotherapy (concurrent vs sequential vs none). Patients on trial were monitored at 4-weekly intervals in order to collect safety data. Computed tomography (CT) scans and chest x-rays were carried out every 8 weeks on alternate monthly visits.

Subject to patient consent, blood samples were collected for measurement of biomarkers at baseline, after 28 days of treatment and at the end of treatment. Archived diagnostic tissue biopsies were also collected retrospectively and used for histopathological assessment and translational endpoints.

Patients continued on trial medication for 2 years or until disease progression, death, unacceptable toxicity, or withdrawal of patient consent for data transfer.

TRIAL SCHEMA

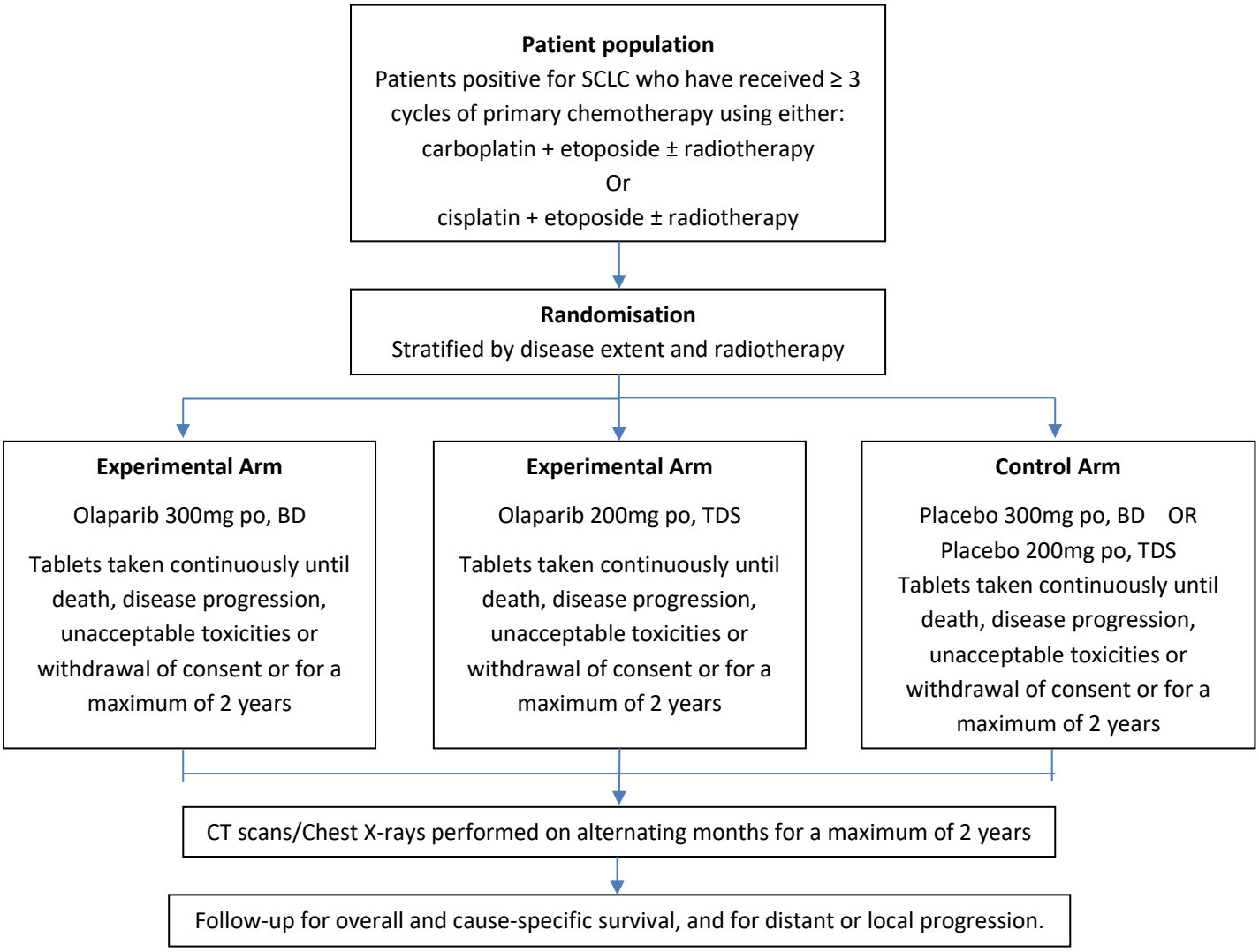


Figure 1. Trial Schema

SCIENTIFIC BACKGROUND

Small cell lung cancer

SCLC comprises 15-20% of lung cancers, representing about 3,500 new cases per annum in the UK. SCLC is initially very chemosensitive, with an objective response rate of about 80% but the majority of patients relapse and die from it. In a London Lung Cancer Group study involving 724 patients, reported in 2007, the median survival was 10.3 months. The standard first line chemotherapy treatment with a platinum based compound (cis- or carbo-platin) and etoposide has been unchanged for 20 years, and the only improvements in survival over this period are attributable to the addition of radiotherapy. Novel active treatment approaches are urgently needed.

Chemoresistant SCLC commonly has multiple abnormalities in oncogenic and tumour suppressor pathways. Abnormalities in p53 (80%), Rb (>90%), FHIT (80%) and inactivation of RASSF1 (90%) are very common in SCLC. These result in increased cell proliferation and deoxyribonucleic acid (DNA) damage requiring repair. Recent data have shown that the association of these with defects in DNA repair pathways, including NBS1, ATM, RAD51, Chk1/2, MDC1 and PTEN can make SCLC cells susceptible to DNA damage.

Polyadenosine 5'-diphosphoribose [poly-(ADP-ribose)] or PAR poly-merisation

Polyadenosine 5'-diphosphoribose [poly-(ADP-ribose)] or PAR polymerisation is a unique post-translational modification of histones and other nuclear proteins that contributes to the survival of proliferating and non-proliferating cells following DNA damage. This event represents an immediate cellular response to DNA damage and involves the modification of glutamate, aspartate and lysine residues with the addition of long chains of Adenosine diphosphate (ADP)-ribose units, derived from Nicotine Adenine Dinucleotide (NAD)+, onto the DNA-binding proteins. The enzymes that catalyse this process, poly-(ADP)-ribose polymerases (PARPs), are critical regulatory components in DNA damage repair and other cellular processes. They now comprise a large and expanding family of 18 proteins, encoded by different genes, and display a conserved catalytic domain in which PARP 1 (113 kDa), the initial member, and PARP 2 (62 kDa) are so far the sole enzymes whose catalytic activity has been shown to be immediately stimulated by DNA strand breaks. Moreover, many of the identified family members interact with each other, share common partners and common sub-cellular localisations, suggesting functional redundancy and possibly fine-tuning in the regulation of post-translational modification of proteins.

The range of biological roles involving PARP proteins is wide. They include: DNA repair and maintenance of genomic integrity, regulation of protein expression at the transcriptional level, regulation of cellular replication and differentiation, regulation of telomerase activity, involvement in cell elimination pathway by necrosis and serving as a signal for protein degradation in oxidatively injured cells.

Of the various members of the PARP enzyme family, only PARP 1 and PARP 2 have been shown to work as DNA damage sensor and signalling molecules. PARP 1 activation leads to DNA repair through the base excision repair (BER) pathway, and cells deficient in PARP 1 have been shown to have delayed DNA repair. Like PARP 1, PARP 2 also responds to DNA damage and is similarly involved in single strand DNA repair. For both proteins, inactivation and cleavage promotes apoptosis and is part of the apoptotic cascade. Loss of PARP 1 activity in cells or in knockout mice leads to both radio and chemo-sensitisation. Moreover, increased PARP 1 activity has been found in many tumour types. The use of PARP inhibitors has confirmed that in combination an enhancement of the anti-tumour activity of radiation and DNA damaging cytotoxic agents occurs.

There is increasing interest in synthetic lethality as a means of selectively killing cancer cells. Two genes are synthetically lethal where mutation of either gene alone is compatible with viability but simultaneous mutation of both genes leads to death. Synthetic lethal interactions between mutated oncogenes or tumour suppressor genes and molecules involved in DNA damage signalling and repair can be therapeutically exploited to preferentially kill tumour cells.

Olaparib

Olaparib (AZD2281, KU-0059436, KuDOS/AstraZeneca) is a PARP inhibitor in development for the treatment of patients who have cancers associated with genetic BRCA mutations and in patients with deficiency in DNA repair, specifically homologous recombination repair deficiency. Clinical study data to date in patients with advanced cancer have shown olaparib to have significant anti-tumour activity as a single agent in ovarian and breast cancer patients with known homologous recombination deficiency: BRCA1-/- or BRCA2-/-. Due to the molecular targeting of olaparib to specific subsets of tumours

and sparing of normal cells, this has raised the opportunity for relatively less toxic cancer monotherapy using such a PARP 1 inhibitor compared with conventional treatments, such as chemotherapy.

Olaparib has been tested in a standard range of safety pharmacology studies e.g. dog cardiovascular and respiratory function tests, and the rat Irwin test. There were no noticeable effects on the cardiovascular or respiratory parameters in the anaesthetised dog or any behavioural, autonomic or motor effects in the rat at the doses studied. The toxicology studies indicate that the target organ of toxicity is the bone marrow. Further information can be found in the current version of the olaparib Investigator's Brochure. More than 950 patients have now received olaparib either as monotherapy (11 studies) or in combination with other chemotherapy agents. Data from these studies indicate that olaparib is generally well tolerated as monotherapy at doses up to 400 mg bd capsules in patients with solid tumours.

TRIAL RATIONALE

Whilst SCLC is initially very chemosensitive (RR 80%), responses are often short-lived and relapse is common. SCLC cells typically exhibit a variety of genetic changes and genomic instability. We hypothesise that this results in “BRCAness” and that such cells will be susceptible to killing by a PARP inhibitor. Olaparib is given by mouth and has an excellent safety and tolerability profile.

This study will evaluate the therapeutic activity, safety and tolerability of the PARP inhibitor olaparib (AZD2281) as maintenance treatment in patients with chemo-sensitive small cell lung cancer. Patients are those with pathologically confirmed SCLC (limited or extensive stage) and who have completed at least 3 cycles of first line chemotherapy with platinum and etoposide ± radiotherapy and achieved at least a partial response.

AIMS, HYPOTHESES AND OUTCOME MEASURES

Aims

This trial will assess the activity and safety of the PARP inhibitor olaparib as maintenance treatment for patients with chemoresponsive SCLC. Stored tumour specimens and, in selected sites, blood samples, will be studied to look for variables that predict response to this treatment.

Hypotheses

Primary: The use of olaparib as a maintenance therapy in patients with chemoresponsive small cell lung cancer prolongs the period of progression free survival beyond that of using a placebo.

Secondary: Olaparib is safe, tolerable and effective as maintenance therapy in patients with chemoresponsive SCLC.

Outcome Measures

Primary outcome measure

- Progression-free survival time

Secondary outcome measures

- Progression-free rate at 4 months from randomisation
- Overall survival time
- Overall survival rate at 6 months
- Changes in performance status
- Quality of life (EQ-5D-3L)
- Adverse events

STATISTICAL CONSIDERATIONS

Power Calculations

The power and sample size calculation is based on the primary outcome measure of PFS. A median PFS time of 4.8 months is assumed on the control arm. This has been calculated from the raw data of the relevant population from a recent large UK study in SCLC (Lee et al 2009). The STOMP trial population will be those patients in the Lee study that were categorised as responders after 4 cycles of chemotherapy. This trial aims to detect an improvement in median PFS to 7.8 months for either of the two experimental arms. A one-tailed significance level of 10% was selected, however, to adjust for multiplicity in comparing the two experimental arms separately to the control arm, the calculation is based on a log rank test with a one-tailed significance level of 5% (equivalent to a two-tailed level of 10%).

