Efficacy of maintenance olaparib plus bevacizumab according to clinical risk in patients with newly diagnosed, advanced ovarian cancer in the phase III PAOLA-1/ENGOT-ov25 trial

This appendix has been provided by the authors to give readers additional information about their work.
Supplement to: Harter P, Mouret-Reynier MA, Pignata S, et al. Efficacy of maintenance olaparib plus bevacizumab according to clinical risk in patients with newly diagnosed, advanced ovarian cancer in the phase III PAOLA-1/ENGOT-ov25 trial

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1. Methods

1.1 Full eligibility criteria

1.1.1 Inclusion criteria

For inclusion in the study, patients should fulfill the following criteria:

1. Female and must be aged ≥18 years
2. Signed informed consent and ability to comply with treatment and follow-up
3. Patients with newly diagnosed:
   - Ovarian cancer, primary peritoneal cancer and/or fallopian tube cancer
   - Histologically confirmed (based on local histopathological findings):
     - High-grade serous or
     - High-grade endometrioid or
     - Other epithelial non-mucinous ovarian cancer in patients with a deleterious germline *BRCA1* and/or *BRCA2* mutation
   - Advanced stage: International Federation of Gynecology and Obstetrics (FIGO) stage IIIB, IIIC or IV (1988 FIGO classification):
     - Using the current 2014 FIGO classification for stage III disease, women would be classified as having stage IIIA–IV ovarian cancer
4. Completed first-line, platinum-taxane chemotherapy prior to randomization:
   - Platinum-taxane-based regimen must have consisted of a minimum of six treatment cycles and a maximum of nine. However, if platinum-based therapy is discontinued early as a result of nonhematological toxicity specifically related to the platinum regimen (i.e. neurotoxicity, hypersensitivity, etc.), the patient must have received a minimum of four cycles of the platinum regimen
   - Intravenous, intraperitoneal or neoadjuvant platinum-based chemotherapy is allowed; for weekly therapy, 3 weeks are considered one cycle. Interval debulking surgery is allowed
5. Prior to randomization, patients must have received a minimum of three cycles of bevacizumab in combination with the three last cycles of platinum-based chemotherapy. Only in the case of interval cytoreductive surgery are patients permitted to receive only two cycles of bevacizumab in combination with the last three cycles of platinum-based chemotherapy. Bevacizumab treatment should be administered at a dose 15 mg/kg every 3 weeks up to a total of 15 months
6. Prior to randomization, patients must have no evidence of disease (NED) or be in complete response or partial response from the first-line treatment. There should be no clinical evidence of disease progression (physical examination, imaging, cancer antigen 125 [CA-125]) throughout first-line treatment and prior to study randomization:
   - Patients without assessable disease after initial cytoreductive surgery were considered to have NED at the end of the first-line chemotherapy and surgery strategy if disease has not progressed
   - Patients with measurable or assessable disease after initial cytoreductive surgery or at the start of neoadjuvant chemotherapy and whose disease was no longer detectable at the end of the chemotherapy and surgery strategy were considered to have a complete response
7. Patients must be randomized at least 3 weeks and no more than 9 weeks after their last dose of chemotherapy (last dose is the day of the last infusion) and all major toxicities from prior chemotherapy must have resolved to Common

Terminology Criteria for Adverse Events (CTCAE) grade 1 or better (except alopecia and peripheral neuropathy)

8. Patients must have normal organ and bone marrow function:
   - Hemoglobin ≥10.0 g/dL
   - Absolute neutrophil count ≥1.5 x 10^9/L
   - Platelet count ≥100 x 10^9/L
   - Total bilirubin ≤1.5 x institutional upper limit of normal (ULN)
   - Aspartate aminotransferase/serum glutamic oxaloacetic transaminase and alanine aminotransferase/serum glutamic pyruvate transaminase ≤2.5 x ULN unless liver metastases are present, in which case they must be ≤5 x ULN
   - Serum creatinine ≤1.25 x institutional ULN and creatinine clearance >50 mL/min
   - Patients not receiving anticoagulant medication who have an international normalized ratio (INR) ≤1.5 and an activated prothrombin time (aPTT) ≤1.5 x ULN. The use of full-dose oral or parenteral anticoagulants is permitted as long as the INR or aPTT is within therapeutic limits (according to the site's medical standard). If the patient is on oral anticoagulants, the dose has to be stable for at least 2 weeks at the time of randomization
   - Urine dipstick for proteinuria <2+. If urine dipstick is ≥2+, 24-hour urine must demonstrate <1 g of protein in 24 hours
   - Normal blood pressure (BP) or adequately treated and controlled hypertension (systolic BP ≤140 mmHg and/or diastolic BP ≤90 mmHg)
9. Eastern Cooperative Oncology Group performance status 0–1
10. Formalin-fixed, paraffin-embedded tumor sample from the primary cancer must be available for central BRCA testing and test result must be available for stratification
11. Postmenopausal or evidence of non-childbearing status for women of childbearing potential prior to the first dose of study treatment
12. **For France only**: in France, a patient will be eligible for randomization in this study only if either affiliated to, or a beneficiary of, a social security category

1.1.2 Exclusion criteria

Patients must not enter the study if any of the following exclusion criteria are fulfilled:

