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LYNPARZA PATIENT MANAGEMENT SUPPORT:
DOSING AND ADVERSE REACTIONS

The following management strategies were derived from clinical studies that tested LYNPARZA (PAOLA-1, SOLO-1, SOLO-2, PROpel, PROfound, OlympiA, OlympiAD, and POLO) and established medical protocols.

The information in this brochure is not meant to replace the clinical judgment of the attending physician.

INDICATIONS

LYNPARZA is a poly (ADP-ribose) polymerase (PARP) inhibitor indicated:

First-Line Maintenance *BRCA*m Advanced Ovarian Cancer

For the maintenance treatment of adult patients with deleterious or suspected deleterious germline or somatic *BRCA*-mutated (g*BRCA*m or s*BRCA*m) advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in complete or partial response to first-line platinum-based chemotherapy. Select patients for therapy based on an FDA-approved companion diagnostic for LYNPARZA.

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 *BRCA* mutation, and/or genomic instability. Select patients for therapy based on an FDA-approved companion diagnostic for LYNPARZA.

Maintenance *BRCA*-mutated Recurrent Ovarian Cancer

For the maintenance treatment of adult patients with deleterious or suspected deleterious germline or somatic *BRCA*-mutated (g*BRCA*m or s*BRCA*m) recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer, who are in complete or partial response to platinum-based chemotherapy. Select patients for therapy based on an FDA-approved companion diagnostic for LYNPARZA.

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

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.

g*BRCA*m, HER2-Negative Metastatic Breast Cancer

For the treatment of adult patients with deleterious or suspected deleterious g*BRCA*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. Select patients for therapy based on an FDA-approved companion diagnostic for LYNPARZA.

First-Line Maintenance g*BRCA*m Metastatic Pancreatic Cancer

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.

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

*BRCA*m Metastatic Castration-Resistant Prostate Cancer in Combination with Abiraterone and Prednisone or Prednisolone

In combination with abiraterone and prednisone or prednisolone (abi/pred) for the treatment of adult patients with deleterious or suspected deleterious *BRCA*-mutated (*BRCA*m) metastatic castration-resistant prostate cancer (mCRPC). Select patients for therapy based on an FDA-approved companion diagnostic for LYNPARZA.

Please see Important Safety Information on pages 3-5, and complete Prescribing Information, including Medication Guide.

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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.

In SOLO-1, patients with newly diagnosed advanced *BRCA*m ovarian cancer, the incidence of MDS/AML was 1.9% (5/260) in patients who received LYNPARZA and 0.8% (1/130) in patients who received placebo based on an updated analysis. In PAOLA-1, of patients with newly diagnosed advanced ovarian cancer with HRD-positive status, the incidence of MDS/AML was 1.6% (4/255) in patients who received LYNPARZA and 2.3% (3/131) in the control arm.

In SOLO-2, patients with *BRCA*m platinum-sensitive relapsed ovarian cancer, the incidence of MDS/AML was 8% (15/195) in patients who received LYNPARZA and 4% (4/99) in patients who received placebo. The duration of LYNPARZA treatment prior to the diagnosis of MDS/AML ranged from 0.6 years to 4.5 years.

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.

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. In the combined data of two randomized, placebo-controlled clinical studies (PROfound and PROpel) in patients with metastatic castration-resistant prostate cancer (N=1180), VTE occurred in 8% of patients who received LYNPARZA, including pulmonary embolism in 6%. In the control arms, VTE occurred in 2.5%, including pulmonary embolism in 1.5%. 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.

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IMPORTANT SAFETY INFORMATION (Cont'd)

ADVERSE REACTIONS—First-Line Maintenance *BRCA*m Advanced Ovarian Cancer

Most common adverse reactions (all Grades) in ≥10% of patients who received 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%), urinary tract infection (13%), thrombocytopenia (11%), and stomatitis (11%).

Most common laboratory abnormalities (Grades 1-4) in ≥25% of patients who received 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 and at a ≥5% frequency compared to 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 thromboembolism 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 g*BRCA*m Recurrent Ovarian Cancer

Most common adverse reactions (Grades 1-4) in ≥20% of patients who received 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)/sinusitis/rhinitis/influenza (36%), diarrhea (33%), arthralgia/myalgia (30%), dysgeusia (27%), headache (26%), decreased appetite (22%), and stomatitis (20%).

Most common laboratory abnormalities (Grades 1-4) in ≥25% of patients who received LYNPARZA in the **maintenance setting** for **SOLO-2** were: increase in mean corpuscular volume (89%), decrease in hemoglobin (83%), decrease in leukocytes (69%), decrease in lymphocytes (67%), decrease in absolute neutrophil count (51%), increase in serum creatinine (44%), and decrease in platelets (42%).

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%).

ADVERSE REACTIONS—g*BRCA*m, HER2-Negative Metastatic Breast Cancer

Most common adverse reactions (Grades 1-4) in ≥20% of patients who received LYNPARZA in the **metastatic setting** for **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 who received LYNPARZA in the **metastatic setting** for **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%).

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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%).

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

Most common adverse reactions (Grades 1-4) in ≥10% of patients who received 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 who received LYNPARZA for **PROfound** were: decrease in hemoglobin (98%), decrease in lymphocytes (62%), decrease in leukocytes (53%), and decrease in absolute neutrophil count (34%).

ADVERSE REACTIONS—Metastatic Castration-Resistant Prostate Cancer in Combination with Abiraterone and Prednisone or Prednisolone

Most common adverse reactions (Grades 1-4) in ≥10% of patients who received LYNPARZA/abiraterone with a difference of ≥5% compared to placebo/abiraterone for **PROpel** were: anemia (48%), fatigue (including asthenia) (38%), nausea (30%), diarrhea (19%), decreased appetite (16%), lymphopenia (14%), dizziness (14%), and abdominal pain (13%).

Most common laboratory abnormalities (Grades 1-4) in ≥20% of patients who received LYNPARZA/abiraterone for **PROpel** were: decrease in hemoglobin (97%), decrease in lymphocytes (70%), decrease in platelets (23%), and decrease in absolute neutrophil count (23%).

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).

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You may report side effects related to AstraZeneca products.

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Clear communication around treatment goals and AR management may inform a patient's experience on therapy[1-3]

Proactive management of select ARs by patients and care teams can help to optimize patient care[3-5]

Before starting treatment with LYNPARZA, review expectations with patients and caregivers on[3,6,7]:

- The types of ARs that may occur
- How ARs may be managed
- The importance of reporting any ARs to their care team

Evaluation for risk of ARs and close monitoring by a multidisciplinary healthcare team can inform treatment planning and help optimize dosing strategy.[2,5,6,8]

Some support methods to consider[2,5,8-10]:

- Individual nurse consultations to educate patients
- Nurse telephone follow-up after the initial nurse education session
- Multidisciplinary care team counseling on managing ARs and the importance of reporting ARs
- Pharmacist counseling supplemented with written educational materials
- Pharmacist telephone follow-up after counseling sessions

Your patients may experience ARs different from those listed in this guide during treatment with LYNPARZA.
You may report side effects related to AstraZeneca products.

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AR=adverse reaction.

LYNPARZA is the PARPi with the most FDA approvals: Approved across 8 indications and 4 tumor types[6,11-14]

ADVANCED OR RECURRENT OVARIAN CANCER	**First-line maintenance treatment in combination with bevacizumab for HRD-positive* advanced ovarian cancer in adult patients** That is in complete or partial response to first-line platinum-based chemotherapy
	First-line maintenance treatment for *BRCA*m* advanced ovarian cancer in adult patients That is in complete or partial response to first-line platinum-based chemotherapy
	Maintenance treatment for *BRCA*m* recurrent ovarian cancer in adult patients That is in complete or partial response to platinum-based chemotherapy
METASTATIC PROSTATE CANCER	**Treatment of *BRCA*m* metastatic castration-resistant prostate cancer in combination with abiraterone and prednisone or prednisolone** In combination with abiraterone and prednisone or prednisolone for the treatment of adult patients with deleterious or suspected deleterious *BRCA*m mCRPC
	Treatment of HRRm* metastatic castration-resistant prostate cancer For the treatment of adult patients with deleterious or suspected deleterious germline or somatic HRRm mCRPC who have progressed following prior treatment with enzalutamide or abiraterone
EARLY BREAST CANCER	**Adjuvant treatment of g*BRCA*m,* HER2-negative, high-risk† early breast cancer in adult patients** After neoadjuvant or adjuvant chemotherapy
METASTATIC BREAST CANCER	**Treatment of g*BRCA*m,* HER2-negative metastatic breast cancer in adult patients** After chemotherapy in the neoadjuvant, adjuvant, or metastatic setting, patients with HR-positive breast cancer should have been treated with a prior endocrine therapy or be considered inappropriate for endocrine therapy
METASTATIC PANCREATIC CANCER	**First-line maintenance therapy in g*BRCA*m* metastatic pancreatic cancer** 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.[8]

†**High-risk criteria:** For patients who received neoadjuvant chemotherapy and surgery, 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 surgery and adjuvant chemotherapy for TNBC, high risk was defined as ≥pN1 or pN0 with ≥pT2. For patients who received surgery and adjuvant chemotherapy for HR-positive, HER2-negative breast cancer, high risk was defined as ≥4 positive lymph nodes. The CPS&EG scoring system estimates relapse probability on the basis of the sum of points attributed to the following features: pre-treatment clinical stage (I/IIA=0, IIB/IIIA=1, and IIIB/IIIC=2 points); post-treatment pathologic stage (0/I=0, IIA/IIB/IIIA/IIIB=1, and IIIC=2 points); ER status (positive=0 and negative=1 point); and nuclear grade (grade 1-2=0 and grade 3=1 point). Higher scores indicate higher relapse risk. Total score of ≥3 was required for patients with HR-positive breast cancer.[6,15]

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*BRCA*m=*BRCA*-mutated; CPS&EG=pre-treatment clinical and post-treatment pathologic stage (CPS), estrogen receptor (ER) status, and histologic grade; g*BRCA*m=germline *BRCA*-mutated; HER2=human epidermal growth factor receptor 2; HR=hormone receptor; HRD=homologous recombination deficiency; HRRm=homologous recombination repair gene–mutated; mCRPC=metastatic castration-resistant prostate cancer; PARPi=poly (ADP-ribose) polymerase inhibitor; pCR=pathologic complete response; TNBC=triple-negative breast cancer.

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Clinical studies supporting the indications for LYNPARZA

ADVANCED OR RECURRENT OVARIAN CANCER	**PAOLA-1**[6,16] A randomized, phase 3 study of 806 patients with newly diagnosed, advanced, high-grade ovarian cancer who were in complete or partial response after first-line platinum-based chemotherapy plus bevacizumab comparing LYNPARZA + bevacizumab with placebo + bevacizumab. The HRD-positive subgroup served as the basis for the FDA-approved indication
	SOLO-1[6,17] A randomized, phase 3 study of 391 patients with advanced high-grade serous or endometrioid *BRCA*m ovarian cancer who were in complete or partial response following completion of first-line platinum-containing chemotherapy comparing LYNPARZA with placebo
	SOLO-2[6,18] A randomized, phase 3 study of 295 patients with a g*BRCA* mutation; platinum-sensitive relapsed ovarian, fallopian tube, or primary peritoneal cancer; and ≥2 prior lines of platinum-containing regimens comparing LYNPARZA with placebo
METASTATIC PROSTATE CANCER	**PROpel**[6,19] A randomized, double-blind, placebo-controlled, multicenter, phase 3 trial comparing LYNPARZA + abiraterone with placebo + abiraterone in 796 patients with mCRPC. Patients in both arms also received either prednisone or prednisolone. All patients received a GnRH analog or had prior bilateral orchiectomy. FDA approval of LYNPARZA + abi/pred in the initial treatment of *BRCA*m mCRPC was based on an exploratory *BRCA*m subgroup (n=85)
METASTATIC PROSTATE CANCER (CONT'D)	**PROfound**[6,20] A randomized, open-label, multicenter, phase 3 trial comparing LYNPARZA with investigator's choice of enzalutamide or abiraterone acetate in 387 men with mCRPC and a tumor mutation in at least 1 of 15 genes involved in the HRR pathway who had progressed on prior enzalutamide or abiraterone for the treatment of metastatic prostate cancer and/or CRPC. All patients received a GnRH analog or had a prior bilateral orchiectomy. Patients with mutations in *BRCA1*, *BRCA2*, or *ATM* were randomized in Cohort A (n=245). Patients with mutations among 12 other HRR genes were randomized in Cohort B (n=142). Patients with co-mutations (*BRCA1/2* or *ATM* plus a Cohort B gene) were assigned to Cohort A
EARLY BREAST CANCER	**OlympiA**[6,15] A phase 3, randomized, double-blind, placebo-controlled, international study in 1836 patients with g*BRCA*m, HER2-negative, high-risk early breast cancer who had completed definitive local treatment and neoadjuvant or adjuvant chemotherapy comparing LYNPARZA with placebo. Patients with HR-positive tumors received endocrine therapy according to institutional guidelines
METASTATIC BREAST CANCER	**OlympiAD**[6,21] An open-label, randomized, controlled, multicenter, phase 3 study of 302 patients with g*BRCA*m, HER2-negative mBC that was HR positive or triple negative, comparing LYNPARZA with healthcare provider's choice of chemotherapy (capecitabine, eribulin, or vinorelbine)
METASTATIC PANCREATIC CANCER	**POLO**[6,22] A multicenter, double-blind, randomized, placebo-controlled, phase 3 trial comparing LYNPARZA with placebo in 154 patients who had g*BRCA*m metastatic pancreatic cancer. Patients previously received ≥16 weeks of first-line platinum-based chemotherapy with no evidence of disease progression. Randomization occurred 4–8 weeks after the last dose of chemotherapy

