

Test early for biomarkers of DNA damage to help inform targeted treatment¹⁻⁵



- NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) recommend:**
- *BRCA1/2* mutation testing for patients with pathologically confirmed ovarian cancer⁶
 - Evaluation of HRR gene mutations in patients with metastatic castration-resistant prostate cancer⁷
 - Germline testing in any patient with confirmed pancreatic cancer, using comprehensive gene panels for hereditary cancer syndromes⁸
 - Germline *BRCA1/2* testing in patients with HER2-negative metastatic breast cancer⁹

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TUMOR TYPE	FDA-APPROVED INDICATION ¹	DIAGNOSTIC TEST	HOW TO ORDER TEST KITS
ADVANCED OVARIAN CANCER	First-line Maintenance HRD-positive* Advanced Ovarian Cancer in Combination With Bevacizumab 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 homologous recombination deficiency (HRD)–positive status defined by either a deleterious or suspected deleterious <i>BRCA</i> mutation and/or genomic instability.	Order Myriad myChoice® CDx¹ at first tissue collection to determine HRD status. ²	To order the Myriad myChoice® CDx , call Myriad Genetics at 1-877-283-6709 or visit MyriadmyChoice.com²
	First-line Maintenance <i>BRCA</i>m* Advanced Ovarian Cancer For the maintenance treatment of adult patients with deleterious or suspected deleterious germline or somatic <i>BRCA</i> -mutated advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in complete or partial response to first-line platinum-based chemotherapy.	Order FoundationOne® CDx at first tissue collection to detect <i>BRCA1/2</i> mutations. ⁴ •Tumor testing cannot distinguish between germline and somatic mutations Order Myriad BRACAnalysis CDx® to detect germline <i>BRCA1/2</i> mutations. ³	To order FoundationOne® CDx , call Foundation Medicine at 1-888-988-3639 or visit www.foundationmedicine.com/order¹⁰ To order Myriad BRACAnalysis CDx® , call Myriad Genetics at 1-800-4-MYRIAD or visit bracanalysiscdx.com/order-test³
	Maintenance Recurrent Ovarian Cancer For the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer, who are in complete or partial response to platinum-based chemotherapy.	Diagnostic testing for this indication is not required. ¹	
	Advanced <i>gBRCA</i>m* Ovarian Cancer For the treatment of adult patients with deleterious or suspected deleterious <i>gBRCA</i> m advanced ovarian cancer who have been treated with 3 or more prior lines of chemotherapy.	Order Myriad BRACAnalysis CDx® to detect germline <i>BRCA1/2</i> mutations. ³	To order Myriad BRACAnalysis CDx® , call Myriad Genetics at 1-800-4-MYRIAD or visit bracanalysiscdx.com/order-test³
METASTATIC PROSTATE CANCER	HRR Gene–mutated* Metastatic Castration-Resistant Prostate Cancer For the treatment of adult patients with deleterious or suspected deleterious germline or somatic homologous recombination repair (HRR) gene-mutated metastatic castration-resistant prostate cancer (mCRPC) who have progressed following prior treatment with enzalutamide or abiraterone.	Order FoundationOne® CDx or FoundationOne® Liquid CDx to detect HRR gene mutations per the LYNPARZA label. ^{4,5†} •Detects both somatic and germline alterations but does not distinguish between the two on reports Order Myriad BRACAnalysis CDx® to detect germline <i>BRCA1/2</i> mutations. ³	To order a FoundationOne® CDx or FoundationOne® Liquid CDx , call 1-888-988-3639 or visit www.foundationmedicine.com/order¹⁰ To order Myriad BRACAnalysis CDx® , call Myriad Genetics at 1-800-4-MYRIAD or visit bracanalysiscdx.com/order-test³
METASTATIC PANCREATIC CANCER	First-line Maintenance <i>gBRCA</i>m* Metastatic Pancreatic Cancer For the maintenance treatment of adult patients with deleterious or suspected deleterious <i>gBRCA</i> m metastatic pancreatic adenocarcinoma whose disease has not progressed on at least 16 weeks of a first-line platinum-based chemotherapy regimen.	Order Myriad BRACAnalysis CDx® to detect germline <i>BRCA1/2</i> mutations. ³	To order Myriad BRACAnalysis CDx® , call Myriad Genetics at 1-800-4-MYRIAD or visit bracanalysiscdx.com/order-test³
METASTATIC BREAST CANCER	<i>gBRCA</i>m*, HER2-negative Metastatic Breast Cancer For the treatment of adult patients with deleterious or suspected deleterious <i>gBRCA</i> m, human epidermal growth factor receptor 2 (HER2)-negative metastatic breast cancer who have been treated with chemotherapy in the neoadjuvant, adjuvant, or metastatic setting. Patients with hormone receptor (HR)-positive breast cancer should have been treated with a prior endocrine therapy or be considered inappropriate for endocrine therapy.	Order Myriad BRACAnalysis CDx® to detect germline <i>BRCA1/2</i> mutations. ³	To order Myriad BRACAnalysis CDx® , call Myriad Genetics at 1-800-4-MYRIAD or visit bracanalysiscdx.com/order-test³

