Supplementary appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Poveda A, Floquet A, Ledermann JA, et al. Overall survival with maintenance olaparib in BRCA1/2-mutated platinum-sensitive relapsed ovarian cancer (SOLO2/ENGOT-Ov21): a randomised, placebo-controlled, phase 3 trial

Table of contents

SOLO2 Investigators

The table below lists the lead investigator for each site that participated in this study.

Site no.	Principal Investigator	No. of patients randomised	Country
4001	Jacob Korach	17	Israel
5702	Tomasz Huzarski/Tomasz Byrski	17	Poland
2307	Patricia Pautier	11	France
302	Michael Friedlander	10	Australia
2601	Philipp Harter	10	Germany
4102	Nicoletta Colombo	9	Italy
4101	Sandro Pignata	8	Italy
4106	Giovanni Scambia	6	Italy
4103	Maria Nicoletto	6	Italy
2801	Fiona Nussey	6	UK
2806	Andrew Clamp	6	UK
7804	Richard Penson	6	USA
1003	Amit Oza	6	Canada
7001	Andrés Poveda Velasco	6	Spain
2312	Manuel Rodrigues	5	France
2309	Jean-Pierre Lotz/Frédéric Selle	5	France
2308	Isabelle Ray-Coquard	5	France
1001	Diane Provencher	5	Canada
7007	Aleix Prat Aparicio/Laura Vidal Boixader	5	Spain
301	Clare Scott	5	Australia
4304	Kenji Tamura/Mayu Yunokawa	5	Japan
6213	Alla Lisyanskaya	5	Russia
2301	Jacques Medioni/Nicolas Pécuchet	4	France
2311	Coraline Dubot/Thibault De La Motte Rouge	4	France
2310	Marie-Christine Kaminsky/Béatrice Weber	4	France
2306	Alain Lortholary	4	France
2808	Christine Parkinson	4	UK
2802	Jonathan Ledermann	4	UK
2803	Sarah Williams	4	UK
2804	Susana Banerjee	4	UK
7854	Jonathan Cosin/James Hoffman	4	USA
7803	Richard Penson	4	USA
1002	Marie Plante	4	Canada
1007	Allan Covens	4	Canada
5001	Gabe Sonke	4	Netherlands
2305	Florence Joly	3	France
2302	Anne Floquet	3	France
2805	Susana Banerjee	3	UK
1005	Holger Hirte	3	Canada
4003	Amnon Amit	3	Israel
2603	Tjoung-Won Park-Simon	3	Germany

Site no.	Principal Investigator	No. of patients randomised	Country
4309	Koji Matsumoto	3	Japan
6215	Sergei Tjulandin	3	Russia
6004	Jae Hoon Kim	3	South Korea
2304	Laurence Gladieff	2	France
4107	Roberto Sabbatini	2	Italy
7846	David O'Malley	2	USA
7826	Patrick Timmins/Daniel Kredentser	2	USA
7009	Nuria Laínez Milagro	2	Spain
7006	Maria Pilar Barretina Ginesta	2	Spain
7005	Ariadna Tibau Martorell/Alfonso Gómez De Liaño Lista/Belén Ojeda González	2	Spain
303	Linda Mileshkin	2	Australia
4311	Masaki Mandai	2	Japan
5003	Ingrid Boere	2	Netherlands
5005	Petronella Ottevanger	2	Netherlands
6001	Joo-Hyun Nam	2	South Korea
708	Elias Filho	2	Brazil
2303	Salima Hamizi	1	France
4105	Francesco Cognetti	1	Italy
7881	David Warshal	1	USA
7859	Elizabeth Dickson-Michelson/Scott Kamelle	1	USA
7806	Nathalie McKenzie	1	USA
7816	Gustavo Rodriguez	1	USA
7872	Deborah Armstrong	1	USA
7808	Eva Chalas	1	USA
7811	Paul Celano	1	USA
7813	Kian Behbakht/Susan Davidson	1	USA
1004	Stephen Welch	1	Canada
4002	Limor Helpman/Ami Fishman/Ilan Bruchim	1	Israel
5705	Magdalena Sikorska	1	Poland
5704	Anna Słowińska/Wojciech Rogowski	1	Poland
5701	Mariusz Bidziński/Beata Śpiewankiewicz	1	Poland
7008	Antonio Casado Herraez	1	Spain
7004	César Mendiola Fernández	1	Spain
2606	Martina Gropp-Meier	1	Germany
4305	Toshiaki Saito	1	Japan
4312	Kazuhiro Takehara	1	Japan
4308	Takayuki Enomoto	1	Japan
4310	Hidemichi Watari	1	Japan
6003	Chel Hun Choi/Byoung-Gie Kim	1	South Korea
6002	Jae Weon Kim	1	South Korea
701	Roberto Hegg	1	Brazil
501	Ignace Vergote	1	Belgium

Supplementary methods

Full eligibility criteria

A complete list of eligibility criteria is given below. Patients who have a known mutation in *BRCA1* and/or *BRCA2* (BRCA) by local testing that is predicted to be deleterious, or suspected deleterious, must fulfil all of the inclusion criteria below.

Patients who do not know their mutation status at entry and are being considered for this trial must fulfil all of the criteria marked with an asterisk below prior to BRCA mutation testing being carried out. All inclusion criteria will then be assessed following confirmation that they harbour an appropriate BRCA mutation. For inclusion in the study, patients should fulfil the following criteria (any marked with an asterisk [*] are also required for pre-randomisation Myriad germline BRCA mutation status sampling to determine study eligibility). Any patient who fulfils the eligibility criteria for the BRCA test is required to have their eligibility assessed again prior to randomisation.

Inclusion criteria

1. *Provision of informed consent prior to any study-specific procedures
2. *Patients must be ≥18 years of age
3. *Female patients with histologically diagnosed relapsed high-grade serous ovarian cancer (including primary peritoneal and/or fallopian tube cancer) or high-grade endometrioid cancer
4. Documented BRCA mutation that is predicted to be deleterious or suspected deleterious (known or predicted to be detrimental/lead to loss of function)
5. *Patients who have received at least two previous lines of platinum-containing therapy prior to randomisation

   (a) *For the penultimate chemotherapy course prior to enrolment in the study:

   - Treatment must have contained a platinum agent (eg, carboplatin or cisplatin according to standard clinical practice; there are no other specific requirements)
   - Patient classified as platinum sensitive after this treatment, defined as disease progression occurring more than 6 months after completion of their last dose of platinum chemotherapy
   - Maintenance treatment is allowed at the end of the penultimate platinum regimen, including bevacizumab

   (b) For the last chemotherapy course immediately prior to randomisation in the study:

   - Patients must be, in the opinion of the investigator, in response (partial or complete radiological response), or they may have no evidence of disease (if optimal cytoreductive surgery was conducted prior to chemotherapy) and no evidence of rising CA-125, as defined below, following completion of this chemotherapy course
   - Patients must have received at least four cycles of a platinum-based chemotherapy regimen (carboplatin or cisplatin)
   - *Patients must **not** have received bevacizumab during this course of treatment
   - Patients must not have received any investigational agent during this course of treatment
   - Patients must be randomised within 8 weeks of their last dose of chemotherapy (last dose is the day of the last infusion)

6. Pre-treatment CA-125 measurements must meet the criteria specified below:

   - If the first value does not exceed the upper limit of normal (ULN), the patient is eligible to be randomised and a second sample is not required
   - If the first value is greater than the ULN, a second assessment must be performed at least 7 days after the first. If the second assessment is ≥15% more than the first, the patient is not eligible

7. Patients must have normal organ and bone marrow function measured within 28 days of randomisation, as defined below:

   - Haemoglobin ≥10·0 g/dL with no blood transfusions in the past 28 days
   - Absolute neutrophil count ≥1·5 x 10^9/L