The PFS analyses will be performed when approximately 105 events per comparison have occurred. With 105 events per comparison (assuming 1:1 randomisation) there is 80% power to detect a difference in treatments at a 5% 1-sided significance level, if the true (alternate) hazard ratio was hypothesised to be 0.62 (a reduction in risk of progression of 38%). If the median PFS in the control arm is expected to be 4.8 months, this equates to a 3 month increase in median PFS. Assuming 105 PFS events occur, an observed hazard ratio of 0.72 (a 28% reduction in risk of progression) will give a 1-sided p-value <0.05 within the trial (a hazard ratio of 0.72 corresponds to 1.9 month increase in median PFS, assuming exponential distribution and proportional hazards).

With the duration of the trial set as 2.5 years (24 months accrual and 6 months follow up) it is estimated that the trial will require 75 patients per treatment arm. Therefore in total a target recruitment of 225 patients is estimated to be required for this trial.

The sample size has been calculated employing the methodology for exponential survival using median survival times reported in Machin D, Campbell MJ, Tan SB, Tan SH: Sample Size Tables for Clinical Studies, 3rd Edition, 2009.

Analyses

The aim was to compare each of the olaparib schedules to the pooled placebo arm, subject to the placebo arms being sufficiently comparable to be combined.

For the primary outcome measure of progression PFS, the survivor function for each treatment arm was estimated using Kaplan-Meier method from which medians are reported with Greenwood's formula used for 90% confidence intervals (in line with the planned one-sided 5% significance level). For each olaparib regimen, the primary analysis tests the null hypothesis of no difference between olaparib and placebo using a stratified log-rank test (stratifying for M-status and prior radiotherapy). In addition, a Cox regression model adjusting for the stratification factors was applied. Regression coefficients from the model provided estimates of hazard ratios (HR) with two-sided 90% confidence intervals (CI) to compare treatment arms. All analyses of the primary outcome measure were based on an intention-to-treat principle (ITT).

OS was analysed using the same approach as PFS. PFS rates at 4 months and OS rates at 6 months were estimated from Kaplan-Meier with 90% confidence intervals. Changes in ECOG performance status and quality of life were analysed descriptively and restricted to the 6 month period from randomisation to incorporate the most clinically relevant survival period. In addition, the utility measures were used in a quality-adjusted survival analysis to report the quality-adjusted life months restricted to 6 months (QALM6) using an area under the curve approach. Incidence of common adverse events (i.e. recorded for ≥10% of trial patients) are reported together with any adverse events graded as 3 or more in >1 patient.

At the design stage, sample size determinations were based on the primary outcome measure of PFS. A median PFS of 4.8 months was assumed for the placebo arm based on relevant data shared from a large UK study in SCLC. Our trial was designed to detect an improvement in median PFS to 7.8 months (equivalent to a HR of 0.62) for either of the two olaparib regimens. As a phase II trial, a relaxed one-sided significance level of 10% was selected, however, this was halved to a one-sided 5% significance level to adjust for multiplicity of comparing two experimental arms separately to the pooled placebo arm. The trial required 105 events per comparison to ensure 80% power. Given the planned accrual time of 24 months and follow-up time of 6 months it was estimated that the trial needed approximately 75 patients per arm to observe this number of events.

Sub-group Analyses

Sensitivity analysis was performed including an analysis with pooling of the olaparib arms and a per-protocol population (i.e. all those that received at least one dose of study drug). In addition, a further sensitivity analysis was undertaken removing ineligible patients who had progressive disease after primary therapy and were randomised in error.

PATIENT SAFETY

This study was carried out in accordance with current guidelines for Good clinical Practice and the Declaration of Helsinki. The protocol gained ethical approval from the NRES Committee Yorkshire & The Humber - Leeds East. Before entering patients into the study, the Principal Investigator ensured that the protocol had approval from their local Research and Development (R&D) Office. Participants were provided with ethically approved comprehensive information about the trial and trial treatments, and given advice on who to contact with any questions or concerns at any time.

A participant's treatment response was determined by their treating physician who reviewed the patient every 4 weeks with: Physical examination, ECOG performance status, blood pressure, pulse and temperature measurements, haematological and biochemical tests, adverse event and concomitant medication reviews and alternate CT and X-ray scans. Prohibited concomitant therapies were listed in the olaparib Investigators Brochure and trial protocol. All concomitant therapies were required to be recorded. Any toxicity observed during the course of the trial was managed by dose interruption or permanent dose reduction if deemed appropriate by the treating physician and in accordance with the protocol. Participants of child bearing potential were required to agree to use two highly effective forms of contraception throughout their participation in the trial and for 3 months after last dose of trial drug.

The independent monitoring committee (IDMC) met on a yearly basis during the trial recruitment phase. The IDMC could consider discontinuing the trial if the recruitment rate or data quality were found to be unacceptable or if any issues are identified which may compromise patient safety.

TRIAL POPULATION

Patients with pathologically confirmed SCLC (M0 or M1a/b with any T or N stage) categorised as responders after completing ≥3 cycles of first line chemotherapy or chemo-radiotherapy with cisplatin/etoposide or carboplatin/etoposide.

Table 1. Baseline age characteristics by treatment group

	Placebo (74)	Olaparib BD (73)	Olaparib TDS (73)	Overall (220)
EudraCT Age Categorisation				
18-64	42 (57)	35 (48)	38 (52)	115 (52)
65-84	31 (42)	37 (51)	35 (48)	103 (47)
85+	1 (1)	1 (1)	0 (0)	2 (1)

SUBJECT DISPOSITION

ELIGIBILITY CRITERIA

Inclusion criteria

1. Pathologically confirmed SCLC (M0 or M1a/b with any T or N stage)
2. Completed ≥3 cycles of first line chemotherapy or chemo-radiotherapy with cisplatin + etoposide or carboplatin + etoposide
3. Complete Response (CR) or Partial Response (PR) to first line chemotherapy (Response Evaluation Criteria in Solid Tumours [RECIST] 1.1)
4. Eastern Co-operative Oncology Group (ECOG) (see Appendix 2) performance status 0-2, and a life expectancy of greater than 12 weeks
5. Resolution of all previous chemotherapy toxicity (except alopecia) to grade 1 or better
6. Adequate physiological function:
    - Calculated or measured creatinine clearance ≥ 50 ml/min (Cockcroft-Gault) and serum creatinine ≤ 1.5 x institutional upper limit of normal (ULN)
    - Haemoglobin (Hb) ≥ 100 g/L
    - White blood cells (WBC) ≥ $3x10^9$/L
    - Absolute neutrophil count (ANC) ≥ 1.5 x 10^9/L
    - Platelet count ≥ 100 x 10^9/L
    - Aspartate aminotransferase (AST) or alanine transaminase (ALT) ≤ 2.5 x institutional ULN unless liver metastases are present in which case it must be ≤ 5x ULN
    - Total bilirubin ≤ 1.5 x institutional ULN
7. Negative pregnancy test (for female patients of child-bearing potential)
8. Agrees to comply with contraceptive measures
9. Provision of written informed consent
10. Able to swallow oral medication
11. Patient is willing and able to comply with the protocol for the duration of the trial including undergoing treatment and scheduled visits and examinations

Exclusion criteria

1. Age ≤18 years
2. Interval from last anticancer treatment to start of trial treatment:
    - last radiotherapy fraction > 21 days*
    - start of final cycle of chemotherapy > 42 days*
    - radiotherapy must begin within 35 days of the start of the last chemotherapy cycle

*If sequential chemotherapy then radiotherapy then apply the interval for the last radiotherapy fraction. If concurrent chemotherapy and radiotherapy then ensure the trial treatment start date is within whichever is the later interval.

3. Patients with symptomatic uncontrolled brain metastases. A scan to confirm the absence of brain metastases is not required. The patient can receive a stable dose of corticosteroids before and during the trial as long as these were started at least 28 days prior to trial treatment

4. Interstitial lung disease
5. Previous malignancies (except curatively treated non-melanoma skin cancer or carcinoma in situ of the cervix or breast) within the past 3 years
6. History of malabsorption or major gastrointestinal tract resection likely to affect trial drug absorption
7. Treatment with any investigational product during the last 14 days (or a longer period depending on the defined characteristics of the agents used)
8. Any previous treatment with a PARP inhibitor, including olaparib
9. Patients receiving the following classes of inhibitors of CYP3A4 (see Section 6.4.2 for guidelines and wash out periods): azole antifungals, macrolide antibiotics, protease inhibitors
10. Patients considered a poor medical risk due to a serious, uncontrolled medical disorder, non-malignant systemic disease or active, uncontrolled infection. Examples include, but are not limited to, uncontrolled ventricular arrhythmia, recent (within 3 months) myocardial infarction, uncontrolled major seizure disorder, unstable spinal cord compression, superior vena cava syndrome, or any psychiatric disorder that prohibits obtaining informed consent
11. Breast feeding women
12. Immunocompromised patients, e.g. patients who are known to be serologically positive for human immunodeficiency virus (HIV)
13. Patients with known active hepatic disease (i.e., Hepatitis B or C)
14. Patients with a known hypersensitivity to olaparib or any of the excipients of the product
15. Patients with uncontrolled seizures
16. Patients with myelodysplastic syndrome (MDS) / acute myeloid leukaemia (AML)
17. Major surgery within 14 days of starting trial treatment and patients must have recovered from any effects of any major surgery

RECRUITMENT

Screening

A total of 831 patients were screened (one patient twice in error), with 397 patients not meeting eligibility criteria, 99 patients declining and 115 patients not entering for other reasons. A total of 220 patients were randomised.

Randomisation

The first patient was randomised into the STOMP trial on the 21st November 2013 and the last patient on the 11th December 2015.

A total of 220 patients were randomised into STOMP. One of these patients was randomised into the trial too early, however, they subsequently met eligibility criteria and were re-randomised. Data from this patient's initial randomisation was not included in the analysis.