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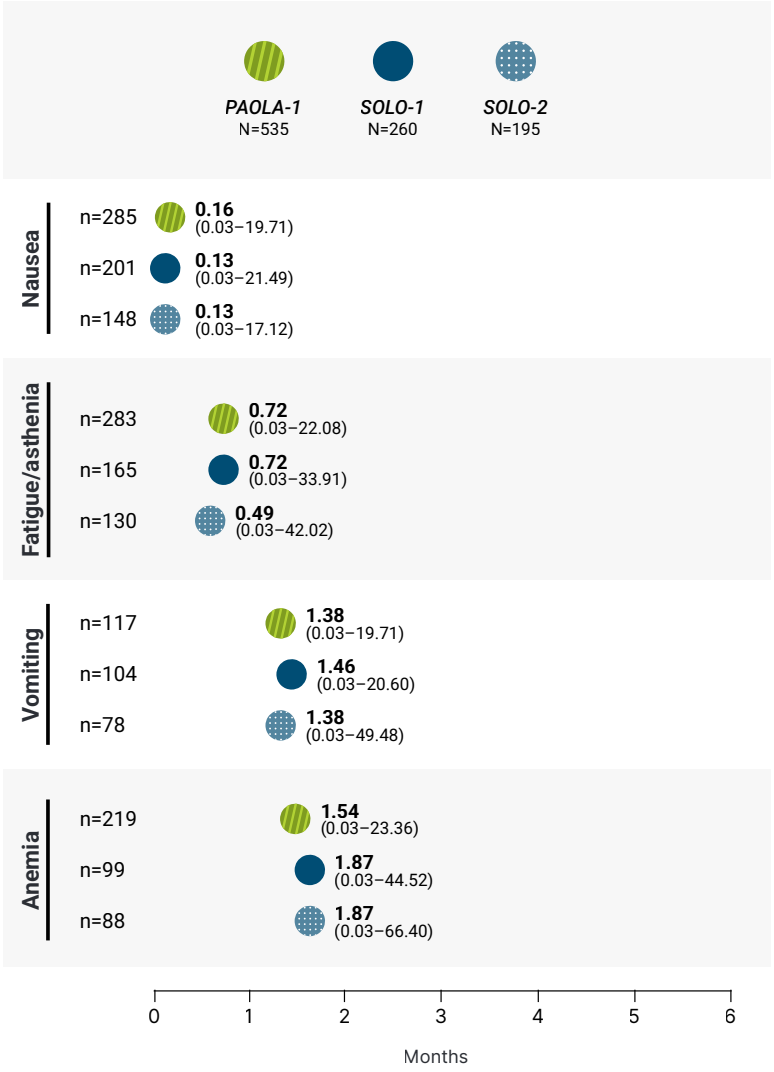
abi/pred=abiraterone plus prednisone or prednisolone; CRPC=castration-resistant prostate cancer; g*BRCA*=germline *BRCA*; GnRH=gonadotropin-releasing hormone; HR=hormone receptor; HRR=homologous recombination repair; mBC=metastatic breast cancer.

Median (range) onset of select common ARs for LYNPARZA in advanced and recurrent ovarian cancer studies[23]



DCO: March 22, 2019 for PAOLA-1; May 17, 2018 for SOLO-1; February 3, 2020 for SOLO-2.

- These are post hoc analyses based on clinical trial data from PAOLA-1, SOLO-1, and SOLO-2
- This information is descriptive only and may not be reflective of clinical practice; it should not replace physician judgment and evaluation of a potential adverse reaction should it occur
- Cross-trial comparisons should not be made
- HCPs should monitor and evaluate patients for the presence of potential adverse reactions throughout treatment with LYNPARZA

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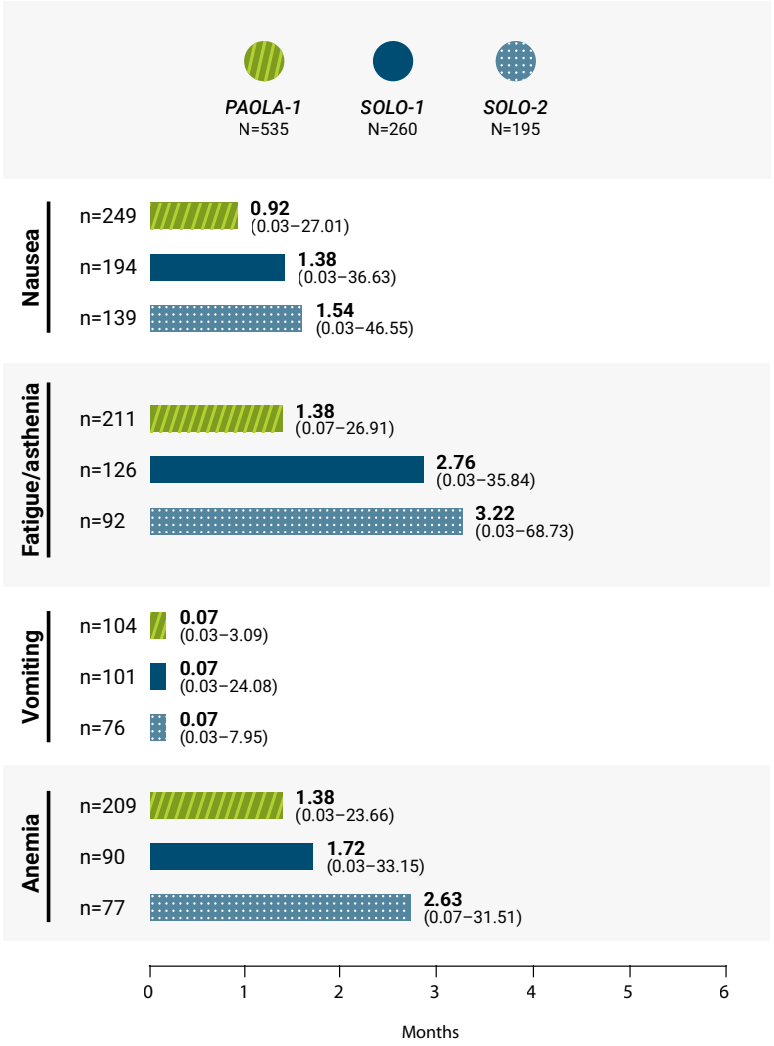
Median (range) duration of select common ARs for LYNPARZA in advanced and recurrent ovarian cancer studies[23]



DCO: March 22, 2019, for PAOLA-1; May 17, 2018, for SOLO-1; February 3, 2020, for SOLO-2.

For calculation of adverse reaction duration, reactions with missing adverse reaction dates were not included in the calculation of duration.

- These are post hoc analyses based on clinical trial data from PAOLA-1, SOLO-1, and SOLO-2
- This information is descriptive only and may not be reflective of clinical practice; it should not replace physician judgment and evaluation of a potential adverse reaction should it occur
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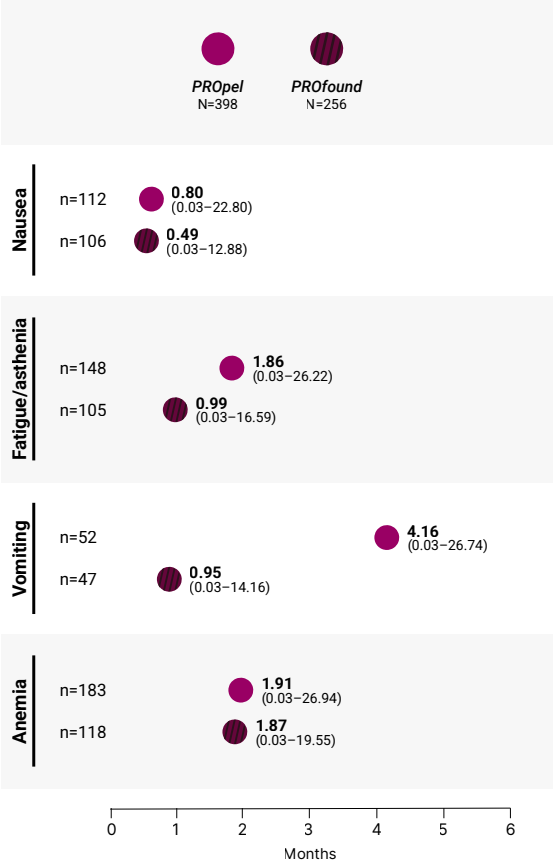
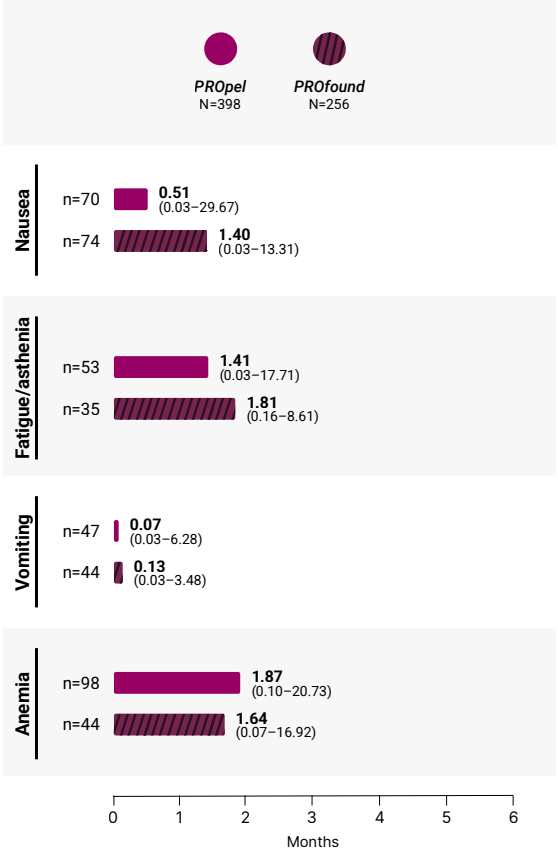
Median (range) onset and duration of select common ARs for LYNPARZA in HRRm and *BRCA*m mCRPC studies[23]

Median (range) onset of first occurrence of select common ARs in PROpel and PROfound



DCO: July 30, 2021 for PROpel; June 4, 2019 for PROfound.

Median (range) duration of first occurrence of select common ARs in PROpel and PROfound



DCO: July 30, 2021 for PROpel; June 4, 2019 for PROfound.

For calculation of adverse reaction duration, reactions with missing adverse reaction dates were not included in the calculation of duration.