1. Non-epithelial origin of the ovary, fallopian tube or peritoneum (i.e. germ-cell tumors)
2. Ovarian tumors of low malignant potential (e.g. borderline tumors) and clear-cell or mucinous carcinoma
3. Synchronous primary endometrial cancer unless both of the following criteria are met:
   - Stage <II
   - Aged <60 years at the time of diagnosis of endometrial cancer with stage IA or IB grade I or II, or stage IA grade III endometrial carcinoma OR aged ≥60 years at the time of diagnosis of endometrial cancer with stage IA grade I or II endometrioid adenocarcinoma. Patients with serous or clear-cell adenocarcinoma or carcinosarcoma of the endometrium are not eligible
4. 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.* Patients with a history of localized malignancy diagnosed over 5 years ago may be eligible provided they completed adjuvant systemic therapy

prior to randomization and remain free of recurrent or metastatic disease. Patients with a history of primary triple-negative breast cancer may be eligible provided they completed definitive anticancer treatment more than 3 years ago and remain breast cancer free prior to start of study treatment

5. Patients with myelodysplastic syndromes/acute myeloid leukemia history
6. Patients who experienced, for at least one cycle, a delay of >2 weeks because of prolonged hematologic recovery during first-line chemotherapy
7. Patients receiving radiotherapy within 6 weeks prior to study treatment
8. Major surgery within 4 weeks of starting study treatment; patients must have recovered from any effects of any major surgery
9. Previous allogenic bone marrow transplantation
10. Any previous treatment with poly(ADP–ribose) polymerase inhibitor, including olaparib
11. Administration of other simultaneous chemotherapy drugs, any other anticancer therapy or antineoplastic hormonal therapy, or simultaneous radiotherapy during the trial treatment period (hormonal replacement therapy is permitted as are steroidal antiemetics)
12. Current or recent (within 10 days prior to randomization) chronic use of aspirin >325 mg/day
13. Concomitant use of known potent cytochrome P450 3A4 inhibitors, such as ketoconazole, itraconazole, ritonavir, indinavir, saquinavir, telithromycin, clarithromycin and nelfinavir
14. History of hypertensive crisis (CTCAE grade 4) or hypertensive encephalopathy
15. Clinically significant (e.g. active) cardiovascular disease, including:
    - Myocardial infarction or unstable angina pectoris within ≤6 months of randomization
    - New York Heart Association grade ≥2 congestive heart failure
    - Poorly controlled cardiac arrhythmia despite medication (patients with rate-controlled atrial fibrillation are eligible), or any clinically significant abnormal finding on resting electrocardiogram
    - Peripheral vascular disease grade ≥3 (e.g. symptomatic and interfering with activities of daily living requiring repair or revision)
16. Previous cerebrovascular accident, transient ischemic attack or subarachnoid hemorrhage within 6 months prior to randomization
17. History or evidence of hemorrhagic disorders within 6 months prior to randomization
18. Evidence of bleeding diathesis or significant coagulopathy (in the absence of coagulation)
19. History or clinical suspicion of brain metastases or spinal cord compression. computed tomography/magnetic resonance imaging (MRI) of the brain is mandatory (within 4 weeks prior to randomization) in the case of suspected brain metastases. Spinal MRI is mandatory (within 4 weeks prior to randomization) in the case of suspected spinal cord compression
20. History or evidence upon neurological examination of central nervous system disease (e.g. uncontrolled seizures), unless adequately treated with standard medical therapy
21. Significant traumatic injury during 4 weeks prior to randomization

22. Non-healing wound, active ulcer or bone fracture. Patients with granulating incisions healing by secondary intention with no evidence of fascial dehiscence or infection are eligible, but require 3-weekly wound examinations
23. History of vascular endothelial growth factor therapy-related abdominal fistula or gastrointestinal perforation or active gastrointestinal bleeding within 6 months prior to the first study treatment
24. Current, clinically relevant bowel obstruction, including sub-occlusive disease, related to underlying disease
25. Patients with evidence of abdominal free air not explained by paracentesis or recent surgical procedure
26. Evidence of any other disease, metabolic dysfunction, physical examination finding or laboratory finding that gives reasonable suspicion of a disease or condition that contraindicates the use of an investigational drug or puts the patient at high risk for treatment-related complications
27. Pregnant or lactating women
28. Participation in another clinical study with an investigational product during the chemotherapy cycle immediately prior to randomization
29. Patients unable to swallow orally administered medication and patients with gastrointestinal disorders likely to interfere with absorption of the study medication
30. Patients with a known hypersensitivity to olaparib or any of the excipients of the product
31. Immunocompromised patients; for example, with known active hepatitis (i.e. hepatitis B or C) due to risk of transmitting the infection through blood or other body fluids or patients known to be serologically positive for human immunodeficiency virus

1.2 Tumor BRCA testing

Before patients entered the trial, archival tumor samples were sent to one of five central French academic laboratories for assessment of BRCA mutation status. The results of tumor BRCA testing were then sent to the principal investigator at each study site for stratification of patients.

Retrospective central tumor BRCA testing, using the myChoice® HRD Plus assay (Myriad Genetic Laboratories, Inc., Salt Lake City, UT, USA), was conducted on tumor samples to determine Myriad tumor homologous recombination deficiency (HRD) status. A genomic instability score (GIS) of ≥42 (positive test) provided evidence of defects in homologous recombination and a GIS of <42 (negative test) provided evidence that homologous recombination was not defective.

1.3 Randomization

Randomization was performed centrally using a block design with stratification according to:

- Outcome of first-line treatment at screening:
  - No evidence of disease with complete macroscopic resection at upfront cytoreductive surgery versus
  - No evidence of disease/complete response with complete macroscopic resection at interval cytoreductive surgery versus
  - No evidence of disease/complete response in patients with either incomplete resection at upfront/interval cytoreductive surgery or no cytoreductive surgery versus
  - Partial response
- Tumor BRCA status:
  - Deleterious mutation versus
  - No deleterious mutation, including tumor BRCA wild-type, a variant of uncertain significance, or an unknown result.