Where testing fails or tissue sample is unavailable/insufficient, or when germline testing is negative, consider using an alternative test, if available.¹

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

[†]HRD positive is defined as either a *tBRCA* mutation and/or an HRD score ≥42 by Myriad myChoice® CDx; HRD negative is defined as either non-*tBRCA*-mutated and/or an HRD score <42 by Myriad myChoice® CDx.

HRD unknown is defined in accordance with a test that fails, is inconclusive, or is missing. Test determines HRD status by detecting *BRCA1* and *BRCA2* variants and assessing genomic instability.^{2,11,12}

[‡]FoundationOne® CDx mutations detected: *BRCA1, BRCA2, ATM, BARD1, BRIPI, CDK12, CHEK1, CHEK2, FANCL, PALB2, RAD51B, RAD51C, RAD51D, RAD54L*; FoundationOne® Liquid CDx mutations detected: *BRCA1, BRCA2, ATM*.^{4,5}

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

There are no contraindications for LYNPARZA.

WARNINGS AND PRECAUTIONS

Myelodysplastic Syndrome/Acute Myeloid Leukemia (MDS/AML): Occurred in <1.5% of patients exposed to LYNPARZA monotherapy, and the majority of events had a fatal outcome. The duration of therapy in patients who developed secondary MDS/AML varied from <6 months to >2 years. All of these patients had previous chemotherapy with platinum agents and/or other DNA-damaging agents, including radiotherapy, and some also had a history of more than one primary malignancy or of bone marrow dysplasia. Do not start LYNPARZA until patients have recovered from hematological toxicity caused by previous chemotherapy (≤Grade 1). Monitor complete blood count for cytopenia at baseline and monthly thereafter for clinically significant changes during treatment. For prolonged hematological toxicities, interrupt LYNPARZA and monitor blood count weekly until recovery.

If the levels have not recovered to Grade 1 or less after 4 weeks, refer the patient to a hematologist for further investigations, including bone marrow analysis and blood sample for cytogenetics. Discontinue LYNPARZA if MDS/AML is confirmed.

Please see additional Important Safety Information on the other side, and the accompanying complete Prescribing Information, including Patient Information (Medication Guide).

*BRCA*m=*BRCA*-mutated; *gBRCA*m=germline *BRCA*-mutated; HER2-negative=human epidermal growth factor receptor 2–negative; HRD-positive=homologous recombination deficiency–positive; HRR=homologous recombination repair; NCCN=National Comprehensive Cancer Network.

Help inform targeted treatment with LYNPARZA using FDA-approved companion diagnostics¹

IMPORTANT SAFETY INFORMATION (Cont'd) WARNINGS AND PRECAUTIONS (Cont'd)

Pneumonitis: Occurred in <1% of patients exposed to LYNPARZA, and some cases were fatal. If patients present with new or worsening respiratory symptoms such as dyspnea, cough, and fever, or a radiological abnormality occurs, interrupt LYNPARZA treatment and initiate prompt investigation. Discontinue LYNPARZA if pneumonitis is confirmed and treat patient appropriately.

Embryo-Fetal Toxicity: Based on its mechanism of action and findings in animals, LYNPARZA can cause fetal harm. A pregnancy test is recommended for females of reproductive potential prior to initiating treatment.

