Lynparza®
olaparib
tablets 150 mg

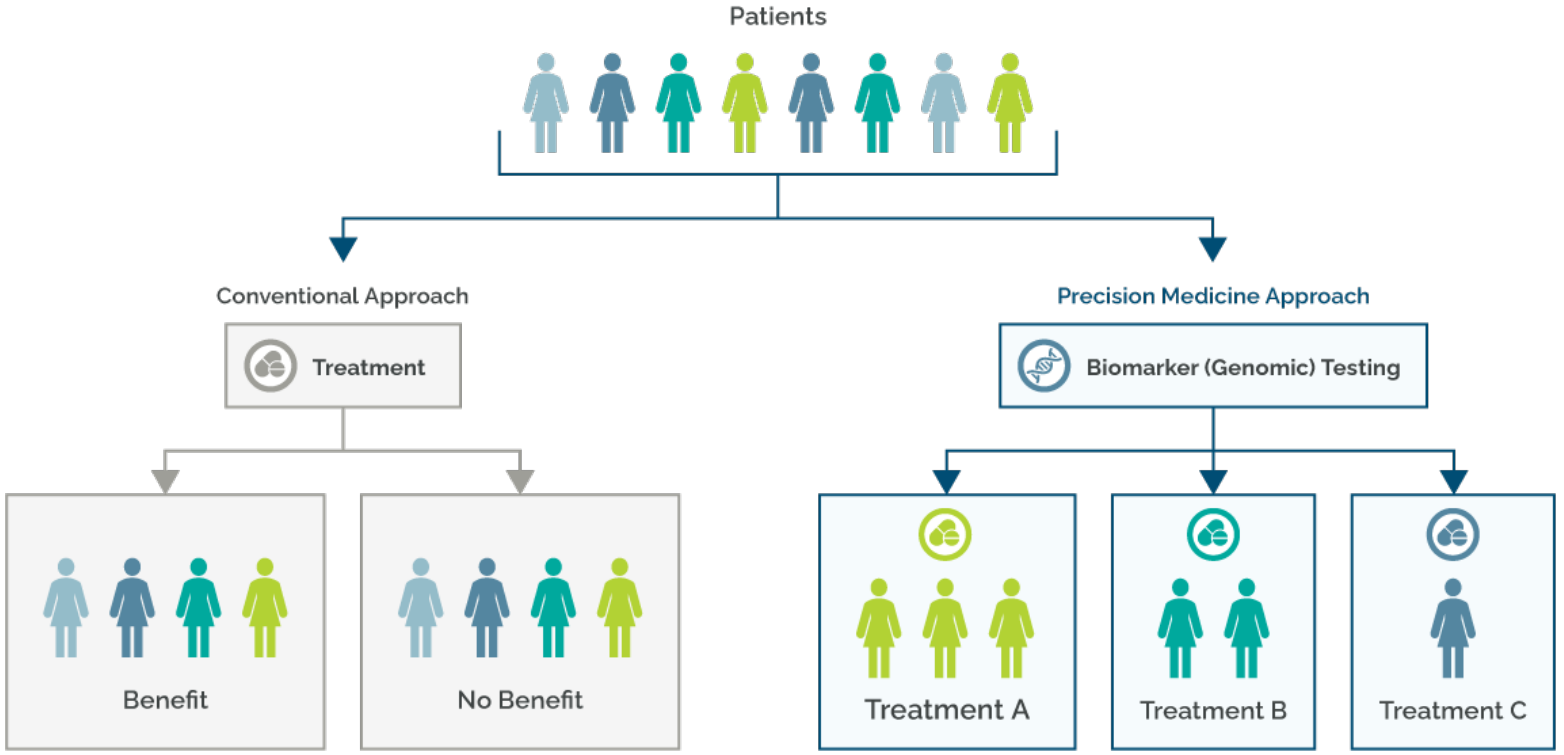
HRD Testing: Why Test?

AstraZeneca

Please see below for Important Safety Information and links to complete Prescribing Information, including Medication Guide.

Biomarker Testing in Precision Medicine

Patient characteristics **inform treatment decisions** that are most likely to provide benefit.[1]



Some patients derive treatment benefit[1,2]

Genomic tumor profiles allow HCPs to select treatments most likely to benefit the patient[1,2]

HCP, healthcare professional.

1. FDA. Precision Medicine. September 2018.
2. Afzal M, et al. *IEEE Access*. 2020;8:13593-13612.

Please see below for Important Safety Information and links to complete Prescribing Information, including Medication Guide.

Genomic Testing in Ovarian Cancer

Genomic testing for advanced ovarian cancer is no longer just for **familial risk assessment.** It can provide insights for **prognosis** and development of a **treatment plan.**[1,2]

Predispositional insights

Germline mutations in *BRCA1/2* aid in familial risk assessment

Prognostic insights

HRD status can provide insight on the course of disease

Predictive insights

HRD status can be used to develop a comprehensive treatment plan

HRD, homologous recombination deficiency.

1. Konstantinopoulos PA, et al. *J Clin Oncol.* 2020;38:1222-1245.
2. Stewart MD, et al. *Oncologist*. 2022;27:167-174.

Please see below for Important Safety Information and links to complete Prescribing Information, including Medication Guide.

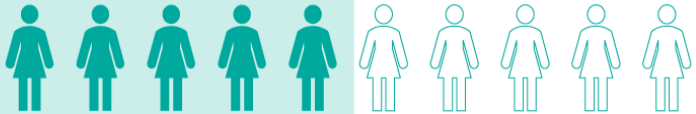
Proportion of Patients With Advanced Ovarian Cancer That Will Test Positive

Tumor sample (germline and somatic)[1-3]

Tumor sample

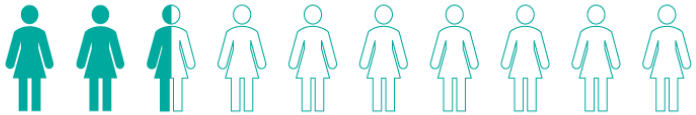
HRD
(including t*BRCA*1 and t*BRCA*2 and/or genomic instability markers LOH, TAI, and LST)

≈50% of women



t*BRCA*

≈25% of women



Blood sample (germline)[1-3]

Blood sample

g*BRCA*

≈18% of women

Testing for HRD including genomic instability tests **identifies more patients** than testing for *BRCA* mutations alone.[1-3]

Testing only for *BRCA*m will **miss half of all patients with HRD**.[1,2]

*BRCA*m, *BRCA* mutation; g*BRCA*, germline *BRCA*; HRD, homologous recombination deficiency; LOH, loss of heterozygosity; LST, large-scale transitions; TAI, telomeric allelic imbalance; t*BRCA*, tumor *BRCA*.

1. Konstantinopoulos PA, et al. *Cancer Discov*. 2015;5:1137-1154.
2. Pennington KP, et al. *Clin Cancer Res*. 2014;20:764-775.
3. Capoluongo E, et al. *Semin Oncol*. 2017;44:187-197.