- These are post hoc analyses based on clinical trial data from PROpel and PROfound
- This information is descriptive only and may not be reflective of clinical practice; it should not replace physician judgment and evaluation of a potential adverse reaction should it occur
- Cross-trial comparisons should not be made
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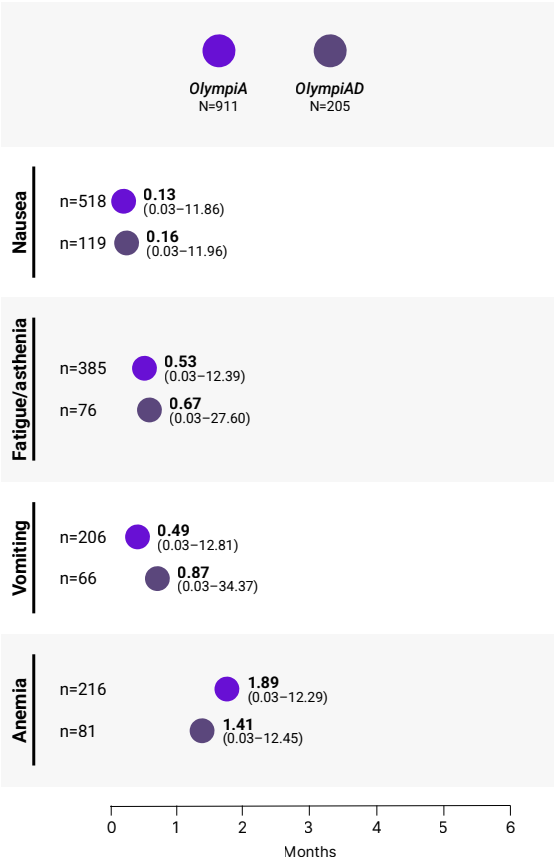
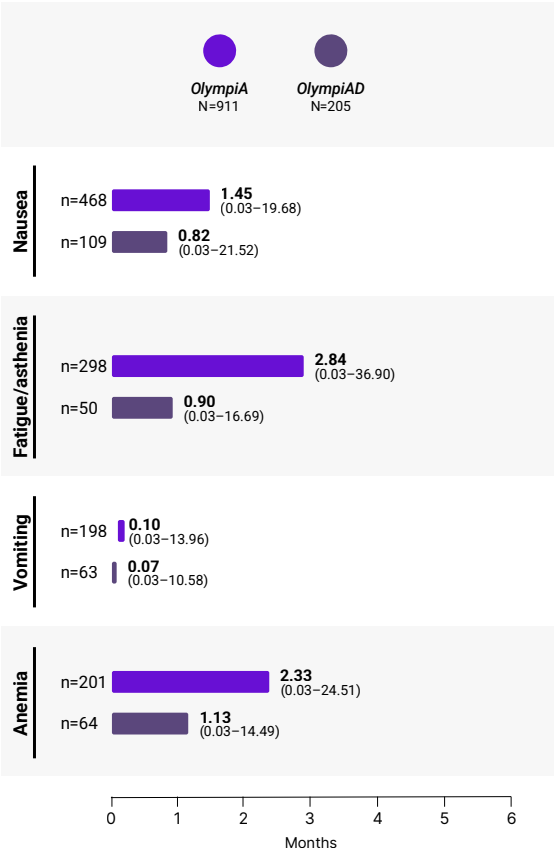
Median (range) onset and duration of select common ARs for LYNPARZA in g*BRCA*m, HER2-negative early and metastatic breast cancer studies[23]

Median (range) onset of first occurrence of select common ARs in OlympiA and OlympiAD



DCO: March 27, 2020 for OlympiA; September 25, 2017 for OlympiAD.

Median (range) duration of first occurrence of select common ARs in OlympiA and OlympiAD



DCO: March 27, 2020 for OlympiA; September 25, 2017 for OlympiAD.

For calculation of adverse reaction duration, reactions with missing adverse reaction dates were not included in the calculation of duration.

- These are post hoc analyses based on clinical trial data from OlympiA and OlympiAD
- This information is descriptive only and may not be reflective of clinical practice; it should not replace physician judgment and evaluation of a potential adverse reaction should it occur
- Cross-trial comparisons should not be made
- HCPs should monitor and evaluate patients for the presence of potential adverse reactions throughout treatment with LYNPARZA

Please see Important Safety Information on pages 3-5, and complete Prescribing Information, including Medication Guide.

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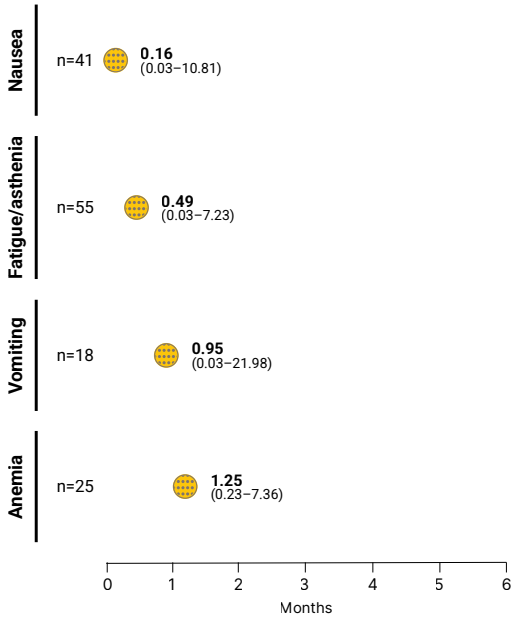
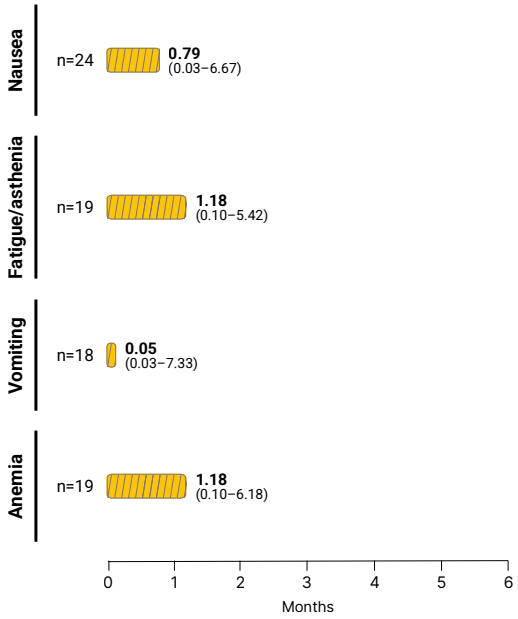
Median (range) onset and duration of select common ARs for LYNPARZA in a g*BRCA*m metastatic pancreatic cancer study[23]

Median (range) onset of first occurrence of select common ARs in POLO (N=91)



DCO: January 15, 2019.

Median (range) duration of first occurrence of select common ARs in POLO (N=91)



DCO: January 15, 2019.

For calculation of adverse reaction duration, reactions with missing adverse reaction dates were not included in the calculation of duration.

- These are post hoc analyses based on clinical trial data from POLO
- This information is descriptive only and may not be reflective of clinical practice; it should not replace physician judgment and evaluation of a potential adverse reaction should it occur
- HCPs should monitor and evaluate patients for the presence of potential adverse reactions throughout treatment with LYNPARZA

Please see Important Safety Information on pages 3-5, and complete Prescribing Information, including Medication Guide.

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Dosing and administration for LYNPARZA[6]

This is not all the information related to LYNPARZA dosing. Please see the LYNPARZA Prescribing Information for additional dosing information.

RECOMMENDED DAILY DOSE

The recommended daily dose of LYNPARZA is:

300 mg (two 150-mg tablets) taken orally twice daily, with or without food (total 600 mg daily)

Tablets shown are not actual size.

If a patient misses a dose of LYNPARZA, instruct the patient to take their next dose at its scheduled time. Instruct patients to swallow tablets whole. Do not chew, crush, dissolve, or divide tablet. Inform patients to avoid grapefruit, grapefruit juice, Seville oranges, and Seville orange juice while taking LYNPARZA.

aOC

PAOLA-1: First-Line Maintenance Treatment of HRD-Positive Advanced Ovarian Cancer in Combination with Bevacizumab

Continue LYNPARZA treatment until disease progression, unacceptable toxicity, or completion of 2 years of treatment. Patients with a complete response (no radiological evidence of disease) at 2 years should stop treatment. Patients with evidence of disease at 2 years, who in the opinion of the treating healthcare provider can derive further benefit from continuous LYNPARZA treatment, can be treated beyond 2 years. When used with LYNPARZA, the recommended dose of bevacizumab is 15 mg/kg every three weeks. Bevacizumab should be given for a total of 15 months including the period given with chemotherapy and given as maintenance. Refer to the Prescribing Information for bevacizumab when used in combination with LYNPARZA for more information.

SOLO-1: First-Line Maintenance Treatment of *BRCA*-Mutated Advanced Ovarian Cancer

Continue treatment until disease progression, unacceptable toxicity, or completion of 2 years of treatment. Patients with a complete response (no radiological evidence of disease) at 2 years should stop treatment. Patients with evidence of disease at 2 years, who in the opinion of the treating healthcare provider can derive further benefit from continuous treatment, can be treated beyond 2 years.

SOLO-2: Maintenance Treatment of *BRCA*-Mutated Recurrent Ovarian Cancer

Continue treatment until disease progression or unacceptable toxicity.

eBC

OlympiA: Adjuvant Treatment of Germline *BRCA*-Mutated, HER2-Negative, High-Risk Early Breast Cancer

Continue treatment for a total of 1 year, or until disease recurrence, or unacceptable toxicity, whichever occurs first. Patients receiving LYNPARZA for hormone receptor–positive HER2-negative breast cancer should continue concurrent treatment with endocrine therapy as per current clinical practice guidelines.

mBC

OlympiAD: Germline *BRCA*-Mutated, HER2-Negative Metastatic Breast Cancer

Continue treatment until disease progression or unacceptable toxicity.

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Dosing and administration for LYNPARZA[6] (Cont'd)

mCRPC

PROpel: *BRCA*-Mutated Metastatic Castration-Resistant Prostate Cancer in Combination with Abiraterone and Prednisone or Prednisolone

Continue treatment until disease progression or unacceptable toxicity. When used with LYNPARZA, the recommended dose of abiraterone is 1000 mg taken orally once daily. Abiraterone should be given in combination with prednisone or prednisolone 5 mg orally twice daily. Refer to the Prescribing Information for abiraterone for dosing information.

Patients with mCRPC should also receive a GnRH analog concurrently or should have had bilateral orchiectomy.

PROfound: HRR Gene-Mutated Metastatic Castration-Resistant Prostate Cancer Following Progression on Enzalutamide or Abiraterone

Continue treatment until disease progression or unacceptable toxicity. Patients with mCRPC should also receive a GnRH analog concurrently or should have had bilateral orchiectomy.

mPaC

POLO: First-line Maintenance of Germline *BRCA*-Mutated Metastatic Pancreatic Adenocarcinoma

Continue treatment until disease progression or unacceptable toxicity.

Dosing and administration for LYNPARZA[6] (Cont'd)

Dosage modifications for concomitant use with strong or moderate CYP3A inhibitors[6]

Avoid concomitant use of strong or moderate CYP3A inhibitors with LYNPARZA. If concomitant use cannot be avoided, reduce LYNPARZA dosage to:

- 100 mg twice daily when used concomitantly with a strong CYP3A inhibitor
- 150 mg twice daily when used concomitantly with a moderate CYP3A inhibitor

After the inhibitor has been discontinued for 3–5 elimination half-lives, resume the LYNPARZA dose taken prior to initiating the CYP3A inhibitor.

Dosage modifications for renal impairment[6]

In patients with moderate renal impairment (CLcr 31–50 mL/min), reduce the LYNPARZA dosage to 200 mg taken orally twice daily.

No dosage modification is recommended in patients with mild renal impairment (CLcr 51–80 mL/min estimated by Cockcroft-Gault).

There are no data in patients with severe renal impairment or end-stage disease (CLcr ≤30 mL/min).

Dosage modifications for hepatic impairment[6]

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).

Avoid coadministration with strong or moderate CYP3A inducers

Concomitant use with a strong or moderate CYP3A inducer decreased olaparib exposure, which may reduce LYNPARZA efficacy.

Dosing and administration for LYNPARZA[6] (Cont'd)

To manage adverse reactions (ARs), consider[6]:

DOSE INTERRUPTION

Consider dose interruption if a patient experiences an AR

OR

DOSE REDUCTION

Consider dose reduction if a patient experiences an AR

INITIAL REDUCTION

Reduce to

150 mg

100 mg

Initial reduction to 250 mg (one 150-mg tablet and one 100-mg tablet) taken twice daily (total 500 mg daily)

FURTHER REDUCTION

Reduce to

100 mg

100 mg

Further reduction to 200 mg (two 100-mg tablets) taken twice daily (total 400 mg daily)

Tablets shown are not actual size.

For dose modifications for specific AR management, including MDS/AML, pneumonitis, VTE, and DILI, please see the Management of Select ARs section later in this guide.

When using LYNPARZA in combination with bevacizumab for the first-line maintenance treatment of HRD-positive advanced ovarian cancer, please refer to the Prescribing Information for bevacizumab for more information on the management of ARs related to bevacizumab and bevacizumab dose adjustments.

When using LYNPARZA in combination with abiraterone and prednisone or prednisolone for the treatment of *BRCA*m mCRPC, please refer to the Prescribing Information for dose instructions for abiraterone.

Dose modifications due to adverse reactions in LYNPARZA pivotal trials[6,16,24,25]

		PAOLA-1	
		LYNPARZA + bevacizumab (LYNPARZA component) (n=535)	**Placebo + bevacizumab** (placebo component) (n=267)
ADVANCED OVARIAN CANCER (IN COMBINATION)	**Discontinuations**	20%	6%
	Reductions*	41%	7%
	Interruptions†	54%	24%

*In PAOLA-1, LYNPARZA dose reduction or discontinuation were considered after a patient resumed treatment after a dose interruption. In the case of dose reduction, the LYNPARZA dose was reduced to 250 mg BID. If further reduction was needed, then the dose could be reduced to 200 mg BID.

†For LYNPARZA, repeat dose interruptions in PAOLA-1 were allowed as required, for a maximum of 4 weeks on each occasion.

8 out of 10 patients remained on LYNPARZA as prescribed in combination with bevacizumab without discontinuing due to ARs

In PAOLA-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. Recorded ARs occurred during study treatment or up to 30 days after discontinuing the intervention.