Females

Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception during treatment and for 6 months following the last dose.

Males

Advise male patients with female partners of reproductive potential or who are pregnant to use effective contraception during treatment and for 3 months following the last dose of LYNPARZA and to not donate sperm during this time.

Venous Thromboembolic Events: Including pulmonary embolism, occurred in 7% of patients with metastatic castration-resistant prostate cancer who received LYNPARZA plus androgen deprivation therapy (ADT) compared to 3.1% of patients receiving enzalutamide or abiraterone plus ADT in the PROfound study. Patients receiving LYNPARZA and ADT had a 6% incidence of pulmonary embolism compared to 0.8% of patients treated with ADT plus either enzalutamide or abiraterone. Monitor patients for signs and symptoms of venous thrombosis and pulmonary embolism, and treat as medically appropriate, which may include long-term anticoagulation as clinically indicated.

ADVERSE REACTIONS—First-Line Maintenance BRCaM Advanced Ovarian Cancer

Most common adverse reactions (Grades 1-4) in ≥10% of patients in clinical trials of LYNPARZA in the **first-line maintenance setting** for **SOLO-1** were: nausea (77%), fatigue (67%), abdominal pain (45%), vomiting (40%), anemia (38%), diarrhea (37%), constipation (28%), upper respiratory tract infection/influenza/nasopharyngitis/bronchitis (28%), dysgeusia (26%), decreased appetite (20%), dizziness (20%), neutropenia (17%), dyspepsia (17%), dyspnea (15%), leukopenia (13%), UTI (13%), thrombocytopenia (11%), and stomatitis (11%).

Most common laboratory abnormalities (Grades 1-4) in ≥25% of patients in clinical trials of LYNPARZA in the **first-line maintenance setting** for **SOLO-1** were: decrease in hemoglobin (87%), increase in mean corpuscular volume (87%), decrease in leukocytes (70%), decrease in lymphocytes (67%), decrease in absolute neutrophil count (51%), decrease in platelets (35%), and increase in serum creatinine (34%).

ADVERSE REACTIONS—First-Line Maintenance Advanced Ovarian Cancer in Combination with Bevacizumab

Most common adverse reactions (Grades 1-4) in ≥10% of patients treated with LYNPARZA/bevacizumab compared to a ≥5% frequency for placebo/bevacizumab in the **first-line maintenance setting** for **PAOLA-1** were: nausea (53%), fatigue (including asthenia) (53%), anemia (41%), lymphopenia (24%), vomiting (22%) and leukopenia (18%). In addition, the most common adverse reactions (≥10%) for patients receiving LYNPARZA/bevacizumab irrespective of the frequency compared with the placebo/bevacizumab arm were: diarrhea (18%), neutropenia (18%), urinary tract infection (15%) and headache (14%).

In addition, venous thromboembolic events occurred more commonly in patients receiving LYNPARZA/bevacizumab (5%) than in those receiving placebo/bevacizumab (1.9%).

Most common laboratory abnormalities (Grades 1-4) in ≥25% of patients for LYNPARZA in combination with bevacizumab in the **first-line maintenance setting** for **PAOLA-1** were: decrease in hemoglobin (79%), decrease in lymphocytes (63%), increase in serum creatinine (61%), decrease in leukocytes (59%), decrease in absolute neutrophil count (35%) and decrease in platelets (35%).

ADVERSE REACTIONS—Maintenance Recurrent Ovarian Cancer

Most common adverse reactions (Grades 1-4) in ≥20% of patients in clinical trials of LYNPARZA in the **maintenance setting** for **SOLO-2** were: nausea (76%), fatigue (including asthenia) (66%), anemia (44%), vomiting (37%), nasopharyngitis/upper respiratory tract infection (URI)/influenza (36%), diarrhea (33%), arthralgia/myalgia (30%), dysgeusia (27%), headache (26%), decreased appetite (22%), and stomatitis (20%).

Study 19: nausea (71%), fatigue (including asthenia) (63%), vomiting (35%), diarrhea (28%), anemia (23%), respiratory tract infection (22%), constipation (22%), headache (21%), decreased appetite (21%) and dyspepsia (20%).