- Platelet count ≥100 x 10^9/l
- Total bilirubin ≤1·5 x institutional ULN
- Aspartate aminotransferase (serum glutamic oxaloacetic transaminase/alanine aminotransferase (serum glutamic pyruvate transaminase) ≤2·5 x institutional ULN unless liver metastases are present, in which case they must be ≤5 x ULN
- Serum creatinine ≤1·5 x institutional ULN

8. *Eastern Cooperative Oncology Group (ECOG) performance status 0–1
9. *Patients must have a life expectancy of ≥16 weeks
10. *Postmenopausal or evidence of non-childbearing status for women of childbearing potential: negative urine or serum pregnancy test prior to Myriad BRCA test during screening part 1, within 28 days of study treatment and confirmed prior to treatment on day 1. Postmenopausal is defined as:

    - Amenorrhoeic for 1 year or more following cessation of exogenous hormonal treatments
    - Levels of luteinising hormone and follicle-stimulating hormone in the postmenopausal range for women under 50 years old, or radiation-induced oophorectomy with last menses >1 year ago, or chemotherapy-induced menopause with last menses >1 year ago, or surgical sterilisation (bilateral oophorectomy or hysterectomy)

11. *Patient is willing and able to comply with the protocol for the duration of the study, including undergoing treatment and scheduled visits and examinations
12. *Formalin-fixed, paraffin-embedded tumour sample from the primary or recurrent cancer **must** be available for central testing. If there is no written confirmation of the availability of an archived tumour sample prior to enrolment, the patient is **not** eligible for the study

Exclusion Criteria

Patients must not enter the study if any of the following exclusion criteria are fulfilled (any marked with an asterisk are also applicable as exclusion criteria for patients who are being screened to determine their BRCA mutation status via Myriad):

1. *Involvement in the planning and/or conduct of the study (applies to both AstraZeneca staff and/or staff at the study site)
2. BRCA mutations that are considered to be non-detrimental (eg, 'variant of uncertain clinical significance', 'variant of unknown significance', 'variant, favour polymorphism', 'benign polymorphism', etc)
3. Patients who have had drainage of their ascites during the final two cycles of their last chemotherapy regimen prior to enrolment in the study
4. *Previous randomisation in the present study
5. *Participation in another clinical study with an investigational product during the chemotherapy course immediately prior to randomisation
6. *Any previous treatment with a poly(ADP-ribose) polymerase (PARP) inhibitor, including olaparib
7. *Patients with a known hypersensitivity to olaparib or any of the excipients of the product
8. *Other malignancy within the last 5 years, except adequately treated non-melanoma skin cancer, curatively treated in-situ cancer of the cervix, ductal carcinoma in-situ, stage 1, grade 1 endometrial carcinoma, and other solid tumours, including lymphomas (without bone marrow involvement) curatively treated with no evidence of disease for ≥5 years. Patients with history of primary breast cancer may be eligible provided their definitive anticancer treatment was completed more than 3 years ago and they remain free of breast cancer disease prior to start of study treatment
9. *Resting electrocardiogram corrected QT (QTc) interval >470 ms at two or more time points within a 24-hour period, or family history of long-QT syndrome
10. Patients receiving any systemic chemotherapy or radiotherapy (except for palliative reasons) within 3 weeks prior to study treatment (or a longer period, depending on the defined characteristics of the agents used)
11. *Concomitant use of known potent cytochrome P450 (CYP) 3A4 inhibitors such as ketoconazole, itraconazole, ritonavir, indinavir, saquinavir, telithromycin, clarithromycin, and nelfinavir
12. *Persistent toxicities (Common Terminology Criteria for Adverse Events [CTCAE] grade >2) caused by previous cancer therapy, excluding alopecia
13. *Patients with myelodysplastic syndrome (MDS)/acute myeloid leukaemia (AML)
14. *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 study as long as these were started at least 4 weeks prior to treatment. Patients with spinal cord compression, unless considered to have received definitive treatment for this and evidence of clinically stable disease for 28 days

15. Major surgery within 2 weeks of starting study treatment, and patients must have recovered from any effects of any major surgery
16. *Patients considered at high medical risk because of 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, superior vena cava syndrome, extensive interstitial bilateral lung disease determined by high-resolution computed tomography, or any psychiatric disorder that prohibits obtaining of informed consent
17. *Patients unable to swallow orally administered medication and patients with gastrointestinal disorders likely to interfere with absorption of the study medication
18. *Breastfeeding women
19. *Immunocompromised patients, eg, patients who are known to be serologically positive for human immunodeficiency virus
20. *Patients with known active hepatitis (ie, hepatitis B or C) because of risk of transmitting the infection through blood or other body fluids
21. *Previous allogeneic bone marrow transplant
22. *Whole blood transfusions in the last 120 days prior to study entry (packed red blood cells and platelet transfusions are acceptable; for timing, refer to inclusion criterion 7)

Discontinuation criteria

Patients could be discontinued from the study treatment in the following situations:

- Patient decision
- Adverse event
- Severe non-compliance with study protocol
- Bone marrow findings consistent with MDS/AML
- Objective radiological disease progression according to Response Evaluation Criteria in Solid Tumors (RECIST; unless, in the investigator's opinion, they were benefiting from treatment and did not meet any other discontinuation criteria)

Overall survival sensitivity analysis using electronic case report form stratification variables

Randomisation was performed centrally using an interactive web or voice-response system with stratification according to:

- Response to previous chemotherapy (complete or partial response)
- Length of the platinum-free interval (>6–12 months or >12 months)

An overall survival sensitivity analysis was conducted using the baseline data collected in the electronic case report form (eCRF) to correct for any patients who were mis-stratified at randomisation (supplementary table 3). Although not anticipated, if patients were randomised in error when they had not had a response to prior platinum-based chemotherapy, they were categorised in the 'partial response' category for the sensitivity analysis using eCRF stratification data. If patients were randomised in error with less than 6 months to disease progression in the penultimate platinum-based chemotherapy prior to enrolment, they were included in the '6–12 months' category for the sensitivity analysis using the eCRF stratification data.

Supplementary results

Time to study treatment discontinuation or death

Median time to study treatment discontinuation or death (243 events in 295 patients: 152 [78%] in the olaparib group *vs* 91 [92%] in the placebo group; 82% maturity) was 19·4 months (95% confidence interval [CI] 14·9–25·9) with olaparib and 5·6 months (95% CI 5·0–6·8) with placebo (hazard ratio [HR] 0·37 [95% CI 0·28–0·49], p<0·0001).

Supplementary table 1: Characteristics of patients at baseline

Characteristic	Olaparib (n=196)	Placebo (n=99)
Age, years	56 (51–63)	56 (49–63)
ECOG performance status*		
0	162 (83%)	77 (78%)
1	32 (16%)	22 (22%)
Missing data	2 (1%)	0
Primary tumour location		
Ovary	162 (83%)	86 (87%)
Fallopian tubes or primary peritoneal	31 (16%)	13 (13%)
Other	2 (1%)	0
Missing data	1 (1%)	0
Histology type		
Serous	183 (93%)	86 (87%)
Endometrioid	9 (5%)	8 (8%)
Mixed	3 (2%)	5 (5%)
Missing data	1 (1%)	0
Patients with >2 cm target lesions at baseline		
Yes	30 (15%)	18 (18%)
Confirmed Myriad germline BRCA mutation		
BRCA1	132 (67%)	61 (62%)
BRCA2	58 (30%)	35 (35%)
Both	0	0
Missing data†	6 (3%)	3 (3%)
Response to previous platinum therapy		
Complete response	91 (46%)	47 (47%)
Partial response	105 (54%)	52 (53%)
Number of prior platinum regimens		
2	110 (56%)	62 (63%)
3	60 (31%)	20 (20%)
4	18 (9%)	12 (12%)
≥5	7 (4%)	5 (5%)
Unknown	1 (1%)	0
Platinum-free interval		
>6–12 months	79 (40%)	40 (40%)
>12 months	117 (60%)	59 (60%)
Prior use of bevacizumab		
Yes	33 (17%)	20 (20%)
No	163 (83%)	79 (80%)

Data are n (%) or median (IQR). Percentages may not total 100% because of rounding. ECOG=Eastern Cooperative Oncology Group. IQR=interquartile range. *An ECOG performance status of 0 indicates that the patient is fully active, and a status of 1 indicates that the patient is restricted in physically strenuous activity, but ambulatory and able to carry out work of a light or sedentary nature. †Denotes patients with a confirmed germline BRCA mutation by local testing, but without confirmed germline BRCA mutation status as part of this trial.

