Lynparza®
olaparib
tablets 150 mg

PAOLA-1 Trial: Safety and HRQoL

HRQoL, health-related quality of life.

AstraZeneca

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Significance of the PAOLA-1 Trial

The combination of the poly (ADP-ribose) polymerase (PARP) inhibitor **LYNPARZA® (olaparib) plus bevacizumab** as **first-line maintenance therapy** after response to first-line platinum-based chemotherapy in advanced ovarian cancer was examined in the **PAOLA-1 clinical trial.**[1,2]

PAOLA-1 resulted in an **approval for use** in selected patients with HRD-positive* advanced ovarian cancer.[1]

Indication: LYNPARZA is indicated in combination with bevacizumab for the maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube or primary peritoneal cancer who are in complete or partial response to first-line platinum-based chemotherapy and whose cancer is associated with HRD-positive status defined by either:

- a deleterious or suspected deleterious *BRCA* mutation, and/or
- genomic instability

Select patients for therapy based on an FDA-approved companion diagnostic for LYNPARZA.

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*Including *BRCA* mutation (as determined by Myriad MyChoice® CDx) and other causes of HRD. HRD+ is defined as either a tumor *BRCA* mutation and/or an HRD score ≥42 by Myriad MyChoice® CDx.[2,3]

BRCA, BReast CAncer gene; CDx, companion diagnostic; FDA, US Food and Drug Administration; HRD, homologous recombination deficiency.

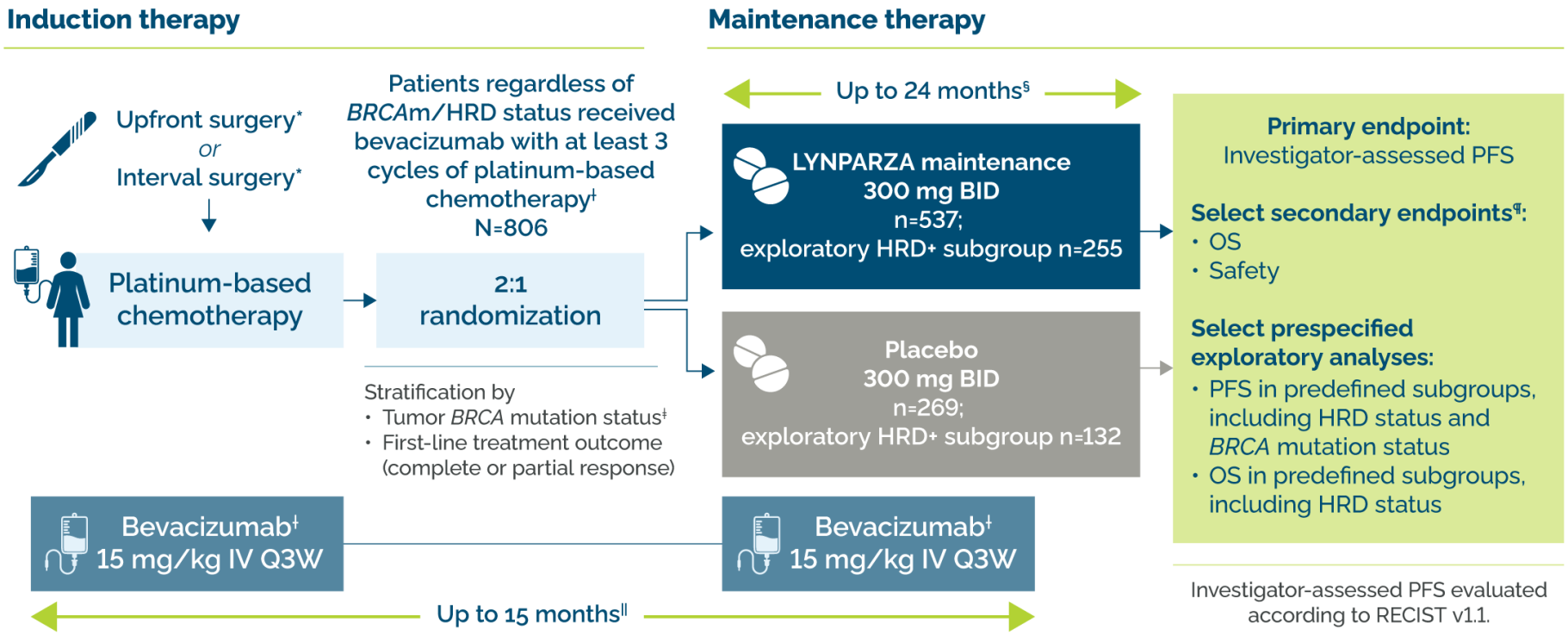
1. LYNPARZA® (olaparib) [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2025.
2. Ray-Coquard I, et al. *Ann Oncol*. 2023;34:681-692.
3. Myriad Genetic Laboratories, Inc. Myriad MyChoice® CDx Technical Information. Accessed June 30, 2025.