Bevacizumab toxicity during PAOLA-1 was managed according to the Prescribing Information for bevacizumab, which could have included dose interruption, modification, or discontinuation. Please refer to the current version of the bevacizumab Prescribing Information for bevacizumab guidance. If LYNPARZA was temporarily interrupted for toxicity related to LYNPARZA, bevacizumab was continued unless the toxicity of LYNPARZA prevented patients from taking bevacizumab or increased the risk of bevacizumab toxicity. In this case, both treatments were interrupted until toxicity resolution (or NCI CTCAE Grade 1).

Dose modifications due to adverse reactions in LYNPARZA pivotal trials[6,17,18,26,27] (Cont'd)

ADVANCED OR RECURRENT OVARIAN CANCER (AS MONOTHERAPY)

	SOLO-1		SOLO-2	
	LYNPARZA (n=260)	**Placebo** (n=130)	**LYNPARZA** (n=195)	**Placebo** (n=99)
Discontinuations	12%	2%	11%	2%
Reductions‡	28%	3%	27%	3%
Interruptions§	52%	17%	45%	18%

‡In SOLO-1 and SOLO-2, LYNPARZA dose reduction or discontinuation were considered after a patient resumed treatment after a dose interruption. In the case of dose reduction, the LYNPARZA dose was reduced to 250 mg BID. If further reduction was needed, then the dose could be reduced to 200 mg BID.

§For LYNPARZA, repeat dose interruptions in SOLO-1 and SOLO-2 were allowed as required, for a maximum of 14 days on each occasion.

~9 out of 10 patients remained on LYNPARZA without an AR-related discontinuation

~3 out of 4 patients remained on LYNPARZA without a dose reduction due to an AR

In SOLO-1: The most frequent ARs leading to dose interruption or reduction of LYNPARZA were anemia (23%), nausea (14%), and vomiting (10%). The most frequent ARs that led to discontinuation were fatigue (3.1%), anemia (2.3%), and nausea (2.3%).

In SOLO-2: The most frequent ARs leading to dose interruption or reduction of LYNPARZA were anemia (22%), neutropenia (9%), and fatigue/asthenia (8%).

Please see Important Safety Information on pages 3-5, and complete Prescribing Information, including Medication Guide.

BID=twice daily; CTCAE=Common Terminology Criteria for Adverse Events; NCI=National Cancer Institute.

Dose modifications due to adverse reactions in LYNPARZA pivotal trials[6,28] (Cont'd)

		PROpel
		LYNPARZA with abiraterone + prednisone or prednisolone (LYNPARZA component) (n=398)
METASTATIC PROSTATE CANCER	**Discontinuations**	16%
	Reductions*	21%
	Interruptions†	48%

*In PROpel, LYNPARZA dose reduction was considered after a patient resumed treatment after a dose interruption; the LYNPARZA dose was reduced to 250 mg BID. If further reduction was needed, then the dose could be reduced to 200 mg BID. If the reduced dose of 200 mg BID was not tolerated, no further dose reduction was allowed and LYNPARZA was discontinued.

†For LYNPARZA, repeat dose interruptions in PROpel were allowed as required, for a maximum of 4 weeks on each occasion.

In PROpel, 84% of patients remained on LYNPARZA without discontinuing due to adverse reactions.

The most common (>2%) adverse reactions requiring dosage interruption of LYNPARZA were anemia (16%), COVID-19 (6%), fatigue (3.5%), nausea (2.8%), pulmonary embolism (2.3%), and diarrhea (2.3%); the most common (>2%) adverse reactions requiring dosage reductions of LYNPARZA were anemia (11%) and fatigue (2.5%); the most common adverse reactions which resulted in permanent discontinuation of LYNPARZA were anemia (4.3%) and pneumonia (1.5%).

Dose modifications due to adverse reactions in LYNPARZA pivotal trials[6,20,29] (Cont'd)

		PROfound	
		LYNPARZA (n=256)	**Investigator's choice of enzalutamide or abiraterone** (n=130)
METASTATIC PROSTATE CANCER	**Discontinuations**	18%	8%
	Reductions*	22%	4%
	Interruptions†	45%	18%

*In PROfound, the LYNPARZA dose was reduced to 250 mg BID. If further reduction was needed, then the dose could be reduced to 200 mg BID. If the reduced dose of 200 mg BID was not tolerated, no further dose reduction was allowed and LYNPARZA was discontinued.

†For LYNPARZA, repeat dose interruptions in PROfound were allowed as required, for a maximum of 4 weeks on each occasion.

In PROfound, 82% of patients remained on LYNPARZA without discontinuing due to adverse reactions.

In PROfound: The most frequent ARs leading to dose interruption of LYNPARZA were anemia (25%) and thrombocytopenia (6%), and the most frequent AR leading to reduction was anemia (16%). The AR that most frequently led to discontinuation was anemia (7%).

Dose modifications due to adverse reactions in LYNPARZA pivotal trials[6,30] (Cont'd)

		OlympiA
		LYNPARZA (n=911)
EARLY BREAST CANCER	**Discontinuations**	10%
	Reductions*	23%
	Interruptions†	31%

*In OlympiA, the LYNPARZA dose was reduced to 250 mg BID. If further reduction was needed, then the dose could be reduced to 200 mg BID. If the reduced dose was not tolerated, no further dose reduction was allowed and LYNPARZA was discontinued.

†For LYNPARZA, dose interruptions in OlympiA were allowed for a maximum of 4 weeks. If the AR causing the dose interruption was not resolved at 4 weeks, LYNPARZA was discontinued.

9 out of 10 patients remained on LYNPARZA without an AR-related discontinuation

In OlympiA: The most frequent ARs leading to dose interruption of LYNPARZA were anemia (11%), neutropenia (6%), nausea (5%), leukopenia (3.5%), fatigue (3%), and vomiting (2.9%) and the most frequent ARs leading to dose reduction of LYNPARZA were anemia (8%), nausea (4.7%), neutropenia (4.2%), fatigue (3.3%), leukopenia (1.8%), and vomiting (1.5%). The ARs that most frequently led to discontinuation of LYNPARZA were nausea (2%), anemia (1.8%), and fatigue (1.3%).

Dose modifications due to adverse reactions in LYNPARZA pivotal trials[6,21,31] (Cont'd)

		OlympiAD	
		LYNPARZA (n=205)	**Chemotherapy** (n=91)
METASTATIC BREAST CANCER	**Discontinuations**	5%	8%
	Reductions*	25%	31%
	Interruptions†	35%	28%

*In OlympiAD, the LYNPARZA dose was reduced to 250 mg BID. If further reduction was needed, then the dose could be reduced to 200 mg BID. If the reduced dose of 200 mg BID was not tolerated, no further dose reduction was allowed and LYNPARZA was discontinued.

†For LYNPARZA, repeat dose interruptions in OlympiAD were allowed as required, for a maximum of 4 weeks on each occasion.

~9 out of 10 patients remained on LYNPARZA without an AR-related discontinuation

~3 out of 4 patients remained on LYNPARZA without a dose reduction due to an AR

In OlympiAD: Patients received LYNPARZA or healthcare provider's choice of chemotherapy (capecitabine, eribulin, or vinorelbine).

Please see Important Safety Information on pages 3-5, and complete Prescribing Information, including Medication Guide.

Lynparza® olaparib tablets 150 mg

Dose modifications due to adverse reactions in LYNPARZA pivotal trials[6,32] (Cont'd)

		POLO
		LYNPARZA (n=90)
METASTATIC PANCREATIC CANCER	**Discontinuations**	6%
	Reductions*	17%
	Interruptions†	35%

*In POLO, the LYNPARZA dose was reduced to 250 mg BID. If further reduction was needed, then the dose could be reduced to 200 mg BID.

†For LYNPARZA, repeat dose interruptions in POLO were allowed as required, for a maximum of 4 weeks on each occasion.

~9 out of 10 patients remained on LYNPARZA without AR-related discontinuation

In POLO: The most frequent ARs leading to dosage interruption or reduction in patients who received LYNPARZA were anemia (11%), vomiting (5%), abdominal pain (4%), asthenia (3%), and fatigue (2%). The most frequent AR that led to discontinuation was fatigue (2.2%).

Considerations in the management of select ARs

The following considerations are based on the Prescribing Information for LYNPARZA, as well as based on information adapted from guidelines developed independently by the organizations cited herein. The most up-to-date and complete information developed by these organizations is available online. This information is not meant to replace the clinical judgment of the attending physician.

Nausea and vomiting

This information is not meant to replace the clinical judgment of the attending physician

LYNPARZA DOSE MANAGEMENT[6]

As part of your assessment and management of a potential adverse reaction, evaluate whether LYNPARZA dosing should be interrupted, reduced, or discontinued. See Dosing & Administration information on pages 14-17.

PATIENT COUNSELING[6]

Advise patients that:

- Mild or moderate nausea and/or vomiting are very common in patients receiving LYNPARZA
- Management strategies exist to aid in the alleviation of the symptoms of nausea and vomiting
- Communication with their care team may inform their experience on therapy
- They should consult with their care team about available antiemetic treatment options
- They should report to their healthcare provider any new or worsening symptoms that they experience while taking medication

Clinical evaluation and management strategies for nausea and vomiting

This information is not meant to replace the clinical judgment of the attending physician

CLINICAL EVALUATION

As part of your clinical evaluation, consider potential causes, including if the patient's cancer has progressed or recurred and evaluate appropriately.

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) recommendations for evaluation include:

Assess:

- Determine the severity of nausea and vomiting[33]

Consider other potential causes of emesis in patients with cancer, including[34]:

- Vestibular dysfunction
- Brain metastasis
- Electrolyte imbalance
- Uremia
- Concomitant drug treatments
- Psychophysiologic (anxiety and anticipatory nausea and vomiting)
- Pancreatitis

See NCCN Guidelines for Palliative Care and NCCN Guidelines for Antiemesis for further information.

MANAGEMENT CONSIDERATIONS

NCCN Guidelines® recommendations for intervention include:

- Appropriate prophylactic antiemetic therapy to reduce the incidence of nausea/vomiting. For more information on emetic risk of cancer therapies including olaparib, and recommendations for antiemetic agents, see the NCCN Guidelines for Antiemesis[34]
- Counsel patients on their eating habits and to adopt other lifestyle measures that may alleviate nausea and/or vomiting such as[34,35]:
  - Small frequent meals, choosing healthy foods, controlling the amount of food consumed, full liquid foods, and eating food at room temperature. A dietary consult may also be useful

Other management strategies include:

- Treat dehydration, uremia, and hypercalcemia

Consider:

- Psychiatric consultation[33]
- Acupuncture, hypnosis, and cognitive behavioral therapy[33]

See NCCN Guidelines for Palliative Care and NCCN Guidelines for Antiemesis for further information.

Diarrhea

This information is not meant to replace the clinical judgment of the attending physician

LYNPARZA DOSE MANAGEMENT[6]

As part of your assessment and management of a potential adverse reaction, evaluate whether LYNPARZA dosing should be interrupted, reduced, or discontinued. See Dosing & Administration information on pages 14-17.

PATIENT COUNSELING[6,36]

Advise patients that:

- Diarrhea is a common side effect when receiving LYNPARZA
- Management strategies exist to aid in the alleviation of the symptoms of diarrhea
- Communication with their care team may inform their experience on therapy
- They should report to their healthcare provider any new or worsening symptoms that they experience while taking medication

Clinical evaluation and management strategies for diarrhea

This information is not meant to replace the clinical judgment of the attending physician

CLINICAL EVALUATION[33]

As part of your clinical evaluation, consider potential causes, including if the patient's cancer has progressed or recurred and evaluate appropriately.

NCCN Guidelines recommend screening and assessment to evaluate diarrhea severity and cause.

See NCCN Guidelines for Palliative Care for further information.

MANAGEMENT CONSIDERATIONS

NCCN Guidelines recommendations for intervention include[33]:

- Provide immediate antidiarrheal therapy indicated by grade
  - May include oral hydration or IV fluids
- Tailor treatment to potential causes
  - Irritable bowel syndrome (IBS) or Crohn's disease
  - Postsurgical or anatomic changes
  - Recent antibiotic use
  - Drugs that frequently induce diarrhea
  - Dietary changes
  - Infection

Other considerations may apply depending on clinical presentation. See the NCCN Guidelines for complete information.

See NCCN Guidelines for Palliative Care for further information.

Additional considerations for management of diarrhea include:

Patients should talk with their healthcare team about management strategies, including[35]:

- Trying the BRAT diet (bananas, rice, applesauce, toast)
- Avoiding caffeine, alcohol, high-fat foods, acidic drinks such as orange and prune juices, and spicy or sugary foods
- Starting a clear liquid diet and drinking at least 1 cup after each loose bowel movement
- Taking medicine for diarrhea only if and as prescribed

IV=intravenous.