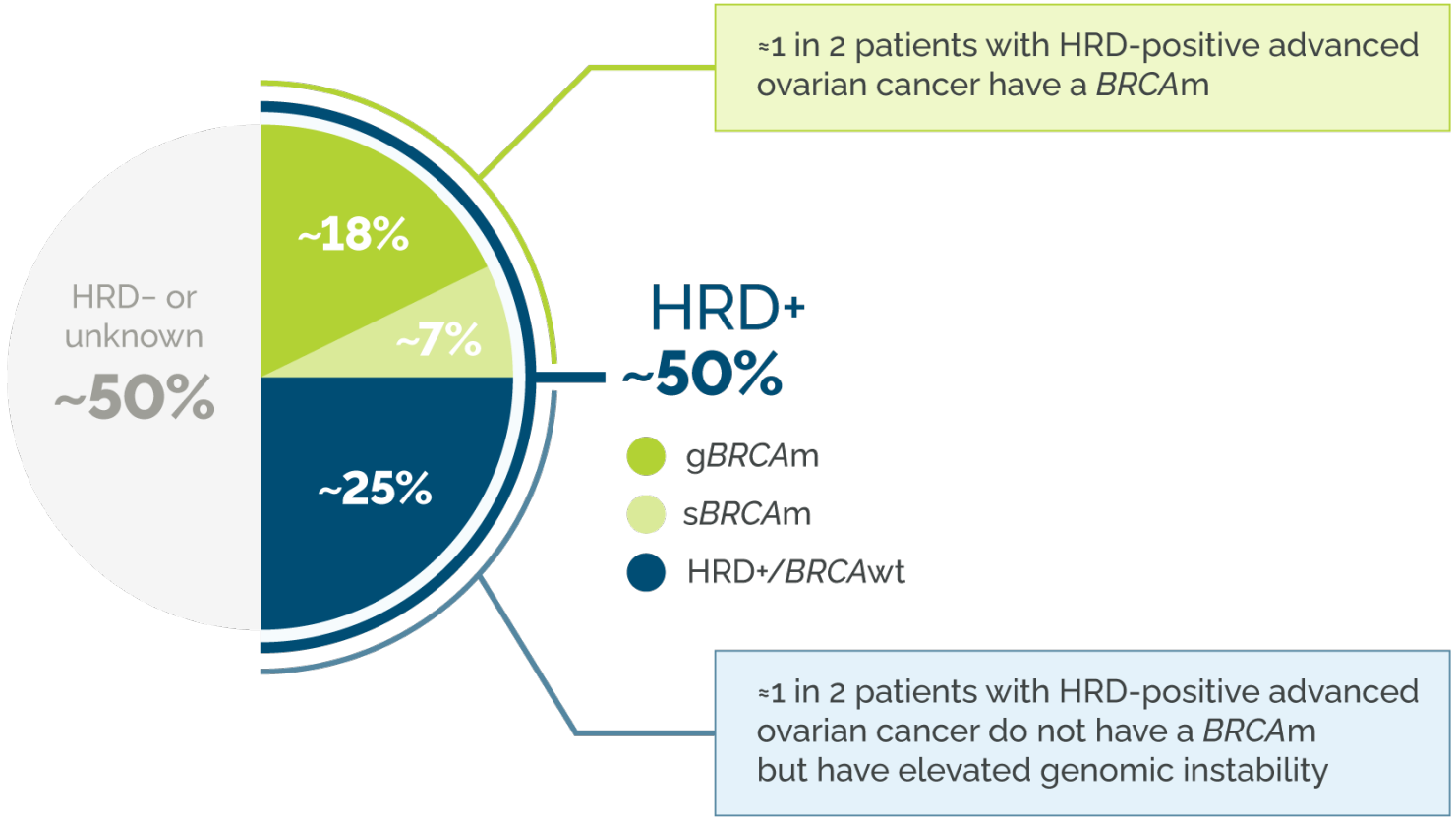
Please see below for Important Safety Information and links to complete Prescribing Information, including Medication Guide.

What Proportion of Advanced Ovarian Cancers Exhibit HRD?

About half of high-grade serous ovarian cancers exhibit HRD; half of these do not have *BRCA*m but have genomic instability.[1,2]

HR status can be characterized as

- ⊕ HRD-positive: HRD or HR deficiency
- ⊖ HRD-negative: HRP or HR proficiency



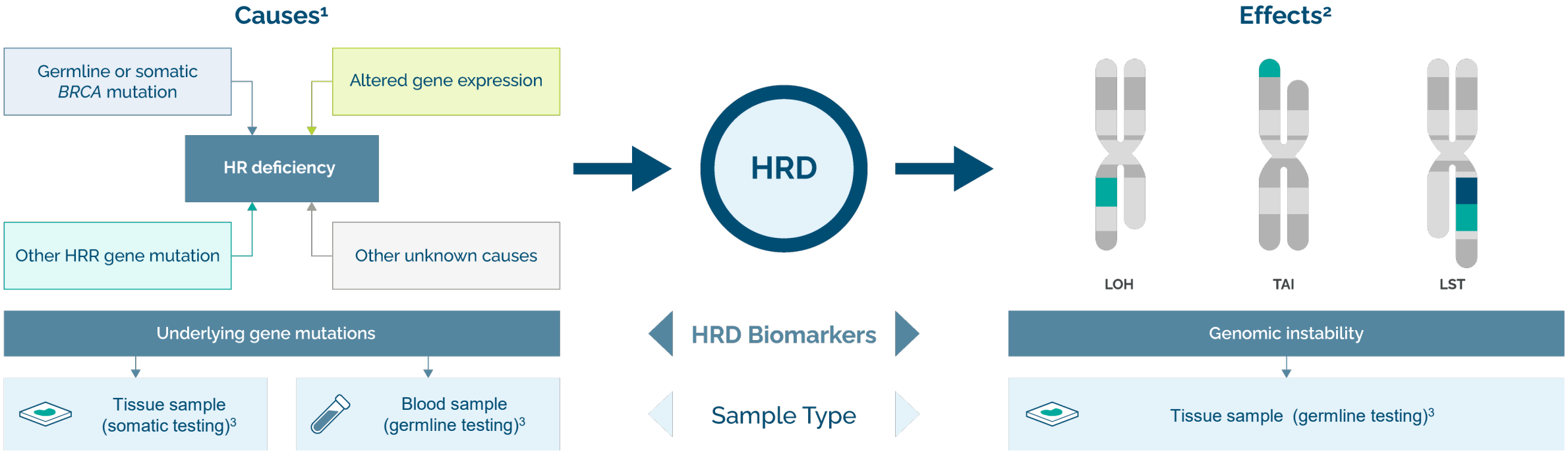
BRCA, BReast CAncer gene; *BRCA*m, *BRCA* mutation; *BRCA*wt, *BRCA* wild-type; g*BRCA*m, germline *BRCA* mutation; HR, homologous recombination; HRD, homologous recombination deficiency; HRD+, homologous recombination deficiency–positive; HRD–, homologous recombination deficiency–negative; HRP, homologous recombination proficient; s*BRCA*m, somatic *BRCA* mutation.