Design of the PAOLA-1 Trial

PAOLA-1

The **combination of LYNPARZA and bevacizumab** as **first-line maintenance therapy** in advanced ovarian cancer was examined in the **PAOLA-1 clinical trial**.[1]

Design of the PAOLA-1 trial[1-4]



Investigator-assessed PFS evaluated according to RECIST v1.1.

*Not all patients received surgery. †Patients continued bevacizumab in the maintenance setting and started treatment with LYNPARZA after a minimum of 3 weeks and up to a maximum of 9 weeks following completion of their last dose of chemotherapy. ‡*BRCA* mutation status was determined by local laboratories. §LYNPARZA or placebo was continued for up to 2 years or until progression of the underlying disease or unacceptable toxicity. Patients, who in the opinion of the treating physician could derive further benefit from continuous treatment, could be treated beyond 2 years. ‖Bevacizumab was administered for a total of up to 15 months, including the period given with chemotherapy and given as maintenance. ¶More endpoints than those noted here were studied in PAOLA-1. Not all results from these endpoints are detailed on this site. This study did not implement a prespecified crossover study design.

BRCA, BReast CAncer gene; *BRCA*m, *BRCA* mutation; BID, twice daily; IV, intravenous; HRD, homologous recombination deficiency; HRD+, homologous recombination deficiency–positive; OS, overall survival; PFS, progression-free survival; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumors.

1. LYNPARZA® (olaparib) [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2025.
2. Ray-Coquard I, et al. *N Engl J Med*. 2019;381:2416-2428.
3. Ray-Coquard I, et al. Supplementary Information. *N Engl J Med*. 2019;381:2416-2428.
4. Ray-Coquard I, et al. *Ann Oncol*. 2023;34:681-692.

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PAOLA-1 Dose Modifications of LYNPARZA Due to an AR

Primary analysis: Dose modifications due to an AR[2]

	LYNPARZA + bevacizumab (n=535)	Placebo + bevacizumab (n=267)
Dose interruptions due to ARs (%)	**54**	24
Dose reductions due to ARs (%)	**41**	7
Discontinuations due to ARs (%)	**20**	6

8 out of 10 patients remained on LYNPARZA as prescribed, in combination with bevacizumab, without discontinuing due to ARs.[1]

- Anemia (4%) and nausea (3%) were reported to cause discontinuation rates ≥2%; all other ARs leading to discontinuation occurred with a frequency of 1% or below[3]
- Recorded ARs occurred during study treatment or up to 30 days after discontinuation of the intervention[3]

Adverse reactions (ARs) and laboratory abnormalities from the primary analysis in PAOLA-1 were mostly Grades 1 and 2; most patients remained on LYNPARZA as prescribed.[1]

Please see bevacizumab Prescribing Information for more information on the management of ARs related to bevacizumab and bevacizumab dosage modifications.

AR, adverse reaction.

1. LYNPARZA® (olaparib) [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2025.
2. Ray-Coquard I, et al. *N Engl J Med*. 2019;381:2416-2428.
3. Ray-Coquard I, et al. Supplementary Information. *N Engl J Med*. 2019;381:2416-2428.

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PAOLA-1 Safety Results

Primary analysis:

- Fatal adverse reactions occurred in 1 patient due to concurrent pneumonia and aplastic anemia. Serious adverse reactions occurred in 31% of patients who received LYNPARZA plus bevacizumab. Serious adverse reactions in >5% of patients included hypertension (19%) and anemia (17%)[1]
- In addition, venous thromboembolism occurred more commonly in patients receiving LYNPARZA plus bevacizumab (5%) than in those receiving placebo plus bevacizumab (1.9%) [1]

At 5-year follow-up analysis:

- No new safety signals were identified[2]
- The incidence of MDS/AML/AA was 1.7% (9/535) in the LYNPARZA plus bevacizumab group and 2.2% (6/267) in the bevacizumab plus placebo group[2]
  - In the HRD-positive subgroup, the incidence of MDS/AML was 1.6% (4/255) in patients who received LYNPARZA plus bevacizumab and 2.3% (3/131) in patients who received bevacizumab plus placebo[1]
- 22 (4.1%) new primary malignancy events occurred in the LYNPARZA plus bevacizumab group and 8 (3.0%) events occurred in the bevacizumab plus placebo group[2]
- 7 (1.3%) pneumonitis events occurred in the LYNPARZA plus bevacizumab group and 2 (0.7%) events occurred in the bevacizumab plus placebo group[2]

AA, aplastic anemia; AML, acute myeloid leukemia; HRD, homologous recombination deficiency; MDS, myelodysplastic syndrome.

1. LYNPARZA® (olaparib) [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2025.
2. Ray-Coquard I, et al. *Ann Oncol*. 2023;34:681-692.

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PAOLA-1 Safety Results

ARs from the primary analysis in PAOLA-1 were **mostly Grades 1 and 2.**

ARs occurring in ≥10% of patients treated with LYNPARZA plus bevacizumab and ≥5% frequency compared with placebo plus bevacizumab

Adverse reactions*	Grades 1–4 (%)	Grades 3–4 (%)
Fatigue (including asthenia)†	53 32	5 1.5
Nausea	53 22	2.4 0.7
Vomiting	22 11	1.7 1.9
Anemia‡	41 10	17 0.4
Lymphopenia§	24 9	7 1.1
Leukopenia‖	18 10	1.9 1.5

LYNPARZA plus bevacizumab (n=535) | Placebo plus bevacizumab (n=267)

*Graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE), version 4.0.
†Includes asthenia and fatigue.
‡Includes anemia, anemia macrocytic, erythropenia, hematocrit decreased, hemoglobin decreased, normochromic anemia, normochromic normocytic anemia, normocytic anemia, and red blood cell count decreased.
§Includes B-lymphocyte count decreased, lymphocyte count decreased, lymphopenia, and T-lymphocyte count decreased.
‖Includes leukopenia and white blood cell count decreased.

AR, adverse reaction.

LYNPARZA® (olaparib) [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2025.

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PAOLA-1 Laboratory Abnormalities

Laboratory abnormalities from the primary analysis in PAOLA-1 were **mostly Grades 1 and 2.**

Primary analysis: Lab abnormalities reported in ≥25% of women treated with LYNPARZA + bevacizumab vs bevacizumab + placebo*

Laboratory parameter†	Grades 1–4 (%)	Grades 3–4 (%)
Decrease in hemoglobin	79 / 55	13 / 0.4
Decrease in lymphocytes	63 / 42	10 / 3
Increase in serum creatinine	61 / 36	0.4 / 0.4
Decrease in leukocytes	59 / 45	3.4 / 2.2
Decrease in absolute neutrophil count	35 / 30	7 / 3.7
Decrease in platelets	35 / 28	2.4 / 0.4

*Reported within 30 days of the last dose.
† Patients were allowed to enter clinical studies with laboratory values of CTCAE Grade 1.
‡This number represents the safety population. The derived values in the table are based on the total number of evaluable patients for each laboratory parameter.

CTCAE, Common Terminology Criteria for Adverse Events.

LYNPARZA® (olaparib) [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2025.

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5-Year Follow-Up Safety Analysis

No new safety signals were identified, and the safety profile remained generally consistent with the primary analysis.[1-3]

AEs of special interest for the PARPi class in PAOLA-1, n (%)	Primary analysis[1]		Final PFS2 analysis[2]		Final OS analysis[3]	
	Olaparib + bevacizumab (n=535)	Placebo + bevacizumab (n=267)	Olaparib + bevacizumab (n=535)	Placebo + bevacizumab (n=267)	Olaparib + bevacizumab (n=535)	Placebo + bevacizumab (n=267)
MDS/AML/AA, n (%)	6 (1.1)	1 (<1)	7 (1.3)	4 (1.5)*	9 (1.7)	6 (2.2)
New primary malignancies, n (%)†	7 (1.3)	3 (1.1)	13 (2.4)	5 (1.9)	22 (4.1)	8 (3.0)
Pneumonitis/ILD/bronchitis, n (%)‡	6 (1.1)	0 (0.0)	6 (1.1)	0 (0.0)	7 (1.3)	2 (0.7)