Most common laboratory abnormalities (Grades 1-4) in ≥25% of patients in clinical trials of LYNPARZA in the **maintenance setting** (**SOLO-2/Study 19**) were: increase in mean corpuscular volume (89%/82%), decrease in hemoglobin (83%/82%), decrease in leukocytes (69%/58%), decrease in lymphocytes (67%/52%), decrease in absolute neutrophil count (51%/47%), increase in serum creatinine (44%/45%), and decrease in platelets (42%/36%).

ADVERSE REACTIONS—Advanced gBRCaM Ovarian Cancer

Most common adverse reactions (Grades 1-4) in ≥20% of patients in clinical trials of LYNPARZA for **advanced gBRCaM ovarian cancer after 3 or more lines of chemotherapy** (pooled from 6 studies) were: fatigue/asthenia (66%), nausea (64%), vomiting (43%), anemia (34%), diarrhea (31%), nasopharyngitis/upper respiratory tract infection (URI) (26%), dyspepsia (25%), myalgia (22%), decreased appetite (22%), and arthralgia/musculoskeletal pain (21%).

Most common laboratory abnormalities (Grades 1-4) in ≥25% of patients in clinical trials of LYNPARZA for **advanced gBRCaM ovarian cancer** (pooled from 6 studies) were: decrease in hemoglobin (90%), mean corpuscular volume elevation (57%), decrease in lymphocytes (56%), increase in serum creatinine (30%), decrease in platelets (30%), and decrease in absolute neutrophil count (25%).

ADVERSE REACTIONS—gBRCaM, HER2-Negative Metastatic Breast Cancer

Most common adverse reactions (Grades 1-4) in ≥20% of patients in **OlympiAD** were: nausea (58%), anemia (40%), fatigue (including asthenia) (37%), vomiting (30%), neutropenia (27%), respiratory tract infection (27%), leukopenia (25%), diarrhea (21%), and headache (20%).

Most common laboratory abnormalities (Grades 1-4) in ≥25% of patients in **OlympiAD** were: decrease in hemoglobin (82%), decrease in lymphocytes (73%), decrease in leukocytes (71%), increase in mean corpuscular volume (71%), decrease in absolute neutrophil count (46%), and decrease in platelets (33%).

ADVERSE REACTIONS—First-Line Maintenance gBRCaM Metastatic Pancreatic Adenocarcinoma

Most common adverse reactions (Grades 1-4) in ≥10% of patients in clinical trials of LYNPARZA in the **first-line maintenance setting** for **POLO** were: fatigue (60%), nausea (45%), abdominal pain (34%), diarrhea (29%), anemia (27%), decreased appetite (25%), constipation (23%), vomiting (20%), back pain (19%), arthralgia (15%), rash (15%), thrombocytopenia (14%), dyspnea (13%), neutropenia (12%), nasopharyngitis (12%), dysgeusia (11%), and stomatitis (10%).

Most common laboratory abnormalities (Grades 1-4) in ≥25% of patients in clinical trials of LYNPARZA in the **first-line maintenance setting** for **POLO** were: increase in serum creatinine (99%), decrease in hemoglobin (86%), increase in mean corpuscular volume (71%), decrease in lymphocytes (61%), decrease in platelets (56%), decrease in leukocytes (50%), and decrease in absolute neutrophil count (25%).

ADVERSE REACTIONS—HRR Gene-mutated Metastatic Castration-Resistant Prostate Cancer

Most common adverse reactions (Grades 1-4) in ≥10% of patients in clinical trials of LYNPARZA for **PROfound** were: anemia (46%), fatigue (including asthenia) (41%), nausea (41%), decreased appetite (30%), diarrhea (21%), vomiting (18%), thrombocytopenia (12%), cough (11%), and dyspnea (10%).

Most common laboratory abnormalities (Grades 1-4) in ≥25% of patients in clinical trials of LYNPARZA for **PROfound** were: decrease in hemoglobin (98%), decrease in lymphocytes (62%), decrease in leukocytes (53%), and decrease in absolute neutrophil count (34%).

DRUG INTERACTIONS

Anticancer Agents: Clinical studies of LYNPARZA with other myelosuppressive anticancer agents, including DNA-damaging agents, indicate a potentiation and prolongation of myelosuppressive toxicity.