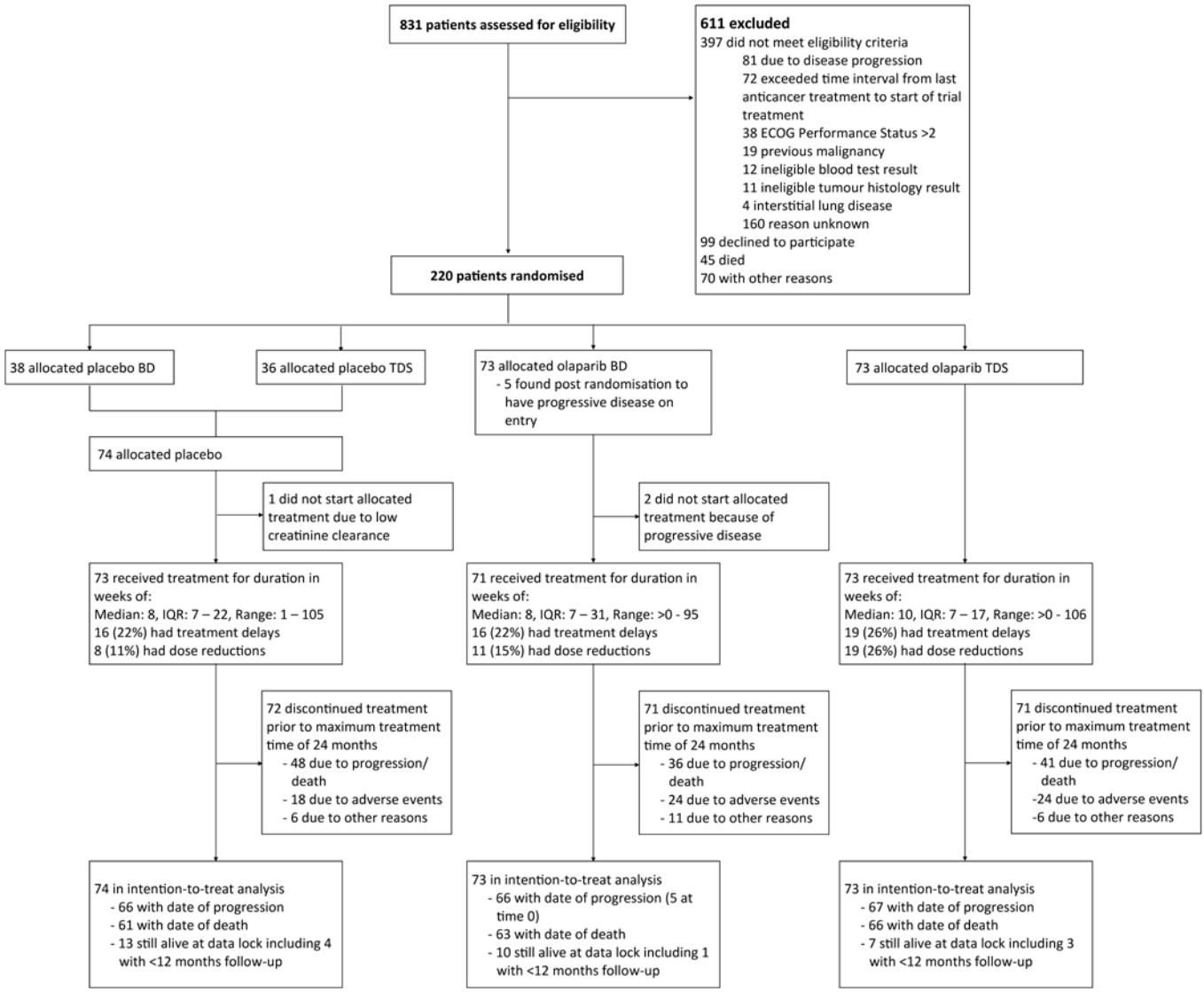


Figure 2. STOMP CONSORT Diagram

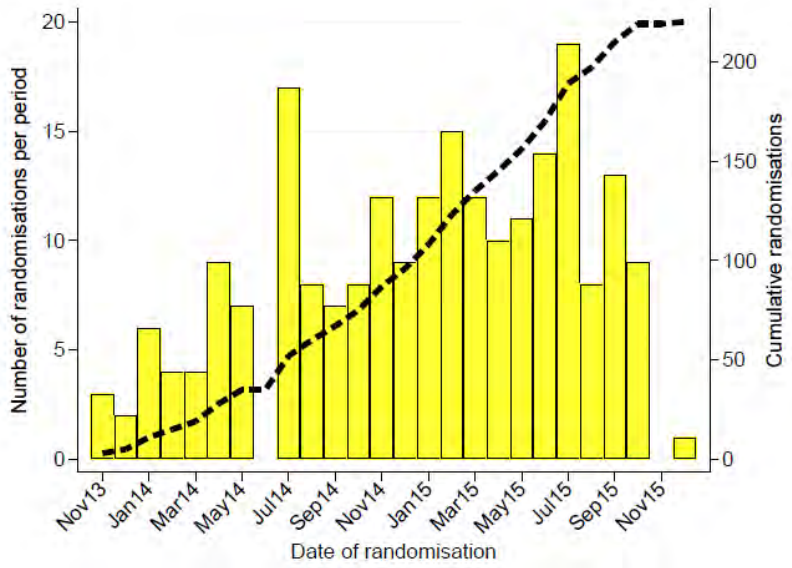


Figure 3. Numbers of patients randomised into the STOMP trial and cumulative recruitment

Table 2. Randomising centres by treatment

Treatment	Placebo (74)	Olaparib BD (73)	Olaparib TDS (73)	Overall (220)
Centre				
Weston Park Hospital	5 (7)	10 (14)	6 (8)	21 (10)
Beatson West of Scotland Cancer Centre	7 (9)	6 (8)	5 (7)	18 (8)
Leicester Royal Infirmary	6 (8)	4 (5)	3 (4)	13 (6)
St James's University Hospital	4 (5)	3 (4)	6 (8)	13 (6)
Maidstone Hospital	4 (5)	4 (5)	3 (4)	11 (5)
Aberdeen Royal Infirmary	3 (4)	3 (4)	3 (4)	9 (4)
Royal Marsden Hospital Sutton	4 (5)	2 (3)	2 (3)	8 (4)
Addenbrooke's Hospital	4 (5)	2 (3)	2 (3)	8 (4)
Guy's Hospital	3 (4)	3 (4)	2 (3)	8 (4)
Western General Hospital	4 (5)	1 (1)	3 (4)	8 (4)
Southampton General Hospital	1 (1)	5 (7)	2 (3)	8 (4)
Huddersfield Royal Infirmary	0 (0)	2 (3)	5 (7)	7 (3)
Velindre Hospital	5 (7)	0 (0)	1 (1)	6 (3)
Christie Hospital	3 (4)	1 (1)	2 (3)	6 (3)
Airedale General Hospital	3 (4)	3 (4)	0 (0)	6 (3)
Royal Bournemouth Hospital	4 (5)	1 (1)	1 (1)	6 (3)
New Cross Hospital	1 (1)	2 (3)	2 (3)	5 (2)
Royal Lancaster Infirmary	1 (1)	1 (1)	3 (4)	5 (2)
Bristol Haematology And Oncology Centre	3 (4)	1 (1)	1 (1)	5 (2)
Princess Royal University Hospital	1 (1)	1 (1)	3 (4)	5 (2)
Pilgrim Hospital	0 (0)	2 (3)	2 (3)	4 (2)
Derriford Hospital	0 (0)	2 (3)	2 (3)	4 (2)
University Hospital Lewisham	1 (1)	0 (0)	3 (4)	4 (2)
Nottingham City Hospital	1 (1)	2 (3)	1 (1)	4 (2)
Queen's Hospital	0 (0)	2 (3)	1 (1)	3 (1)
Royal Derby Hospital	0 (0)	1 (1)	2 (3)	3 (1)
North Devon District Hospital	0 (0)	2 (3)	1 (1)	3 (1)
Royal Marsden Hospital London	1 (1)	1 (1)	1 (1)	3 (1)
Bradford Royal Infirmary	0 (0)	2 (3)	1 (1)	3 (1)
Raigmore Hospital	1 (1)	0 (0)	1 (1)	2 (1)
King's Mill Hospital	0 (0)	2 (3)	0 (0)	2 (1)
Harrogate District Hospital	1 (1)	0 (0)	1 (1)	2 (1)
Birmingham Heartlands Hospital	1 (1)	0 (0)	1 (1)	2 (1)
The Queen Elizabeth Hospital	1 (1)	0 (0)	1 (1)	2 (1)
Lincoln County Hospital	1 (1)	1 (1)	0 (0)	2 (1)
Conquest Hospital	0 (0)	1 (1)	0 (0)	1 (0)
Total	74 (100)	73 (100)	73 (100)	220 (100)

Withdrawals

In total, of 220 trial patients, 7 patients withdrew from the trial.

Table 3. Patients who withdrew consent to any further involvement in STOMP trial

Treatment	Placebo (74)	Olaparib BD (73)	Olaparib TDS (73)	Overall (220)
Patient wishes				
Patient has not withdrawn consent to further data	71 (96)	72 (99)	70 (96)	213 (97)
Patient would like to withdraw from trial and is not willing for further data to be supplied to the Trials Office	3 (4)	1 (1)	3 (4)	7 (3)
Time to Withdrawal from Randomisation (months)				
N	3	1	3	7
Mean (sd)	3 (4)	2 (.)	3 (1)	3 (2)
Median	1	2	3	2
IQR	0, 8	2, 2	2, 4	1, 4
Range	0, 8	2, 2	2, 4	0, 8

BASELINE CHARACTERISTICS

AGE & GENDER

Table 4. Baseline age and sex by treatment group

Treatment	Placebo (74)	Olaparib BD (73)	Olaparib TDS (73)	Overall (220)
Age (years)				
N	74	73	73	220
Mean (sd)	63 (8)	64 (9)	62 (9)	63 (9)
Median	64	66	63	64
IQR	58, 68	58, 70	55, 69	57, 69
Range	43, 86	43, 89	42, 82	42, 89
Sex				
Male	34 (46)	36 (49)	31 (42)	101 (46)
Female	40 (54)	37 (51)	42 (58)	119 (54)

STUDY SPECIFIC CHARACTERISTICS

Table 5. Overview of baseline characteristics

	Placebo N = 74	**Olaparib BD N = 73**	**Olaparib TDS N = 73**
Time from diagnosis to randomisation			
Weeks, median (range)	22 (15, 34)	25 (16, 38)	24 (15, 32)
Chemotherapy regimen			
Carboplatin, etoposide	52 (70%)	56 (77%)	54 (74%)
Cisplatin, etoposide	18 (24%)	16 (22%)	13 (18%)
Cisplatin, carboplatin, etoposide	4 (5%)	1 (1%)	6 (8%)
Chemotherapy, number of cycles			
3	1 (1%)	0	2 (3%)
4	31 (42%)	27 (37%)	23 (32%)
5	5 (7%)	3 (4%)	4 (5%)
6	37 (50%)	43 (59%)	44 (60%)
Radiotherapy schedule			
Concurrent	10 (14%)	6 (8%)	4 (5%)
Sequential	57 (77%)	57 (78%)	61 (84%)
None	7 (9%)	10 (14%)	8 (11%)
Radiotherapy sites			
Thoracic & cranial	40 (54%)	33 (45%)	36 (49%)
Thoracic only	2 (3%)	5 (7%)	5 (7%)
Cranial only	25 (34%)	25 (34%)	24 (33%)
None	7 (9%)	10 (14%)	8 (11%)
Response to primary treatment			
Complete response	5 (7%)	4 (5%)	7 (10%)
Partial response	69 (93%)	64 (88%)	66 (90%)
Progression	0	5 (7%)	0

ECOG performance status			
0	18 (24%)	17 (23%)	25 (34%)
1	48 (65%)	51 (70%)	44 (60%)
2	8 (11%)	5 (7%)	3 (4%)
Not known	0	0	1 (1%)

Table 6. TNM staging at diagnosis

Treatment	Placebo (74)	Olaparib BD (73)	Olaparib TDS (73)	Overall (220)
T-stage at diagnosis				
TX	4 (5)	4 (5)	1 (1)	9 (4)
T0	0 (0)	1 (1)	2 (3)	3 (1)
T1	3 (4)	5 (7)	5 (7)	13 (6)
T1a	3 (4)	1 (1)	3 (4)	7 (3)
T1b	2 (3)	0 (0)	3 (4)	5 (2)
T2	4 (5)	2 (3)	3 (4)	9 (4)
T2a	4 (5)	3 (4)	4 (5)	11 (5)
T2b	0 (0)	5 (7)	1 (1)	6 (3)
T3	18 (24)	20 (27)	13 (18)	51 (23)
T4	36 (49)	32 (44)	38 (52)	106 (48)
N-stage at diagnosis				
NX	2 (3)	0 (0)	0 (0)	2 (1)
N0	4 (5)	5 (7)	3 (4)	12 (5)
N1	9 (12)	6 (8)	4 (5)	19 (9)
N2	24 (32)	28 (38)	29 (40)	81 (37)
N3	35 (47)	34 (47)	37 (51)	106 (48)
M-stage at diagnosis				
M0	21 (28)	22 (30)	23 (32)	66 (30)
M1a	6 (8)	6 (8)	5 (7)	17 (8)
M1b	47 (64)	45 (62)	45 (62)	137 (62)

ENDPOINTS

DEFINITIONS

Progression-free survival time

PFS time is defined as the interval in whole days between the date of randomisation into the trial and either the earliest date of detection of progression or date of death without recorded progression. For those patients who neither died nor experienced progression during the course of the trial, PFS time will be censored at the date when they were last known to be alive and free of progression.