1. Konstantinopoulos PA, et al. *Cancer Discov.* 2015;5:1137-1154.
2. Pennington KP, et al. *Clin Cancer Res.* 2014;20:764-775.

Please see below for Important Safety Information and links to complete Prescribing Information, including Medication Guide.

Biomarkers Examined in an HRD Test

HRD is a tumor characteristic determined by germline and somatic mutations and genomic aberrations. Biomarkers of HRD in ovarian cancer include **germline and somatic *BRCA1/2* mutations** and **genomic instability**.[1]



HRD testing examines biomarkers including ***BRCA* mutations and genomic instability.**[1]

HRD, homologous recombination deficiency; HRR, homologous recombination repair; LOH, loss of heterozygosity; LST, large-scale transitions; TAI, telomeric allelic imbalance.

1. Miller RE, et al. *Ann Oncol*. 2020;31:1606-1622.
2. Stewart MD, et al. *Oncologist*. 2022;27:167-174.
3. Capoluongo E, et al. *Semin Oncol*. 2017;44:187-197.

Please see below for Important Safety Information and links to complete Prescribing Information, including Medication Guide.

Types of Tissue Samples

Test type	Somatic	Germline
Sample type	Tumor tissue Can use fresh-frozen sample or archived FFPE specimen[1]	Blood[1]
Clinical relevance	Determines total mutation status (somatic + germline)[1] May be used to assess genomic instability[2]	May have familial implications[3]
Limitations	Samples can contain both malignant and normal cells; low cancer cell content can affect results[1,2] Does not distinguish between somatic and germline mutations[1]	Does not identify somatic mutations[1]

Germline testing only **does not detect tumor mutations**, and tumor testing only **cannot distinguish between germline and somatic mutations**.[1]

FFPE, formalin-fixed, paraffin-embedded.

1. Capoluongo E, et al. *Semin Oncol*. 2017;44:187-197.
2. Miller RE, et al. *Ann Oncol*. 2020;31:1606-1622.
3. Konstantinopoulos PA, et al. *J Clin Oncol*. 2020;38:1222-1245.

Please see below for Important Safety Information and links to complete Prescribing Information, including Medication Guide.

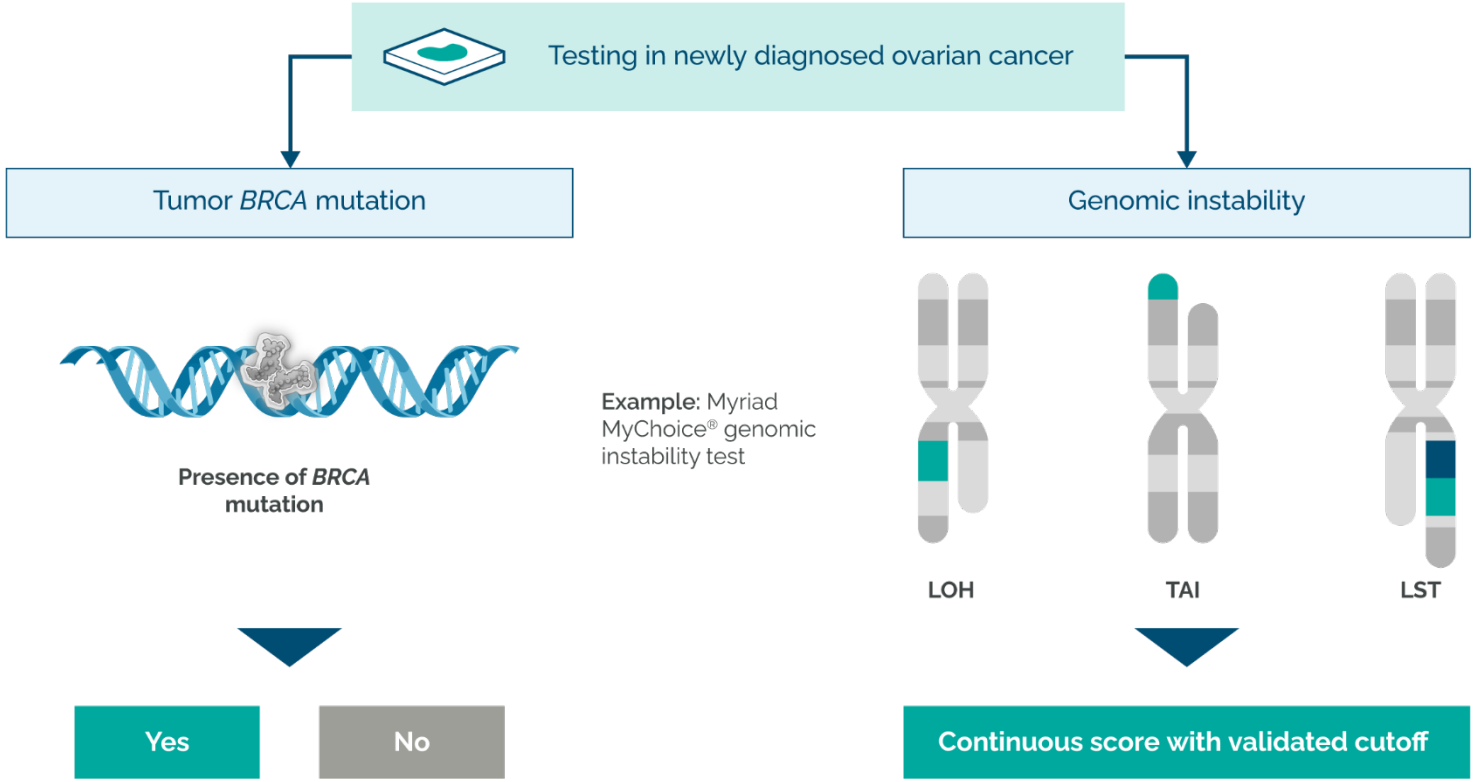
How Is a Positive HRD Test Defined?

Clinically validated methods to detect HRD in newly diagnosed ovarian cancer require ***BRCA*m testing and scoring of genomic instability.**[1]

Analysis is performed on DNA isolated from FFPE tumor tissue and assesses 2 factors to determine HRD status[1,2]:

- Tumor *BRCA* mutation
- Genomic instability

*BRCA*m, *BRCA* mutation; FFPE, formalin-fixed, paraffin-embedded; HRD, homologous recombination deficiency; LOH, loss of heterozygosity; LST, large-scale transitions; TAI, telomeric allelic imbalance.