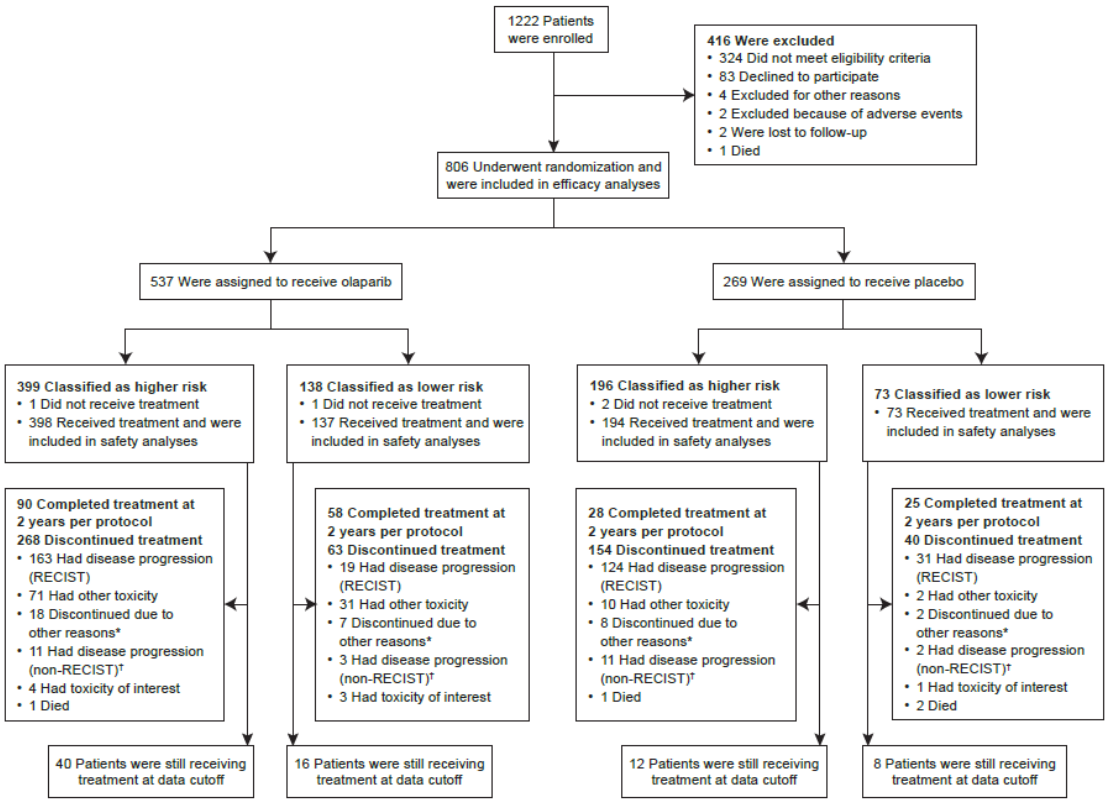
No evidence of disease was defined as complete macroscopic resection after cytoreductive surgery and no radiologic evidence of disease and a normal CA-125 level after chemotherapy, clinical complete response was defined as the disappearance of all measurable/assessable disease present at the start of chemotherapy and normalization of CA-125 levels, and clinical partial response was defined as radiologic evidence of disease and/or an abnormal CA-125 level.

2. Results

2.1 Median follow-up for progression-free survival

The median (interquartile range) follow-up for PFS was 22.3 (17.2–27.7) months in the olaparib plus bevacizumab arm and 24.6 (17.2–27.9) months in the placebo plus bevacizumab arm in the higher-risk subgroup, and 23.9 (20.8–27.7) months in the olaparib plus bevacizumab arm and 22.3 (21.9–27.6) months in the placebo plus bevacizumab arm in the lower-risk subgroup.

Figure S1. Patient disposition



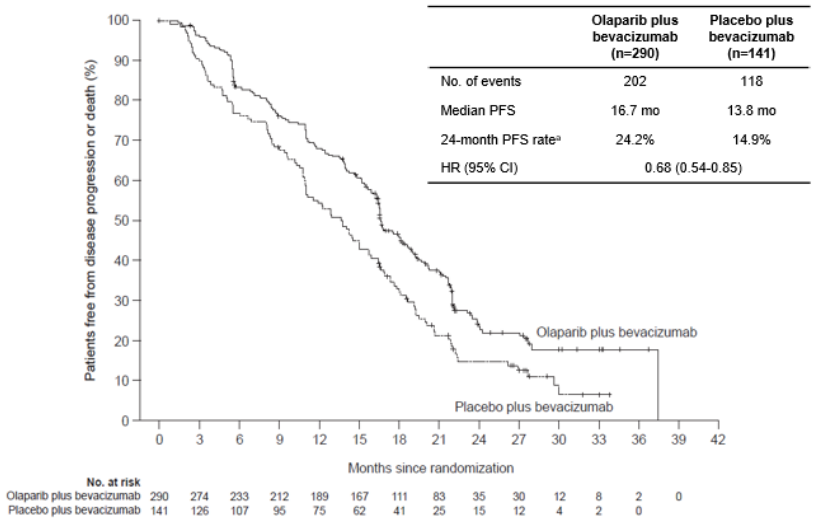
*Other reasons included consent withdrawn (higher-risk group: n = 3, olaparib plus bevacizumab and *n* = 2, placebo plus bevacizumab; lower-risk group: n = 1, olaparib plus bevacizumab and n = 2, placebo plus bevacizumab), lost to follow-up (lower-risk group: n = 1, olaparib plus bevacizumab), missing (higher-risk group: n = 1, olaparib plus bevacizumab) and other (higher-risk group: n = 14, olaparib plus bevacizumab and n = 6, placebo plus bevacizumab; lower-risk group: n = 5, olaparib plus bevacizumab).