Primary analysis DCO: March 22, 2019. Median duration of follow-up for primary analysis: olaparib, 22.7 months; placebo, 24.0 months.[1]

Final PFS2 DCO: March 22, 2020. Median duration of follow-up: olaparib, 35.5 months; placebo, 36.5 months.[2]

Final OS DCO: March 22, 2022. Median duration of follow-up: olaparib, 61.7 months; placebo, 61.9 months.[3]

*3 of the 4 patients in the placebo plus bevacizumab group who developed MDS/AML/AA received a PARP inhibitor as the first subsequent treatment before onset of AML. †At primary PFS analysis, new primary malignancies in the olaparib plus bevacizumab group were acute lymphocytic leukemia (n=1), breast cancer (n=2), lung cancer (n=1), myeloma (n=1), squamous skin cancer (n=1), and pancreatic cancer (n=1), and in the placebo group were breast cancer (n=2) and thyroid cancer (n=1). Additional new primary malignancies reported at the final PFS2 analysis in the olaparib plus bevacizumab group were breast cancer (n=5), squamous skin cancer (n=1), and colon cancer (n=1), and in the placebo group were breast cancer (n=1) and malignant neoplasm (n=1). New primary malignancies occurring between the PFS2 and OS DCO were 1 plasma cell myeloma, 2 basal cell carcinoma, 7 breast cancer, 1 bronchial carcinoma, 1 colon cancer, 1 glioblastoma, 3 invasive ductal breast carcinoma, 1 invasive lobular breast carcinoma, 1 malignant neoplasm, 1 pancreatic carcinoma, 2 squamous cell carcinoma, and 1 ureteric cancer in the olaparib arm; and 1 papillary thyroid cancer, 3 breast cancer, 1 diffuse large B-cell lymphoma, 1 invasive ductal breast carcinoma, 1 malignant lung neoplasm, and 1 malignant neoplasm in the placebo arm.
‡New pneumonitis/ILD/bronchiolitis events at the OS DCO were 1 bronchiolitis, 1 pneumonia, 1 acute respiratory distress syndrome, 2 interstitial lung disease, and 2 pneumonitis in the olaparib arm; and 1 corona virus infection and 1 pneumonitis case in the placebo arm.

AA, aplastic anemia; AE, adverse event; AML, acute myeloid leukemia; DCO, data cutoff; ILD, interstitial lung disease; MDS, myelodysplastic syndrome; OS, overall survival; PARPi, poly (ADP-ribose) polymerase inhibitor; PFS2, time from randomization to second progression or death.

1. Ray-Coquard I, et al. *N Engl J Med.* 2019;381:2416-2428.
2. González-Martín A, et al. Presented at ESMO Virtual Congress; September 19-21, 2020. Abstract #LBA33.
3. Ray-Coquard I, et al. *Ann Oncol.* 2023;34:681-692.

