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olaparib
tablets 150 mg

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Pancreatic Adenocarcinoma

NCCN Guidelines® recommend all patients with confirmed pancreatic cancer receive genetic testing for inherited mutations, including gBRCAm, at diagnosis to help inform therapy[1]

LYNPARZA is the ONLY FDA-approved PARP inhibitor for first-line maintenance therapy in patients with g*BRCA*-mutated* metastatic pancreatic cancer whose disease has not progressed on at least 16 weeks of a first-line platinum-based chemotherapy.[2-5]

***Select patients for therapy based on an FDA-approved companion diagnostic for LYNPARZA.**[2]

NCCN Guidelines®

NCCN Guidelines for Pancreatic Adenocarcinoma

Olaparib is included as a Category 2A† preferred option for maintenance therapy for patients with germline *BRCA1/2*-mutated metastatic adenocarcinoma of the pancreas, and no disease progression following first-line platinum-based chemotherapy for at least 16 weeks.[1]

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†Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus (≥ 85% support of the panel) that the intervention is appropriate.

INDICATION

LYNPARZA is a poly (ADP-ribose) polymerase (PARP) inhibitor indicated for the maintenance treatment of adult patients with deleterious or suspected deleterious g*BRCA*m metastatic pancreatic adenocarcinoma whose disease has not progressed on at least 16 weeks of a first-line platinum-based chemotherapy regimen. Select patients for therapy based on an FDA-approved companion diagnostic for LYNPARZA.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

There are no contraindications for LYNPARZA.

WARNINGS AND PRECAUTIONS

Myelodysplastic Syndrome/Acute Myeloid Leukemia (MDS/AML): Occurred in approximately 1.2% of patients (26/2219) with various *BRCA*m, g*BRCA*m, HRR gene-mutated or HRD-positive cancers who received LYNPARZA in clinical studies as a single agent or as part of a combination regimen, consistent with the approved indications, and the majority of events had a fatal outcome. The median duration of therapy in patients who developed MDS/AML was approximately 2 years (range: <6 months to >4 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 counts 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 throughout and complete Prescribing Information, including Medication Guide.

*BRCA*m=*BRCA*-mutated; g*BRCA*=germline *BRCA*; g*BRCA*m=germline *BRCA*-mutated or germline *BRCA* mutation(s); HRD=homologous recombination deficiency; HRR=homologous recombination repair; NCCN=National Comprehensive Cancer Network® (NCCN®); PARP=poly (ADP-ribose) polymerase.

POLO: a phase 3 trial establishing use of LYNPARZA[2,6]

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The POLO trial was a multicenter, double-blind, randomized, placebo-controlled, phase 3 trial of LYNPARZA maintenance therapy in patients with g*BRCA*-mutated metastatic pancreatic cancer

Eligibility criteria

- Patients had deleterious or suspected deleterious g*BRCA*m and were tested using BRACAnalysis CDx® (Myriad Genetic Laboratories) or local testing with subsequent confirmation via BRACAnalysis CDx®
- ≥16 weeks of first-line platinum-based chemotherapy with no limit to duration, without evidence of disease progression (complete response, partial response, or stable disease)

Randomization

- 3:2 N=154 (no stratification)

Treatment until disease progression or unacceptable toxicity

- LYNPARZA 300 mg BID (n=92)
- Placebo BID (n=62)

Trial endpoints

Primary endpoint

- PFS (BICR per modified RECIST, version 1.1)

Select secondary endpoints

- OS
- ORR (BICR per modified RECIST, version 1.1)

Safety objective

- Safety and tolerability[2,6,7]

Prior treatment

- Previous chemotherapy (LYNPARZA n=92, placebo n=62): 75% received FOLFIRINOX, 12% received variants of FOLFIRINOX, and 3% received gemcitabine plus cisplatin
- A complete or partial response to first-line platinum-based chemotherapy was seen in 49% of patients (LYNPARZA n=92, placebo n=62)

IMPORTANT SAFETY INFORMATION (Cont'd)

WARNINGS AND PRECAUTIONS (Cont'd)

Pneumonitis: Including severe and fatal cases, has occurred in patients treated with LYNPARZA. In clinical studies, among patients who received LYNPARZA as a single agent or as part of a combination regimen, the incidence of pneumonitis, including fatal cases, was 1.0% (29/2851). If patients present with new or worsening respiratory symptoms such as dyspnea, cough, and fever, or a radiological abnormality occurs, interrupt LYNPARZA treatment and promptly assess the source of the symptoms. If pneumonitis is confirmed, discontinue LYNPARZA treatment and treat the patient appropriately.

Venous Thromboembolism (VTE): Including severe or fatal pulmonary embolism (PE), occurred in patients treated with LYNPARZA. 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.

Hepatotoxicity, including Drug-Induced Liver Injury (DILI): Hepatotoxicity, including severe and potentially fatal cases of DILI has occurred in patients treated with LYNPARZA. Evaluate bilirubin and transaminases at baseline and throughout treatment with LYNPARZA. For patients who develop abnormal liver tests after LYNPARZA, monitor more frequently for liver test abnormalities and clinical signs and symptoms of hepatic toxicity. If DILI is suspected, withhold LYNPARZA. Upon confirmation of DILI, discontinue LYNPARZA.