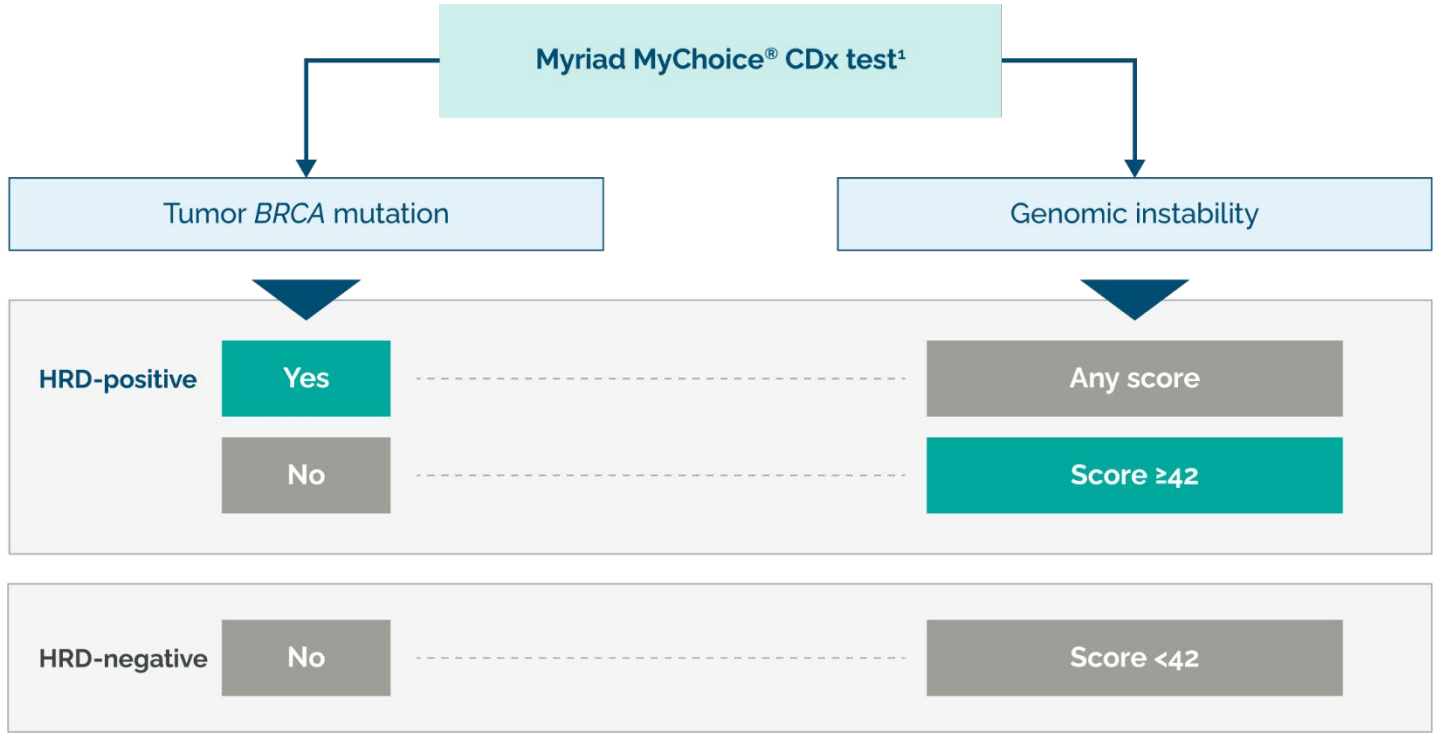
A positive HRD test is defined as either **the presence of a tumor *BRCA* mutation and/or a genomic instability score** above a validated cutoff.[1,2]

1. Miller RE, et al. *Ann Oncol*. 2020;31:1606-1622.
2. Myriad Genetic Laboratories, Inc. Myriad MyChoice® CDx Technical Information. Accessed June 30, 2025.

Please see below for Important Safety Information and links to complete Prescribing Information, including Medication Guide.

Example: Myriad MyChoice® CDx Test

For example, the Myriad MyChoice® CDx test defines patients as HRD-positive **if they have a *BRCA* mutation and/or a genomic instability score ≥42**.[1,2]



CDx, companion diagnostic; HRD, homologous recombination deficiency.

The Myriad MyChoice® CDx test is **approved for use with LYNPARZA® (olaparib) as a companion diagnostic**.[1]

1. Myriad Genetic Laboratories, Inc. Myriad MyChoice® CDx Technical Information. Accessed June 30, 2025.
2. Ray-Coquard I, et al. *N Engl J Med*. 2019;381:2416-2428.

Please see below for Important Safety Information and links to complete Prescribing Information, including Medication Guide.

National Comprehensive Cancer Network® (NCCN®) Recommendations Regarding HRD Testing in Ovarian Cancer

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) **recommend germline testing for *BRCA1* and *BRCA2* mutations and somatic testing for *BRCA1* and *BRCA2* mutations and HRD in the absence of a germline *BRCA* mutation** at diagnosis in all patients with ovarian cancer.[1*]

WHOM TO TEST

All patients with ovarian cancer, fallopian tube cancer, or primary peritoneal cancer should have genetic risk evaluation and germline and somatic testing (if not previously done).

HOW TO TEST

Germline testing:
- *BRCA1* and *BRCA2*

Tumor (somatic) testing:
- *BRCA1* and *BRCA2*
- LOH or HRD status in the absence of a germline *BRCA* mutation.

WHAT TO TEST

BRCA1* and *BRCA2 status should be tested. In the absence of *BRCA1/2* status, **HRD status** may provide information on the magnitude of benefit of PARP inhibitor therapy.

WHEN TO TEST

Upon pathologic confirmation of ovarian cancer.

NCCN recommend *BRCA* mutation and HRD testing at diagnosis in all patients with ovarian cancer.[1]

*Not all NCCN recommendations regarding *BRCA1/2* testing in patients with ovarian cancer are listed.
HR, homologous recombination; HRD, homologous recombination deficiency; NCCN, National Comprehensive Cancer Network; PARP, poly (ADP-ribose) polymerase.

Please see below for Important Safety Information and links to complete Prescribing Information, including Medication Guide.

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** 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, based on an FDA-approved test.[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.

LYNPARZA is associated with serious and potentially fatal adverse events including myelodysplastic syndrome/acute myeloid leukemia (MDS/AML), pneumonitis, venous thromboembolism (VTE) and drug-induced liver injury (DILI). Monitor patients for signs and symptoms and discontinue LYNPARZA if MDS/AML or pneumonitis is confirmed. Monitor patients for signs and symptoms of VTE and treat as medically appropriate. Evaluate bilirubin and transaminases at baseline and throughout treatment with LYNPARZA. If DILI is suspected, interrupt LYNPARZA. If DILI is confirmed, discontinue LYNPARZA. LYNPARZA can cause fetal harm. Advise of the potential risk to a fetus and to use effective contraception.