†Disease progression defined by criteria other than RECIST (higher-risk group: n = 6, olaparib plus bevacizumab and n = 8, placebo plus bevacizumab; lower-risk group: n = 3, olaparib plus bevacizumab and n = 2, placebo plus bevacizumab) or symptomatic deterioration (higher-risk group: n = 5, olaparib plus bevacizumab and n=3, placebo plus bevacizumab).

RECIST, Response Evaluation Criteria in Solid Tumors.

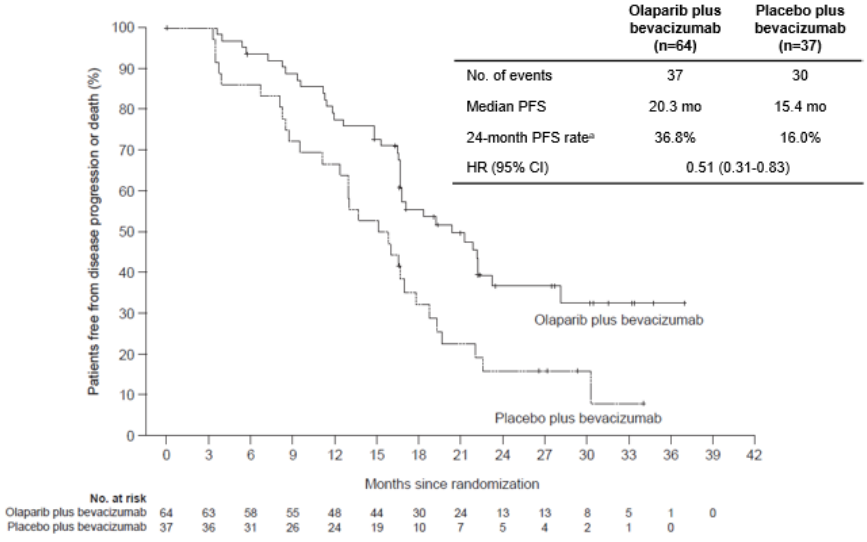
Figure S2. Kaplan–Meier estimate of progression-free survival in higher-risk patients (A) without a tumor BRCA mutation, (B) who are HRD positive excluding a BRCA mutation, (C) who are HRD negative/unknown, (D) who are HRD negative and (E) who are HRD unknown

A. No tumor BRCA mutation



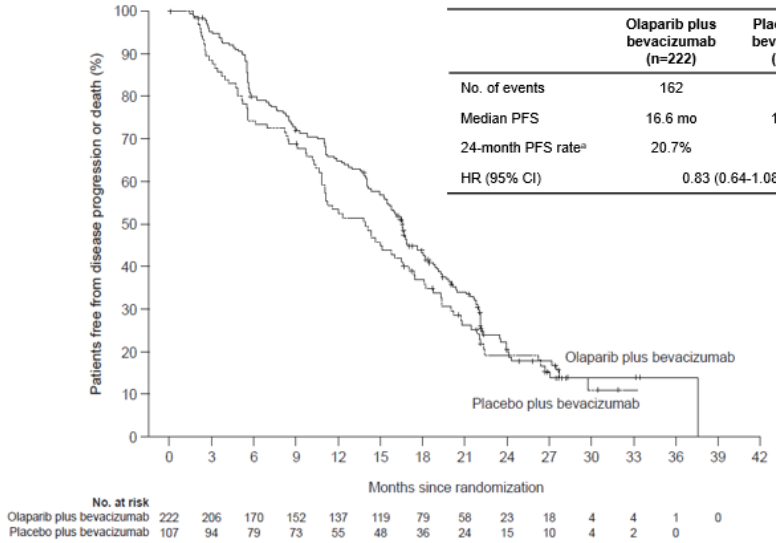
	Olaparib plus bevacizumab (n=290)	Placebo plus bevacizumab (n=141)
No. of events	202	118
Median PFS	16.7 mo	13.8 mo
24-month PFS rate[a]	24.2%	14.9%
HR (95% CI)	0.68 (0.54-0.85)	

B. HRD positive excluding a BRCA mutation



	Olaparib plus bevacizumab (n=64)	Placebo plus bevacizumab (n=37)
No. of events	37	30
Median PFS	20.3 mo	15.4 mo
24-month PFS rate[a]	36.8%	16.0%
HR (95% CI)	0.51 (0.31-0.83)	