Supplementary table 2: Subsequent anticancer therapy modalities*

	Olaparib (n=196)	Placebo (n=99)
Total	130 (66%)	81 (82%)
Platinum-containing regimen	89 (45%)	43 (43%)
Platinum in combination with bevacizumab	9 (5%)	4 (4%)
Other bevacizumab-containing regimen	20 (10%)	9 (9%)
Any other chemotherapy-containing regimen (excluding platinum or bevacizumab)	74 (38%)	55 (56%)
PARP inhibitor	20 (10%)	38 (38%)
Hormonal agent	9 (5%)	6 (6%)
Other investigational agents	3 (2%)	4 (4%)

Data are n (%). Patients may have received a post-discontinuation treatment modality in more than one subsequent line of anticancer therapy. PARP=poly(ADP-ribose) polymerase. *Includes patients who received a post-discontinuation treatment modality under any subsequent line of anticancer therapy.

Supplementary table 3: Subsequent PARP inhibitor therapy

	Olaparib (n=196)	Placebo (n=99)
Patients who received a PARP inhibitor*	20 (10%)	38 (38%)
First subsequent anticancer therapy	15 (8%)	28 (28%)
Second subsequent anticancer therapy	2 (1%)	8 (8%)
Third subsequent anticancer therapy	3 (2%)	3 (3%)
Fourth subsequent anticancer therapy	0	2 (2%)
Fifth subsequent anticancer therapy	0	1 (1%)
Sixth subsequent anticancer therapy	1 (1%)	1 (1%)

Data are n (%). Patients may have received a PARP inhibitor in more than one subsequent line of anticancer therapy. PARP=poly(ADP-ribose) polymerase. *Includes patients who received a PARP inhibitor under any subsequent line of anticancer therapy.

Supplementary table 4: Overall survival analyses

Analysis	Median OS [months (95% CI)]		HR (95% CI) p value
	Olaparib	Placebo	
FAS per randomisation*	n=196 51·7 (41·5–59·1)	n=99 38·8 (31·4–48·6)	0·74 (0·54–1·00) p=0·054
FAS adjusted for PARP inhibitor therapy in the placebo group†	n=196 51·7	n=99 35·4	0·56 (0·35–0·97)
FAS per eCRF‡	n=196 51·7 (41·5–59·1)	n=99 38·8 (31·4–48·6)	0·70 (0·52–0·96) p=0·023
Patients with a Myriad germline BRCA mutation	n=190 52·4 (41·5–61·4)	n=96 37·4 (29·8–44·2)	0·71 (0·52–0·97) p=0·031

Data are n (%) or median (95% CI). CI=confidence interval. eCRF=electronic case report form. FAS=full analysis set. HR=hazard ratio. OS=overall survival. PARP=poly(ADP-ribose) polymerase. *Randomisation was performed by investigators with stratification according to response to previous chemotherapy and length of the platinum-free interval. †The rank preserving structural failure time model (re-censored) was used to adjust for subsequent PARP inhibitor therapy in the placebo group. ‡ eCRF stratification variables were used as covariates to correct for any patients who were mis-stratified at randomisation.

Supplementary table 5: Stratification data for the full analysis set per randomisation and per the eCRF

Response to previous platinum chemotherapy	Platinum-free interval (months)	Number of patients		
		Olaparib (n=196)	Placebo (n=99)	Total (n=295)
FAS per randomisation				
Complete response	>6–12	31 (16%)	16 (16%)	47 (16%)
	>12	60 (31%)	31 (31%)	91 (31%)
Partial response	>6–12	48 (24%)	24 (24%)	72 (24%)
	>12	57 (29%)	28 (28%)	85 (29%)
FAS per eCRF*				
Complete response	>6–12	26 (13%)	11 (11%)	37 (13%)
	>12	48 (24%)	29 (29%)	77 (26%)
Partial response	>6–12	53 (27%)	23 (23%)	76 (26%)
	>12	68 (35%)	36 (36%)	104 (35%)

Data are n (%). Percentages may not total 100% because of rounding. eCRF=electronic case report form. FAS=full analysis set. *Data from one patient in the olaparib group were not available to allow a derivation of the time to progression from the penultimate platinum-based chemotherapy regimen.

Supplementary table 6: Summary of grade 1–2 treatment-emergent adverse events in ≥10% of patients in either group, and grade 3, grade 4, and grade 5 adverse events at the final analysis

Event	Olaparib (n=195)				Placebo (n=99)			
	Grade 1–2	Grade 3	Grade 4	Grade 5	Grade 1–2	Grade 3	Grade 4	Grade 5
Grade 1–2 adverse events occurring in ≥10% of patients in either group								
Nausea	142 (72·8%)	6 (3·1%)	0	0	35 (35·4%)	0	0	0
Fatigue/asthenia*	119 (61·0%)	11 (5·6%)	0	0	37 (37·4%)	2 (2·0%)	0	0
Anaemia†	48 (24·6%)	39 (20·0%)	2 (1·0%)	0	8 (8·1%)	2 (2·0%)	0	0
Vomiting	73 (37·4%)	5 (2·6%)	0	0	19 (19·2%)	1 (1·0%)	0	0
Diarrhoea	65 (33·3%)	2 (1·0%)	0	0	20 (20·2%)	0	0	0
Abdominal pain	49 (25·1%)	6 (3·1%)	0	0	28 (28·3%)	3 (3·0%)	0	0
Headache	49 (25·1%)	1 (0·5%)	0	0	14 (14·1%)	0	0	0
Constipation	46 (23·6%)	0	0	0	20 (20·2%)	3 (3·0%)	0	0
Decreased appetite	43 (22·1%)	1 (0·5%)	0	0	11 (11·1%)	0	0	0
Leukopenia‡	27 (13·8%)	4 (2·1%)	3 (1·5%)	0	2 (2·0%)	0	0	0
Neutropenia§	32 (16·4%)	11 (5·6%)	3 (1·5%)	0	2 (2·0%)	3 (3·0%)	1 (1·0%)	0
Dysgeusia	38 (19·5%)	0	0	0	6 (6·1%)	0	0	0
Cough	36 (18·5%)	1 (0·5%)	1 (0·5%)	0	6 (6·1%)	0	0	0
Dizziness	33 (16·9%)	1 (0·5%)	0	0	6 (6·1%)	0	0	0
Back pain	31 (15·9%)	0	0	0	12 (12·1%)	2 (2·0%)	0	0
Thrombocytopenia¶	28 (14·4%)	3 (1·5%)	1 (0·5%)	0	3 (3·0%)	1 (1·0%)	0	0
Arthralgia	31 (15·9%)	0	0	0	14 (14·1%)	0	0	0
Dyspepsia	29 (14·9%)	0	0	0	9 (9·1%)	0	0	0
Hypomagnesaemia	28 (14·4%)	1 (0·5%)	0	0	10 (10·1%)	0	0	0
Pyrexia	28 (14·4%)	0	0	0	6 (6·1%)	0	0	0
Nasopharyngitis	25 (12·8%)	0	0	0	11 (11·1%)	0	0	0
Dyspnoea	23 (11·8%)	2 (1·0%)	0	0	1 (1·0%)	0	0	0
Upper abdominal pain	23 (11·8%)	1 (0·5%)	0	0	13 (13·1%)	0	0	0
Elevated blood creatinine	21 (10·8%)	0	0	0	1 (1·0%)	0	0	0
Urinary tract infection	17 (8·7%)	3 (1·5%)	0	0	10 (10·1%)	0	0	0
Grade 3, grade 4, and grade 5 adverse events¶								
AML	0	0	1 (0·5%)	2 (1·0%)	0	0	0	0
MDS	0	1 (0·5%)	2 (1·0%)	1 (0·5%)	0	0	0	0
Plasma cell myeloma	0	0	0	1 (0·5%)	0	0	0	0
Decreased lymphocyte count	6 (3·1%)	0	2 (1·0%)	0	0	0	0	0
Hypokalaemia	10 (5·1%)	0	1 (0·5%)	0	1 (1·0%)	1 (1·0%)	1 (1·0%)	0
Hypercalcaemia	3 (1·5%)	0	1 (0·5%)	0	1 (1·0%)	0	0	0
Osteoarthritis	2 (1·0%)	0	1 (0·5%)	0	1 (1·0%)	0	0	0
Anaphylactic reaction	0	0	1 (0·5%)	0	0	0	0	0
Drug reaction with eosinophilia and systemic symptoms	0	0	1 (0·5%)	0	0	0	0	0
Enteritis	0	0	1 (0·5%)	0	0	0	0	0
Gastric adenocarcinoma	0	0	1 (0·5%)	0	0	0	0	0