A PFS event is defined as the earliest of the following:

- Progression reported as a result of CT scan in accordance with RECIST v1.1. Essentially an increase by 20% in the sum of tumour diameters or the appearance of new lesions
- If progression is suspected by an abnormal chest X-ray and subsequently confirmed by the immediate next CT scan then the date of progression will be taken as the date of the chest X-ray. NB: If the subsequent CT scan does not show progression then the patient will not be considered to have progressed at the abnormal chest X-ray time point.

- If unequivocal progression is detected by a method other than a CT scan or Chest X-ray then the date of that assessment shall be taken as the date of progression. E.g. Brain scan, Bone scan, clinical progression.
- Death

Overall survival time/ rate

OS time is defined as the interval in whole days between the date of randomisation into the trial and date of death from any cause. Patients who did not die during the course of the trial will be censored at the date when they were last known to be alive.

Changes in performance status

ECOG performance status (PS) is collected on the baseline and treatment CRFs. The PS can be 0, 1 or 2 at baseline. On the treatment CRFs PS can range from 0 to 5.

The PS scores are as follows:

0 - Fully active, able to carry on all pre-disease performance without restriction

1 - Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g. light house work, office work

2 - Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours

3 - Capable of only limited self-care, confined to bed or chair more than 50% of waking hours

4 - Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair

5 - Dead

Quality of life (EQ-5D-3L)

The EQ-5D-3L overall utility score is determined from the answers given to the 5 individual questions in accordance with the scoring manual. The EQ-5D questionnaire also has a thermometer component asking the patient to evaluate their health status on a continuous scale of 0-100.

Adverse event

Any untoward medical occurrence in a patient or clinical trial subject administered a medicinal product and which does not necessarily have a causal relationship with this treatment. These events are graded according to the National Cancer Institute CTCAE v4.0.

Serious adverse event

Any untoward medical occurrence or effect that at any dose:

- Results in death (unrelated to original cancer)
- Is life-threatening
- Requires hospitalisation or prolongation of existing inpatients' hospitalisation
- Results in persistent or significant disability or incapacity
- Is a congenital anomaly/birth defect
- Or is otherwise considered medically significant by the Investigator

For the purposes of the STOMP trial, development of MDS/AML is considered significant and should be reported as an SAE

Primary Outcome

Progression-free survival & progression-free rate at 4 months from randomisation (secondary outcome)

There have been 132 PFS events in the Olaparib BD vs Placebo comparison (66 on Olaparib BD and 66 on Placebo). There have been 133 PFS events in the Olaparib TDS vs Placebo comparison (67 on Olaparib TDS and 66 on Placebo). Median PFS in months and weeks are reported in the tables below.

Table 7. PFS outcomes

Treatment	Median PFS (months)	4m PFS rate
Placebo	2.50 (90%CI; 1.81, 3.68)	36% (90%CI; 27, 45)
Olaparib BD	3.65 (90%CI; 3.12, 4.60)	45% (90%CI; 35, 54)
Olaparib TDS	3.58 (90%CI; 2.79, 4.67)	45% (90%CI; 35, 54)

Table 8. Median PFS (weeks)

Treatment	Median PFS (weeks)
Placebo	10.86 (90%CI; 7.86, 16.00)
Olaparib BD	15.86 (90%CI; 13.57, 20.00)
Olaparib TDS	15.57 (90%CI; 12.14, 20.29)

The p-values below were determined using a stratified log-rank test for the stratification factors of disease extent (M stage) at diagnosis and prior radiotherapy.

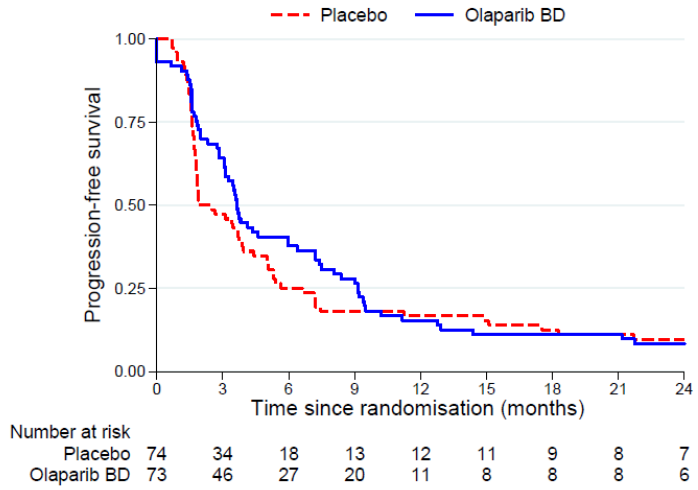
Table 9. Stratified log-rank p-values for PFS

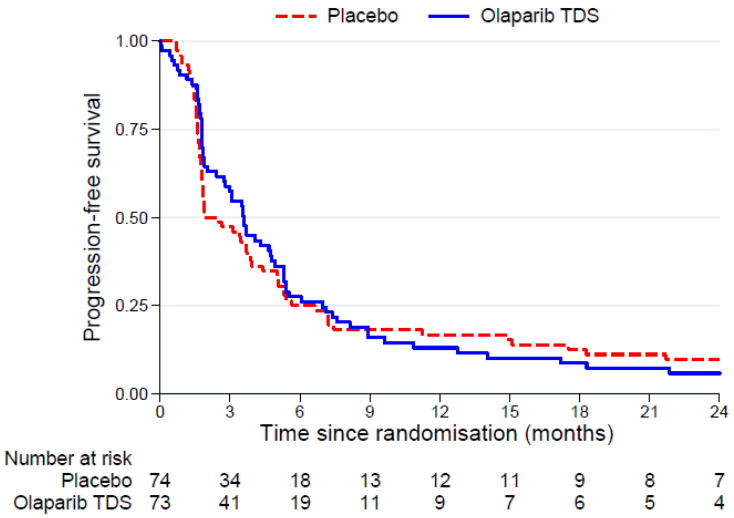
Treatment comparison	p-value
Olaparib BD vs. Placebo	0.1801
Olaparib TDS vs. Placebo	0.1641

The hazard ratios are generated from a Cox model adjusted for the stratification factors of disease extent (M stage) at diagnosis and prior radiotherapy.

Table 10. Hazard ratios for PFS

Treatment comparison	Hazard Ratio (90%CI)	p-value
Olaparib BD vs. Placebo	0.76 (90%CI; 0.57, 1.02)	0.125
Olaparib TDS vs. Placebo	0.86 (90%CI; 0.64, 1.15)	0.402





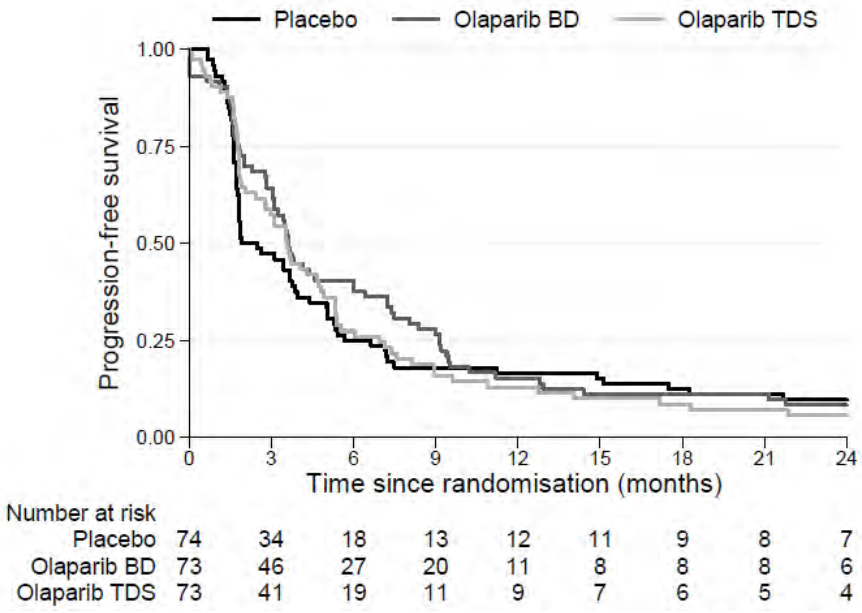


Figure 4. Kaplan-Meier plot of Progression-free survival to compare placebo to Olaparib BD and TDS

The tables below report analyses where the survival times for patients who had progressed prior to randomisation were censored. There have been 127 PFS events in the Olaparib BD vs Placebo comparison. There have been 133 PFS events in the Olaparib TDS vs Placebo comparison.

Table 11. Progression free survival outcomes for sensitivity analysis

Treatment	Median PFS (months)	4m PFS
Placebo	2.50 (90%CI; 1.81, 3.68)	36% (90%CI; 27, 45)
Olaparib BD	3.75 (90%CI; 3.45, 6.41)	48% (90%CI; 38, 58)
Olaparib TDS	3.58 (90%CI; 2.79, 4.67)	45% (90%CI; 35, 54)

Table 12. Median progression free survival (weeks) for sensitivity analysis with patients progressed at randomisation censored

Treatment	Median PFS (weeks)
Placebo	10.86 (90%CI; 7.86, 16.00)
Olaparib BD	16.29 (90%CI; 15.00, 27.86)
Olaparib TDS	15.57 (90%CI; 12.14, 20.29)

The hazard ratios are generated from a Cox model adjusted for the stratification factors of disease extent (M stage) at diagnosis and prior radiotherapy.

Table 13. Hazard ratios for progression free survival sensitivity analysis with patients progressed at randomisation censored

Treatment	Hazard Ratio (90%CI)	p-value
Olaparib BD	0.69 (90%CI; 0.51, 0.93)	0.043
Olaparib TDS	0.86 (90%CI; 0.64, 1.15)	0.385

Secondary outcome measures

Progression-free rate at 4 months from randomisation – see above

Overall survival time & overall survival at 6 months

There have been 124 OS events in the Olaparib BD vs Placebo comparison (63 Olaparib BD and 61 Placebo events). There have been 127 OS events in the Olaparib TDS vs Placebo comparison (66 Olaparib TDS and 61 Placebo events).

Table 14. Overall survival outcomes

Treatment	Median OS (months)	6m OS	12m OS
Placebo	9.69 (90%CI; 7.13, 12.19)	66% (90%CI; 56, 75)	42% (90%CI; 32, 51)
Olaparib BD	11.01 (90%CI; 7.85, 12.94)	69% (90%CI; 60, 77)	42% (90%CI; 32, 51)
Olaparib TDS	9.63 (90%CI; 6.80, 11.76)	66% (90%CI; 56, 75)	39% (90%CI; 29, 48)

Table 15. Median overall survival (weeks)

Treatment	Median OS (weeks)
Placebo	42.14 (90%CI; 31.00, 53.00)
Olaparib BD	47.86 (90%CI; 34.14, 56.29)
Olaparib TDS	41.86 (90%CI; 29.57, 51.14)

The p-values below were determined using a stratified log-rank test for the stratification factors of disease extent (M stage) at diagnosis and prior radiotherapy.