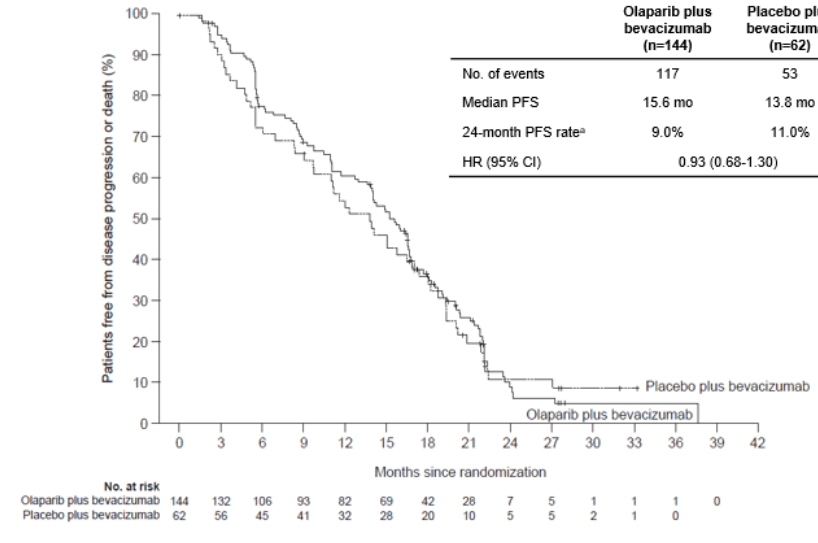
C. HRD negative/unknown



	Olaparib plus bevacizumab (n=222)	Placebo plus bevacizumab (n=107)
No. of events	162	87
Median PFS	16.6 mo	13.9 mo
24-month PFS rate[a]	20.7%	19.3%
HR (95% CI)	0.83 (0.64-1.08)	

No. at risk													
Olaparib plus bevacizumab	222	206	170	152	137	119	79	58	23	18	4	4	1	0
Placebo plus bevacizumab	107	94	79	73	55	48	36	24	15	10	4	2	0	

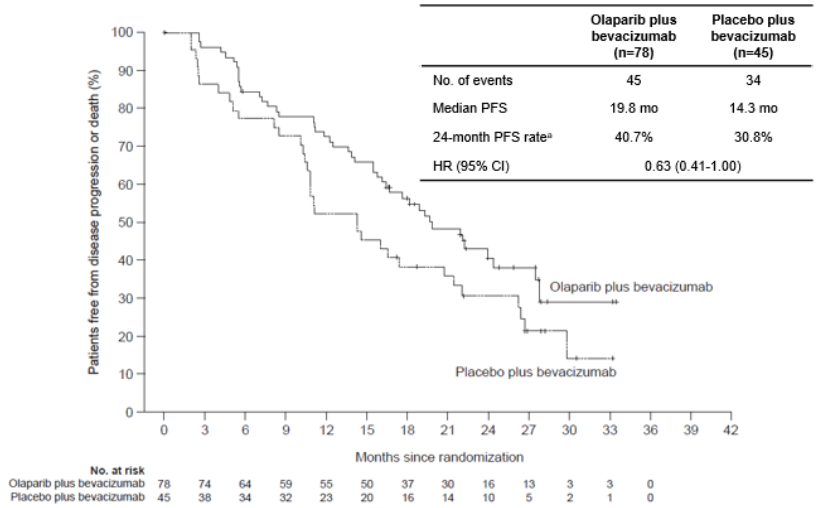
D. HRD negative



	Olaparib plus bevacizumab (n=144)	Placebo plus bevacizumab (n=62)
No. of events	117	53
Median PFS	15.6 mo	13.8 mo
24-month PFS rate[a]	9.0%	11.0%
HR (95% CI)	0.93 (0.68-1.30)	

No. at risk													
Olaparib plus bevacizumab	144	132	106	93	82	69	42	28	7	5	1	1	1	0
Placebo plus bevacizumab	62	56	45	41	32	28	20	10	5	5	2	1	0	

E. HRD unknown

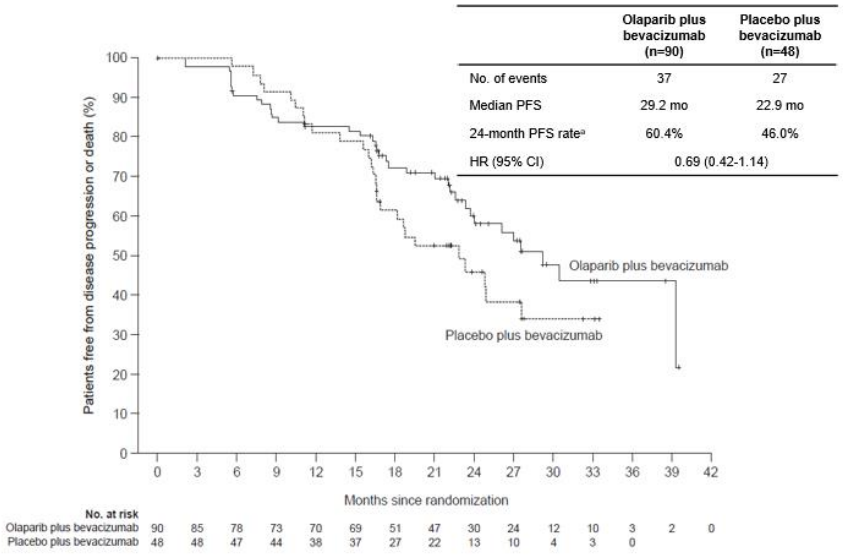


	Olaparib plus bevacizumab (n=78)	Placebo plus bevacizumab (n=45)
No. of events	45	34
Median PFS	19.8 mo	14.3 mo
24-month PFS rate[a]	40.7%	30.8%
HR (95% CI)	0.63 (0.41-1.00)	

