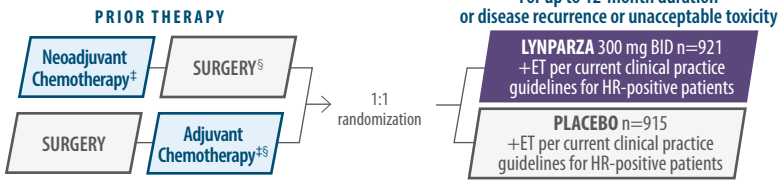
New indication approved in March 2022

LYNPARZA® (olaparib) is the first and only PARPi indicated for the adjuvant treatment of patients with g*BRCA*m,* HER2-negative, high-risk† early breast cancer (eBC)[1]

LYNPARZA is indicated for the adjuvant treatment of adult patients with deleterious or suspected deleterious g*BRCA*m, human epidermal growth factor receptor 2 (HER2)-negative high-risk early breast cancer who have been treated with neoadjuvant or adjuvant chemotherapy. Select patients for therapy based on an FDA-approved companion diagnostic for LYNPARZA.[1]

OlympiA trial overview[1]

- Patient population included those with **g*BRCA*m, HER2-negative (TNBC or HR-positive), high-risk† eBC**



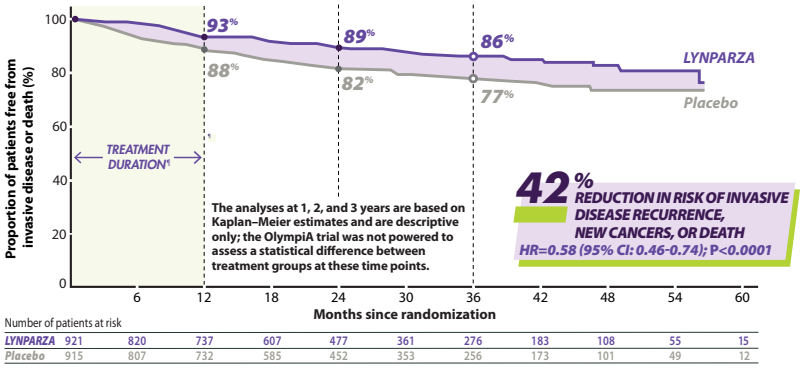
Primary endpoint: IDFS[1]
Key secondary endpoints: OS and safety[1,2]

IDFS is a composite endpoint consisting of the most commonly accepted DFS events based on expert consensus.[3]

*Select patients for this indication based on an FDA-approved companion diagnostic for LYNPARZA.
†For patients who received prior neoadjuvant chemotherapy, high risk was defined as non-pCR in TNBC and as non-pCR with CPS&EG score ≥3 in HR-positive, HER2-negative disease. For patients who received prior adjuvant chemotherapy, high risk was defined as ≥pN1 or ≥pN0 with ≥pT2 in TNBC and as ≥4 positive lymph nodes in HR-positive, HER2-negative disease.[1]
‡At least 6 cycles of neoadjuvant or adjuvant chemotherapy containing anthracyclines, taxanes, or both agents. Platinum-based chemotherapy was allowed.[1]
§Radiation therapy was given when appropriate.[2]

Efficacy endpoints

Primary endpoint: LYNPARZA demonstrated a statistically significant improvement in IDFS vs placebo[1,2‖]



The threshold for statistical significance was 0.005. Data from the pre-specified interim analysis (86% of the number of events for the planned final analysis).

- The number of IDFS events observed was 106 with LYNPARZA vs 178 with placebo[1]

‖IDFS was defined as time from randomization to date of first recurrence, where recurrence is defined as invasive loco-regional, distant recurrence, contralateral invasive breast cancer, new cancer, or death from any cause.[1]
¶LYNPARZA was administered for up to 12 months or until disease recurrence or unacceptable toxicity.[1]

Key secondary endpoint:

Patients treated with LYNPARZA experienced a statistically significant improvement in OS# vs placebo[1]

32% RELATIVE RISK REDUCTION IN OS WITH ADJUVANT LYNPARZA
HR=0.68 (95% CI: 0.50-0.91); P=0.0091

The threshold for statistical significance was 0.015.