Event	Olaparib (n=195)				Placebo (n=99)			
	Grade 1–2	Grade 3	Grade 4	Grade 5	Grade 1–2	Grade 3	Grade 4	Grade 5
Pericarditis	0	0	1 (0·5%)	0	0	0	0	0
Increased amylase	0	0	0	0	0	0	1 (1·0%)	0
Intestinal obstruction	1 (0·5%)	3 (1·5%)	0	0	1 (1·0%)	1 (1·0%)	0	0
Deep vein thrombosis	1 (0·5%)	3 (1·5%)	0	0	0	1 (1·0%)	0	0
Lymphopenia	1 (0·5%)	3 (1·5%)	0	0	0	0	0	0
Stomatitis	18 (9·2%)	2 (1·0%)	0	0	6 (6·1%)	0	0	0
Mouth ulceration	3 (1·5%)	2 (1·0%)	0	0	1 (1·0%)	0	0	0
Pulmonary embolism	2 (1·0%)	2 (1·0%)	0	0	0	0	0	0
Syncope	0	2 (1·0%)	0	0	0	1 (1·0%)	0	0
Increased gamma-glutamyltransferase	4 (2·1%)	1 (0·5%)	0	0	2 (2·0%)	2 (2·0%)	0	0
Small intestinal obstruction	0	0	0	0	1 (1·0%)	2 (2·0%)	0	0
Peripheral oedema	16 (8·2%)	1 (0·5%)	0	0	7 (7·1%)	0	0	0
Cystitis	14 (7·2%)	1 (0·5%)	0	0	0	0	0	0
Anxiety	12 (6·2%)	1 (0·5%)	0	0	5 (5·1%)	0	0	0
Depression	12 (6·2%)	1 (0·5%)	0	0	0	0	0	0
Peripheral neuropathy	10 (5·1%)	1 (0·5%)	0	0	4 (4·0%)	0	0	0
Elevated ALT	9 (4·6%)	1 (0·5%)	0	0	3 (3·0%)	1 (1·0%)	0	0
Insomnia	14 (7·2%)	0	0	0	8 (8·1%)	1 (1·0%)	0	0
Gastroenteritis	8 (4·1%)	0	0	0	2 (2·0%)	1 (1·0%)	0	0
Hyperglycaemia	8 (4·1%)	1 (0·5%)	0	0	4 (4·0%)	0	0	0
Pneumonia	8 (4·1%)	1 (0·5%)	0	0	0	0	0	0
Malaise	5 (2·6%)	1 (0·5%)	0	0	2 (2·0%)	0	0	0
Elevated AST	4 (2·1%)	1 (0·5%)	0	0	4 (4·0%)	0	0	0
Muscular weakness	4 (2·1%)	1 (0·5%)	0	0	1 (1·0%)	0	0	0
Tooth infection	3 (1·5%)	1 (0·5%)	0	0	2 (2·0%)	0	0	0
Dental caries	3 (1·5%)	1 (0·5%)	0	0	1 (1·0%)	0	0	0
Hydronephrosis	2 (1·0%)	1 (0·5%)	0	0	0	0	0	0
Hypertransaminasaemia	1 (0·5%)	1 (0·5%)	0	0	1 (1·0%)	0	0	0
Aortic stenosis	1 (0·5%)	1 (0·5%)	0	0	0	0	0	0
Dyspraxia	1 (0·5%)	1 (0·5%)	0	0	0	0	0	0
Fibromyalgia	1 (0·5%)	1 (0·5%)	0	0	0	0	0	0
Increased blood creatine phosphokinase	1 (0·5%)	1 (0·5%)	0	0	0	0	0	0
Presyncope	1 (0·5%)	1 (0·5%)	0	0	0	0	0	0
Chest pain	0	1 (0·5%)	0	0	0	1 (1·0%)	0	0
Coronary artery stenosis	0	1 (0·5%)	0	0	0	0	0	0
Haematuria	0	1 (0·5%)	0	0	3 (3·0%)	0	0	0
Device related infection	0	1 (0·5%)	0	0	1 (1·0%)	0	0	0
Cholecystitis	0	1 (0·5%)	0	0	0	0	0	0
Femoral fracture	0	1 (0·5%)	0	0	0	0	0	0
Gastric cancer	0	1 (0·5%)	0	0	0	0	0	0
Gastrointestinal carcinoma	0	1 (0·5%)	0	0	0	0	0	0
Increased erythroblast count	0	1 (0·5%)	0	0	0	0	0	0
Infection	0	1 (0·5%)	0	0	0	0	0	0

Event	Olaparib (n=195)				Placebo (n=99)			
	Grade 1–2	Grade 3	Grade 4	Grade 5	Grade 1–2	Grade 3	Grade 4	Grade 5
Lymphoma	0	1 (0·5%)	0	0	0	0	0	0
Malignant lung neoplasm	0	1 (0·5%)	0	0	0	0	0	0
Myocardial infarction	0	1 (0·5%)	0	0	0	0	0	0
Nail infection	0	1 (0·5%)	0	0	0	0	0	0
Spinal cord infection	0	1 (0·5%)	0	0	0	0	0	0
Squamous cell carcinoma	0	1 (0·5%)	0	0	0	0	0	0
Squamous cell carcinoma of skin	0	1 (0·5%)	0	0	0	0	0	0
Squamous cell carcinoma of tongue	0	1 (0·5%)	0	0	0	0	0	0
Thyroid cancer	0	1 (0·5%)	0	0	0	0	0	0
Ulcerative colitis	0	1 (0·5%)	0	0	0	0	0	0
Hypertension	7 (3·6%)	0	0	0	3 (3·0%)	1 (1·0%)	0	0
Abdominal discomfort	5 (2·6%)	0	0	0	3 (3·0%)	1 (1·0%)	0	0
Spinal compression fracture	2 (1·0%)	0	0	0	0	1 (1·0%)	0	0
Invasive ductal breast carcinoma	0	0	0	0	0	1 (1·0%)	0	0

Data are n (%). Data are shown for TEAEs that occurred in at least 10% of patients in either treatment group during study treatment or up to 30 days after discontinuation of the intervention. The TEAEs were graded using CTCAE version 4·0. Where indicated, the *Medical Dictionary for Regulatory Activities* (MedDRA) preferred terms for some adverse events have been combined. ALT=alanine aminotransferase increased. AML=acute myeloid leukaemia. AST=aspartate aminotransferase increased. CMML=chronic myelomonocytic leukaemia. MDS=myelodysplastic syndrome. *Includes patients with fatigue and patients with asthenia. †Includes patients with anaemia, decreased haemoglobin level, decreased haematocrit, or decreased red blood cell count. ‡Includes patients with leukopenia and decreased white blood cell count. §Includes patients with neutropenia, febrile neutropenia, neutropenic sepsis, or decreased neutrophil count. ¶Includes patients with thrombocytopenia or decreased platelet count.