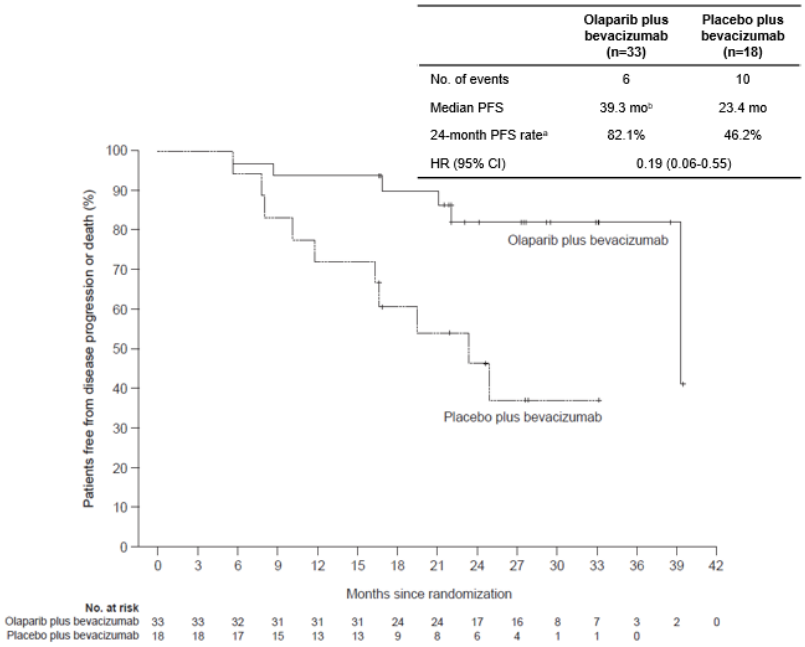
CI, confidence interval; HRD, homologous recombination deficiency.

Figure S3. Kaplan–Meier estimate of progression-free survival in lower-risk patients (A) without a tumor BRCA mutation, (B) who are HRD positive excluding a BRCA mutation, (C) who are HRD negative/unknown and (D) who are HRD negative

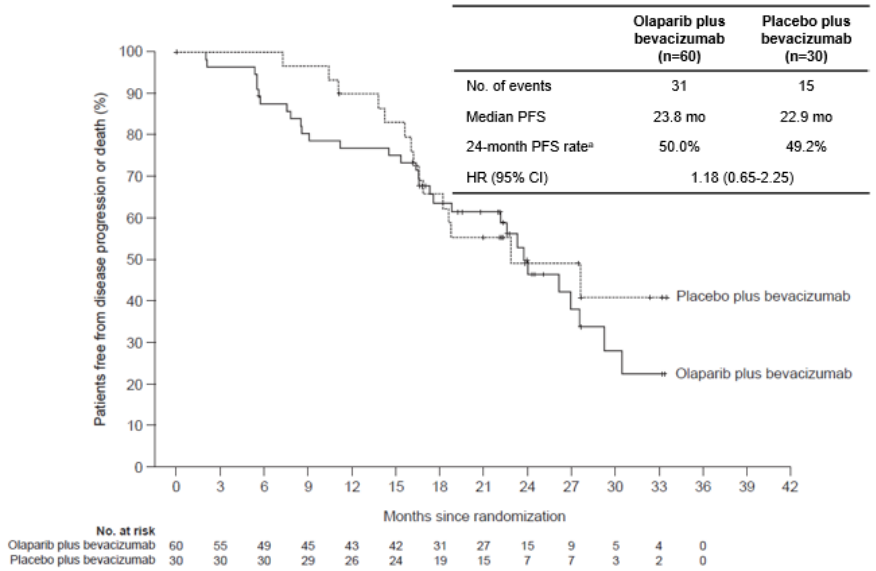
A. No tumor BRCA mutation



B. HRD positive excluding a BRCA mutation

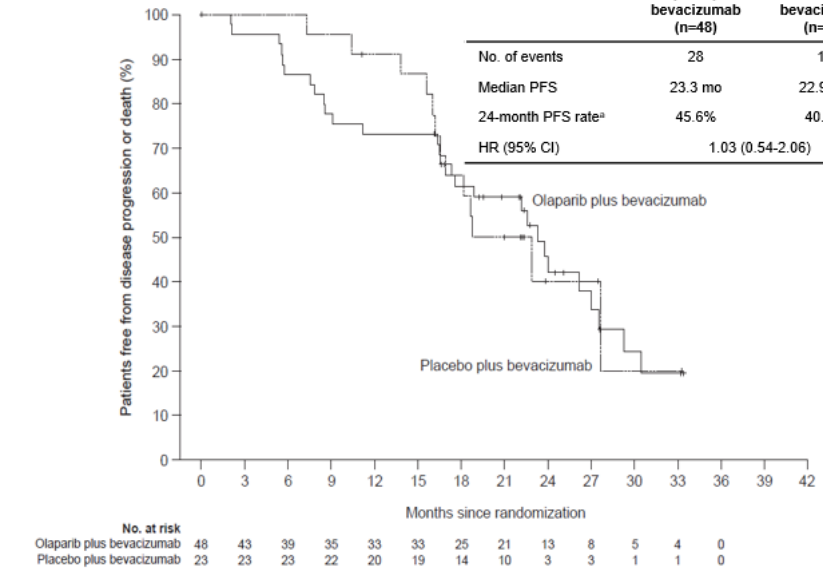


C. HRD negative/unknown



	Olaparib plus bevacizumab (n=60)	Placebo plus bevacizumab (n=30)
No. of events	31	15
Median PFS	23.8 mo	22.9 mo
24-month PFS rate[a]	50.0%	49.2%
HR (95% CI)	1.18 (0.65-2.25)	

D. HRD negative



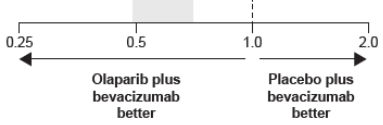
	Olaparib plus bevacizumab (n=48)	Placebo plus bevacizumab (n=23)
No. of events	28	13
Median PFS	23.3 mo	22.9 mo
24-month PFS rate[a]	45.6%	40.2%
HR (95% CI)	1.03 (0.54-2.06)	

CI, confidence interval; HRD, homologous recombination deficiency.