*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]

Please see Important Safety Information below on this website and links to the complete Prescribing Information, including Medication Guide.

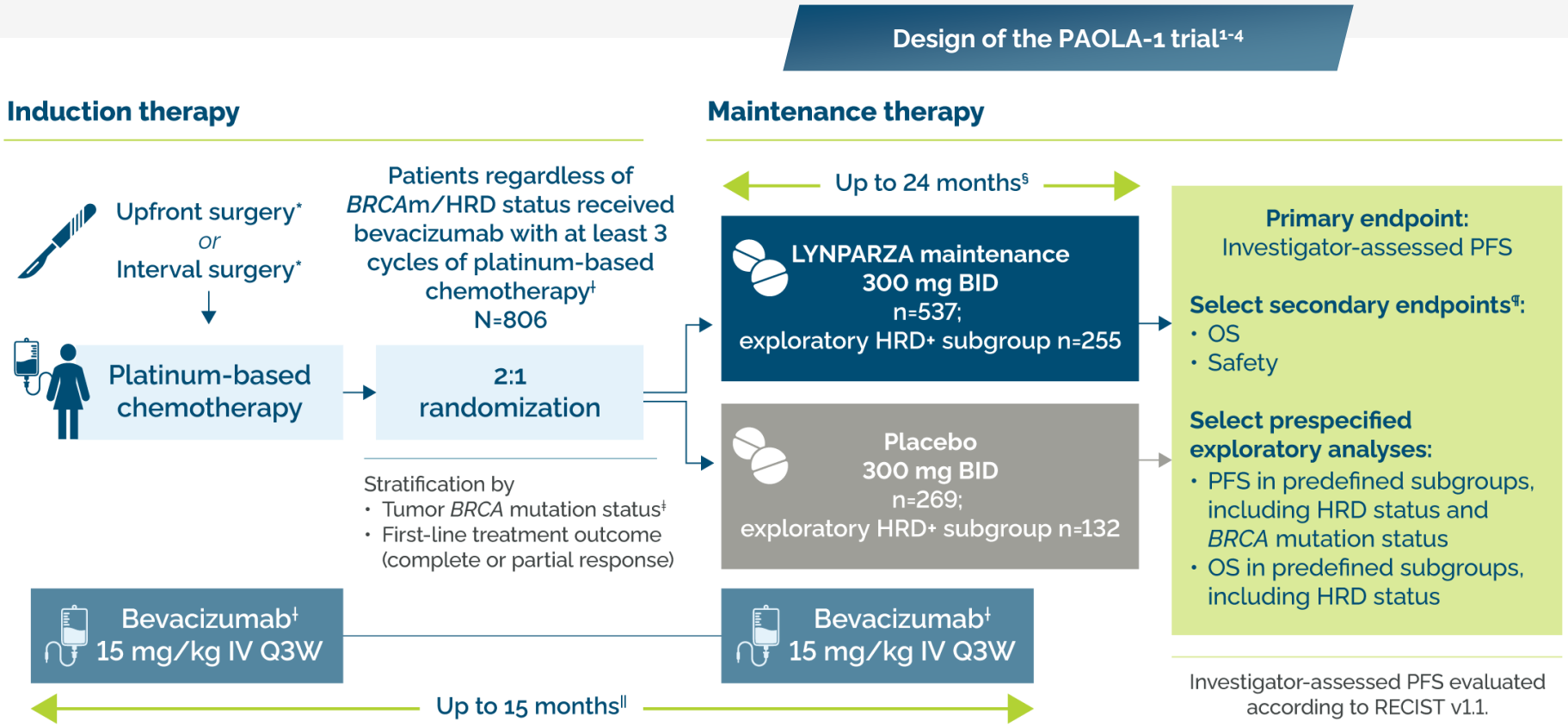
CDx, companion diagnostic; FDA, US Food and Drug Administration; HRD, homologous recombination deficiency.

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

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]



*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.

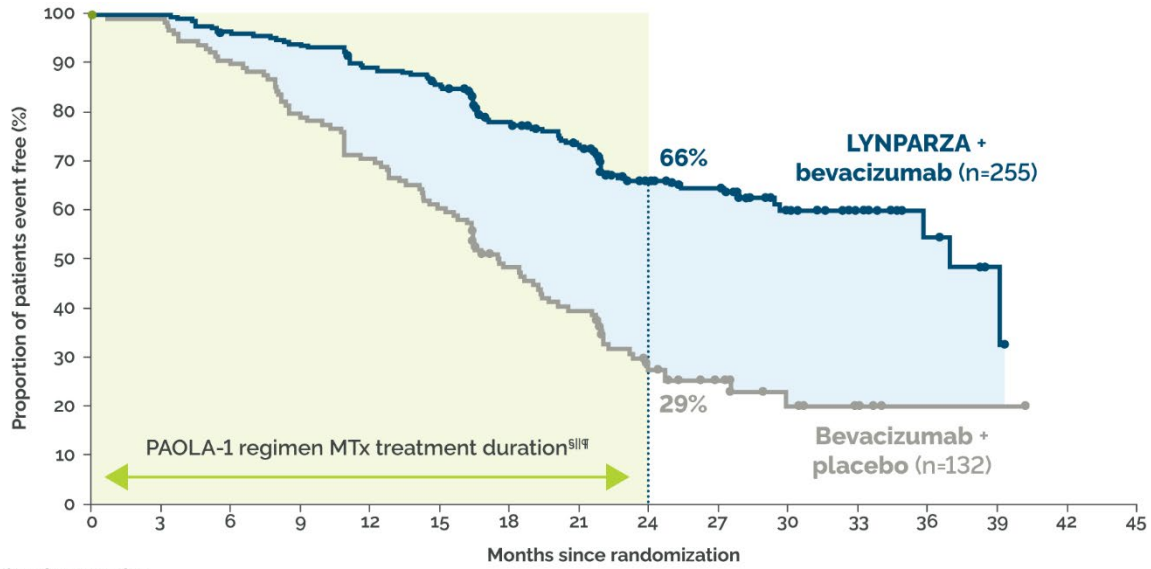
Please see below for Important Safety Information and links to complete Prescribing Information, including Medication Guide.