Supplementary table 7: Summary of treatment-emergent adverse events in ≥10% of patients at the primary and final analyses

Event	Olaparib (n=195)				Placebo (n=99)			
	All grades		Grade ≥3		All grades		Grade ≥3	
	Primary	Final	Primary	Final	Primary	Final	Primary	Final
Any	192 (98·5%)	194 (99·5%)	72 (36·9%)	90 (46·2%)	94 (94·9%)	94 (94·9%)	18 (18·2%)	19 (19·2%)
Nausea	148 (75·9%)	148 (75·9%)	5 (2·6%)	6 (3·1%)	33 (33·3%)	35 (35·4%)	0	0
Fatigue or asthenia*	128 (65·6%)	130 (66·7%)	8 (4·1%)	11 (5·6%)	39 (39·4%)	39 (39·4%)	2 (2·0%)	2 (2·0%)
Anaemia†	85 (43·6%)	89 (45·6%)	38 (19·5%)	41 (21·0%)	8 (8·1%)	10 (10·1%)	2 (2·0%)	2 (2·0%)
Vomiting	73 (37·4%)	78 (40·0%)	5 (2·6%)	5 (2·6%)	19 (19·2%)	20 (20·2%)	1 (1·0%)	1 (1·0%)
Diarrhoea	64 (32·8%)	67 (34·4%)	2 (1·0%)	2 (1·0%)	20 (20·2%)	20 (20·2%)	0	0
Abdominal pain	47 (24·1%)	55 (28·2%)	5 (2·6%)	6 (3·1%)	31 (31·3%)	31 (31·3%)	3 (3·0%)	3 (3·0%)
Headache	49 (25·1%)	50 (25·6%)	1 (0·5%)	1 (0·5%)	13 (13·1%)	14 (14·1%)	0	0
Constipation	40 (20·5%)	46 (23·6%)	0	0	23 (23·2%)	23 (23·2%)	3 (3·0%)	3 (3·0%)
Decreased appetite	43 (22·1%)	44 (22·6%)	0	1 (0·5%)	11 (11·1%)	11 (11·1%)	0	0
Neutropenia‡	38 (19·5%)	46 (23·6%)	10 (5·1%)	14 (72%)	6 (6·1%)	6 (6·1%)	4 (4·0%)	4 (4·0%)
Dysgeusia	52 (26·7%)	38 (19·5%)	0	0	7 (7·1%)	6 (6·1%)	0	0
Cough	33 (16·9%)	38 (19·5%)	1 (0·5%)	2 (1·0%)	5 (5·1%)	6 (6·1%)	0	0
Dizziness	26 (13·3%)	34 (17·4%)	1 (0·5%)	1 (0·5%)	5 (5·1%)	6 (6·1%)	0	0
Back pain	23 (11·8%)	32 (16·4%)	0	0	13 (13·1%)	14 (14·1%)	2 (2·0%)	2 (2·0%)
Thrombocytopenia§	27 (13·8%)	32 (16·4%)	2 (1·0%)	4 (2·1%)	3 (3·0%)	4 (4·0%)	1 (1·0%)	1 (1·0%)
Arthralgia	29 (14·9%)	31 (15·9%)	0	0	15 (15·2%)	14 (14·1%)	0	0
Hypomagnesaemia	28 (14·4%)	29 (14·9%)	0	1 (0·5%)	10 (10·1%)	10 (10·1%)	0	0
Dyspepsia	22 (11·3%)	29 (14·9%)	0	0	8 (8·1%)	9 (9·1%)	0	0
Pyrexia	26 (13·3%)	28 (14·4%)	0	0	6 (6·1%)	6 (6·1%)	0	0
Dyspnoea	23 (11·8%)	25 (12·8%)	2 (1·0%)	2 (1·0%)	1 (1·0%)	1 (1·0%)	0	0
Upper abdominal pain	21 (10·8%)	24 (12·3%)	0	1 (0·5%)	12 (12·1%)	13 (13·1%)	0	0
Leukopenia	20 (10·3%)	21 (10·8%)	3 (1·5%)	4 (2·1%)	1 (1·0%)	1 (1·0%)	0	0
Increased blood creatinine	21 (10·8%)	21 (10·8%)	0	0	1 (1·0%)	1 (1·0%)	0	0
Nasopharyngitis	21 (10·8%)	25 (12·8%)	0	0	11 (11·1%)	11 (11·1%)	0	0
Urinary tract infection	18 (9·2%)	20 (10·3%)	1 (0·5%)	3 (1·5%)	10 (10·1%)	10 (10·1%)	0	0
Stomatitis	20 (10·3%)	20 (10·3%)	2 (1·0%)	2 (1·0%)	6 (6·1%)	6 (6·1%)	0	0
Muscle spasms	19 (9·7%)	19 (9·7%)	0	0	5 (5·1%)	5 (5·1%)	0	0
Led to dose interruption	88 (45·1%)	97 (49·7%)	··	··	18 (18·2%)	19 (19·2%)	··	··
Led to dose reduction	49 (25·1%)	54 (27·7%)	··	··	3 (3·0%)	3 (3·0%)	··	··
Led to discontinuation	21 (10·8%)	33 (16·9%)	··	··	2 (2·0%)	3 (3·0%)	··	··

Data are n (%). Data are shown for TEAEs that occurred in at least 10% of patients in either treatment group during study treatment or up to 30 days after discontinuation of the intervention. The TEAEs were graded using CTCAE version 4·0. Where indicated, the *Medical Dictionary for Regulatory Activities* (MedDRA) preferred terms for some adverse events have been combined. TEAE=treatment-emergent adverse event.
*Includes patients with fatigue and patients with asthenia. †Includes patients with anaemia, decreased haemoglobin level, decreased haematocrit, or decreased red blood cell count. ‡Includes patients with neutropenia, febrile neutropenia, neutropenic sepsis, or decreased neutrophil count. § Includes patients with thrombocytopenia or decreased platelet count.

Supplementary table 8: Summary of serious treatment-emergent adverse events

Event	Olaparib (n=195)	Placebo (n=99)
Any	50 (25·6%)	8 (8·1%)
Anaemia	8 (4·1%)	0
Intestinal obstruction	4 (2·1%)	1 (1·0%)
Myelodysplastic syndrome	4 (2·1%)	0
Abdominal pain	4 (2·1%)	0
Deep vein thrombosis	3 (1·5%)	1 (1·0%)
Acute myeloid leukaemia	3 (1·5%)	0
Urinary tract infection	2 (1·0%)	1 (1·0%)
Cough	2 (1·0%)	0
Device-related infection	1 (0·5%)	0
Neutropenic sepsis	1 (0·5%)	0
Pneumonia	1 (0·5%)	0
Spinal cord infection	1 (0·5%)	0
Gastric adenocarcinoma	1 (0·5%)	0
Gastric cancer	1 (0·5%)	0
Gastrointestinal carcinoma	1 (0·5%)	0
Lymphoma	1 (0·5%)	0
Malignant lung neoplasm	1 (0·5%)	0
Plasma-cell myeloma	1 (0·5%)	0
Squamous-cell carcinoma	1 (0·5%)	0
Squamous-cell carcinoma of the skin	1 (0·5%)	0
Squamous-cell carcinoma of the tongue	1 (0·5%)	0
Thyroid cancer	1 (0·5%)	0
Febrile neutropenia	1 (0·5%)	0
Neutropenia	1 (0·5%)	0
Anaphylactic reaction	1 (0·5%)	0
Hypersensitivity	1 (0·5%)	0
Coronary artery stenosis	1 (0·5%)	0
Myocardial infarction	1 (0·5%)	0
Pericarditis	1 (0·5%)	0
Dyspnoea	1 (0·5%)	0
Pneumonitis	1 (0·5%)	0
Ascites	1 (0·5%)	0
Dysphagia	1 (0·5%)	0
Enteritis	1 (0·5%)	0
Nausea	1 (0·5%)	0
Subileus	1 (0·5%)	0
Vomiting	1 (0·5%)	0
Cholecystitis	1 (0·5%)	0
Drug reaction*	1 (0·5%)	0
Fibromyalgia	1 (0·5%)	0
Muscular weakness	1 (0·5%)	0
Osteoarthritis	1 (0·5%)	0
Haematuria	1 (0·5%)	0
Fatigue	1 (0·5%)	0
Malaise	1 (0·5%)	0
Peripheral oedema	1 (0·5%)	0
Pyrexia	1 (0·5%)	0
Increased blood creatine phosphokinase	1 (0·5%)	0
Increased blood creatinine	1 (0·5%)	0
Incisional hernia	1 (0·5%)	0
Post-procedural complication	1 (0·5%)	0
Constipation	0	2 (2·0%)
Small intestinal obstruction	0	2 (2·0%)
Invasive ductal breast carcinoma	0	1 (1·0%)
Hypokalaemia	0	1 (1·0%)
Abdominal hernia	0	1 (1·0%)
Back pain	0	1 (1·0%)
Increased amylase	0	1 (1·0%)
Post-procedural fistula	0	1 (1·0%)