Table 16. Stratified log-rank p-values for overall survival

Treatment comparison	p-value
Olaparib BD vs. Placebo	0.7094
Olaparib TDS vs. Placebo	0.9904

The hazard ratios are generated from a Cox model adjusted for the stratification factors of disease extent (M stage) at diagnosis and prior radiotherapy.

Table 17. Hazard ratios for overall survival

Treatment	Hazard Ratio (90%CI)	p-value
Olaparib BD	0.85 (90%CI; 0.63, 1.15)	0.376
Olaparib TDS	1.03 (90%CI; 0.77, 1.39)	0.850

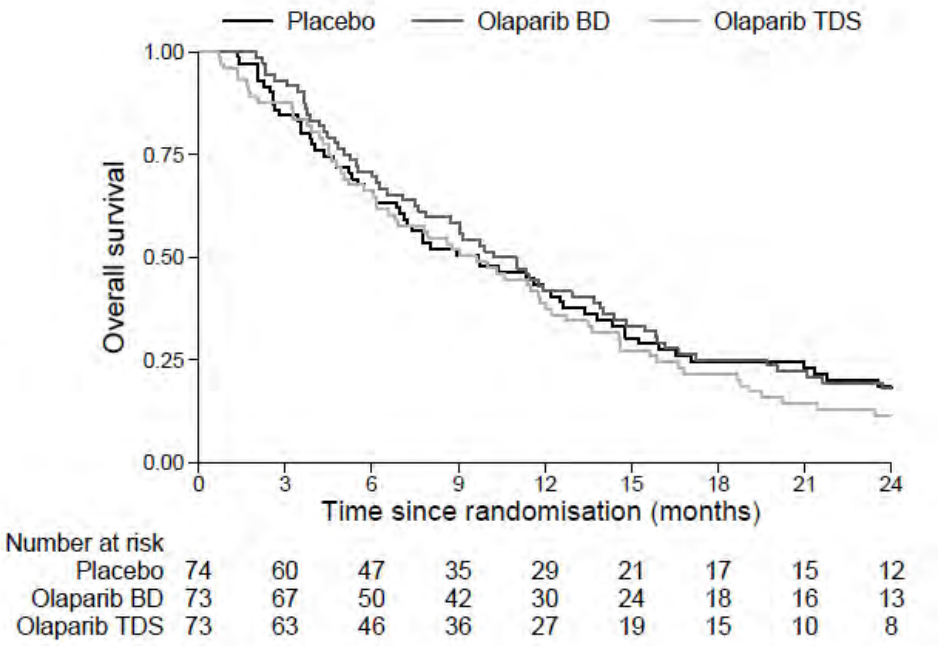


Figure 5. Kaplan-Meier plot of overall survival to compare placebo to olaparib BD and TDS

Overall survival rate at 6 months – see above

Changes in performance status

The plots below present changes in ECOG performance status over time in the three treatment groups

Quality of life (EQ-5D-3L)

The utility scores were used in a quality-adjusted survival analysis to report the quality-adjusted life months restricted to 6 months (QALM6) using an area under the curve (AUC) approach. At this point 70 of the 220 patients had died. The time period selected (6 months) was deemed clinically relevant.

The AUC calculation was performed for each patient with the following assumptions bring made;

- if a patient has died then their EQ-5D scores (Utility and Thermometer) were imputed as 0 at the date of death.
- if a patient has missed a QoL completion point then the data can be interpolated between those scores.
- if a patient is censored alive then their QoL was carried forward from their last completed form to 183 days (i.e. 6 months)

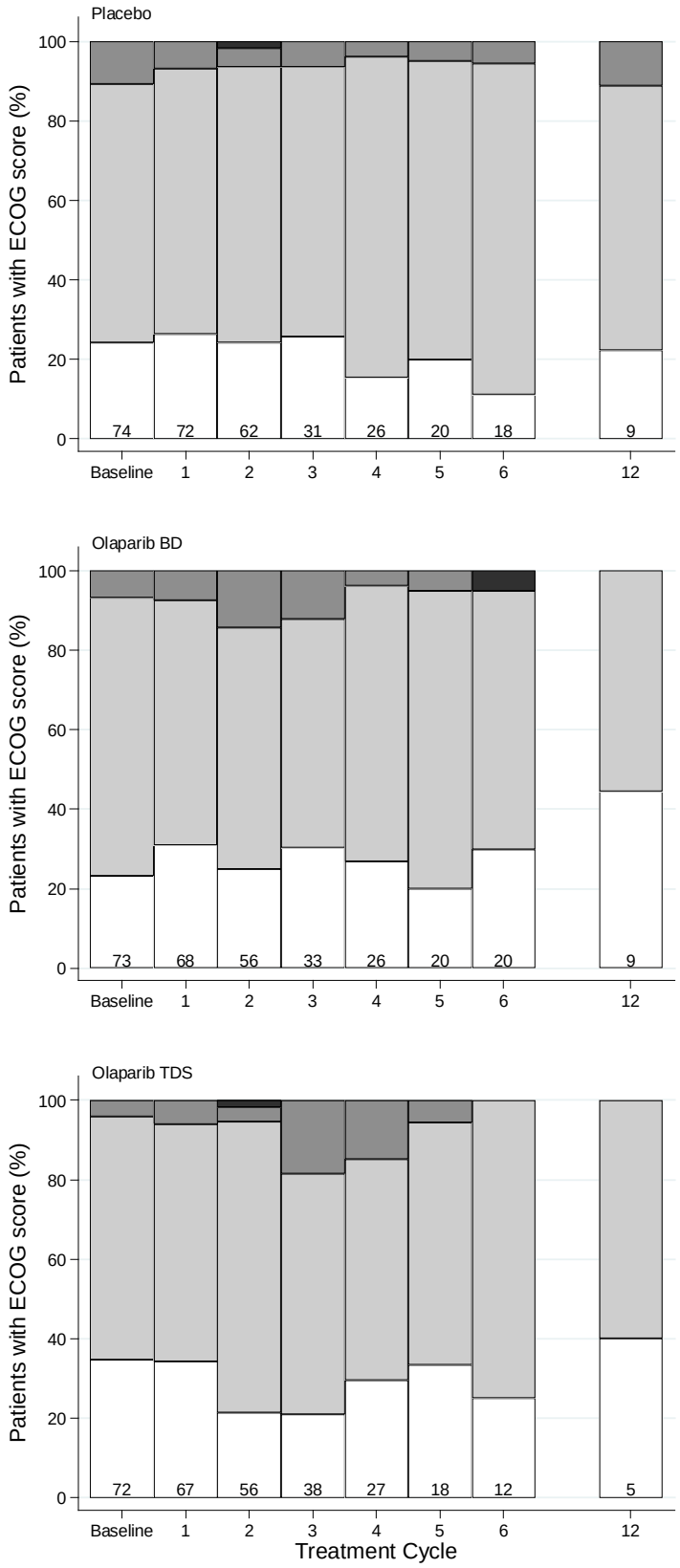
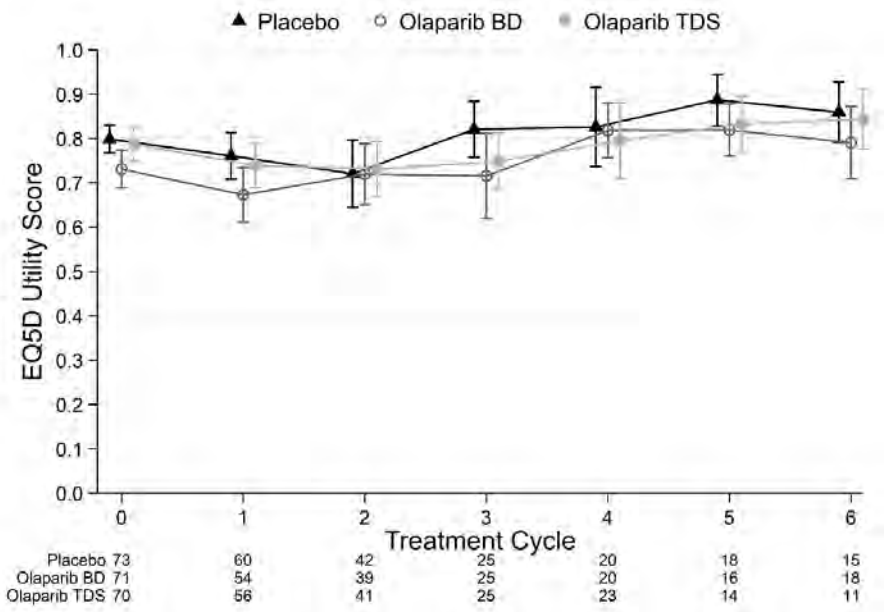


Figure 6. Change in ECOG performance status over time in the three treatment groups. Top: placebo; middle: olaparib BD; bottom: Olaparib TDS. White = performance status 0, light = performance status 1, dark = performance status 2, black = performance status 3. Numbers of patients included at each time point are shown at the bottom of each bar.

Table 18. Quality-Adjusted Life Months – at 6 months (QALM6)

Treatment	Utility QALM (90%CI)	Thermometer QALM (90%CI)
Placebo	3.16 (90%CI; 2.80, 3.52)	292.25 (90%CI; 259.21, 325.30)
Olaparib BD	2.98 (90%CI; 2.65, 3.31)	301.60 (90%CI; 273.38, 329.82)
Olaparib TDS	3.21 (90%CI; 2.87, 3.56)	294.13 (90%CI; 264.37, 323.89)

(A)



(B)

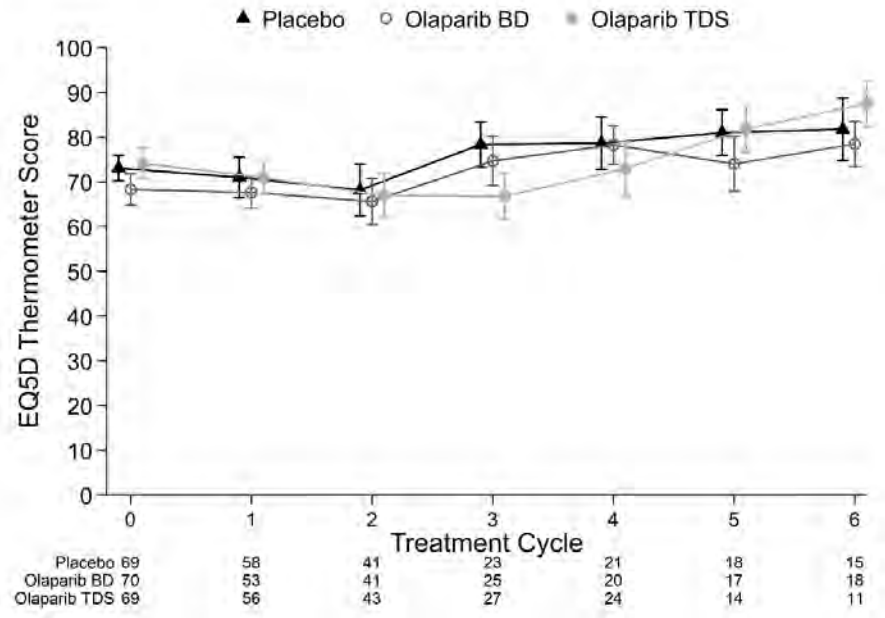


Figure 7: Quality of life measures over time from EQ-5D-3L questionnaires. (A) EQ-5D-3L utility measures – means and 90% CI. (B) EQ-5D-3L visual analogue scores – means and 90% CI.