- The number of deaths was 75 with LYNPARZA (n=921) vs 109 with placebo (n=915)[1]
- OS was cOS was controlled for Type 1 error within a hierarchical statistical analysis in OlympiA[4]

#Data from the prespecified second interim analysis of OS (at ~330 IDFS events).[1]

Select safety in the OlympiA trial[1]

Adverse reactions that occurred in ≥10% of patients who received LYNPARZA

	LYNPARZA (n=911)	Placebo (n=904)
Adverse reactions**	Grades 1-4 (%)	Grades 1-4 (%)
Nausea	57	23
Fatigue (including asthenia)	42	28
Anemia††	24	3.9
Vomiting	23	8
Headache	20	17
Diarrhea	18	14
Leukopenia‡‡	17	6
Neutropenia§§	16	7
Decreased appetite	13	6
Dysgeusia‖‖	12	4.8
Dizziness	11	7
Stomatitis¶¶	10	4.5

Adverse reactions leading to death were cardiac arrest in 1 patient who received LYNPARZA and AML/ovarian cancer in 1 patient each who received placebo.
**Graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE), version 4.03.
††Includes anemia, anemia macrocytic, erythropenia, hematocrit decreased, hemoglobin decreased, normochromic anemia, normochromic normocytic anemia, normocytic anemia, red blood cell count decreased.
‡‡Includes leukopenia, white blood cell count decreased.
§§Includes agranulocytosis, febrile neutropenia, granulocyte count decreased, granulocytopenia, idiopathic neutropenia, neutropenia, neutropenic infection, neutropenic sepsis, neutrophil count decreased.
‖‖Includes dysgeusia, taste disorder.
¶¶Includes aphthous ulcer, mouth ulceration, stomatitis.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

There are no contraindications for LYNPARZA.

WARNINGS AND PRECAUTIONS

Myelodysplastic Syndrome/Acute Myeloid Leukemia (MDS/AML): Occurred in approximately 1.5% of patients exposed to LYNPARZA monotherapy, and the majority of events had a fatal outcome. The median duration of therapy in patients who developed MDS/AML was 2 years (range: <6 months to >10 years). All of these patients had previous chemotherapy with platinum agents and/or other DNA-damaging agents, including radiotherapy.

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 reverse side and complete Prescribing Information, including Medication Guide.

BID=twice daily; CI=confidence interval; DDFS=distant disease-free survival; DFS=disease-free survival; ET=endocrine therapy; g*BRCA*m=germline breast cancer susceptibility gene-mutated; HER2=human epidermal growth factor receptor 2; HR=hazard ratio; HR-positive=hormone receptor positive; IDFS=invasive disease-free survival; non-pCR=pathologic non-complete response; OS=overall survival; PARPi=poly (ADP-ribose) polymerase inhibitor; TNBC=triple-negative breast cancer.

Lynparza® olaparib tablets 150 mg

Tolerability of LYNPARZA in the OlympiA trial[1,2]

	Dose interruptions due to ARs	Discontinuations due to ARs*	Dose reductions due to ARs†
LYNPARZA (n=911)	31%	10%	23%

*Include ARs with an onset from the date of first dose up to 30 days following the date of last dose.
†Dose reductions are based on investigator-initiated decisions. Reductions due to patient noncompliance are omitted.