Data are n (%). *Drug reaction with oeospinophilia and systemic symptoms.

Supplementary table 9: Summary of adverse events of special interest at the primary and final analyses

Event	Olaparib (n=195)		Placebo (n=99)	
	Primary	Final	Primary	Final
Myelodysplastic syndrome or acute myeloid leukaemia	4 (2%)	16 (8%)	4 (4%)	4 (4%)
TEAE*	..	7 (4%)	..	0
Non-TEAE†	..	9 (5%)	..	4 (4%)
New primary malignancies	1 (1%)	8 (4%)	1 (1%)	2 (2%)
Pneumonitis	3 (2%)	3 (2%)	0	0

Data are n (%). Data are shown for adverse events that occurred outside the follow-up period for safety (duration of treatment and up to 30 days after discontinuation). TEAE=treatment-emergent adverse event. *Occurred during the follow-up period for safety. †Occurred after the follow-up period for safety.

Supplementary table 10: Summary of treatment-emergent adverse events leading to dose interruptions, dose reductions, and treatment discontinuations in the olaparib and placebo groups

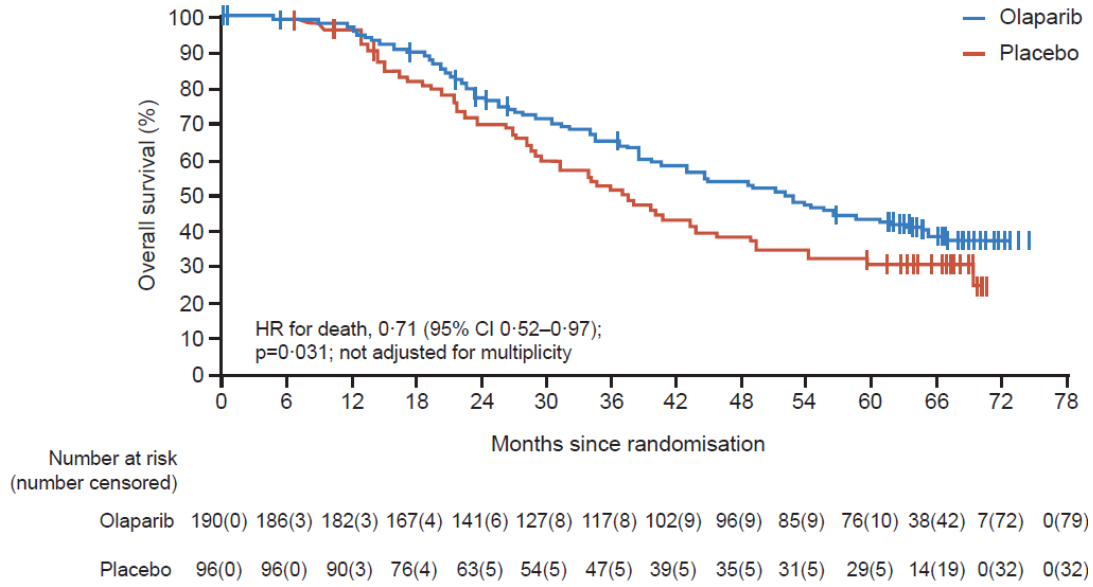
Event	Olaparib (n=195)	Placebo (n=99)
*Patients with a TEAE leading to dose interruption**	*97 (49·7%)*	*19 (19·2%)*
Anaemia	44 (22·6%)	0
Vomiting	18 (9·2%)	1 (1·0%)
Nausea	13 (6·7%)	4 (4·0%)
Neutropenia	12 (6·2%)	3 (3·0%)
Abdominal pain	8 (4·1%)	2 (2·0%)
Diarrhoea	8 (4·1%)	0
Fatigue	8 (4·1%)	0
Leukopenia	7 (3·6%)	0
Asthenia	5 (2·6%)	1 (1·0%)
Neutrophil count decreased	5 (2·6%)	0
Pyrexia	5 (2·6%)	0
Thrombocytopenia	5 (2·6%)	1 (1·0%)
Dyspnoea	4 (2·1%)	0
Intestinal obstruction	4 (2·1%)	0
Pneumonia	4 (2·1%)	0
Dizziness	3 (1·5%)	0
Dyspepsia	3 (1·5%)	0
Headache	3 (1·5%)	1 (1·0%)
Influenza	3 (1·5%)	0
Platelet count decreased	3 (1·5%)	0
Stomatitis	3 (1·5%)	0
Abdominal pain upper	2 (1·0%)	1 (1·0%)
Cough	2 (1·0%)	0
Decreased appetite	2 (1·0%)	0
Dyspraxia	2 (1·0%)	0
Gastroenteritis	2 (1·0%)	0
Gastroenteritis viral	2 (1·0%)	0
Nasopharyngitis	2 (1·0%)	0
Oedema peripheral	2 (1·0%)	0
Rash	2 (1·0%)	0
White blood cell decreased	2 (1·0%)	0
Abdominal discomfort	1 (0·5%)	0
Alanine aminotransferase increased	1 (0·5%)	1 (1·0%)
Animal bite	1 (0·5%)	0
Aspartate aminotransferase increased	1 (0·5%)	1 (1·0%)
Blood creatine phosphokinase increased	1 (0·5%)	0
Bronchitis	1 (0·5%)	0
Chills	1 (0·5%)	0
Cholecystitis	1 (0·5%)	0
Conjunctival irritation	1 (0·5%)	0
Dental carries	1 (0·5%)	1 (1·0%)
Dermatitis allergic	1 (0·5%)	0
Discomfort	1 (0·5%)	0
Dysphagia	1 (0·5%)	0
Enteritis	1 (0·5%)	0
Erythema	1 (0·5%)	0
Erythroblast count increased	1 (0·5%)	0
Gastric cancer	1 (0·5%)	0
Gastrointestinal infection	1 (0·5%)	0
Haemorrhoidal haemorrhage	1 (0·5%)	0
Hypocalcaemia	1 (0·5%)	0
Influenza-like illness	1 (0·5%)	0