Dyspepsia

This information is not meant to replace the clinical judgment of the attending physician

LYNPARZA DOSE MANAGEMENT[6]

As part of your assessment and management of a potential adverse reaction, evaluate whether LYNPARZA dosing should be interrupted, reduced, or discontinued. See Dosing & Administration information on pages 14-17.

PATIENT COUNSELING[6,37]

Advise patients that:

- Dyspepsia is a potential side effect when receiving LYNPARZA
- Management strategies exist to aid in the alleviation of the symptoms of dyspepsia
- Communication with their care team may inform their experience on therapy
- They should report to their healthcare provider any new or worsening symptoms that they experience while taking medication

Clinical evaluation and management strategies for dyspepsia

This information is not meant to replace the clinical judgment of the attending physician

CLINICAL EVALUATION[37]

As part of your clinical evaluation, consider potential causes, including if the patient's cancer has progressed or recurred and evaluate appropriately.

Clinical evaluation considerations include:

- Completing a history and physical examination to determine possible etiologies of dyspepsia symptoms
- Assessing medication history for any drugs associated with dyspepsia

Causes of dyspepsia may include:

- *Helicobacter pylori* infection
- Acid secretion
- Abnormal gastric or duodenal motility
- Impaired gastric myoelectrical activity
- Immune activation
- Anxiety and/or depression

MANAGEMENT CONSIDERATIONS[37]

Management considerations include:

- Recommending the limitation of foods that may contribute to dyspepsia (eg, wheat, high-fat foods, FODMAPs, caffeine)
- Eradication of *H. pylori*
- Acid suppression

Constipation

This information is not meant to replace the clinical judgment of the attending physician

LYNPARZA DOSE MANAGEMENT[6]

As part of your assessment and management of a potential adverse reaction, evaluate whether LYNPARZA dosing should be interrupted, reduced, or discontinued. See Dosing & Administration information on pages 14-17.

PATIENT COUNSELING[6,38]

Advise patients that:

- Constipation is a potential side effect when receiving LYNPARZA
- Management strategies exist to aid in alleviation of the symptoms of constipation
- Communication with their care team may inform their experience on therapy
- They should report to their healthcare provider any new or worsening symptoms that they experience while taking medication

Clinical evaluation and management strategies for constipation

This information is not meant to replace the clinical judgment of the attending physician

CLINICAL EVALUATION[38]

As part of your clinical evaluation, consider potential causes, including if the patient's cancer has progressed or recurred and evaluate appropriately.

Causes of constipation may include:

- Colorectal or advanced cancers
- Other medicines such as opioids, antidepressants, and barium sulfate (contrast for CT and MRI imaging scans)
- Lack of exercise
- Low fluid intake and low fiber diet
- Overuse of laxatives

MANAGEMENT CONSIDERATIONS[38]

Management considerations include:

- Eating more insoluble fiber and avoiding soluble fiber
- Use of a laxative or enema and suppositories, if appropriate
- Physical activity
- Medicines for constipation
- Trying pelvic therapy and biofeedback

Ensure patients understand the symptoms and the importance of communicating these symptoms to their healthcare team to help avoid the risk of complications.

Fatigue

This information is not meant to replace the clinical judgment of the attending physician

LYNPARZA DOSE MANAGEMENT[6]

As part of your assessment and management of a potential adverse reaction, evaluate whether LYNPARZA dosing should be interrupted, reduced, or discontinued. See Dosing & Administration information on pages 14-17.

PATIENT COUNSELING[6,39]

Advise patients that:

- Fatigue is a common side effect when receiving LYNPARZA
  - Anemia is frequently an underlying cause of fatigue (Please see pages 41-42 for the Anemia Section.)
- Management strategies exist to aid in the alleviation of the symptoms of fatigue
- Communication with their care team may inform their experience on therapy
- It's important for them to report to you if they experience weakness and/or feeling tired, as these may be signs of hematological toxicity or of a more serious uncommon bone marrow problem (MDS/AML), which have been reported in patients treated with LYNPARZA
- They should report to their healthcare provider any new or worsening symptoms that they experience while taking medication

Clinical evaluation and management strategies for fatigue

This information is not meant to replace the clinical judgment of the attending physician

CLINICAL EVALUATION[39]

As part of your clinical evaluation, consider potential causes, including if the patient's cancer has progressed or recurred and evaluate appropriately.

Screen for and treat fatigue at cancer diagnosis, and monitor fatigue throughout cancer treatment.

Communicate with patients to assess:

- Severity
- Onset
- When they feel most tired
- Duration
- Changes over time
- What triggers or relieves tiredness
- How their fatigue affects the activities they enjoy and their daily routine

Causes of cancer-related fatigue may include:

- Cancer treatments
- Chronic pain
- Depression, anxiety, and distress
- Sleep problems
- Problems eating and drinking
- Anemia
- Arthritis, heart or breathing problems, and hormone problems

MANAGEMENT CONSIDERATIONS[39]

Patients should talk with their healthcare team about management strategies, including:

- Physical activity
- Energy conservation
- Stress management (eg, mindfulness and relaxation exercises, counseling, and other strategies)
- Trying to get good sleep
- Balanced nutrition and good hydration

Headache

This information is not meant to replace the clinical judgment of the attending physician

LYNPARZA DOSE MANAGEMENT[6]

As part of your assessment and management of a potential adverse reaction, evaluate whether LYNPARZA dosing should be interrupted, reduced, or discontinued. See Dosing & Administration information on pages 14-17.

PATIENT COUNSELING[6,40]

Advise patients that:

- Headache is a common side effect when receiving LYNPARZA
- Management strategies exist to aid in alleviation of the symptoms of headache
- Communication with their care team may inform their experience on therapy
- They should report to their healthcare provider any new or worsening symptoms that they experience while taking medication

Clinical evaluation and management strategies for headache

This information is not meant to replace the clinical judgment of the attending physician

CLINICAL EVALUATION[40,41]

As part of your clinical evaluation, consider potential causes, including if the patient's cancer has progressed or recurred and evaluate appropriately.

Causes of headache may include:

- Brain or spine tumor
- Cancer treatments
- Acute sinusitis
- Meningitis
- Medications to treat other disorders
- Dehydration
- Changes in sleep or lack of sleep, skipped meals, and stress

MANAGEMENT CONSIDERATIONS[40,42]

Patients should talk with their healthcare team about management strategies, including:

- Seeking rest in a quiet, dark room
- Reducing stress through therapy (eg, CBT, biofeedback, massage, acupuncture)
- Identifying causes or triggers for headaches
- Keeping a daily log of headaches

Consider medication that may prevent and treat headaches or reduce the pain.

CBT=cognitive behavioral therapy.

Dysgeusia

This information is not meant to replace the clinical judgment of the attending physician

LYNPARZA DOSE MANAGEMENT[6]

As part of your assessment and management of a potential adverse reaction, evaluate whether LYNPARZA dosing should be interrupted, reduced, or discontinued. See Dosing & Administration information on pages 14-17.

PATIENT COUNSELING[6,43]

Advise patients that:

- Dysgeusia is a potential side effect when receiving LYNPARZA
- Management strategies exist to aid in alleviation of the symptoms of dysgeusia
- Communication with their care team may inform their experience on therapy
- They should report to their healthcare provider any new or worsening symptoms that they experience while taking medication

Clinical evaluation and management strategies for dysgeusia

This information is not meant to replace the clinical judgment of the attending physician

CLINICAL EVALUATION[43,44]

As part of your clinical evaluation, consider potential causes, including if the patient's cancer has progressed or recurred and evaluate appropriately.

Perform detailed history and physical exam to determine the causality of dysgeusia.

Causes of dysgeusia may include:

- Certain cancer treatments
- ENT surgery
- Mouth sores or dryness
- Dental or gum problems
- COVID-19

MANAGEMENT CONSIDERATIONS[43]

Considerations include:

- Keep a food diary to track what works
- Choose what tastes and smells good
- Serve foods cold or at room temperature
- Use plastic utensils and glass cups and plates to reduce metallic taste
- Avoid red meats if unappetizing, and try other protein-rich foods
- Marinate meats in fruit juices, sweet wines, salad dressings, or other sauces
- Flavor foods with herbs, spices, sugar, or tart flavors
- Practice good dental hygiene
- Rinse with a baking soda, salt, and water mouthwash before eating

ENT=ear, nose, and throat.

Dizziness

This information is not meant to replace the clinical judgment of the attending physician

LYNPARZA DOSE MANAGEMENT[6]

As part of your assessment and management of a potential adverse reaction, evaluate whether LYNPARZA dosing should be interrupted, reduced, or discontinued. See Dosing & Administration information on pages 14-17.

PATIENT COUNSELING[6,45,46]

Advise patients that:

- Dizziness is a common side effect when receiving LYNPARZA
- Management strategies exist to aid in alleviation of the symptoms of dizziness
- Communication with their care team may inform their experience on therapy
- They should report to their healthcare provider any new or worsening symptoms that they experience while taking medication

Clinical evaluation and management strategies for dizziness

This information is not meant to replace the clinical judgment of the attending physician

CLINICAL EVALUATION[45,46]

As part of your clinical evaluation, consider potential causes, including if the patient's cancer has progressed or recurred and evaluate appropriately.

Communicate with patients to assess:

- When dizziness occurs and/or gets worse (eg, when sitting or standing up suddenly, walking, moving head, etc)
- How long dizziness has been occurring
- Whether there are sight or hearing issues accompanying the dizziness
- Medications, vitamins, or supplements

Causes of dizziness may include:

- Medications (eg, antiseizure drugs, antidepressants, sedatives, tranquilizers, antihypertensive medications)
- Anemia
- Drop in blood pressure
- Poor blood circulation
- Low blood sugar
- Overheating and dehydration
- Inner ear infection or disease
- Anxiety disorders

MANAGEMENT CONSIDERATIONS[45]

Patients should talk with their healthcare team about management strategies, including:

- Staying hydrated, eating healthy, getting enough sleep, and avoiding stress
- Using a cane for stability and avoiding sudden movement
- Avoiding driving a car or operating heavy machinery if dizziness occurs without warning
- Avoiding caffeine, alcohol, salt, and tobacco

If no cause is found or if dizziness persists, consider recommending prescription drugs and other treatments to make symptoms more manageable.

Decreased appetite

This information is not meant to replace the clinical judgment of the attending physician

LYNPARZA DOSE MANAGEMENT[6]

As part of your assessment and management of a potential adverse reaction, evaluate whether LYNPARZA dosing should be interrupted, reduced, or discontinued. See Dosing & Administration information on pages 14-17.

PATIENT COUNSELING[6,35]

Advise patients that:

- Decreased appetite is a common side effect when receiving LYNPARZA
- Management strategies exist to aid in alleviation of the symptoms of decreased appetite
- Communication with their care team may inform their experience on therapy
- They should report to their healthcare provider any new or worsening symptoms that they experience while taking medication

Clinical evaluation and management strategies for decreased appetite

This information is not meant to replace the clinical judgment of the attending physician

CLINICAL EVALUATION[35]

As part of your clinical evaluation, consider potential causes, including if the patient's cancer has progressed or recurred and evaluate appropriately.

Perform detailed history and physical exam to determine the causality of decreased appetite.

Causes of decreased appetite may include:

- The cancer itself
- Fatigue
- Pain
- Medicines
- Feelings such as stress, fear, depression, and anxiety
- Cancer treatment side effects such as nausea, vomiting, constipation, or changes in how foods taste or smell

MANAGEMENT CONSIDERATIONS[35]

Management considerations include:

- Drink a liquid meal replacement
- Eat 5 or 6 smaller meals each day
- Keep snacks nearby
- Drink liquids throughout the day
- Choose liquids that add calories
- Eat a bedtime snack
- Talk with a dietician

NCI=National Cancer Institute.

Pneumonitis in patients receiving LYNPARZA[6]

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.

Cough and dyspnea

This information is not meant to replace the clinical judgment of the attending physician

LYNPARZA DOSE MANAGEMENT[6]

As part of your assessment and management of a potential adverse reaction, evaluate whether LYNPARZA dosing should be interrupted, reduced, or discontinued. See Dosing & Administration information on pages 14-17.

PATIENT COUNSELING[6,33,47]

Advise patients that:

- Cough and dyspnea are potential side effects when receiving LYNPARZA
- Management strategies exist to aid in the alleviation of the symptoms of cough and dyspnea
- Communication with their care team may inform their experience on therapy
- Advise patients to contact their healthcare provider if they experience any new or worsening respiratory symptoms including shortness of breath, fever, cough, or wheezing
- They should report to their healthcare provider any new or worsening symptoms that they experience while taking medication

Clinical evaluation and management strategies for cough and dyspnea

This information is not meant to replace the clinical judgment of the attending physician

CLINICAL EVALUATION[47]

As part of your clinical evaluation, consider potential causes, including if the patient's cancer has progressed or recurred and evaluate appropriately.