CYP3A Inhibitors: Avoid coadministration of strong or moderate CYP3A inhibitors when using LYNPARZA. If a strong or moderate CYP3A inhibitor must be coadministered, reduce the dose of LYNPARZA. Advise patients to avoid grapefruit, grapefruit juice, Seville oranges, and Seville orange juice during LYNPARZA treatment.

CYP3A Inducers: Avoid coadministration of strong or moderate CYP3A inducers when using LYNPARZA.

USE IN SPECIFIC POPULATIONS

Lactation: No data are available regarding the presence of olaparib in human milk, its effects on the breastfed infant or on milk production. Because of the potential for serious adverse reactions in the breastfed infant, advise a lactating woman not to breastfeed during treatment with LYNPARZA and for 1 month after receiving the final dose.

Pediatric Use: The safety and efficacy of LYNPARZA have not been established in pediatric patients.

Hepatic Impairment: No adjustment to the starting dose is required in patients with mild or moderate hepatic impairment (Child-Pugh classification A and B). There are no data in patients with severe hepatic impairment (Child-Pugh classification C).

Renal Impairment: No dosage modification is recommended in patients with mild renal impairment (CLcr 51-80 mL/min estimated by Cockcroft-Gault). In patients with moderate renal impairment (CLcr 31-50 mL/min), reduce the dose of LYNPARZA to 200 mg twice daily. There are no data in patients with severe renal impairment or end-stage renal disease (CLcr ≤30 mL/min).

You are encouraged to report negative side effects of AstraZeneca prescription drugs by calling 1-800-236-9933.

If you prefer to report these to the FDA, either visit www.FDA.gov/medwatch or call 1-800-FDA-1088.

Please see accompanying complete Prescribing Information, including Patient Information (Medication Guide).

References: **1.** LYNPARZA® (olaparib) [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2020. **2.** Myriad myChoice® CDx Technical Information. Myriad Genetic Laboratories. Accessed November 11, 2020. <https://bit.ly/myChoiceCDxSpecs> **3.** BRACAnalysis CDx® Technical Information. Myriad Genetics Laboratories. Accessed November 30, 2020. <https://s3.amazonaws.com/myriad-web/BRACAnalysisCDxTS.pdf> **4.** FoundationOne® CDx Technical Information. Foundation Medicine, Inc. Accessed November 11, 2020. <http://www.F1CDxlabel.com> **5.** FoundationOne® Liquid CDx Technical Information. Foundation Medicine, Inc. Accessed November 11, 2020. <http://www.F1LCDxlabel.com> **6.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Ovarian Cancer V.1.2020. © National Comprehensive Cancer Network, Inc. 2020. All rights reserved. Accessed November 11, 2020. To view the most recent and complete version of the guideline, go online to NCCN.org. **7.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Prostate Cancer V.3.2020. © National Comprehensive Cancer Network, Inc. 2020. All rights reserved. Accessed November 24, 2020. To view the most recent and complete version of the guideline, go online to NCCN.org. **8.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Pancreatic Adenocarcinoma V.1.2021. © National Comprehensive Cancer Network, Inc. 2020. All rights reserved. Accessed November 11, 2020. To view the most recent and complete version of the guideline, go online to NCCN.org. **9.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer V.6.2020. © National Comprehensive Cancer Network, Inc. 2020. All rights reserved. Accessed November 11, 2020. To view the most recent and complete version of the guideline, go online to NCCN.org. **10.** Order a Test. Foundation Medicine, Inc. Accessed December 11, 2020. <https://www.foundationmedicine.com/info/detail/order-a-test> **11.** Ray-Coquard I, Pautier P, Pignata S, et al. Olaparib plus bevacizumab as first-line maintenance in ovarian cancer. *N Engl J Med.* 2019;381(25):2416-2428. **12.** Ray-Coquard I, Pautier P, Pignata S, et al. Olaparib plus bevacizumab as first-line maintenance in ovarian cancer. PAOLA-1 Protocol. *N Engl J Med.* 2019;381(25):2416-2428.

For more information, visit LYNPARZAhcp.com