Event	Olaparib (n=195)	Placebo (n=99)
Lung neoplasm malignant	1 (0·5%)	0
Lymphocyte count decreased	1 (0·5%)	0
Lymphoma	1 (0·5%)	0
Memory impairment	1 (0·5%)	0
Mouth ulceration	1 (0·5%)	0
Myelocytosis	1 (0·5%)	0
Myelodysplastic syndrome	1 (0·5%)	0
Neutropenic sepsis	1 (0·5%)	0
Oral pain	1 (0·5%)	0
Osteoarthritis	1 (0·5%)	0
Pain in extremity	1 (0·5%)	0
Pallor	1 (0·5%)	0
Pollakiuria	1 (0·5%)	0
Presyncope	1 (0·5%)	0
Spinal cord infection	1 (0·5%)	0
Squamous cell carcinoma of the tongue	1 (0·5%)	0
Subileus	1 (0·5%)	0
Syncope	1 (0·5%)	1 (1·0%)
Tachycardia	1 (0·5%)	0
Thyroid cancer	1 (0·5%)	0
Tinnitus	1 (0·5%)	0
Tooth abscess	1 (0·5%)	1 (1·0%)
Tooth infection	1 (0·5%)	0
Toothache	1 (0·5%)	0
Upper limb fracture	1 (0·5%)	0
Upper respiratory tract infection	1 (0·5%)	0
Urinary tract infection	1 (0·5%)	1 (1·0%)
Vertigo	1 (0·5%)	0
Blood alkaline phosphatase increased	0	1 (1·0%)
Constipation	0	1 (1·0%)
Deep vein thrombosis	0	1 (1·0%)
Gamma-glutamyltranferase increased	0	1 (1·0%)
Hypokalaemia	0	1 (1·0%)
Pleural effusion	0	1 (1·0%)
Post procedural fistula	0	1 (1·0%)
Rhinitis	0	1 (1·0%)
Skin infection	0	1 (1·0%)
Small intestinal obstruction	0	1 (1·0%)
Patients with a TEAE leading to dose reduction[†]	*54 (27·7%)*	*3 (3·0%)*
Anaemia	27 (13·8%)	0
Fatigue	8 (4·1%)	0
Asthenia	7 (3·6%)	0
Neutropenia	4 (2·1%)	0
Leukopenia	3 (1·5%)	0
Nausea	2 (1·0%)	2 (2·0%)
Neutrophil count decreased	2 (1·0%)	0
Thrombocytopenia	2 (1·0%)	0
White blood cell count decreased	2 (1·0%)	0
Abdominal pain	1 (0·5%)	1 (1·0%)
Arthralgia	1 (0·5%)	0
Dysgeusia	1 (0·5%)	0
Dyspepsia	1 (0·5%)	0
Dyspnoea	1 (0·5%)	0
Dyspraxia	1 (0·5%)	0
Erythema	1 (0·5%)	0
Genital herpes simplex	1 (0·5%)	0
Headache	1 (0·5%)	0
Memory impairment	1 (0·5%)	0
Mouth ulceration	1 (0·5%)	0
Myalgia	1 (0·5%)	0
Oedema peripheral	1 (0·5%)	0
Peripheral sensory neuropathy	1 (0·5%)	0
Rash	1 (0·5%)	0
Syncope	0	1 (1·0%)
Patients with a TEAE leading to treatment discontinuation[‡]	*33 (16·9%)*	*3 (3·0%)*
Neoplasms benign, malignant and unspecified (including cysts and polyps)		
Acute myeloid leukaemia	3 (1·5%)	0
Myelodysplastic syndrome	2 (1·0%)	0
Gastrointestinal carcinoma	1 (0·5%)	0
Lymphoma	1 (0·5%)	0
Plasma cell myeloma	1 (0·5%)	0
Squamous cell carcinoma	1 (0·5%)	0
Squamous cell carcinoma of the tongue	1 (0·5%)	0

Event	Olaparib (n=195)	Placebo (n=99)
Invasive ductal breast carcinoma	0	1 (1·0%)
Blood and lymphatic system disorders		
Anaemia	8 (4·1%)	0
Neutropenia	2 (1·0%)	0
Thrombocytopenia	2 (1·0%)	1 (1·0%)
Leukopenia	1 (0·5%)	0
Psychiatric disorders		
Depression	1 (0·5%)	0
Nervous system disorders		
Disturbance in attention	1 (0·5%)	0
Memory impairment	0	1 (1·0%)
Respiratory, thoracic and mediastinal disorder		
Cough	1 (0·5%)	0
Pneumonitis	1 (0·5%)	0

Data are n (%). Data are shown for TEAEs with an onset date during study treatment or up to 30 days after discontinuation of the intervention. TEAE = treatment-emergent adverse event. *Patients may have had more than one TEAE leading to dose interruption (temporary discontinuation of study treatment). †Patients may have had more than one TEAE leading to dose reduction. ‡Patients with multiple TEAEs leading to treatment discontinuation are counted once for each system organ class or preferred term.

Supplementary figure 1: Kaplan-Meier estimates of overall survival in patients with a Myriad germline BRCA mutation

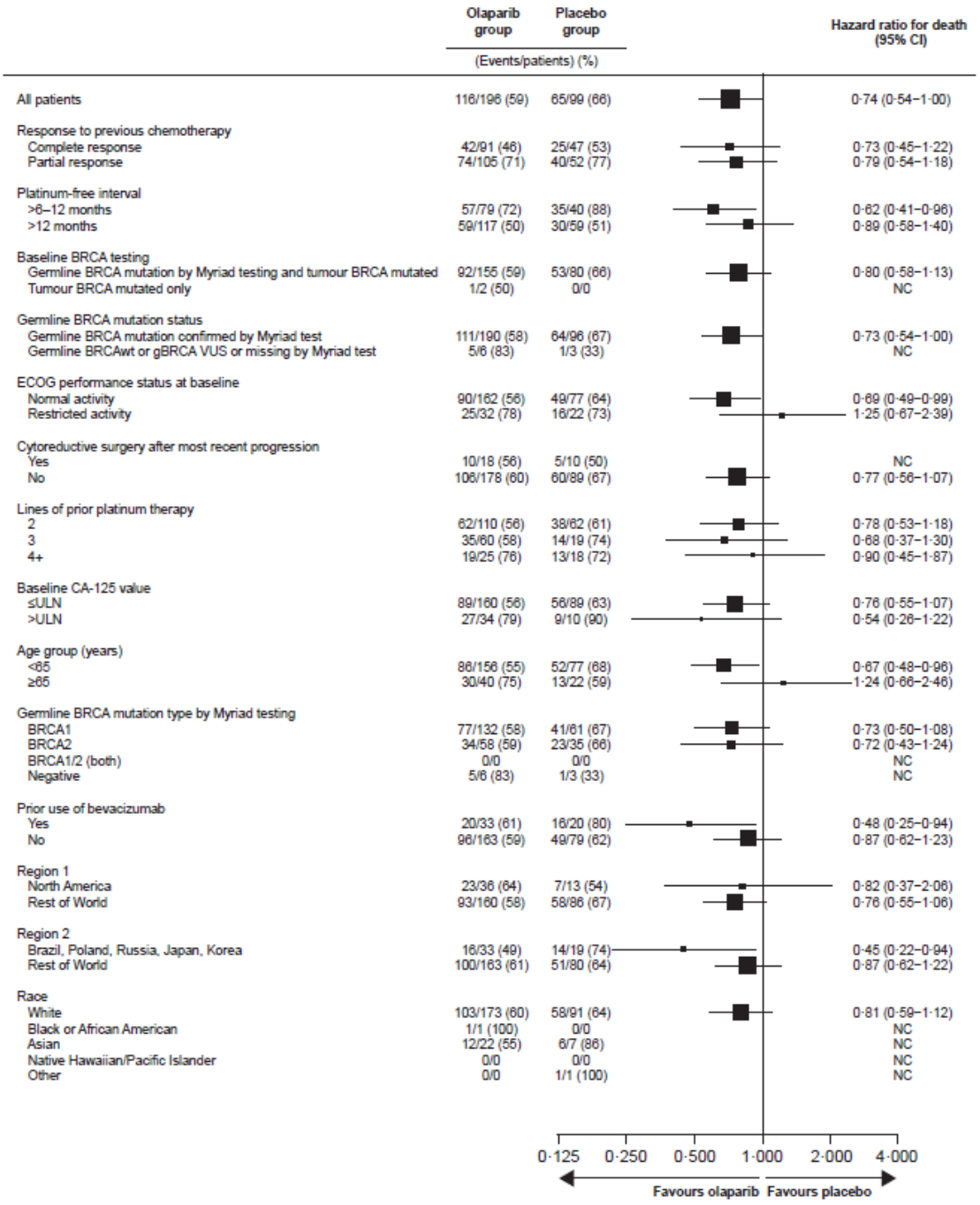


Number at risk (number censored)