Embryo-Fetal Toxicity: Based on its mechanism of action and findings in animals, LYNPARZA can cause fetal harm. Verify pregnancy status in 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.

Please see additional Important Safety Information throughout and complete Prescribing Information, including Medication Guide.

BICR=blinded independent central review; BID=twice daily; *BRCA*m=*BRCA*-mutated; CDx=companion diagnostic; FOLFIRINOX= folinic acid/fluorouracil/irinotecan/oxaliplatin; ORR=objective response rate; OS=overall survival; PFS=progression-free survival; RECIST=Response Evaluation Criteria in Solid Tumors.

In the POLO trial, LYNPARZA nearly doubled median PFS (7.4 months vs 3.8 months with placebo)[2,6]

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PRIMARY ENDPOINT: PROGRESSION-FREE SURVIVAL
LYNPARZA nearly doubled median PFS compared with placebo

7.4 MONTHS LYNPARZA (95% CI: 4.1–11)

vs

3.8 MONTHS PLACEBO (95% CI: 3.5–4.9)

47%
reduction in relative risk of disease progression or death

HR=0.53
95% CI: 0.35–0.81, P=0.0035

In POLO, PFS was defined as the time from randomization to disease progression or death from any cause. In the LYNPARZA arm (n=92), there were 55 progression events and 5 death events. Deaths occurred before BICR-documented progression. In the placebo arm (n=62), there were 44 progression events and no deaths.

OS in the POLO trial: **The final analysis of OS did not reach statistical significance (HR=0.83, 95% CI: 0.56–1.22, P=0.3487). Events, n (%): 61 (66) for LYNPARZA and 47 (76) for placebo. Median overall survival was 19.0 months (95% CI: 15.3–26.3) for LYNPARZA vs 19.2 months (95% CI: 14.3–26.1) for placebo.**

IMPORTANT SAFETY INFORMATION (Cont'd)

ADVERSE REACTIONS—First-Line Maintenance g*BRCA*m Metastatic Pancreatic Adenocarcinoma

Most common adverse reactions (all Grades) in ≥10% of patients who received 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 who received 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%).

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.

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CI=confidence interval; HR=hazard ratio.

NCCN Guidelines recommend all patients with confirmed pancreatic cancer receive genetic testing for inherited mutations, including gBRCAm, at diagnosis to help inform therapy[1]

NCCN Guidelines for Pancreatic Adenocarcinoma

Genetic testing for inherited mutations is recommended for any patient with confirmed pancreatic cancer, using comprehensive gene panels for hereditary cancer syndromes.[1]

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WHO — Test all patients

~7% prevalence of g*BRCA*m in metastatic pancreatic cancer in a clinical trial (N=3315)[6]

In another study of patients with pancreatic cancer, among those with a genetic mutation (n=167), >80% had no family history of pancreatic cancer[8]

WHEN — Test at diagnosis

At diagnosis, collaborate with your multidisciplinary healthcare team to facilitate prompt germline testing, including for *BRCA* mutations[1]

g*BRCA*m should be determined by an FDA-approved companion diagnostic for LYNPARZA[2]

WHY — Test to inform treatment options

g*BRCA* testing helps to inform treatment choices, including eligibility for olaparib (LYNPARZA), a targeted maintenance therapy for patients with metastatic pancreatic cancer and g*BRCA*m whose disease has not progressed on ≥16 weeks of first-line platinum-based chemotherapy[1,2]

HOW — Test your patients with the FDA-approved

BRACAnalysis CDx® from Myriad Genetics[9]

Call Myriad Genetics at **1-800-4-MYRIAD or visit myriad-oncology.com/bracanalysiscdx** to order test kits.

IMPORTANT SAFETY INFORMATION (Cont'd)

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 may report side effects related to AstraZeneca products.

References: 1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Pancreatic Adenocarcinoma V.2.2025. © National Comprehensive Cancer Network, Inc. 2025. All rights reserved. Accessed February 3, 2025. To view the most recent and complete version of the guideline, go online to NCCN.org. **2.** LYNPARZA® (olaparib) [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2025. **3.** Zejula® (niraparib) [prescribing information]. Durham, NC: GlaxoSmithKline; 2025. **4.** Rubraca® (rucaparib) [prescribing information]. Vienna, Austria: zr pharma& GmbH; 2024. **5.** Talzenna® (talazoparib) [prescribing information]. New York, NY: Pfizer, Inc.; 2025. **6.** Golan T, Hammel P, Reni M, et al. Maintenance olaparib for germline *BRCA*-mutated metastatic pancreatic cancer. *N Engl J Med*. 2019;381(4):317-327. doi:10.1056/NEJMoa1903387 **7.** Golan T, Hammel P, Reni M, et al. Maintenance olaparib for germline *BRCA*-mutated metastatic pancreatic cancer. Trial Protocol. *N Engl J Med*. 2019;381(4):317-327. **8.** Hu C, Hart SN, Polley EC, et al. Association between inherited germline mutations in cancer predisposition genes and risk of pancreatic cancer. *JAMA*. 2018;319(23):2401-2409. **9.** BRACAnalysis CDx® Technical Information. Myriad Genetics Laboratories, Inc. Accessed June 20, 2025. https://s3.amazonaws.com/myriad-web/BRACAnalysisCDxTS.pdf

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