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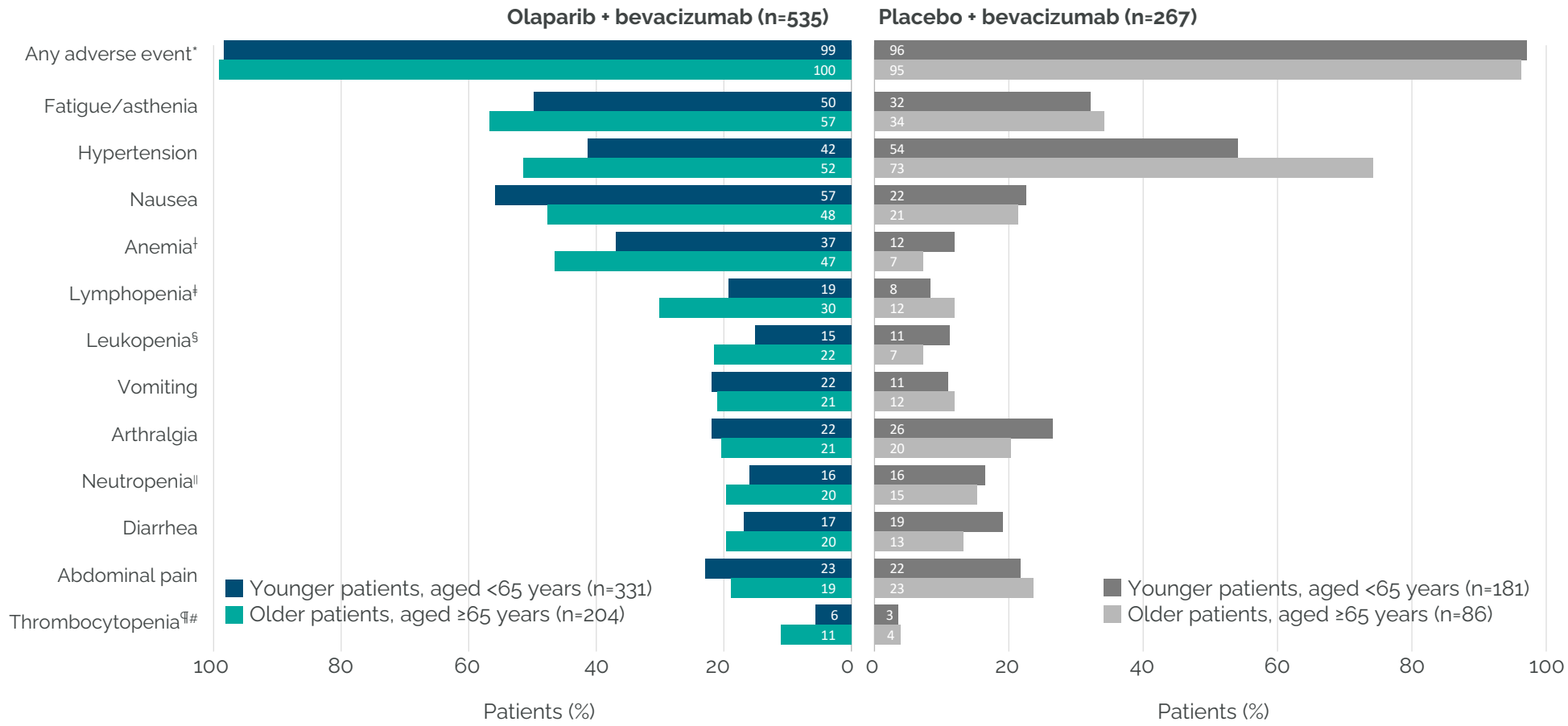
PAOLA-1 Adverse Event Profile in Older Patients

A prespecified **subgroup analysis of safety by age subgroup** (aged ≥65 and <65 years) in the PAOLA-1 trial was conducted.[1]

This age subgroup analysis was exploratory, was not tested for statistical significance, and was not powered to show differences between treatment arms.

*Data are based on prespecified subgroup analyses in 2 clinical subgroups (<65 years and ≥65 years). Age was not a stratification factor in PAOLA-1. Adverse events were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.03.
†Anemia was a grouped term including patients with anemia, decreased hemoglobin level, decreased hematocrit, decreased red blood cell count, erythropenia, macrocytic anemia, normochromic anemia, normochromic normocytic anemia, or normocytic anemia.
‡Lymphopenia includes patients with a decreased lymphocyte count, lymphopenia, a decreased B-lymphocyte count, or a decreased T-cell count.
§Leukopenia includes patients with leukopenia or a decreased white blood cell count.
‖Neutropenia includes patients with neutropenia, febrile neutropenia, neutropenic sepsis, neutropenic infection, a decreased neutrophil count, idiopathic neutropenia, granulocytopenia, a decreased granulocyte count, or agranulocytosis.
¶Thrombocytopenia includes patients with thrombocytopenia, decreased platelet production, a decreased platelet count, or a decreased plateletcrit.
#Occurred in <20% of patients in either arm but included to provide more complete information on the hematologic safety profiles.

Most common adverse events by age subgroup[1,2]



1. Sabatier R, et al. Presented at: ESMO Congress; September 16-21, 2021. Poster 1990.
2. Ray-Coquard I, et al. Supplementary Information. *N Engl J Med*. 2019;381:2416-2428.

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PAOLA-1 Safety Profile in Older Patients

Further results from the prespecified **subgroup analysis of safety by age subgroup** (aged ≥65 and <65 years) in the PAOLA-1 trial included*:

- The most common adverse reactions in patients in both age subgroups were fatigue/asthenia, nausea, anemia, and hypertension
- In patients aged ≥65 years, 1 patient with LYNPARZA plus bevacizumab had MDS and 0 patients with placebo plus bevacizumab had MDS/AA/AML
- In patients aged <65 years, 4 patients with LYNPARZA plus bevacizumab (1 had AA, 1 had AML, 2 had MDS) and 0 patients with placebo plus bevacizumab had MDS/AA/AML
- Adverse reactions led to death in 1 patient aged ≥65 years who received placebo plus bevacizumab and 1 patient aged <65 years who received LYNPARZA plus bevacizumab

This age subgroup analysis was exploratory, was not tested for statistical significance, and was not powered to show differences between treatment arms.