Figure S4. Analysis of progression-free survival according to biomarker status in (A) higher-risk patients and (B) lower-risk patients

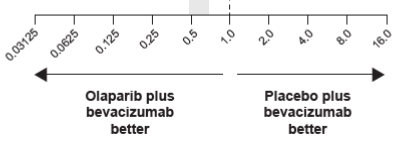
A Higher-risk patients

Subgroup	Olaparib plus bevacizumab *no. of patients with disease progression or death/total no. (%)*	Placebo plus bevacizumab *no. of patients with disease progression or death/total no. (%)*	Hazard ratio for disease progression or death (95% CI)
Higher-risk patients	239/399 (59.9)	154/196 (78.6)	0.60 [0.49–0.74]
Tumor BRCA status*			
Tumor BRCAm	37/109 (33.9)	36/55 (65.5)	0.37 [0.23–0.59]
No tumor BRCAm	202/290 (69.7)	118/141 (83.7)	0.68 [0.54–0.85]
Tumor HRD status (2 modalities)			
HRD-positive, including BRCAm	77/177 (43.5)	67/89 (75.3)	0.39 [0.28–0.54]
HRD-negative/unknown	162/222 (73)	87/107 (81.3)	0.83 [0.64–1.08]
Tumor HRD status (3 modalities)			
HRD-positive, including BRCAm	77/177 (43.5)	67/89 (75.3)	0.38 [0.28–0.54]
HRD-negative	117/144 (81.3)	53/62 (85.5)	0.93 [0.68–1.30]
HRD-unknown	45/78 (57.7)	34/45 (75.6)	0.63 [0.41–1.00]
Tumor HRD status excluding tumor BRCAm			
HRD-positive, excluding BRCAm	37/64 (57.8)	30/37 (81.1)	0.51 [0.31–0.83]
HRD-negative	117/144 (81.3)	53/62 (85.5)	0.94 [0.68–1.31]



B Lower-risk patients

Subgroup	Olaparib plus bevacizumab *no. of patients with disease progression or death/total no. (%)*	Placebo plus bevacizumab *no. of patients with disease progression or death/total no. (%)*	Hazard ratio for disease progression or death (95% CI)
Lower-risk patients	41/138 (29.7)	40/73 (54.8)	0.46 [0.30–0.72]
Tumor BRCA status*			
Tumor BRCAm	4/48 (8.3)	13/25 (52)	0.11 [0.03–0.31]
No tumor BRCAm	37/90 (41.1)	27/48 (56.3)	0.69 [0.42–1.14]
Tumor HRD status (2 modalities)			
HRD-positive, including BRCAm	10/78 (12.8)	25/43 (58.1)	0.15 [0.07–0.30]
HRD-negative/unknown	31/60 (51.7)	15/30 (50)	1.18 [0.65–2.25]
Tumor HRD status (3 modalities)			
HRD-positive, including BRCAm	10/78 (12.8)	25/43 (58.1)	0.15 [0.07–0.30]
HRD-negative	28/48 (58.3)	13/23 (56.5)	1.03 [0.54–2.06]
HRD-unknown	3/12 (25)	2/7 (28.6)	1.46 [0.24–11.15]
Tumor HRD status excluding tumor BRCAm			
HRD-positive, excluding BRCAm	6/33 (18.2)	10/18 (55.6)	0.19 [0.06–0.55]
HRD-negative	28/48 (58.3)	13/23 (56.5)	1.03 [0.54–2.06]



For the hazard ratios, the size of the circle is proportional to the number of events. The gray band represents the 95% CI for the overall population, and the dashed line indicates the point of no effect.
*As per the electronic case report form.
BRCAm, BRCA mutation; CI, confidence interval; HRD, homologous recombination deficiency.

Table S1. Adverse events with olaparib plus bevacizumab versus placebo plus bevacizumab[a]