~90% **of patients continued treatment with LYNPARZA without discontinuation due to ARs.**

- The most common ARs leading to discontinuation were nausea, anemia, and fatigue

Treatment recommendations[5]

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) state that addition of adjuvant LYNPARZA for 1 year‡ is a preferred treatment option for those patients with a g*BRCA1/2* mutation.§

After preoperative (neoadjuvant) chemotherapy if:

- TNBC and residual disease (category 1)
- HR-positive, HER2-negative tumors and residual disease with a CPS+EG score ≥3 (category 2A)

After adjuvant chemotherapy if:

- TNBC and ≥pT2 or ≥pN1 disease (category 1)
- HR-positive, HER2-negative tumors and ≥4 positive lymph nodes (category 2A)

Adjuvant LYNPARZA can be used concurrently with endocrine therapy in patients with HR-positive, HER2-negative disease.

‡Adjuvant LYNPARZA may be administered for a total of 1 year, or until disease recurrence, or unacceptable toxicity, whichever occurs first.
§Patients in the OlympiA trial did not receive capecitabine, thus there are no data on sequencing or to guide selection of one over the other.

Testing recommendations

In patients with HER2-negative, high-risk eBC, test for g*BRCA* mutations at diagnosis to help determine eligibility for adjuvant treatment with LYNPARZA based on an FDA-approved companion diagnostic[1,5,6]

AR=adverse reaction; CPS=clinical stage and post-treatment pathologic state; EG=estrogen receptor status and tumor grade; g*BRCA1/2*=germline breast cancer susceptibility genes 1 and/or 2; NA=not available; NCCN=National Comprehensive Cancer Network; NR=not reported; pN1=axillary node positive; pT2=tumor pathological size >2 cm.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd):

Pneumonitis: Occurred in 0.8% of patients exposed to LYNPARZA monotherapy, 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.

ADVERSE REACTIONS—Adjuvant Treatment of g*BRCA*m, HER2-Negative, High-Risk Early Breast Cancer

Most common adverse reactions (Grades 1-4) in ≥10% of patients who received LYNPARZA in the **adjuvant setting** for **OlympiA** were: nausea (57%), fatigue (including asthenia) (42%), anemia (24%), vomiting (23%), headache (20%), diarrhea (18%), leukopenia (17%), neutropenia (16%), decreased appetite (13%), dysgeusia (12%), dizziness (11%), and stomatitis (10%).
Most common laboratory abnormalities (Grades 1-4) in ≥25% of patients who received LYNPARZA in the **adjuvant setting** for **OlympiA** were: decrease in lymphocytes (77%), increase in mean corpuscular volume (67%), decrease in hemoglobin (65%), decrease in leukocytes (64%), and decrease in absolute neutrophil count (39%).

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).

Please see additional Important Safety Information on reverse side and complete Prescribing Information, including Medication Guide.

You may report side effects related to AstraZeneca products by clicking here. If you prefer to report these to the FDA, either visit www.FDA.gov/medwatch or call 1-800-FDA-1088.

References: 1. LYNPARZA® (olaparib) [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2022. **2.** Tutt JE, Garber B, Kaufman, G, et al. Adjuvant olaparib for patients with *BRCA1*- or *BRCA2*-mutated breast cancer. *N Engl J Med.* 2021;384(25):2394-2405. doi: 10.1056/NEJMoa2105215 **3.** Hudis CA, Barlow WE, Constantino JP, et al. Proposal for standardized definitions for efficacy end points in adjuvant breast cancer trials: The STEEP system. *J Clin Oncol.* 2007;25(15):2127-2132. doi:10.1200/JCO.2006.10.3523 **4.** Tutt ANJ, Garber JE, Kaufman, B, et al. Adjuvant olaparib for patients with *BRCA1*- or *BRCA2*-mutated breast cancer. Clinical Study Protocol. *N Engl J Med.* 2021;384(25):2394-2405. doi:10.1056/NEJMoa2105215 **5.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer. V.2.2022. © 2021 National Comprehensive Cancer Network, Inc. All rights reserved. Accessed February 15, 2022. To view the most recent and complete version of the guideline, go online to NCCN.org. **6.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic. V.1.2022. © 2021 National Comprehensive Cancer Network, Inc.
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