PAOLA-1 PFS Results in the HRD-Positive Subgroup

US Food and Drug Administration (FDA) approval of LYNPARZA plus bevacizumab was based on a **prespecified exploratory HRD-positive**[*†] **subgroup** in the PAOLA-1 trial.[1,2]

- A prespecified exploratory subgroup analysis showed clinically meaningful PFS benefit in HRD-positive patients after response to first-line platinum-based chemotherapy[1-3‡]
- Median PFS was 3.1 years (37.2 months) with LYNPARZA plus bevacizumab vs ~1.5 years (17.7 months) with bevacizumab plus placebo[2§‖¶]
- 67% risk reduction of disease progression or death; HR=0.33 (95% CI: 0.25–0.45)[2]
- Data was based upon a prespecified exploratory subgroup analysis, which was not controlled for Type 1 error. HRD status was not a stratification factor in PAOLA-1[4]

PFS in the HRD+ subgroup[1,2]



Number of patients at risk

LYNPARZA + bevacizumab	255	252	242	236	223	213	169	155	103	85	46	29	11	3	0
Bevacizumab + placebo	132	128	117	103	91	79	54	44	28	18	8	5	1	1	0

*Select patients for this indication based on an FDA-approved companion diagnostic for LYNPARZA.[1] †Including *BRCA* mutation (as determined by Myriad MyChoice® CDx) and other causes of HRD. HRD-positive is defined as either a tumor *BRCA* mutation and/or an HRD score ≥42 by Myriad MyChoice® CDx.[2,5] ‡Prespecified exploratory analysis of PFS in the HRD-positive subgroup. Data based upon a prespecified exploratory subgroup analysis, which was not controlled for Type 1 error. HRD status was not a stratification factor in PAOLA-1. The analysis is based on Kaplan–Meier estimates and is descriptive only. This trial was not designed to assess a statistical difference between treatment groups at 2 years.[4] §Bevacizumab was administered for a total of up to 15 months, including the period given with chemotherapy and given as maintenance.[1] ‖LYNPARZA was continued for up to 2 years or until progression of the underlying disease or unacceptable toxicity.[1] Patients, who in the opinion of the treating physician could derive further benefit from continuous treatment, could be treated beyond 2 years. ¶Patients with a complete response should stop treatment at 2 years. Patients with evidence of disease at 2 years can remain on therapy at physician discretion.[1] In PAOLA-1, it was unknown how many HRD-positive patients remained on therapy longer than 2 years; therefore, results should be interpreted with caution.
CI, confidence interval; FDA, US Food and Drug Administration; HR, hazard ratio; HRD, homologous recombination deficiency; PFS, progression-free survival.

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. Ellis LM, et al. *J Clin Oncol*. 2014;32:1277-1280.
4. Ray-Coquard I, et al. *Ann Oncol*. 2023;34:681-692.
5. Myriad Genetic Laboratories, Inc. Myriad MyChoice® CDx Technical Information. Accessed June 30, 2025.

Please see below for Important Safety Information and links to complete Prescribing Information, including Medication Guide.

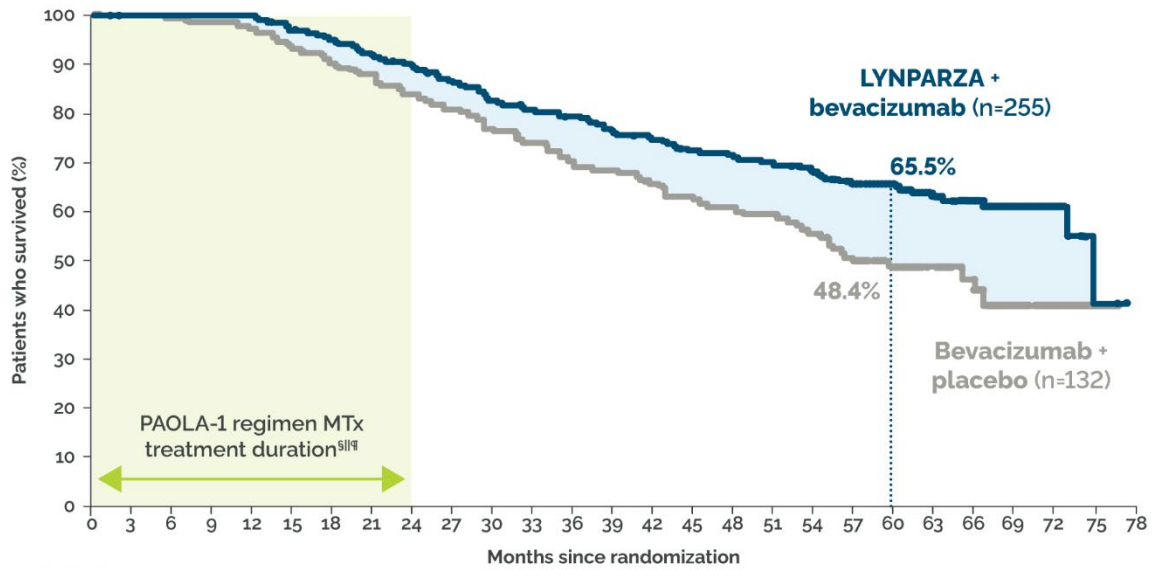
PAOLA-1 OS Results in the HRD-Positive Subgroup

Prespecified exploratory analysis of the secondary endpoint **overall survival (OS) in the HRD-positive*† subgroup** showed a clinically meaningful survival benefit after response to first-line platinum-based chemotherapy.[1-3‡]

- Median OS was ~6.3 years (75.2 months) with LYNPARZA plus bevacizumab vs ~4.8 years (57.3 months) with bevacizumab plus placebo[1§‖¶]
- 38% reduction in the risk of death; HR=0.62 (95% CI: 0.45–0.85)[1]
- Data based upon a prespecified exploratory subgroup analysis, which was not controlled for Type 1 error. HRD status was not a stratification factor in PAOLA-1[2]

PAOLA-1 reported clinically meaningful PFS and OS results in HRD-positive*† advanced ovarian cancer after response to first-line platinum-based chemotherapy.[1-4‡]

OS in the HRD+ subgroup[1,2]



Number of patients at risk

LYNPARZA + bevacizumab	255	253	253	252	252	244	238	231	225	215	205	200	195	189	183	176	174	170	164	142	116	83	62	32	17	4	0
Bevacizumab + placebo	132	130	129	128	126	121	117	114	109	105	100	96	91	89	86	82	174	77	70	59	44	29	21	9	2	1	0

*Select patients for this indication based on an FDA-approved companion diagnostic for LYNPARZA.[1] †Including *BRCA* mutation (as determined by Myriad MyChoice® CDx) and other causes of HRD. HRD-positive is defined as either a tumor *BRCA* mutation and/or an HRD score ≥42 by Myriad MyChoice® CDx.[4,5] ‡Secondary endpoint: Prespecified exploratory analysis of OS in the HRD-positive subgroup. Data based upon a prespecified exploratory subgroup analysis, which was not controlled for Type 1 error. HRD status was not a stratification factor in PAOLA-1. The analysis is based on Kaplan–Meier estimates and is descriptive only. This trial was not designed to assess a statistical difference between treatment groups at 5 years.[2] §Bevacizumab was administered for a total of up to 15 months, including the period given with chemotherapy and given as maintenance.[1] ‖LYNPARZA was continued for up to 2 years or until progression of the underlying disease or unacceptable toxicity.[1] Patients, who in the opinion of the treating physician could derive further benefit from continuous treatment, could be treated beyond 2 years. ¶Patients with a complete response should stop treatment at 2 years. Patients with evidence of disease at 2 years can remain on therapy at physician discretion.[1] In PAOLA-1, it was unknown how many HRD-positive patients remained on therapy longer than 2 years; therefore, results should be interpreted with caution.
CI, confidence interval; FDA, US Food and Drug Administration; HR, hazard ratio; HRD, homologous recombination deficiency; OS, overall survival.