Adverse event, *n* (%)	Higher-risk patients				Lower-risk patients			
	Olaparib plus bevacizumab (N = 398)		Placebo plus bevacizumab (N = 194)		Olaparib plus bevacizumab (N = 137)		Placebo plus bevacizumab (N = 73)	
	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3
Any	395 (99)	227 (57)	184 (95)	98 (51)	136 (99)	76 (55)	72 (99)	38 (52)
Fatigue or asthenia	206 (52)	19 (5)	60 (31)	4 (2)	77 (56)	9 (7)	26 (36)	0
Nausea	204 (51)	10 (3)	43 (22)	2 (1)	81 (59)	3 (2)	15 (21)	0
Hypertension	183 (46)	73 (18)	116 (60)	59 (30)	62 (45)	27 (20)	44 (60)	22 (30)
Anemia[b]	162 (41)	66 (17)	19 (10)	0	57 (42)	27 (20)	8 (11)	1 (1)
Lymphopenia[c]	89 (22)	26 (7)	22 (11)	2 (1)	37 (27)	12 (9)	3 (4)	1 (1)
Abdominal pain	87 (22)	6 (2)	42 (22)	5 (3)	29 (21)	2 (1)	17 (23)	0
Arthralgia	82 (21)	3 (1)	44 (23)	3 (2)	34 (25)	0	20 (27)	1 (1)
Vomiting	81 (20)	6 (2)	22 (11)	3 (2)	36 (26)	2 (1)	7 (10)	2 (3)
Diarrhea	70 (18)	11 (3)	31 (16)	2 (1)	28 (20)	1 (1)	14 (19)	3 (4)
Neutropenia[d]	68 (17)	22 (6)	31 (16)	5 (3)	27 (20)	10 (7)	11 (15)	3 (4)
Leukopenia[e]	68 (17)	9 (2)	20 (10)	2 (1)	27 (20)	1 (1)	6 (8)	2 (3)
UTI	62 (16)	1 (<1)	19 (10)	1 (1)	17 (12)	0	8 (11)	0
Headache	53 (13)	1 (<1)	26 (13)	1 (1)	20 (15)	1 (1)	10 (14)	1 (1)
Musculoskeletal pain	48 (12)	4 (1)	19 (10)	1 (1)	14 (10)	1 (1)	9 (12)	0
Peripheral neuropathy	43 (11)	2 (1)	15 (8)	2 (1)	16 (12)	1 (1)	3 (4)	1 (1)
Constipation	40 (10)	0	22 (11)	0	13 (9)	0	6 (8)	1 (1)
Decreased appetite	28 (7)	1 (<1)	9 (5)	1 (1)	14 (10)	0	1 (1)	0
Dysgeusia	26 (7)	0	3 (2)	0	16 (12)	1 (1)	0	0
Dyspnea	22 (6)	2 (1)	5 (3)	0	20 (15)	3 (2)	4 (5)	1 (1)
Thrombocytopenia[f]	33 (8)	7 (2)	8 (4)	1 (1)	9 (7)	2 (1)	1 (1)	0
Proteinuria	25 (6)	4 (1)	28 (14)	0	6 (4)	1 (1)	12 (16)	1 (1)
Nasopharyngitis	18 (5)	0	12 (6)	0	3 (2)	0	8 (11)	0
Led to dose interruption	209 (53)		50 (26)		82 (60)		15 (21)	
Led to dose reduction	163 (41)		17 (9)		57 (42)		3 (4)	
Led to discontinuation	75 (19)		11 (6)		34 (25)		4 (5)	

UTI, urinary tract infection.

[a]Data are shown on adverse events that occurred in at least 10% of patients in either treatment group (except where noted) during study treatment or up to 30 days after discontinuation of the intervention. The adverse events were graded using National Cancer Institute Common Terminology Criteria for Adverse Events (version 4.03).

[b]The data include patients with anemia, decreased hemoglobin level, decreased hematocrit, decreased red blood cell count, erythropenia, macrocytic anemia, normochromic anemia, normochromic normocytic anemia or normocytic anemia.

[c]The data include patients with decreased lymphocyte count, lymphopenia, decreased B-lymphocyte count or decreased T-lymphocyte count.

[d]The data include patients with neutropenia, febrile neutropenia, neutropenic sepsis, neutropenic infection, decreased neutrophil count, idiopathic neutropenia, granulocytopenia, decreased granulocyte count or agranulocytosis.

[e]The data include patients with leukopenia or decreased white blood cell count.

[f]Thrombocytopenia occurred in <10% of patients in each treatment group, but the data are provided to complete the profile of hematologic toxic effects. The data include patients with thrombocytopenia, decreased platelet production, decreased platelet count or decreased plateletcrit.

Table S2. PFS results from key maintenance therapy trials in patients with newly diagnosed advanced ovarian cancer

Patient population	Intervention [no. of patients]	PFS	
		Median, months	HR (95% CI)
Higher-risk patients from PAOLA-1 (NCT02477644)			
FIGO stage III disease with upfront surgery and residual disease or NACT, or FIGO stage IV disease	Olaparib 300 mg bid[a] plus bevacizumab 15 mg/kg q3w[b] [399]	20.3[c]	0.60 (0.49–0.74)
	Placebo plus bevacizumab 15 mg/kg q3w[b] [196]	14.7[c]	
PRIMA [1] (NCT02655016)			
FIGO stage III disease with upfront surgery and residual disease, inoperable FIGO stage III disease or NACT, or FIGO stage IV disease	Niraparib 200 or 300 mg od individualized or fixed starting dose[d] [484]	13.8[c]	0.62 (0.50–0.76)
	Placebo [244]	8.2[c]	
GOG-0218 [2] (NCT00262847)			
FIGO stage III disease with residual disease after cytoreductive surgery, or FIGO stage IV disease	Arm 1: 6 cycles of carboplatin + paclitaxel + placebo for cycles 2–22 [625]	10.3[e]	
	Arm 2: 6 cycles of carboplatin + paclitaxel + bevacizumab 15 mg/kg on day 1 of cycles 2–6 and + placebo for cycles 7–22 [625]	11.2[e]	Arm 2 versus Arm 1: 0.91 (0.80–1.0)
	Arm 3: 6 cycles of carboplatin + paclitaxel + bevacizumab 15 mg/kg on day 1 of cycles 2–22 [623]	14.1[e]	Arm 3 versus Arm 1: 0.72 (0.63–0.82)

bid, twice daily; CI, confidence interval; FIGO, International Federation of Gynecology and Obstetrics; HR, hazard ratio; NACT, neoadjuvant chemotherapy; od, once daily; PFS, progression-free survival; q3w, every 3 weeks.

[a]For up to 2 years or until investigator-assessed objective disease progression or unacceptable toxicity.

[b]For 15 months in total, including when administered with chemotherapy.

[c]Randomization occurred after the end of chemotherapy.

[d]For up to 3 years or until investigator-assessed objective disease progression.

[e]Randomization occurred prior to the first cycle of cycle of chemotherapy with or without bevacizumab.

References

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