Perform comprehensive history and physical exam focused on identifying underlying causes and optimizing comorbidities including:

- Pneumonia
- Anemia
- Pleural effusion
- Congestive heart failure
- Asthma
- COPD
- Pulmonary embolism

MANAGEMENT CONSIDERATIONS[33,47]

- Optimizing the management of underlying comorbidities
- Referral to palliative care where available
- Nonpharmacologic interventions
  - Airflow interventions
  - Supplemental oxygen for patients with hypoxemia experiencing dyspnea

NCCN Guidelines recommendations for intervention include:
Relieve symptoms:

- Oxygen therapy for symptomatic hypoxia
- Educational, psychosocial-spiritual, and emotional support for the patient/family/caregiver
- Nonpharmacologic therapies, including fans, cooler temperatures, stress management, relaxation therapy, and physical comfort measures
- Noninvasive positive-pressure ventilation support if clinically indicated for severe reversible condition

If outcomes are acceptable, continue intervention and monitor symptoms and quality of life. If there are ongoing needs, reevaluate care interventions and intensify if possible, or consult or refer to palliative care or hospice.

Refer to NCCN Guidelines for more information.

See NCCN Guidelines for Palliative Care for further information.

MDS/AML and VTE in patients receiving LYNPARZA[6]

Myelodysplastic Syndrome/Acute Myeloid Leukemia (MDS/AML) has occurred in patients treated with LYNPARZA and some cases were fatal. In clinical studies, among 2219 patients with various *BRCA*m, g*BRCA*m, HRR gene–mutated or HRD-positive cancers who received LYNPARZA as a single agent or as part of a combination regimen, consistent with approved indications, the cumulative incidence of MDS/AML was approximately 1.2% (26/2219). Of these, 54% (14/26) had a fatal outcome. The median duration of therapy with LYNPARZA in patients who developed MDS/AML was approximately 2 years (range: <6 months to >4 years). All of these patients had received previous chemotherapy with platinum agents and/or other DNA-damaging agents including radiotherapy.

In SOLO-1, patients with newly diagnosed advanced *BRCA*m ovarian cancer, the incidence of MDS/AML was 1.9% (5/260) in patients who received LYNPARZA and 0.8% (1/130) in patients who received placebo based on an updated analysis. In PAOLA-1, of patients with newly diagnosed advanced ovarian cancer with HRD-positive status, the incidence of MDS/AML was 1.6% (4/255) in patients who received LYNPARZA and 2.3% (3/131) in the control arm.

In SOLO-2, patients with *BRCA*m platinum-sensitive relapsed ovarian cancer, the incidence of MDS/AML was 8% (15/195) in patients who received LYNPARZA and 4% (4/99) in patients who received placebo. The duration of LYNPARZA treatment prior to the diagnosis of MDS/AML ranged from 0.6 years to 4.5 years.

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.

Venous Thromboembolism (VTE): Including severe or fatal pulmonary embolism (PE), occurred in patients treated with LYNPARZA. In the combined data of two randomized, placebo-controlled clinical studies (PROfound and PROpel) in patients with metastatic castration-resistant prostate cancer (N=1180), VTE occurred in 8% of patients who received LYNPARZA, including pulmonary embolism in 6%. In the control arms, VTE occurred in 2.5%, including pulmonary embolism in 1.5%. 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.

Anemia

This information is not meant to replace the clinical judgment of the attending physician

LYNPARZA DOSE MANAGEMENT[6]

As part of your assessment and management of a potential adverse reaction, evaluate whether LYNPARZA dosing should be interrupted, reduced, or discontinued. See Dosing & Administration information on pages 14-17.

PATIENT COUNSELING[6]

Advise patients that:

- Regular blood tests are necessary to monitor for hematological ARs including anemia
  - Blood tests should occur before treatment with LYNPARZA, every month during treatment with LYNPARZA, and weekly in case of low blood count that lasts a long time. Treatment with LYNPARZA may need to be stopped until blood cell counts improve
- Anemia was a common side effect reported in clinical studies with LYNPARZA
- Management strategies exist to aid in the alleviation of the symptoms of anemia[48]
- There is the possibility that a blood transfusion may be required[48]
- Communication with their care team may inform their experience on therapy
- They should contact their healthcare provider if they experience weakness, feeling tired, fever, weight loss, frequent infections, bruising, bleeding easily, breathlessness, blood in urine or stool, and/or laboratory findings of low blood cell counts, or a need for blood transfusions. This may be a sign of hematological toxicity or a more serious uncommon bone marrow problem called myelodysplastic syndrome (MDS) or acute myeloid leukemia (AML), which have been reported in patients treated with LYNPARZA
- Patients should immediately report any signs or symptoms of thromboembolism such as pain or swelling in an extremity, shortness of breath, chest pain, tachypnea, and tachycardia
- They should report to their healthcare provider any new or worsening symptoms that they experience while taking medication

Clinical evaluation and management strategies for anemia

This information is not meant to replace the clinical judgment of the attending physician

CLINICAL EVALUATION[48]

As part of your clinical evaluation, consider potential causes, including if the patient's cancer has progressed or recurred and evaluate appropriately.

NCCN Guidelines recommendations include investigating causality and treating underlying conditions as indicated:

First perform:

- Detailed history and physical exam

Check:

- CBC with differential, peripheral blood smear, and reticulocyte count

Then consider possible causes including:

- Hemorrhage
- Hemolysis
- Nutrition
- Inherited
- Renal dysfunction
- Treatment-induced myelosuppression
- Hormone dysfunction
- Anemia of chronic inflammation

See NCCN Guidelines for Hematopoietic Growth Factors for further information.

MANAGEMENT CONSIDERATIONS[48]

NCCN Guidelines recommendations for intervention include:
If the cause is identified, treat as indicated. If no cause is identified, perform risk assessment and consider transfusion if indicated.

Observe with periodic reevaluation:

- Asymptomatic patients without significant comorbidities*

Consider RBC transfusion per AABB Guidelines†:

- High-risk patients (ie, progressive decline in Hb with recent intensive chemotherapy or radiation)

OR

- Asymptomatic patients with comorbidities*:
  - Cardiac disease
  - Chronic pulmonary disease
  - Cerebral vascular disease

RBC transfusion per AABB Guidelines†:

- Symptomatic (physiologic) patients:
  - Sustained tachycardia
  - Tachypnea
  - Chest pain
  - Dyspnea on exertion
  - Lightheadedness
  - Syncope
  - Severe fatigue preventing work and usual activity‡

See NCCN Guidelines for Hematopoietic Growth Factors for further information.

*Degree of severity of comorbidities in combination with the degree of severity of anemia should be taken into consideration when initiating RBC transfusion.
†The AABB has made recommendations regarding appropriate indications for RBC transfusion. Further details are included in the NCCN Guidelines.
‡Fatigue (FACT-F) and Anemia (FACT-An) subscales of the Functional Assessment of Cancer Therapy (FACT) and Brief Fatigue Inventory (BFI) are examples of standardized measures for assessing patient-reported fatigue.

NCCN Guidelines also include information on the use of ESAs or evaluation of iron deficiency. Refer to the NCCN Guidelines for more information.

AABB=American Association of Blood Banks; CBC=complete blood count; ESA=erythropoiesis-stimulating agent.

Leukopenia and neutropenia

This information is not meant to replace the clinical judgment of the attending physician

LYNPARZA DOSE MANAGEMENT[6]

As part of your assessment and management of a potential adverse reaction, evaluate whether LYNPARZA dosing should be interrupted, reduced, or discontinued. See Dosing & Administration information on pages 14-17.

PATIENT COUNSELING[6]

Advise patients that:

- Leukopenia and neutropenia are common side effects with LYNPARZA
- Regular blood tests are necessary to monitor for hematological ARs, including leukopenia and neutropenia
  - Blood tests should occur before treatment with LYNPARZA, every month during treatment with LYNPARZA, and weekly in case of low blood count that lasts a long time. Treatment with LYNPARZA may need to be stopped until blood cell counts improve
- Communication with their care team may inform their experience on therapy
- They should contact their healthcare provider if they experience weakness, feeling tired, fever, weight loss, frequent infections, bruising, bleeding easily, breathlessness, blood in urine or stool, and/or laboratory findings of low blood cell counts, or a need for blood transfusions. This may be a sign of hematological toxicity or a more serious uncommon bone marrow problem called myelodysplastic syndrome (MDS) or acute myeloid leukemia (AML), which has been reported in patients treated with LYNPARZA
- Patients should immediately report any signs or symptoms of thromboembolism such as pain or swelling in an extremity, shortness of breath, chest pain, tachypnea, and tachycardia
- They should report to their healthcare provider any new or worsening symptoms that they experience while taking medication

Clinical evaluation and management strategies for leukopenia and neutropenia

This information is not meant to replace the clinical judgment of the attending physician

CLINICAL EVALUATION[49]

As part of your clinical evaluation, consider potential causes, including if the patient's cancer has progressed or recurred and evaluate appropriately.

NCCN Guidelines recommendations include evaluation and risk assessment for febrile neutropenia in patients with certain cancers based on clinical presentation and treatment history.

- If fever and/or neutropenia is present, perform a complete history and physical examination and laboratory assessment
- Perform blood cultures, urine culture, site-specific diagnostics, and viral diagnostics as appropriate
- Consider chest x-ray

See NCCN Guidelines for Prevention and Treatment of Cancer-Related Infections for further information.

MANAGEMENT CONSIDERATIONS[49]

NCCN Guidelines recommend initial risk assessment for febrile neutropenic patients, including:

Factors indicating low risk, which include most of the following, and none of the high-risk factors:

- Outpatient status when fever develops
- No associated acute comorbid illness, independently indicating inpatient treatment or close observation
- Anticipated short duration of severe neutropenia (≤100 cells/mcL for <7 days)
- Good performance status (ECOG 0-1)
- No hepatic or renal insufficiency
- MASCC* Risk-Index Score of ≥21 or CISNE score of <3

A factor indicating high risk, which includes any of the following factors:

- Inpatient when fever develops
- Significant medical comorbidity or clinically unstable
- Anticipated prolonged severe neutropenia (≤100 cells/mcL and ≥7 days)
- Hepatic or renal insufficiency
- Pneumonia or other complex infections
- Mucositis Grade 3–4
- MASCC* Risk-Index Score of <21 or CISNE score of ≥3
- Allogeneic HCT
- Uncontrolled/progressive cancer
- Use of immune or targeted treatments

*Risk categorization refers to risk of serious complications, including mortality, in patients with neutropenic fever. Risk stratification is validated in adults; no generalizable, cross-validated, risk-stratified management exists for pediatric patients with febrile neutropenia. Refer to the NCCN Guidelines for complete recommendations.

If febrile neutropenia is confirmed:

- Consider appropriateness of hospitalization vs outpatient management
- Consider appropriate pharmaceutical interventions and supportive care

See NCCN Guidelines for Prevention and Treatment of Cancer-Related Infections for further information.

Please see Important Safety Information on pages 3-5, and complete Prescribing Information, including Medication Guide.

CISNE=Clinical Index of Stable Febrile Neutropenia; ECOG=Eastern Cooperative Oncology Group;
HCT=hematopoietic cell transplantation; MASCC=Multinational Association of Supportive Care in Cancer; mcL=microliter.

Thrombocytopenia

This information is not meant to replace the clinical judgment of the attending physician

LYNPARZA DOSE MANAGEMENT[6]

As part of your assessment and management of a potential adverse reaction, evaluate whether LYNPARZA dosing should be interrupted, reduced, or discontinued. See Dosing & Administration information on pages 14-17.

PATIENT COUNSELING[6]

Advise patients that:

- Thrombocytopenia is a potential adverse reaction reported in patients receiving LYNPARZA
- Regular blood tests are necessary to monitor for hematological ARs including thrombocytopenia
  - Blood tests should occur before treatment with LYNPARZA, every month during treatment with LYNPARZA, and weekly in case of low blood count that lasts a long time. Treatment with LYNPARZA may need to be stopped until blood cell counts improve
- There is the possibility that a platelet transfusion may be required[48]
- Communication with their care team may inform their experience on therapy
- They should contact their healthcare provider if they experience weakness, feeling tired, fever, weight loss, frequent infections, bruising, bleeding easily, breathlessness, blood in urine or stool, and/or laboratory findings of low blood cell counts, or a need for blood transfusions. This may be a sign of hematological toxicity or a more serious uncommon bone marrow problem called myelodysplastic syndrome (MDS) or acute myeloid leukemia (AML), which has been reported in patients treated with LYNPARZA
- They should report to their healthcare provider any new or worsening symptoms that they experience while taking medication

Clinical evaluation and management strategies for thrombocytopenia

This information is not meant to replace the clinical judgment of the attending physician

CLINICAL EVALUATION[48]

As part of your clinical evaluation, consider potential causes, including if the patient's cancer has progressed or recurred and evaluate appropriately.