1. LYNPARZA® (olaparib) [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2025.
2. Ray-Coquard I, et al. *Ann Oncol*. 2023;34:681-692.
3. Ellis LM, et al. *J Clin Oncol*. 2014;32:1277-1280.
4. Ray-Coquard I, et al. *N Engl J Med*. 2019;381:2416-2428.
5. Myriad Genetic Laboratories, Inc. Myriad MyChoice® CDx Technical Information. Accessed June 30, 2025.

Please see below for Important Safety Information and links to complete Prescribing Information, including Medication Guide.

PAOLA-1 Safety Results

ARs occurring in ≥10% of patients treated with LYNPARZA plus bevacizumab and ≥5% frequency compared with placebo plus bevacizumab[1]

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

*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.

Adverse reactions (ARs) and laboratory abnormalities from the primary analysis in PAOLA-1 were **mostly Grades 1 and 2**.[1]

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]

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

Please see below for Important Safety Information and links to complete Prescribing Information, including Medication Guide.

PAOLA-1 Dose Modifications Due to an AR

Primary analysis: Dose modifications due to an AR[1]

	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.[2]

- 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.[2]

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

AR, adverse reaction.

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

Please see below for Important Safety Information and links to complete Prescribing Information, including Medication Guide.

Treatment Guidelines on Combination Maintenance Therapy

Treatment guidelines recommend the combination of olaparib with or without bevacizumab as **first-line maintenance therapy** as a treatment option in selected patients with advanced ovarian cancer in complete or partial response to first-line therapy, depending on biomarker status.[1-3]

	*BRCA*m	HRD+/*BRCA*wt	Notes
NCCN[1]	✓	✓	**NCCN Category 1* recommendation,** only in patients that received bevacizumab as part of primary therapy.
ASCO[2,3]	✓	✓	

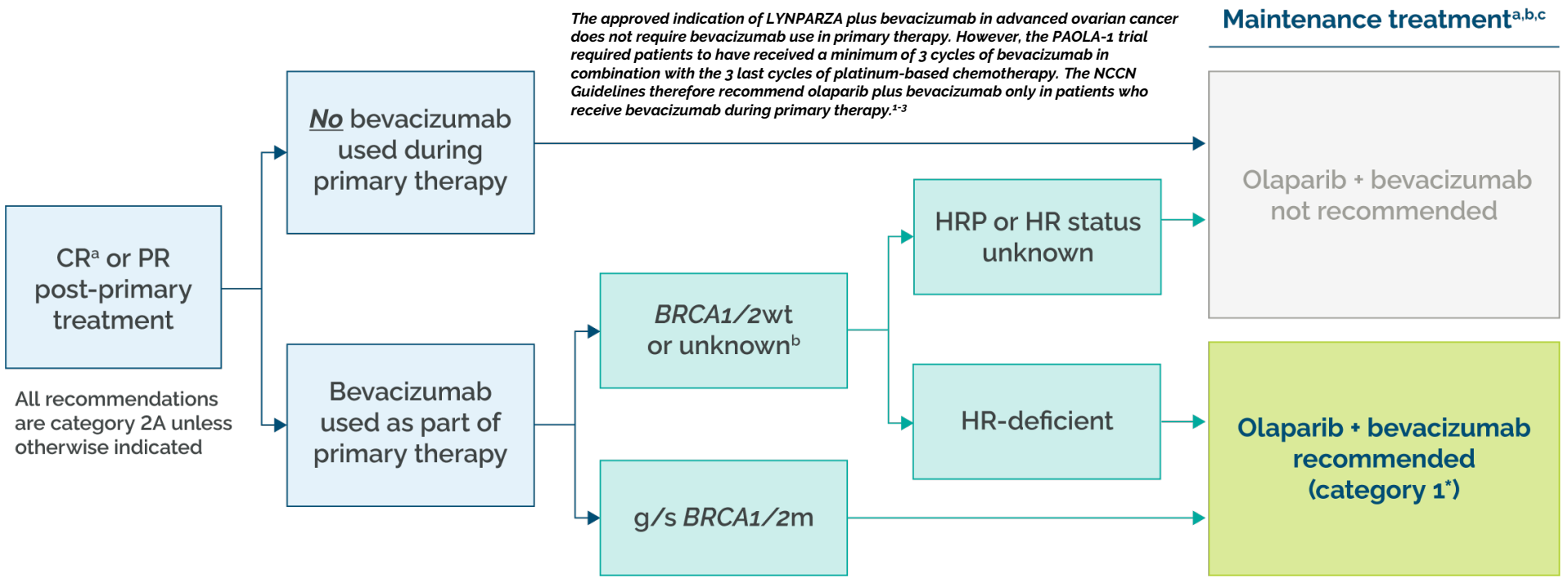
*NCCN Category 1: Based upon high-level evidence (≥1 randomized phase 3 trials or high quality, robust meta-analyses), there is uniform NCCN consensus (≥85% support of the Panel) that the intervention is appropriate. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.
ASCO, American Society of Clinical Oncology; *BRCA*m, *BRCA*-mutated; *BRCA*wt, *BRCA* wild-type; HRD+, homologous recombination deficiency–positive; NCCN, National Comprehensive Cancer Network®(NCCN®).

1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Ovarian Cancer, Including Fallopian Tube Cancer and Primary Peritoneal Cancer. V.3.2025. © National Comprehensive Cancer Network, Inc. 2025. All rights reserved. Accessed July 29, 2025. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.
2. Tew WP, et al. *J Clin Oncol.* 2022;40:3878-3881.
3. Gaillard S, et al. *J Clin Oncol.* 2025;43:868-891.

Please see below for Important Safety Information and links to complete Prescribing Information, including Medication Guide.

NCCN Guidelines® Regarding Olaparib Plus Bevacizumab in Advanced Ovarian Cancer

Olaparib plus bevacizumab is recommended as a maintenance therapy option in select patients with advanced ovarian cancer following surgery and first-line platinum-based chemotherapy with bevacizumab.[1]



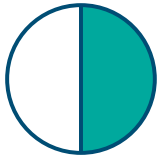
Olaparib plus bevacizumab is a **category 1* recommendation** in selected patients with *BRCA1/2*m/HR-deficient disease who received bevacizumab as part of primary therapy.[1]

[a] No definitive evidence of disease. [b] In the absence of a *BRCA1/2* mutation, HRD status may provide information on the magnitude of benefit of PARP inhibitor therapy. [c] See Principles of Systemic Therapy (OV-C) and Management of Drug Reactions (OV-D), NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Ovarian Cancer (including Fallopian Tube Cancer and Primary Peritoneal Cancer) V.3.2025. *Category 1: Based upon high-level evidence (≥1 randomized phase 3 trials or high-quality, robust meta-analyses), there is uniform NCCN consensus (≥85% support of the Panel) that the intervention is appropriate.
*BRCA1/2*m, *BRCA1/2* mutation; *BRCA1/2*wt, *BRCA1/2* wild-type; CR, complete response; g/s, germline or somatic; HR, homologous recombination; HRP, homologous recombination proficient; PARP, poly (ADP-ribose) polymerase; PR, partial response.