Olaparib	190(0)	186(3)	182(3)	167(4)	141(6)	127(8)	117(8)	102(9)	96(9)	85(9)	76(10)	38(42)	7(72)	0(79)
Placebo	96(0)	96(0)	90(3)	76(4)	63(5)	54(5)	47(5)	39(5)	35(5)	31(5)	29(5)	14(19)	0(32)	0(32)

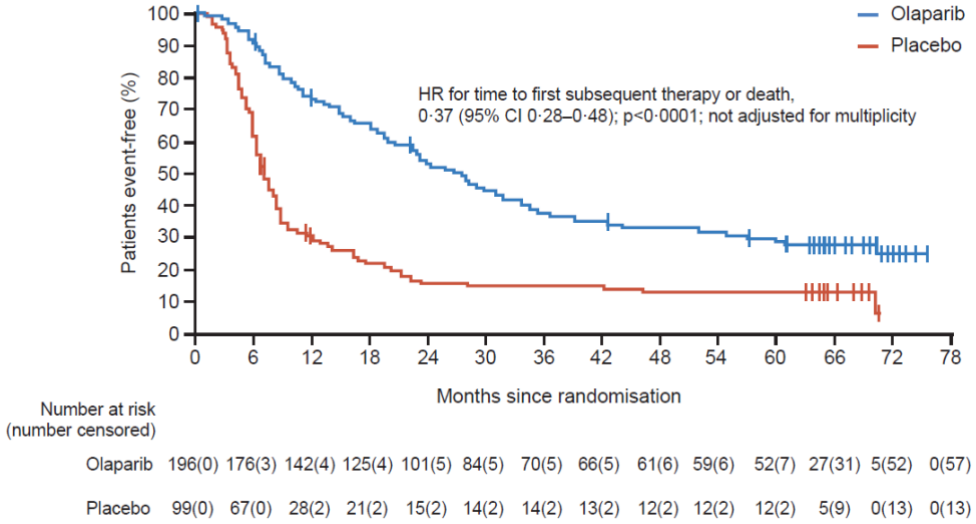
CI=confidence interval. HR=hazard ratio.

Supplementary figure 2: Subgroup analysis of overall survival



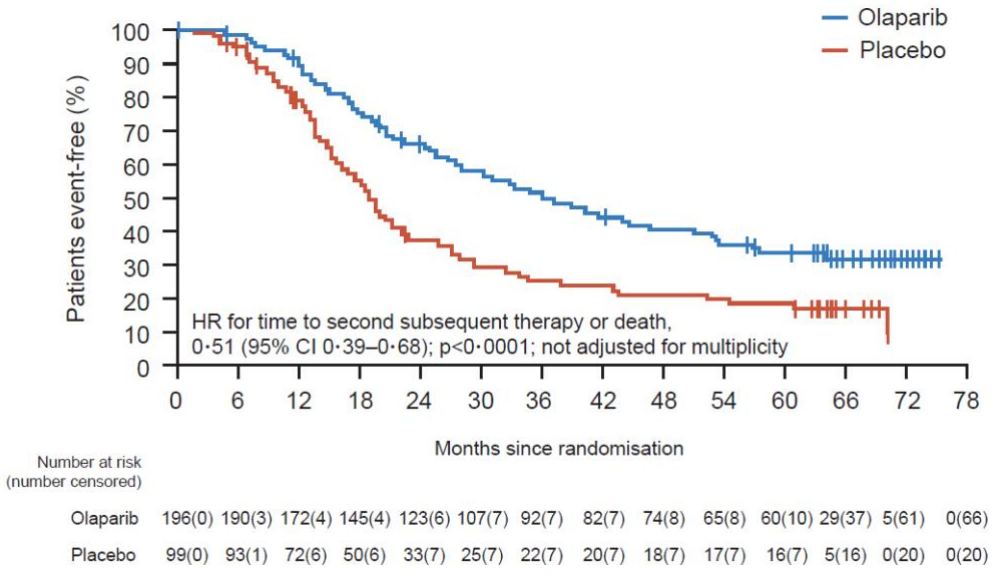
For the hazard ratios, the size of the square is proportional to the number of events. The vertical solid line indicates the point of no effect. Estimated from a Cox proportional hazards model including treatment, subgroup of interest and subgroup by treatment interaction. CI=confidence interval. ECOG=Eastern Cooperative Oncology Group. g=germline. NC=not calculated. ULN=upper limit of the normal range. VUS=variant of unknown significance. wt=wild type.

Supplementary figure 3: Kaplan-Meier estimates of time to first subsequent therapy in the full analysis set



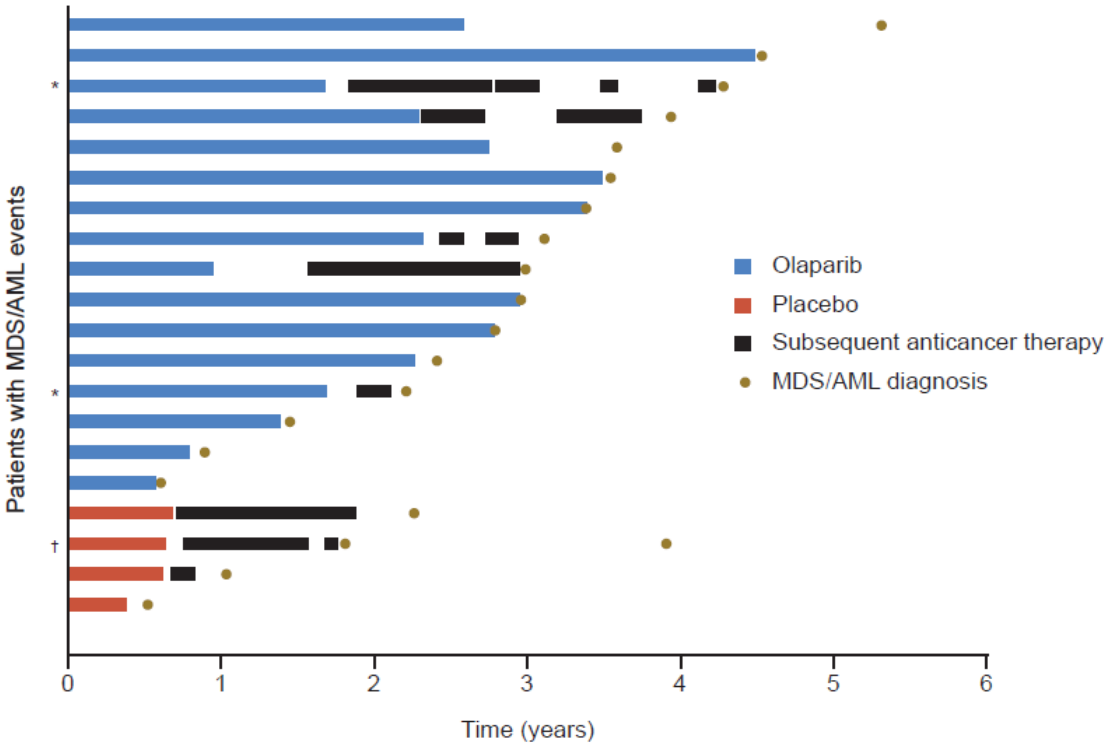
CI=confidence interval. HR=hazard ratio.

Supplementary figure 4: Kaplan-Meier estimates of time to second subsequent therapy in the full analysis set



CI=confidence interval. HR=hazard ratio.

Supplementary figure 5: Swimmer plot of study treatment, subsequent therapy, and diagnosis of MDS/AML in the safety analysis set



AML=acute myeloid leukaemia. MDS=myelodysplastic syndrome. *Two patients in the olaparib group received olaparib as part of subsequent anticancer therapy. †One patient in the placebo group received olaparib as part of subsequent anticancer therapy.