NCCN Guidelines recommendations for evaluation include investigating causality as follows:

First perform:

- Detailed history and physical exam

Check:

- CBC with differential, including evaluations for other cytopenias
- Blood smear morphology, including evaluation for platelet clumping

Consider possible causes including, but not limited to:

- Nutritional deficiencies
- Medications and supplements suppressing platelet production
- Infection
- Immune thrombocytopenia

See NCCN Guidelines for Hematopoietic Growth Factors for further information.

MANAGEMENT CONSIDERATIONS[48]

Underlying conditions should be treated as indicated. If a patient has chemotherapy-induced thrombocytopenia, consider platelet transfusion per AABB guidelines, change in chemotherapy regimen/dose reduction, clinical trial of a thrombopoietin receptor agonist, or romiplostim.

See NCCN Guidelines for Hematopoietic Growth Factors for further information.

Hepatotoxicity, including severe and potentially fatal cases of DILI

This information is not meant to replace the clinical judgment of the attending physician

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.

Clinical trials experience

The following information reflects safety data of LYNPARZA in patients with[6]:

- Advanced ovarian cancer in combination with bevacizumab in PAOLA-1
- *BRCA*m advanced ovarian cancer in SOLO-1
- Recurrent g*BRCA*m platinum-sensitive ovarian cancer in SOLO-2
- Metastatic castration-resistant prostate cancer in combination with abiraterone and prednisone or prednisolone in PROpel
- HRRm metastatic castration-resistant prostate cancer in PROfound
- g*BRCA*m, HER2-negative, high-risk early breast cancer in OlympiA
- g*BRCA*m, HER2-negative metastatic breast cancer in OlympiAD
- g*BRCA*m metastatic pancreatic cancer in POLO

Because clinical trials are conducted under widely varying conditions, AR rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.[6]

Adverse reactions* reported in ≥10% of patients treated with LYNPARZA/bevacizumab and at ≥5% frequency compared to the placebo/bevacizumab arm in PAOLA-1 (primary analysis)[6]

Adverse Reactions	LYNPARZA + bevacizumab (n=535)		Placebo + bevacizumab (n=267)	
	Grades 1–4 (%)	Grades 3–4 (%)	Grades 1–4 (%)	Grades 3–4 (%)
General disorders and administration site conditions				
Fatigue (including asthenia)†	53	5	32	1.5
Gastrointestinal disorders				
Nausea	53	2.4	22	0.7
Vomiting	22	1.7	11	1.9

Adverse Reactions	LYNPARZA + bevacizumab (n=535)		Placebo + bevacizumab (n=267)	
	Grades 1–4 (%)	Grades 3–4 (%)	Grades 1–4 (%)	Grades 3–4 (%)
Blood and lymphatic system disorders				
Anemia‡	41	17	10	0.4
Lymphopenia§	24	7	9	1.1
Leukopenia‖	18	1.9	10	1.5

*Graded according to the 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 β-lymphocyte count decreased, lymphocyte count decreased, lymphopenia, and T-lymphocyte count decreased.
‖Includes leukopenia and white blood cell count decreased.

At primary analysis[6]:

- The median duration of treatment with LYNPARZA was 17.3 months and 11 months for bevacizumab post-randomization on the LYNPARZA/bevacizumab arm
- **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/bevacizumab. Serious adverse reactions in >5% of patients included hypertension (19%) and anemia (17%)
- **Venous thromboembolism** occurred more commonly in patients receiving LYNPARZA + bevacizumab (5%) than in those receiving placebo + bevacizumab (1.9%)

At 5-year follow-up analysis:

- No new safety signals were identified and the safety profile remained generally consistent with the primary analysis[50]
- At the final OS analysis, the incidence of MDS/AML/AA was 1.7% (9/535) in the LYNPARZA + bevacizumab group (MDS/AML was 1.6% [4/255] in the HRD-positive subgroup) and 2.2% (6/267) in the bevacizumab + placebo group (MDS/AML was 2.3% [3/131] in the HRD-positive subgroup)[8]; 22 (4.1%) new primary malignancy events occurred in the LYNPARZA + bevacizumab group and 8 (3.0%) events occurred in the bevacizumab + placebo group; 7 (1.3%) pneumonitis events occurred in the LYNPARZA + bevacizumab group and 2 (0.7%) events occurred in the bevacizumab + placebo group[6,50]

Please see Important Safety Information on pages 3-5, and complete Prescribing Information, including Medication Guide.

OS=overall survival.

Laboratory abnormalities reported in ≥25% of patients in PAOLA-1 (primary analysis)[6]*

Laboratory Parameter†	LYNPARZA + bevacizumab (n=535)‡		Placebo + bevacizumab (n=267)‡	
	Grades 1–4 (%)	Grades 3–4 (%)	Grades 1–4 (%)	Grades 3–4 (%)
Decrease in hemoglobin	79	13	55	0.4
Decrease in lymphocytes	63	10	42	3.0
Increase in serum creatinine	61	0.4	36	0.4
Decrease in leukocytes	59	3.4	45	2.2
Decrease in absolute neutrophil count	35	7	30	3.7
Decrease in platelets	35	2.4	28	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.

Adverse reactions* reported in ≥10% of patients treated with LYNPARZA in SOLO-1 (primary analysis)[6]

Adverse Reactions	LYNPARZA (n=260)		Placebo (n=130)	
	Grades 1–4 (%)	Grades 3–4 (%)	Grades 1–4 (%)	Grades 3–4 (%)
Gastrointestinal disorders				
Nausea	77	1	38	0
Abdominal pain†	45	2	35	1
Vomiting	40	0	15	1
Diarrhea‡	37	3	26	0
Constipation	28	0	19	0
Dyspepsia	17	0	12	0
Stomatitis§	11	0	2	0

Adverse Reactions	LYNPARZA (n=260)		Placebo (n=130)	
	Grades 1–4 (%)	Grades 3–4 (%)	Grades 1–4 (%)	Grades 3–4 (%)
General disorders and administration site conditions				
Fatigue‖	67	4	42	2
Blood and lymphatic system disorders				
Anemia	38	21	9	2
Neutropenia¶	17	6	7	3
Leukopenia#	13	3	8	0
Thrombocytopenia**	11	1	4	2

*Graded according to the NCI CTCAE, version 4.0.
†Includes abdominal pain, abdominal pain lower, abdominal pain upper, abdominal distension, abdominal discomfort, and abdominal tenderness.
‡Includes colitis, diarrhea, and gastroenteritis.
§Includes stomatitis, aphthous ulcer, and mouth ulceration.
‖Includes asthenia, fatigue, lethargy, and malaise.
¶Includes neutropenia and febrile neutropenia.
#Includes leukopenia and white blood cell count decreased.
**Includes platelet count decreased and thrombocytopenia.

Please see Important Safety Information on pages 3-5, and complete Prescribing Information, including Medication Guide.

Lynparza® olaparib tablets 150 mg

Adverse reactions* reported in ≥10% of patients treated with LYNPARZA in SOLO-1 (primary analysis)[6] (Cont'd)

Adverse Reactions	LYNPARZA (n=260)		Placebo (n=130)	
	Grades 1–4 (%)	Grades 3–4 (%)	Grades 1–4 (%)	Grades 3–4 (%)
Infections and infestations				
Upper respiratory tract infection/influenza/ nasopharyngitis/bronchitis	28	0	23	0
UTI†	13	1	7	0
Nervous system disorders				
Dysgeusia	26	0	4	0
Dizziness	20	0	15	1
Metabolism and nutrition disorders				
Decreased appetite	20	0	10	0
Respiratory, thoracic, and mediastinal disorders				
Dyspnea‡	15	0	6	0

*Graded according to the NCI CTCAE, version 4.0.
†Includes urosepsis, urinary tract infection, urinary tract pain, and pyuria.
‡Includes dyspnea and dyspnea exertional.

At primary analysis:

- The median duration of study treatment was 25 months for patients who received LYNPARZA and 14 months for patients who received placebo

At 7-year follow-up analysis[6,51,52]:

- No new safety signals were identified and the safety profile remained generally consistent with the primary analysis (May 17, 2018) and DCO2 (March 5, 2020)
- 4 (1.5%) cases of MDS/AML were reported in the LYNPARZA group and 1 (0.8%) case was reported in the placebo group
  - Another case of MDS/AML was reported based on an updated analysis (5/260: 1.9%)[6];
- 14 (5.4%) cases of new primary malignancies were reported in the LYNPARZA group and 8 (6.2%) cases were reported in the placebo group;
- 5 (1.9%) cases of pneumonitis were reported in the LYNPARZA group and none were reported in the placebo group

Please see Important Safety Information on pages 3-5, and complete Prescribing Information, including Medication Guide.

DCO2=data cutoff 2; UTI=urinary tract infection.

Laboratory abnormalities reported in ≥25% of patients in SOLO-1 (primary analysis)[6]

Laboratory Parameter*	LYNPARZA (n=260)†		Placebo (n=130)†	
	Grades 1–4 (%)	Grades 3–4 (%)	Grades 1–4 (%)	Grades 3–4 (%)
Decrease in hemoglobin	87	19	63	2
Increase in mean corpuscular volume	87	–	43	–
Decrease in leukocytes	70	7	52	1
Decrease in lymphocytes	67	14	29	5
Decrease in absolute neutrophil count	51	9	38	6
Decrease in platelets	35	1	20	2
Increase in serum creatinine	34	0	18	0

*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.

Adverse reactions* reported in ≥20% of patients treated with LYNPARZA in SOLO-2[6]

Adverse Reactions	LYNPARZA (n=195)		Placebo (n=99)	
	Grades 1–4 (%)	Grades 3–4 (%)	Grades 1–4 (%)	Grades 3–4 (%)
Gastrointestinal disorders				
Nausea	76	3	33	0
Vomiting	37	3	19	1
Diarrhea	33	2	22	0
Stomatitis†	20	1	16	0
General disorders and administration site conditions				
Fatigue including asthenia	66	4	39	2
Blood and lymphatic system disorders				
Anemia‡	44	20	9	2
Infections and infestations				
Nasopharyngitis/URI/sinusitis/ rhinitis/influenza	36	0	29	0
Musculoskeletal and connective tissue disorders				
Arthralgia/myalgia	30	0	28	0
Nervous system disorders				
Dysgeusia	27	0	7	0
Headache	26	1	14	0
Metabolism and nutrition disorders				
Decreased appetite	22	0	11	0

*Graded according to the NCI CTCAE, version 4.0.
†Represents grouped term consisting of abscess oral, aphthous ulcer, gingival abscess, gingival disorder, gingival pain, gingivitis, mouth ulceration, mucosal infection, mucosal inflammation, oral candidiasis, oral discomfort, oral herpes, oral infection, oral mucosal erythema, oral pain, oropharyngeal discomfort, and oropharyngeal pain.
‡Represents grouped term consisting of anemia, hematocrit decreased, hemoglobin decreased, iron deficiency, mean cell volume increased, and red blood cell count decreased.

- The median duration of study treatment was 19.4 months for patients who received LYNPARZA and 5.6 months for patients who received placebo
- The incidence of MDS/AML was 8% (15/195) in patients who received LYNPARZA and 4% (4/99) in patients who received placebo. The duration of LYNPARZA treatment prior to the diagnosis of MDS/AML ranged from 0.6 years to 4.5 years

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URI=upper respiratory infection.

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Laboratory abnormalities reported in ≥25% of patients in SOLO-2[6]

Laboratory Parameter*	LYNPARZA (n=195)†		Placebo (n=99)†	
	Grades 1–4 (%)	Grades 3–4 (%)	Grades 1–4 (%)	Grades 3–4 (%)
Increase in mean corpuscular volume‡	89	–	52	–
Decrease in hemoglobin	83	17	69	0
Decrease in leukocytes	69	5	48	1
Decrease in lymphocytes	67	11	37	1
Decrease in absolute neutrophil count	51	7	34	3
Increase in serum creatinine	44	0	29	0
Decrease in platelets	42	2	22	1

*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.
‡Represents the proportion of subjects whose mean corpuscular volume was >ULN.

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ULN=upper limit of normal.

Adverse reactions* reported in ≥10% of patients who received LYNPARZA (with a difference of ≥5% vs placebo) in PROpel[6]

Adverse Reactions	LYNPARZA + abiraterone (n=398)		Placebo + abiraterone (n=396)	
	Grades 1–4 (%)	Grades 3–4 (%)	Grades 1–4 (%)	Grades 3–4 (%)
Blood and lymphatic disorders				
Anemia†	48	16	18	3.3
Lymphopenia‡	14	5	6	1.8
General disorders and administration site conditions				
Fatigue (including asthenia)	38	2.3	30	1.5
Gastrointestinal disorders				
Nausea	30	0.3	14	0.3
Diarrhea	19	1	10	0.3
Abdominal pain§	13	0	7	0.5
Metabolism and nutrition disorders				
Decreased appetite	16	1	7	0
Nervous system disorders				
Dizziness‖	14	0.3	7	0

*Graded according to the NCI CTCAE, version 4.03.
†Includes anemia, anemia macrocytic, and red blood cell count decreased.
‡Includes lymphocyte count decreased and lymphopenia.
§Includes abdominal discomfort, abdominal pain, abdominal pain upper, and abdominal pain lower.
‖Includes dizziness and vertigo.