*Data are based on prespecified subgroup analyses in 2 clinical subgroups (<65 years and ≥65 years). Age was not a stratification factor in PAOLA-1.

AA, aplastic anemia; AML, acute myeloid leukemia; MDS, myelodysplastic syndrome.

Sabatier R, et al. Presented at: ESMO Congress; September 16-21, 2021. Poster 1990.

Health-Related Quality of Life Assessments in PAOLA-1

Health-related quality of life was assessed using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30).[1*]

- EORTC QLQ-C30 was completed by patients at baseline and then every 12 weeks for 2 years or until data cutoff[1]
- 498 of 537 (93%) patients in the olaparib plus bevacizumab group and 246 of 269 (91%) patients in the placebo plus bevacizumab group had baseline and at least one post-baseline global health status score[2]
- The change from baseline in the global health status–quality of life score was assessed with the use of a mixed model for repeated measures; results were not powered for statistical significance[1]

*The EORTC QLQ-C30 is a cancer-specific questionnaire assessing 15 HRQoL scales through 30 items: a global health status, five functional scales (physical, role, emotional, cognitive, and social) and nine symptomatic scales (fatigue, nausea and vomiting, pain, dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties). For each dimension, one score is generated on a 0–100 scale, with higher score representing better HRQoL.[2]

A minimal clinically important difference is defined as ±10 points.

This analysis was a secondary endpoint and was not controlled for type 1 error or powered for statistical significance.

	Olaparib + bevacizumab[1,2]	Placebo + bevacizumab
n	**498**	246
Adjusted mean change from baseline in GHS/QoL score	**−1.33**	−2.89
95% CI	**−2.47 to −0.19**	−4.52 to −1.26
Estimated difference	**1.56**	
95% CI	−0.42 to 3.55	

Primary analysis DCO: March 22, 2019. Median duration of follow-up for primary analysis: olaparib, 22.7 months; placebo, 24.0 months.[2]

CI, confidence interval; DCO, data cutoff; HRQol, health-related quality of life; GHS, global health status; QoL, quality of life.

1. Ray-Coquard I, et al. *N Engl J Med.* 2019;381:2416-2428.
2. Ray-Coquard I, et al. Supplementary Information. *N Engl J Med.* 2019;381:2416-2428.