ADVERSE EVENTS

ADVERSE EVENTS

There were 2 reported grade 5 (fatal) events within the STOMP trial. One patient (placebo) died suddenly due to unknown cause and one patient (Olaparib TDS) died from a stroke.

Any adverse events that were classified under the CTCAE, version 4.0 category "Investigations" at grade 1 or 2 were not required to be reported as part of a protocol amendment and are therefore not included within this report. Therefore, any adverse events documented in the Investigations section will only be grade 3 or above.

Table 19. Summary of adverse events for ITT and per protocol analyses

(a) Summary for ITT analyses

Treatment	Placebo (74)	Olaparib BD (73)	Olaparib TDS (73)	Overall (220)
Patient reported any adverse event post randomisation				
No AEs	2 (3)	3 (4)	1 (1)	6 (3)
AEs experienced	72 (97)	70 (96)	72 (99)	214 (97)
Patient reported any grade 3 or above adverse event post randomisation				
No G3 or above AEs	41 (55)	35 (48)	37 (51)	113 (51)
G3 or above AEs experienced	33 (45)	38 (52)	36 (49)	107 (49)

(b) Summary for patients who had at least 1 dose of treatment

Treatment	Placebo (73)	Olaparib BD (71)	Olaparib TDS (73)	Overall (217)
Patient reported any adverse event post randomisation				
No AEs	1 (1)	1 (1)	1 (1)	3 (1)
AEs experienced	72 (99)	70 (99)	72 (99)	214 (99)
Patient reported any grade 3 or above adverse event post randomisation				
No G3 or above AEs	40 (55)	33 (46)	37 (51)	110 (51)
G3 or above AEs experienced	33 (45)	38 (54)	36 (49)	107 (49)

Table 20. All grade 3 and above adverse events occurring at least twice on the STOMP trial

CTCAE Category	Toxicity	Placebo	Olaparib BD	Olaparib TDS	Sum
General disorders and administration site conditions	Fatigue	14	20	11	45
Investigations	Lymphocyte count decreased	0	20	19	39
Metabolism and nutrition disorders	Hyponatremia	11	12	6	29
Blood and lymphatic system disorders	Anemia	0	5	20	25
Vascular disorders	Hypertension	9	1	11	21
Investigations	Platelet count decreased	2	7	7	16
Investigations	Neutrophil count decreased	0	10	4	14
Vascular disorders	Thromboembolic event	3	8	3	14
Infections and infestations	Lung infection	7	1	4	12
Respiratory, thoracic and mediastinal disorders	Dyspnea	6	1	4	11
Gastrointestinal disorders	Nausea	3	2	3	8
Gastrointestinal disorders	Diarrhea	5	1	2	8
Injury, poisoning and procedural complications	Spinal fracture	7	0	0	7
Gastrointestinal disorders	Vomiting	4	0	2	6
Musculoskeletal and connective tissue disorders	Back pain	2	0	3	5
Investigations	White blood cell decreased	0	4	1	5
Metabolism and nutrition disorders	Anorexia	0	2	3	5
Skin and subcutaneous tissue disorders	Dry skin	0	3	0	3
Metabolism and nutrition disorders	Dehydration	1	1	1	3
Investigations	GGT increased	1	1	1	3
Psychiatric disorders	Confusion	2	1	0	3
Musculoskeletal and connective tissue disorders	Muscle weakness lower limb	0	1	2	3
Musculoskeletal and connective tissue disorders	Flank pain	1	1	1	3
Metabolism and nutrition disorders	Hypomagnesemia	3	0	0	3
Infections and infestations	Urinary tract infection	1	0	1	2
Skin and subcutaneous tissue disorders	Pruritus	2	0	0	2
Nervous system disorders	Neuralgia	2	0	0	2
Nervous system disorders	Seizure	0	0	2	2
Gastrointestinal disorders	Dyspepsia	0	2	0	2
Investigations	Specified as C-reactive protein increased	0	0	2	2
Gastrointestinal disorders	Dysphagia	0	1	1	2
Infections and infestations	Sepsis	1	1	0	2
Nervous system disorders	Stroke	1	0	1	2
Investigations	Alanine aminotransferase increased	1	0	1	2
Respiratory, thoracic and mediastinal disorders	Specified as Pneumonia	0	0	2	2
Nervous system disorders	Headache	0	2	0	2

Table 21. All grade 3 and above adverse events occurring at least twice on the STOMP trial

CTCAE Category	Toxicity	Placebo	Olaparib BD	Olaparib TDS	Sum
Blood and lymphatic system disorders	Specified as Neutropenic sepsis	0	0	1	1
Ear and labyrinth disorders	Hearing impaired	0	0	1	1
General disorders and administration site conditions	Gait disturbance	0	1	0	1
Musculoskeletal and connective tissue disorders	Generalized muscle weakness	1	0	0	1
Respiratory, thoracic and mediastinal disorders	Pleural effusion	1	0	0	1
Investigations	Aspartate aminotransferase increased	1	0	0	1
Vascular disorders	Superior vena cava syndrome	1	0	0	1
Gastrointestinal disorders	Rectal hemorrhage	0	0	1	1
Cardiac disorders	Atrial fibrillation	0	1	0	1
Injury, poisoning and procedural complications	Specified as Injury to right side of chest	1	0	0	1
Musculoskeletal and connective tissue disorders	Muscle weakness right-sided	0	0	1	1
Nervous system disorders	Dysarthria	0	0	1	1
Respiratory, thoracic and mediastinal disorders	Pneumonitis	0	0	1	1
General disorders and administration site conditions	Specified as Deteriorating condition	0	1	0	1
Nervous system disorders	Peripheral sensory neuropathy	0	1	0	1
Psychiatric disorders	Insomnia	0	0	1	1
Renal and urinary disorders	Urinary incontinence	1	0	0	1
Injury, poisoning and procedural complications	Specified as Splenic rupture	1	0	0	1
Nervous system disorders	Paresthesia	0	0	1	1
Cardiac disorders	Heart failure	0	1	0	1
Infections and infestations	Upper respiratory infection	0	1	0	1
Gastrointestinal disorders	Mucositis oral	0	0	1	1
General disorders and administration site conditions	Sudden death NOS	1	0	0	1
Metabolism and nutrition disorders	Hypokalemia	0	0	1	1
Vascular disorders	Hypotension	0	0	1	1
Gastrointestinal disorders	Constipation	0	0	1	1
Gastrointestinal disorders	Specified as Melaena	0	0	1	1
Musculoskeletal and connective tissue disorders	Specified as Cord compression	1	0	0	1
Metabolism and nutrition disorders	Hypophosphatemia	1	0	0	1
Respiratory, thoracic and mediastinal disorders	Hypoxia	0	0	1	1
Gastrointestinal disorders	Esophageal stenosis	0	0	1	1
Respiratory, thoracic and mediastinal disorders	Respiratory failure	1	0	0	1

The following two tables (Tables 22 and 23) report p-values in order to highlight adverse events that may need to be brought to the attention of the clinical community, however they are not provided for the purposes of formal statistical analyses or decision making.

Table 22. Adverse event categories and toxicities where the number of intention to treat patients with the event was >5% in either Placebo or Olaparib arm (or both)

	Placebo (N=73)	Olaparib BD (N=71)	p-value	Olaparib TDS (N=73)	p-value
Anemia	15 (21%)	37 (52%)	**0.000**	41 (56%)	**0.000**
Sinus tachycardia	4 (5%)	0 (0%)	0.120	1 (1%)	0.366
Abdominal pain	6 (8%)	6 (8%)	0.980	8 (11%)	0.556
Bloating	2 (3%)	4 (6%)	0.442	1 (1%)	1.000
Constipation	19 (26%)	16 (23%)	0.593	14 (19%)	0.345
Diarrhea	18 (25%)	13 (18%)	0.333	12 (16%)	0.236
Dry mouth	3 (4%)	1 (1%)	0.620	7 (10%)	0.183
Dyspepsia	13 (18%)	11 (15%)	0.682	6 (8%)	0.091
Dysphagia	5 (7%)	5 (7%)	1.000	3 (4%)	0.719
Mucositis oral	10 (14%)	7 (10%)	0.457	2 (3%)	**0.017**
Nausea	44 (60%)	47 (66%)	0.539	51 (70%)	0.187
Stomach pain	2 (3%)	3 (4%)	0.681	5 (7%)	0.275
Vomiting	21 (29%)	25 (35%)	0.443	33 (45%)	**0.034**
Fatigue	55 (75%)	64 (90%)	**0.039**	58 (79%)	0.461
Non-cardiac chest pain	9 (12%)	10 (14%)	0.781	3 (4%)	0.075
Pain	6 (8%)	3 (4%)	0.494	5 (7%)	0.772
Lung infection	12 (16%)	14 (20%)	0.638	12 (16%)	0.971
Mucosal infection	6 (8%)	7 (10%)	0.752	4 (5%)	0.527
Upper respiratory infection	5 (7%)	7 (10%)	0.531	7 (10%)	0.531
Urinary tract infection	3 (4%)	3 (4%)	1.000	6 (8%)	0.327
Lymphocyte count decreased	0 (0%)	8 (11%)	**0.003**	9 (12%)	**0.001**
Neutrophil count decreased	0 (0%)	5 (7%)	**0.028**	2 (3%)	0.245
Platelet count decreased	2 (3%)	4 (6%)	0.442	5 (7%)	0.275
Anorexia	30 (41%)	34 (48%)	0.461	28 (38%)	0.786
Hyperglycemia	4 (5%)	2 (3%)	0.681	6 (8%)	0.498
Hypoalbuminemia	4 (5%)	4 (6%)	1.000	7 (10%)	0.335
Hypocalcemia	2 (3%)	9 (13%)	**0.027**	3 (4%)	0.681
Hypokalemia	4 (5%)	4 (6%)	1.000	4 (5%)	1.000
Hypomagnesemia	5 (7%)	2 (3%)	0.442	1 (1%)	0.209
Hyponatremia	12 (16%)	7 (10%)	0.231	10 (14%)	0.669
Arthralgia	17 (23%)	6 (8%)	**0.014**	9 (12%)	0.091
Back pain	18 (25%)	13 (18%)	0.333	14 (19%)	0.450
Bone pain	7 (10%)	2 (3%)	0.166	0 (0%)	**0.013**
Joint effusion	2 (3%)	5 (7%)	0.275	4 (5%)	0.442
Myalgia	4 (5%)	2 (3%)	0.681	3 (4%)	1.000
Pain in extremity	2 (3%)	13 (18%)	**0.002**	5 (7%)	0.275
Dizziness	14 (19%)	16 (23%)	0.652	15 (21%)	0.804
Dysgeusia	12 (16%)	12 (17%)	0.971	12 (16%)	0.971
Headache	18 (25%)	19 (27%)	0.812	17 (23%)	0.883
Paresthesia	5 (7%)	2 (3%)	0.442	7 (10%)	0.531
Peripheral sensory neuropathy	2 (3%)	4 (6%)	0.442	4 (5%)	0.442
Anxiety	8 (11%)	2 (3%)	0.097	4 (5%)	0.238
Confusion	3 (4%)	1 (1%)	0.620	5 (7%)	0.494
Depression	7 (10%)	7 (10%)	0.979	6 (8%)	0.791
Insomnia	10 (14%)	8 (11%)	0.637	5 (7%)	0.182
Cough	26 (36%)	22 (31%)	0.518	25 (34%)	0.910
Dyspnea	21 (29%)	26 (37%)	0.347	28 (38%)	0.199
Productive cough	1 (1%)	4 (6%)	0.209	4 (5%)	0.209
Wheezing	5 (7%)	2 (3%)	0.442	2 (3%)	0.442
Alopecia	11 (15%)	13 (18%)	0.629	16 (22%)	0.270
Dry skin	5 (7%)	6 (8%)	0.736	4 (5%)	1.000
Pruritus	7 (10%)	4 (6%)	0.359	4 (5%)	0.359
Rash maculo-papular	8 (11%)	5 (7%)	0.398	5 (7%)	0.398
Hypertension	8 (11%)	5 (7%)	0.398	4 (5%)	0.238
Hypotension	1 (1%)	1 (1%)	1.000	4 (5%)	0.209
Thromboembolic event	3 (4%)	3 (4%)	1.000	6 (8%)	0.327