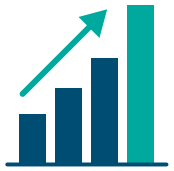
1. Adapted with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Ovarian Cancer, including Fallopian Tube Cancer and Primary Peritoneal Cancer V.3.2025. © 2025 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines® and illustrations herein may not be reproduced in any form for any purpose without the express written permission of NCCN. To view the most recent and complete version of the NCCN Guidelines, go online to NCCN.org. The NCCN Guidelines are a work in progress that may be refined as often as new significant data becomes available. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.
2. LYNPARZA® (olaparib) [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2025.
3. Ray-Coquard I, et al. Supplementary Information. *N Engl J Med*. 2019;381:2416-2428.

Please see below for Important Safety Information and links to complete Prescribing Information, including Medication Guide.

Implications of HRD on Selecting Maintenance Therapy



About half of newly diagnosed, high-grade serous ovarian cancers **exhibit HRD**.[1]



HRD is associated with **increased sensitivity to PARP inhibitor maintenance therapy**.[2]

Testing for ***BRCA*m only will miss half** of all HRD+ patients.[1,3]

The FDA-approved indication of LYNPARZA plus bevacizumab **requires a positive HRD test*** with a companion diagnostic.[4-6]

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.

*HRD-positive is defined as either a tumor *BRCA* mutation and/or an HRD score ≥42 by Myriad MyChoice® CDx.[4-6]
*BRCA*m, *BRCA* mutated; FDA, US Food and Drug Administration; HRD, homologous recombination deficiency; PARP, poly (ADP-ribose) polymerase.

Testing for HRD is required to identify HRD-positive* patients eligible for LYNPARZA plus bevacizumab.[4-6]

1. Konstantinopoulos PA, et al. *Cancer Discov*. 2015;5:1137-1154.
2. Ngoi NYL, et al. *ESMO Open*. 2021;6:100144.
3. Pennington KP, et al. *Clin Cancer Res*. 2014;20:764-775.
4. LYNPARZA® (olaparib) [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2025.
5. Myriad Genetic Laboratories, Inc. Myriad MyChoice® CDx Technical Information. Accessed June 30, 2025.
6. Ray-Coquard I, et al. *N Engl J Med*. 2019;381:2416-2428.

Please see below for Important Safety Information and links to complete Prescribing Information, including Medication Guide.

Take-Home Message

- About half of high-grade serous ovarian cancers exhibit HRD; half of these do not have *BRCA* mutations but have genomic instability.[1,2]
- Testing only for *BRCA*m will miss half of all patients with HRD.[1-3]
- HRD testing examines biomarkers including *BRCA* mutations and genomic instability.[4]
- Germline testing only does not detect tumor mutations, and tumor testing only cannot distinguish between germline and somatic mutations.[3]
- A positive HRD test is defined as the presence of a tumor *BRCA* mutation and/or a genomic instability score above a validated cutoff.[4,5]
- The Myriad MyChoice® CDx test is approved for use with LYNPARZA as a companion diagnostic.[5]
- NCCN recommend *BRCA* mutation and HRD testing at diagnosis in all patients with ovarian cancer.[6]
- PAOLA-1 reported clinically meaningful PFS and OS results in HRD-positive*‡ advanced ovarian cancer after response to first-line platinum-based chemotherapy.‡[7-10]
- ARs and laboratory abnormalities from the primary analysis in PAOLA-1 were mostly Grades 1 and 2; most patients remained on LYNPARZA as prescribed.[7]
- Treatment guidelines recommend olaparib (LYNPARZA) in combination with bevacizumab as first-line maintenance therapy in selected patients with advanced ovarian cancer.[6,11,12]
- Testing for HRD is required to identify HRD-positive‡ patients eligible for LYNPARZA plus bevacizumab.[5,7]
- Olaparib plus bevacizumab is a category 1 recommendation in selected patients with *BRCA*m/HRD disease who received bevacizumab as part of primary therapy.[6]
- **To identify patients eligible for LYNPARZA plus bevacizumab, use an FDA-approved CDx test that includes genomic instability tests on all patients with advanced ovarian cancer.[5,7]**

*Select patients for this indication based on an FDA-approved companion diagnostic for LYNPARZA.[7] ‡Including *BRCA* mutation (as determined by Myriad MyChoice® CDx) and other causes of HRD. HRD-positive is defined as either a tumor *BRCA* mutation and/or an HRD score ≥42 by Myriad MyChoice® CDx.[5,8]
‡Prespecified exploratory analysis of PFS and OS in the HRD-positive subgroup. Data based upon a prespecified exploratory subgroup analysis, which was not controlled for Type 1 error. HRD status was not a stratification factor in PAOLA-1.[8]

AR, adverse reaction; *BRCA*m, *BRCA* mutation; CDx, companion diagnostic; HRD, homologous recombination deficiency; OS, overall survival; NCCN, National Comprehensive Cancer Network® (NCCN®); PARP, poly (ADP-ribose) polymerase; PFS, progression-free survival.

1. Konstantinopoulos PA, et al. *Cancer Discov*. 2015;5:1137-1154.
2. Pennington KP, et al. *Clin Cancer Res.* 2014;20:764-775.
3. Capoluongo E, et al. *Semin Oncol.* 2017;44:187-197.
4. Miller RE, et al. *Ann Oncol.* 2020;31:1606-1622.
5. Myriad Genetic Laboratories, Inc. Myriad MyChoice® CDx Technical Information. Accessed June 30, 2025.
6. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Ovarian Cancer, Including Fallopian Tube Cancer and Primary Peritoneal Cancer. V.3.2025. © National Comprehensive Cancer Network, Inc. 2025. All rights reserved. Accessed July 29, 2025. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.
7. LYNPARZA® (olaparib) [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2025.
8. Ray-Coquard I, et al. *N Engl J Med*. 2019;381:2416-2428.
9. Ray-Coquard I, et al. *Ann Oncol*. 2023;34:681-692.
10. Ellis LM, et al. *J Clin Oncol.* 2014;32:1277-1280.
11. Tew WP, et al. *J Clin Oncol.* 2022;40:3878-3881.
12. Gaillard S, et al. *J Clin Oncol*. 2025;43:868-891.

Please see below for Important Safety Information and links to complete Prescribing Information, including Medication Guide.