- **Fatal adverse reactions** occurred in 6% of patients, including COVID-19 (3%) and pneumonias (0.5%)
- **Serious adverse reactions** occurred in 39% of patients. Serious adverse reactions reported in >2% of patients included anemia (6%), COVID-19 (6%), pneumonia (4.5%), pulmonary embolism (3.5%), and urinary tract infection (3%)
- **Venous thromboembolism (VTE),** including severe or fatal pulmonary embolism (PE), occurred in patients treated with LYNPARZA. In the combined data of two randomized, placebo-controlled clinical studies (PROfound and PROpel) in patients with metastatic castration-resistant prostate cancer (N=1180), VTE occurred in 8% of patients who received LYNPARZA, including pulmonary embolism in 6%. In the control arms, VTE occurred in 2.5%, including pulmonary embolism in 1.5%

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Select laboratory abnormalities reported in ≥20% of patients in PROpel[6]

Laboratory Parameter	LYNPARZA + abiraterone (n=398)*		Placebo + abiraterone (n=396)*	
	Grades 1–4 (%)	Grades 3–4 (%)	Grades 1–4 (%)	Grades 3–4 (%)
Decrease in hemoglobin	97	12	81	1.3
Decrease in lymphocytes	70	23	49	11
Decrease in platelets	23	1.2	20	0.3
Decrease in absolute neutrophil count	23	5	6	0

*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.

Adverse reactions* reported in ≥10% of patients treated with LYNPARZA in PROfound[6]

Adverse Reactions	LYNPARZA (n=256)		Investigator's choice of enzalutamide or abiraterone (n=130)	
	Grades 1–4 (%)	Grades 3–4 (%)	Grades 1–4 (%)	Grades 3–4 (%)
Blood and lymphatic system disorders				
Anemia†	46	21	15	5
Thrombocytopenia‡	12	4	3	0
Gastrointestinal disorders				
Nausea	41	1	19	0
Diarrhea	21	1	7	0
Vomiting	18	2	12	1
General disorders and administration site conditions				
Fatigue (including asthenia)	41	3	32	5
Metabolism and nutrition disorders				
Decreased appetite	30	1	18	1
Respiratory, thoracic, and mediastinal disorders				
Cough	11	0	2	0
Dyspnea	10	2	3	0

*Graded according to the NCI CTCAE, version 4.03.
†Includes anemia and hemoglobin decreased.
‡Includes platelet count decreased and thrombocytopenia.

- Among patients receiving LYNPARZA, 62% were exposed for 6 months or longer and 20% were exposed for greater than one year
- **Fatal adverse reactions** occurred in 4% of patients treated with LYNPARZA. These included pneumonia (1.2%), cardiopulmonary failure (0.4%), aspiration pneumonia (0.4%), intestinal diverticulum (0.4%), septic shock (0.4%), Budd–Chiari Syndrome (0.4%), sudden death (0.4%), and acute cardiac failure (0.4%)
- **Serious adverse reactions** occurred in 36% of patients receiving LYNPARZA. The most frequent serious adverse reactions (≥2%) were anemia (9%), pneumonia (4%), pulmonary embolism (2%), fatigue/asthenia (2%), and urinary tract infection (2%)
- **Venous thromboembolism (VTE),** including severe or fatal pulmonary embolism (PE), occurred in patients treated with LYNPARZA. In the combined data of two randomized, placebo-controlled clinical studies (PROfound and PROpel) in patients with metastatic castration-resistant prostate cancer (N=1180), VTE occurred in 8% of patients who received LYNPARZA, including pulmonary embolism in 6%. In the control arms, VTE occurred in 2.5%, including pulmonary embolism in 1.5%

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Laboratory abnormalities reported in ≥25% of patients in PROfound[6]

Laboratory Parameter*	LYNPARZA (n=256)†		Investigator's choice of enzalutamide or abiraterone (n=130)†	
	Grades 1–4 (%)	Grades 3–4 (%)	Grades 1–4 (%)	Grades 3–4 (%)
Decrease in hemoglobin	98	13	73	4
Decrease in lymphocytes	62	23	34	13
Decrease in leukocytes	53	4	21	0
Decrease in absolute neutrophil count	34	3	9	0

*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.

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Adverse reactions* reported in ≥10% of patients treated with LYNPARZA in OlympiA[6]

Adverse Reactions	LYNPARZA (n=911)		Placebo (n=904)	
	Grades 1–4 (%)	Grades 3–4 (%)	Grades 1–4 (%)	Grades 3–4 (%)
Gastrointestinal disorders				
Nausea	57	0.8	23	0
Vomiting	23	0.7	8	0
Diarrhea	18	0.3	14	0.3
Stomatitis†	10	0.1	4.5	0
General disorders and administration site conditions				
Fatigue (including asthenia)	42	1.8	28	0.7
Blood and lymphatic disorders				
Anemia‡	24	9	3.9	0.3
Leukopenia§	17	3	6	0.3
Neutropenia‖	16	5	7	0.8

Adverse Reactions	LYNPARZA (n=911)		Placebo (n=904)	
	Grades 1–4 (%)	Grades 3–4 (%)	Grades 1–4 (%)	Grades 3–4 (%)
Nervous system disorders				
Headache	20	0.2	17	0.1
Dysgeusia¶	12	0	4.8	0
Dizziness	11	0.1	7	0.1
Metabolism and nutrition disorders				
Decreased appetite	13	0.2	6	0

*Graded according to NCI CTCAE, version 4.03.
†Includes aphthous ulcer, mouth ulceration, and stomatitis.
‡Includes anemia, anemia macrocytic, erythropenia, hematocrit decreased, hemoglobin decreased, normochromic anemia, normochromic normocytic anemia, normocytic anemia, and red blood cell count decreased.
§Includes leukopenia and white blood cell count decreased.
‖Includes agranulocytosis, febrile neutropenia, granulocyte count decreased, granulocytopenia, idiopathic neutropenia, neutropenia, neutropenic infection, neutropenic sepsis, and neutrophil count decreased.
¶Includes dysgeusia and taste disorder.

- The median duration of treatment with LYNPARZA and placebo was 1 year

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Laboratory abnormalities reported in ≥25% of patients in OlympiA[6]

Laboratory Parameter*	LYNPARZA (n=911)†		Placebo (n=904)†	
	Grades 1–4 (%)	Grades 3–4 (%)	Grades 1–4 (%)	Grades 3–4 (%)
Decrease in lymphocytes	77	13	59	3.7
Increase in mean corpuscular volume‡	67	0	4.8	0
Decrease in hemoglobin	65	8	31	0.9
Decrease in leukocytes	64	5	42	0.7
Decrease in absolute neutrophil count	39	7	27	1.1

*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.
‡Represents the proportion of subjects whose mean corpuscular volume was >ULN.

Adverse reactions* reported in ≥20% of patients treated with LYNPARZA in OlympiAD[6]

Adverse Reactions	LYNPARZA (n=205)		Chemotherapy (n=91)	
	Grades 1–4 (%)	Grades 3–4 (%)	Grades 1–4 (%)	Grades 3–4 (%)
Gastrointestinal disorders				
Nausea	58	0	35	1
Vomiting	30	0	15	1
Diarrhea	21	1	22	0
Blood and lymphatic disorders				
Anemia†	40	16	26	4
Neutropenia‡	27	9	50	26
Leukopenia§	25	5	31	13

Adverse Reactions	LYNPARZA (n=205)		Chemotherapy (n=91)	
	Grades 1–4 (%)	Grades 3–4 (%)	Grades 1–4 (%)	Grades 3–4 (%)
General disorders and administration site conditions				
Fatigue (including asthenia)	37	4	36	1
Infections and infestations				
Respiratory tract infection‖	27	1	22	0
Nervous system disorders				
Headache	20	1	15	2

*Graded according to NCI CTCAE, version 4.0.
†Represents grouped terms consisting of anemia (anemia erythropenia, hematocrit decreased, hemoglobin decreased, and red blood cell count decreased).
‡Represents grouped terms consisting of neutropenia (febrile neutropenia, granulocyte count decreased, granulocytopenia, neutropenia, neutropenic infection, neutropenic sepsis, and neutrophil count decreased).
§Represents grouped terms consisting of leukopenia (leukopenia and white blood cell count decreased).
‖Represents grouped terms consisting of bronchitis, influenza, lower respiratory tract infection, nasopharyngitis, pharyngitis, respiratory tract infection, rhinitis, sinusitis, upper respiratory tract infection, and upper respiratory tract infection bacterial.

- The median duration of study treatment was 8.2 months for patients who received LYNPARZA and 3.4 months for patients who received chemotherapy

Laboratory abnormalities reported in ≥25% of patients in OlympiAD[6]

Laboratory Parameter*	LYNPARZA (n=205)†		Chemotherapy (n=91)†	
	Grades 1–4 (%)	Grades 3–4 (%)	Grades 1–4 (%)	Grades 3–4 (%)
Decrease in hemoglobin	82	17	66	3
Decrease in lymphocytes	73	21	63	3
Decrease in leukocytes	71	8	70	23
Increase in mean corpuscular volume‡	71	–	33	–
Decrease in absolute neutrophil count	46	11	65	38
Increase in serum creatinine	33	3	28	0

*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.
‡Represents the proportion of subjects whose mean corpuscular volume was >ULN.

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Adverse reactions* reported in ≥10% of patients treated with LYNPARZA in POLO[6]

Adverse Reactions	LYNPARZA (n=91)†		Placebo (n=60)†	
	Grades 1–4 (%)	Grades 3–4 (%)	Grades 1–4 (%)	Grades 3–4 (%)
General disorders and administration site conditions				
Fatigue‡	60	5	35	2
Gastrointestinal disorders				
Nausea	45	0	23	2
Abdominal pain§	34	2	37	5
Diarrhea	29	0	15	0
Constipation	23	0	10	0
Vomiting	20	1	15	2
Stomatitis‖	10	0	5	0
Blood and lymphatic disorders				
Anemia	27	11	17	3
Thrombocytopenia¶	14	3	7	0
Neutropenia#	12	4	8	3

Adverse Reactions	LYNPARZA (n=91)†		Placebo (n=60)†	
	Grades 1–4 (%)	Grades 3–4 (%)	Grades 1–4 (%)	Grades 3–4 (%)
Metabolism and nutrition disorders				
Decreased appetite	25	3	7	0
Musculoskeletal and connective tissue disorders				
Back pain	19	0	17	2
Arthralgia	15	1	10	0
Skin and subcutaneous tissue disorders				
Rash**	15	0	5	0
Respiratory, thoracic, and mediastinal disorders				
Dyspnea††	13	0	5	2
Infections and infestations				
Nasopharyngitis	12	0	3	0
Nervous system disorders				
Dysgeusia	11	0	5	0

*Graded according to the NCI CTCAE, version 4.0.
†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.
‡Includes asthenia and fatigue.
§Includes abdominal pain, abdominal pain upper, and abdominal pain lower.
‖Includes stomatitis and mouth ulceration.
¶Includes platelet count decreased and thrombocytopenia.
#Includes neutropenia, febrile neutropenia, and neutrophil count decreased.
**Includes rash erythematous, rash macular, and rash maculopapular.
††Includes dyspnea and dyspnea exertional.

- Among patients receiving LYNPARZA, 34% were exposed for 6 months or longer and 25% were exposed for greater than 1 year

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Laboratory abnormalities reported in ≥25% of patients in POLO[6]

Laboratory Parameter*	LYNPARZA (n=91)†		Placebo (n=60)†	
	Grades 1–4 (%)	Grades 3–4 (%)	Grades 1–4 (%)	Grades 3–4 (%)
Increase in serum creatinine	99	2	85	0
Decrease in hemoglobin	86	11	65	0
Increase in mean corpuscular volume‡	71	–	30	–
Decrease in lymphocytes	61	9	27	0
Decrease in platelets	56	2	39	0
Decrease in leukocytes	50	3	23	0
Decrease in absolute neutrophil count	25	3	10	0

*Patients were allowed to enter POLO with hemoglobin ≥9 g/dL (CTCAE Grade 2) and other 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.
‡Represents the proportion of subjects whose mean corpuscular volume was >ULN.

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Please see Important Safety Information on pages 3-5, and complete Prescribing Information, including Medication Guide.

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TOOLS FOR YOUR PATIENTS

Help your patients better understand potential side effects

Share the link below with your patients to connect them to information and resources on side effects that they may experience while taking LYNPARZA.

Access Information and Resources

Remember to refer your patients to the
***MyLYNPARZA* support program**
for additional support while taking LYNPARZA.

Direct patients to **MyLYNPARZA.com** to sign up.

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