Table 23. Adverse event categories and toxicities where the number of intention to treat patients with the event was >10% in either Placebo or Olaparib arm (or both)

	Placebo (N=74)	Olaparib BD (N=73)	p-value	Olaparib TDS (N=73)	p-value
Anemia	15 (20%)	37 (51%)	**0.000**	41 (56%)	**0.000**
Abdominal pain	6 (8%)	6 (8%)	0.980	8 (11%)	0.556
Constipation	19 (26%)	16 (22%)	0.593	14 (19%)	0.345
Diarrhea	18 (24%)	13 (18%)	0.333	12 (16%)	0.236
Dyspepsia	13 (18%)	11 (15%)	0.682	6 (8%)	0.091
Mucositis oral	10 (14%)	7 (10%)	0.457	2 (3%)	**0.017**
Nausea	44 (59%)	47 (64%)	0.539	51 (70%)	0.187
Vomiting	21 (28%)	25 (34%)	0.443	33 (45%)	**0.034**
Fatigue	55 (74%)	64 (88%)	**0.039**	58 (79%)	0.461
Non-cardiac chest pain	9 (12%)	10 (14%)	0.781	3 (4%)	0.075
Lung infection	12 (16%)	14 (19%)	0.638	12 (16%)	0.971
Lymphocyte count decreased	0 (0%)	8 (11%)	**0.003**	9 (12%)	**0.001**
Anorexia	30 (41%)	34 (47%)	0.461	28 (38%)	0.786
Hypocalcemia	2 (3%)	9 (12%)	**0.027**	3 (4%)	0.681
Hyponatremia	12 (16%)	7 (10%)	0.231	10 (14%)	0.669
Arthralgia	17 (23%)	6 (8%)	**0.014**	9 (12%)	0.091
Back pain	18 (24%)	13 (18%)	0.333	14 (19%)	0.450
Pain in extremity	2 (3%)	13 (18%)	**0.002**	5 (7%)	0.275
Dizziness	14 (19%)	16 (22%)	0.652	15 (21%)	0.804
Dysgeusia	12 (16%)	12 (16%)	0.971	12 (16%)	0.971
Headache	18 (24%)	19 (26%)	0.812	17 (23%)	0.883
Anxiety	8 (11%)	2 (3%)	0.097	4 (5%)	0.238
Insomnia	10 (14%)	8 (11%)	0.637	5 (7%)	0.182
Cough	26 (35%)	22 (30%)	0.518	25 (34%)	0.910
Dyspnea	21 (28%)	26 (36%)	0.347	28 (38%)	0.199
Alopecia	11 (15%)	13 (18%)	0.629	16 (22%)	0.270
Rash maculo-papular	8 (11%)	5 (7%)	0.398	5 (7%)	0.398
Hypertension	8 (11%)	5 (7%)	0.398	4 (5%)	0.238

SERIOUS ADVERSE EVENTS

In total there have been 98 Serious Adverse Events in 73 patients.

Table 24. Number of SAEs experienced per patient by treatment arm

	Placebo (N=74)	Olaparib BD (N=73)	Olaparib TDS (N=73)	Overall (N=220)
Number of SAEs	29	26	43	98
Number of Patients with an SAE	23	21	29	73
Number of Patients with 1 SAE	18	16	19	53
Number of Patients with 2 SAEs	4	5	7	16
Number of Patients with 3 SAEs	1	0	2	3
Number of Patients with 4 SAEs	0	0	1	1

Table 25. Reported SAEs by outcome, categorisation and relatedness

Treatment	Placebo (32)	Olaparib BD (28)	Olaparib TDS (46)	Overall (106)
Outcome of Event				
Resolved - no sequelae	19 (59)	14 (50)	30 (65)	63 (59)
Resolved - with sequelae	8 (25)	14 (50)	5 (11)	27 (25)
Unresolved	4 (13)	0 (0)	5 (11)	9 (8)
Death	1 (3)	0 (0)	6 (13)	7 (7)
Category				
Unrelated SAE	29 (91)	13 (46)	30 (65)	72 (68)
SAR	3 (9)	11 (39)	9 (20)	23 (22)
Non fatal/life-threatening SUSAR	0 (0)	4 (14)	6 (13)	10 (9)
Fatal/life-threatening SUSAR	0 (0)	0 (0)	1 (2)	1 (1)
SAE duration (days)				
N	28	28	43	99
Mean (sd)	13 (16)	11 (14)	7 (8)	10 (13)
Median	5	5	3	4
IQR	2, 20	3, 14	2, 7	2, 12
Range	0, 49	0, 55	0, 42	0, 55
Relatedness				
Unrelated	15 (47)	5 (18)	10 (22)	30 (28)
Unlikely to be related	9 (28)	7 (25)	17 (37)	33 (31)
Possibly Related	6 (19)	10 (36)	11 (24)	27 (25)
Probably related	0 (0)	4 (14)	5 (11)	9 (8)
Definitely related	0 (0)	2 (7)	3 (7)	5 (5)
.	2 (6)	0 (0)	0 (0)	2 (2)

Table 26. List of SAEs reported as SUSARs

Treatment	SAE Reference	Category	Toxicity	Grade	Did this AE prompt the SAE?
Olaparib BD	LU2006/001013/02	Non fatal/life-threatening SUSAR	Thromboembolic event	3	Yes
Olaparib BD	LU2006/001013/02	Non fatal/life-threatening SUSAR	Edema limbs	3	No
Olaparib BD	LU2006/007001/01	Non fatal/life-threatening SUSAR	Fatigue	3	No
Olaparib BD	LU2006/007001/01	Non fatal/life-threatening SUSAR	Nausea	3	No
Olaparib BD	LU2006/007001/01	Non fatal/life-threatening SUSAR	Anorexia	3	Yes
Olaparib BD	LU2006/034001/01	Non fatal/life-threatening SUSAR	Dizziness	1	No
Olaparib BD	LU2006/034001/01	Non fatal/life-threatening SUSAR	Lethargy	1	No
Olaparib BD	LU2006/034001/01	Non fatal/life-threatening SUSAR	Atrial fibrillation	3	Yes
Olaparib BD	LU2006/038001/01	Non fatal/life-threatening SUSAR	Heart failure	3	No
Olaparib BD	LU2006/038001/01	Non fatal/life-threatening SUSAR	Dyspnea	3	No
Olaparib BD	LU2006/038001/01	Non fatal/life-threatening SUSAR	Anemia	3	Yes
Olaparib TDS	LU2006/001010/01	Fatal/life-threatening SUSAR	Fever	2	No
Olaparib TDS	LU2006/001010/01	Fatal/life-threatening SUSAR	Lung infection	3	Yes
Olaparib TDS	LU2006/001010/01	Fatal/life-threatening SUSAR	Pneumonitis	3	No
Olaparib TDS	LU2006/001010/01	Fatal/life-threatening SUSAR	Dyspnea	3	No
Olaparib TDS	LU2006/001010/01	Fatal/life-threatening SUSAR	Hypotension	2	No
Olaparib TDS	LU2006/006001/01	Non fatal/life-threatening SUSAR	Anemia	3	Yes
Olaparib TDS	LU2006/006001/01	Non fatal/life-threatening SUSAR	Mucositis oral	2	No
Olaparib TDS	LU2006/006001/04	Non fatal/life-threatening SUSAR	Dyspnea	2	No
Olaparib TDS	LU2006/006001/04	Non fatal/life-threatening SUSAR	Pneumonitis	2	No
Olaparib TDS	LU2006/006001/04	Non fatal/life-threatening SUSAR	Pneumonia	2	Yes
Olaparib TDS	LU2006/023002/01	Non fatal/life-threatening SUSAR	Vomiting	3	Yes
Olaparib TDS	LU2006/024002/02	Non fatal/life-threatening SUSAR	Fatigue	2	No
Olaparib TDS	LU2006/024002/02	Non fatal/life-threatening SUSAR	Anemia	3	Yes
Olaparib TDS	LU2006/028004/01	Non fatal/life-threatening SUSAR	Fever	1	Yes
Olaparib TDS	LU2006/032002/01	Non fatal/life-threatening SUSAR	Anemia	3	No
Olaparib TDS	LU2006/032002/01	Non fatal/life-threatening SUSAR	Platelet count decreased	2	No
Olaparib TDS	LU2006/032002/01	Non fatal/life-threatening SUSAR	Neutrophil count decreased	3	Yes

Table 27. Toxicities reported for SAEs for patients on Placebo by Grade

Grade	1 (6)	2 (16)	3 (25)	4 (6)	5 (0)	Overall (54)
Toxicity						
Alanine aminotransferase increased	0 (0)	1 (6)	0 (0)	0 (0)	0 (.)	1 (2)
Back pain	0 (0)	0 (0)	2 (8)	0 (0)	0 (.)	2 (4)
Bone pain	0 (0)	1 (6)	0 (0)	0 (0)	0 (.)	1 (2)
Chills	2 (33)	0 (0)	0 (0)	0 (0)	0 (.)	2 (4)
Confusion	0 (0)	1 (6)	1 (4)	0 (0)	0 (.)	2 (4)
Constipation	0 (0)	1 (6)	0 (0)	0 (0)	0 (.)	1 (2)
Cough	0 (0)	1 (6)	0 (0)	0 (0)	0 (.)	1 (2)
Diarrhea	0 (0)	0 (0)	1 (4)	0 (0)	0 (.)	1 (2)
Dizziness	1 (17)	0 (0)	0 (0)	0 (0)	0 (.)	1 (2)
Dyspnea	0 (0)	0 (0)	4 (16)	0 (0)	0 (.)	4 (8)
Edema limbs	1 (17)	0 (0)	0 (0)	0 (0)	0 (.)	1 (2)
Fatigue	0 (0)	1 (6)	0 (0)	0 (0)	0 (.)	1 (2)
Generalized muscle weakness	0 (0)	1 (6)	1 (4)	0 (0)	0 (.)	2 (4)
Hyponatremia	0 (0)	0 (0)	1 (4)	1 (17)	0 (.)	2 (4)
Ischemia cerebrovascular	0 (0)	0 (0)	0 (0)	1 (17)	0 (.)	1 (2)
Left ventricular systolic dysfunction	0 (0)	0 (0)	1 (4)	0 (0)	0 (.)	1 (2)
Lethargy	0 (0)	2 (13)	0 (0)	0 (0)	0 (.)	2 (4)
Lung infection	0 (0)	1 (6)	3 (12)	0 (0)	0 (.)	4 (8)
Malaise	0 (0)	1 (6)	0 (0)	0 (0)	0 (.)	1 (2)
Nausea	1 (17)	2 (13)	2 (8)	0 (0)	0 (.)	5 (9)
Neoplasms benign, malignant and unspecified	1 (17)	0 (0)	0 (0)	0 (0)	0 (.)	1 (2)
New primary tumour	0 (0)	0 (0)	1 (4)	0 (0)	0 (.)	1 (2)
Pain	0 (0)	1 (6)	0 (0)	0 (0)	0 (.)	1 (2)
Peripheral motor neuropathy	0 (0)	0 (0)	1 (4)	0 (0)	0 (.)	1 (2)
Pleural effusion	0 (0)	0 (0)	1 (4)	0 (0)	0 (.)	1 (2)
Pleural infection	0 (0)	0 (0)	1 (4)	0 (0)	0 (.)	1 (2)
Respiratory failure	0 (0)	0 (0)	0 (0)	1 (17)	0 (.)	1 (2)
Seizure	0 (0)	0 (0)	0 (0)	0 (0)	0 (.)	0 (0)
Sepsis	0 (0)	0 (0)	0 (0)	1 (17)	0 (.)	1 (2)
Splenic rupture	0 (0)	0 (0)	0 (0)	1 (17)	0 (.)	1 (2)
Superior vena cava syndrome	0 (0)	0 (0)	1 (4)	0 (0)	0 (.)	1 (2)
Thromboembolic event	0 (0)	0 (0)	0 (0)	1 (17)	0 (.)	1 (2)
Urinary incontinence	0 (0)	1 (6)	0 (0)	0 (0)	0 (.)	1 (2)
Urinary tract infection	0 (0)	0 (0)	1 (4)	0 (0)	0 (.)	1 (2)
Vomiting	0 (0)	1 (6)	3 (12)	0 (0)	0 (.)	4 (8)