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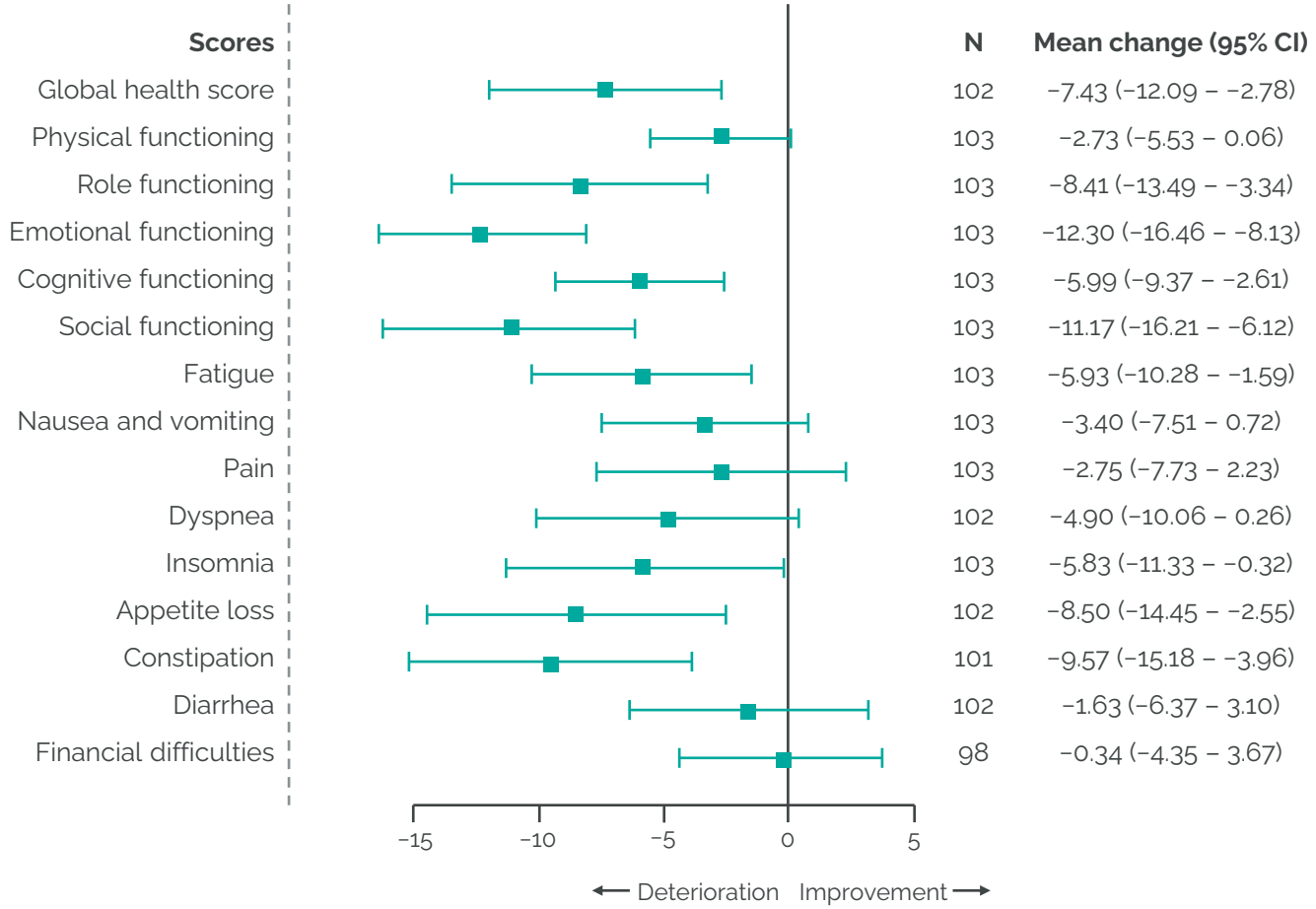
Health-Related QoL Results After Progression in PAOLA-1

Mean change in EORTC QLQ-C30 HRQoL scores after progression*



These results should be interpreted with caution, as this was a post-hoc exploratory analysis of patient-reported EORTC QLQ-C30 HRQoL data. GHS/HRQoL change from baseline results were a secondary endpoint of the PAOLA-1 trial and were not powered for statistical significance.

*HRQoL analyses at disease progression (±60 days) based on responses to EORTC QLQ-C30 health-related QoL questionnaires in 806 patients in the PAOLA-1 trial.

EORTC-QLQ, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire; CI, confidence interval; HRQoL, health-related quality of life; GHS, global health status; QoL, quality of life.

Kurtz JE, et al. Poster presented at the American Society of Clinical Oncology (ASCO) Annual Meeting 2022; June 3-7, 2022; Chicago, IL, USA. Abstract 5560.

Take-Home Messages

- ARs and laboratory abnormalities from the primary analysis in PAOLA-1 were mostly Grades 1 and 2; most patients remained on LYNPARZA as prescribed.[1]
- At the 5–year follow-up safety analysis, no new safety signals were identified, and the safety profile remained generally consistent with the primary analysis.[2-4]
- A subgroup analysis of safety by age subgroup (aged ≥65 and <65 years) in the PAOLA-1 trial has been conducted.[5]
- HRQoL results from the PAOLA-1 trial are available.[2,6]

AR, adverse reaction; HRQol, health-related quality of life.

1. LYNPARZA® (olaparib) [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2025.
2. Ray-Coquard I, et al. *N Engl J Med.* 2019;381:2416-2428.
3. González-Martín A, et al. Presented at ESMO Virtual Congress; September 19-21, 2020. Abstract #LBA33.
4. Ray-Coquard I, et al. *Ann Oncol.* 2023;34:681-692.
5. Sabatier R, et al. Presented at: ESMO Congress; September 16-21, 2021. Poster 1990.
6. Kurtz JE, et al. Poster presented at the American Society of Clinical Oncology (ASCO) Annual Meeting 2022; June 3-7, 2022; Chicago, IL, USA. Abstract 5560.

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