Table 28. Toxicities reported for SAEs on Olaparib BD by Grade

Grade	1 (18)	2 (19)	3 (30)	4 (1)	5 (0)	Overall (68)
Toxicity						
Anemia	0 (0)	5 (26)	3 (10)	0 (0)	0 (.)	8 (12)
Anorexia	1 (6)	1 (5)	2 (7)	0 (0)	0 (.)	4 (6)
Atrial fibrillation	0 (0)	0 (0)	1 (3)	0 (0)	0 (.)	1 (1)
Back pain	0 (0)	0 (0)	2 (7)	0 (0)	0 (.)	2 (3)
Chills	1 (6)	0 (0)	0 (0)	0 (0)	0 (.)	1 (1)
Confusion	0 (0)	0 (0)	1 (3)	0 (0)	0 (.)	1 (1)
Cough	1 (6)	2 (11)	0 (0)	0 (0)	0 (.)	3 (4)
Dehydration	0 (0)	0 (0)	1 (3)	0 (0)	0 (.)	1 (1)
Deteriorating condition	0 (0)	0 (0)	0 (0)	1 (100)	0 (.)	1 (1)
Dizziness	3 (17)	0 (0)	0 (0)	0 (0)	0 (.)	3 (4)
Double vision	0 (0)	1 (5)	0 (0)	0 (0)	0 (.)	1 (1)
Dyspnea	2 (11)	1 (5)	2 (7)	0 (0)	0 (.)	5 (7)
Edema limbs	0 (0)	0 (0)	1 (3)	0 (0)	0 (.)	1 (1)
Fatigue	2 (11)	0 (0)	4 (13)	0 (0)	0 (.)	6 (9)
Fever	1 (6)	1 (5)	0 (0)	0 (0)	0 (.)	2 (3)
Flank pain	0 (0)	0 (0)	1 (3)	0 (0)	0 (.)	1 (1)
Headache	1 (6)	0 (0)	1 (3)	0 (0)	0 (.)	2 (3)
Heart failure	0 (0)	0 (0)	1 (3)	0 (0)	0 (.)	1 (1)
Hypomagnesemia	1 (6)	0 (0)	0 (0)	0 (0)	0 (.)	1 (1)
Hypotension	0 (0)	0 (0)	1 (3)	0 (0)	0 (.)	1 (1)
Hypoxia	0 (0)	0 (0)	1 (3)	0 (0)	0 (.)	1 (1)
Lethargy	1 (6)	0 (0)	0 (0)	0 (0)	0 (.)	1 (1)
Lung infection	0 (0)	1 (5)	0 (0)	0 (0)	0 (.)	1 (1)
Mucosal infection	0 (0)	1 (5)	0 (0)	0 (0)	0 (.)	1 (1)
Mucositis oral	0 (0)	1 (5)	0 (0)	0 (0)	0 (.)	1 (1)
Nausea	0 (0)	1 (5)	1 (3)	0 (0)	0 (.)	2 (3)
Pain	0 (0)	0 (0)	1 (3)	0 (0)	0 (.)	1 (1)
Pain in extremity	0 (0)	1 (5)	0 (0)	0 (0)	0 (.)	1 (1)
Pancytopenia	0 (0)	1 (5)	0 (0)	0 (0)	0 (.)	1 (1)
Platelet count decreased	3 (17)	1 (5)	1 (3)	0 (0)	0 (.)	5 (7)
Pleuritic pain	0 (0)	0 (0)	1 (3)	0 (0)	0 (.)	1 (1)
Pneumonitis	0 (0)	1 (5)	0 (0)	0 (0)	0 (.)	1 (1)
Sepsis	0 (0)	0 (0)	1 (3)	0 (0)	0 (.)	1 (1)
Thromboembolic event	0 (0)	0 (0)	1 (3)	0 (0)	0 (.)	1 (1)
Upper respiratory infection	0 (0)	0 (0)	1 (3)	0 (0)	0 (.)	1 (1)
Urinary tract infection	0 (0)	0 (0)	1 (3)	0 (0)	0 (.)	1 (1)
Vomiting	1 (6)	0 (0)	0 (0)	0 (0)	0 (.)	1 (1)

Table 29. Toxicities reported for SAEs on Olaparib TDS by Grade

Grade	1 (11)	2 (36)	3 (39)	4 (3)	5 (5)	Overall (95)
Toxicity						
Abdominal pain	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	1 (1)
Acute exacerbation of COPD	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	1 (1)
Agitation	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	1 (1)
Anemia	1 (9)	0 (0)	6 (15)	0 (0)	0 (0)	7 (7)
Anorexia	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	1 (1)
Back pain	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	1 (1)
Blurred vision	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	1 (1)
Confusion	1 (9)	2 (6)	0 (0)	0 (0)	0 (0)	3 (3)
Conjunctivitis infective	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	1 (1)
Constipation	0 (0)	2 (6)	0 (0)	0 (0)	0 (0)	2 (2)
Dehydration	0 (0)	1 (3)	1 (3)	0 (0)	0 (0)	2 (2)
Diarrhea	0 (0)	0 (0)	2 (5)	0 (0)	0 (0)	2 (2)
Dizziness	1 (9)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)
Dysarthria	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	1 (1)
Dyspnea	0 (0)	5 (14)	4 (10)	0 (0)	0 (0)	9 (10)
Facial muscle weakness	1 (9)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)
Fatigue	0 (0)	2 (6)	1 (3)	0 (0)	0 (0)	3 (3)
Fever	1 (9)	1 (3)	0 (0)	0 (0)	0 (0)	2 (2)
Flank pain	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	1 (1)
Hypercalcemia	1 (9)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)
Hypokalemia	0 (0)	0 (0)	0 (0)	1 (33)	0 (0)	1 (1)
Hypotension	1 (9)	1 (3)	0 (0)	0 (0)	0 (0)	2 (2)
Intracranial hemorrhage	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	1 (1)
Ischemia cerebrovascular	0 (0)	0 (0)	0 (0)	0 (0)	1 (20)	1 (1)
Lethargy	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	1 (1)
Lung infection	0 (0)	1 (3)	5 (13)	0 (0)	0 (0)	6 (6)
Melaena	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	1 (1)
Mucositis oral	0 (0)	1 (3)	1 (3)	0 (0)	0 (0)	2 (2)
Muscle weakness left-sided	1 (9)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)
Muscle weakness lower limb	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	1 (1)
Muscle weakness right-sided	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	1 (1)
Nausea	0 (0)	2 (6)	2 (5)	0 (0)	0 (0)	4 (4)
Neoplasms ovarian tumour	0 (0)	0 (0)	0 (0)	0 (0)	1 (20)	1 (1)
Neoplasms small cell lung cancer	0 (0)	0 (0)	0 (0)	0 (0)	1 (20)	1 (1)
Neutropenic sepsis	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	1 (1)
Neutrophil count decreased	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	1 (1)
Non-cardiac chest pain	1 (9)	1 (3)	0 (0)	0 (0)	0 (0)	2 (2)
Pancytopenia	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	1 (1)
Peripheral sensory neuropathy	1 (9)	1 (3)	0 (0)	0 (0)	0 (0)	2 (2)
Platelet count decreased	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	1 (1)
Pneumonia	0 (0)	2 (6)	1 (3)	0 (0)	0 (0)	3 (3)
Pneumonitis	0 (0)	1 (3)	1 (3)	1 (33)	0 (0)	3 (3)
Productive cough	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	1 (1)
Rectal hemorrhage	0 (0)	1 (3)	1 (3)	0 (0)	0 (0)	2 (2)
Seizure	0 (0)	1 (3)	0 (0)	1 (33)	0 (0)	2 (2)
Sepsis	0 (0)	0 (0)	0 (0)	0 (0)	2 (40)	2 (2)
Thromboembolic event	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	1 (1)
Urinary incontinence	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	1 (1)
Urinary tract infection	0 (0)	1 (3)	1 (3)	0 (0)	0 (0)	2 (2)
Vomiting	1 (9)	1 (3)	1 (3)	0 (0)	0 (0)	3 (3)

MORE INFORMATION

SUBSTANTIAL AMENDMENTS

Date of Amendment	Description of amendment
13-Mar-2013	• A change in the design of the trial to placebo controlled 3 arm study • Change from capsules to tablets • Increase in recruitment target • Change in primary outcome measure
02-Oct-2013	• Change to eligibility criteria • Clarification of types of tumour sample
25-Aug-2015	• Change to definition of end of study • Clarification of indemnity arrangements • Clarification of treatment schedule assessments • Clarification of data reporting requirements • Change to SAE reporting period
31-May-2016	• Addition of AML as an SAE reporting requirement.
10-May-2019	• Change to definition of end of study • Clarification to translational study details

CONCLUSIONS

We conclude that olaparib monotherapy is well tolerated and the observed data showed some benefit but our trial did not reach the pre-planned level of evidence of improved efficacy when given as a maintenance treatment in SCLC in an unselected population to warrant further research. However, PARP inhibition may be effective in this tumour type when combined with other agents. Combinations of PARP inhibitors with immunotherapy should be investigated further.

DISSEMINATION

The interim trial results were published as a conference abstract presented in the 17th World Conference on Lung Cancer: Penella Woll, Piers Gaunt, Nicola Steele, Samreen Ahmed, Clive Mulatero, Riyaz Shah, et al. STOMP: A UK National Cancer Research Network Randomised, Double Blind, Multicentre Phase II Trial of Olaparib as Maintenance Therapy in SCLC. Journal of Thoracic Oncology 2017; Volume 12, Issue 1, Supplement, Pages S704-S705.

The final trial results will be published in a well stablished peer-reviewed journal in 2022.

A summary of the results will be included in the publicly available Cancer Research UK webpage: https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-olaparib-small-cell-lung-cancer-stomp and the ISRCTN registry (https://www.isrctn.com/ISRCTN73164486).

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