Transcript Details

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BRCA and HRD Biomarker Testing in Advanced Ovarian Cancer: A KOL Panel Discussion

Dr Lewin and Dr Chase have been compensated by AstraZeneca for their participation.

Indications and Select Safety Information:

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

- as maintenance therapy for women with *BRCA*m* advanced ovarian cancer after response to first-line platinum-based chemotherapy.
- in combination with bevacizumab as maintenance therapy for women with HRD- positive* advanced ovarian cancer after response to first-line platinum-based chemotherapy.

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

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

Please see full Important Safety Information at the end of the video.

Dr Lewin:
Greetings and welcome. My name is Dr Sharyn Lewin and I'm the Director of the Division of Gynecologic Oncology at Holy Name Medical Center in Teaneck, New Jersey.

Dr Chase:
And I'm Dana Chase. I am a gynecologic oncologist in Los Angeles, California.

Our conversation today will focus on biomarker testing in newly diagnosed advanced ovarian cancer patients in first line, specifically *BRCA* mutation testing and testing for homologous recombination deficiency, or HRD.

Dr Lewin:
Before we proceed, we need to note that the opinions expressed in this video are solely our own and do not reflect those of AstraZeneca.

Our objectives today include answering the following questions:

- What is *BRCA* and HRD biomarker testing?
- Why is *BRCA* and HRD testing so important?
- Who should be tested, and when?

Dr Chase:
We should mention that in our conversation today we will be talking about LYNPARZA® [or] (olaparib), a poly (ADP-ribose) polymerase,

or PARP, inhibitor.[16]

LYNPARZA has two first-line maintenance therapy indications in advanced ovarian cancer, as shown on the screen. There's a monotherapy indication, for patients with germline or somatic *BRCA* mutations, and a combination therapy indication with an antiangiogenic agent bevacizumab, for patients who are HRD-positive.[16]

Dr Lewin:
That's right, and we must also note that both of these indications were approved for patient populations with specific biomarkers and we use FDA-approved diagnostic tests, either for *BRCA* mutations or for HRD, to help identify those patients. As we will discuss, this is why up-front *BRCA* and HRD biomarker testing is so important in patients with newly diagnosed advanced ovarian cancer.[16]

Dr Chase:
So, let's get to our first question, "what is *BRCA* and HRD testing, and why should we talk about it in the context of newly diagnosed advanced ovarian cancer?"

Dr Lewin:
First, I think it's important to talk about the management of newly diagnosed advanced ovarian cancer in general. When a woman is diagnosed with advanced, that is, stage 3 or 4, ovarian cancer, she is typically treated with surgery and platinum-based chemotherapy.[7] Most patients respond to first-line therapy, but in the absence of maintenance therapy, most of these patients will experience disease recurrence within 3 years, as shown on this slide.[3,14]

Because we now know that certain patients—those with *BRCA* mutations and/or HRD who are in response to first-line platinum-based chemotherapy—may show improved outcomes when treated with PARP inhibitor maintenance therapy.[16,18,28] Identifying these patients through biomarker testing can be essential to inform maintenance treatment decisions for these women.[7]

Dr Chase:
That's right, so instead of treating all patients the same, we are now able to personalize treatment based on the characteristics of the patient and the tumor, which we determine by genetic and biomarker testing.[7]

Dr Lewin:
Next, let's discuss how these tests work.

Dr Chase:
Of course - so, germline, or inherited, mutations in *BRCA* genes can be identified by a germline test, such as the BRACAnalysis companion diagnostic, or CDx. A patient's DNA is isolated from a blood sample and the *BRCA1* and *BRCA2* genes are sequenced to detect any deleterious or suspected deleterious *BRCA* mutations.[21]

Dr Lewin:
Exactly, but it's important to note that germline testing is performed on a blood sample, not a tumor sample, and therefore cannot detect tumor-specific mutations.[21] On the other hand, HRD tests are conducted on a tumor sample, obtained through biopsy.

One important point to keep in mind about tumor sample collection is that some patients who receive neoadjuvant chemotherapy before their interval debulking surgery, or IDS, may respond so well that there isn't enough viable tumor left after surgery for successful HRD testing. In these patients, the only tumor sample available may be a specimen collected by biopsy during initial diagnosis, or even during surgery itself. Therefore, in patients who are being considered for neoadjuvant chemotherapy and IDS, it's critical that biopsy samples are collected early enough while sufficient tumor is available and successful biomarker testing is ensured.[10,26]

Dr Chase:
That's a great point. An HRD test does two things. First, it sequences the *BRCA1* and *BRCA2* genes to identify mutations. Then, it uses NGS to quantify genomic aberrations characteristic of HRD. These are sometimes referred to as genomic scar tests. These aberrations include loss of heterozygosity, or LOH, large-scale transitions, or LST, and telomeric allelic imbalance, or TAI. The extent of these genomic changes is then used to generate a genomic instability score, which can be used to characterize the tumor as HRD.[10,18]

Now, one common misconception is that all HRD tests are the same; I think we need to clarify this.

Dr Lewin:
I totally agree, this is a misconception. Different HRD tests may measure genomic instability in different ways, such as measuring only LOH.[18] The Myriad MyChoice® CDx test, which is the test approved for use with LYNPARZA, is the one I usually prefer to use, as it

measures all three genomic aberrations - those are LOH, LST, and TAI. A genomic instability score of 42 has been set as the cutoff for an HRD-positive test. So, a positive HRD test is defined as either the presence of a tumor *BRCA* mutation, and/or a genomic instability score of 42 or higher.[20,23]

We've covered some important points about *BRCA* and HRD testing – what these tests tell us. So, we come to our next question. "Why is *BRCA* and HRD testing so important?" As we mentioned earlier, PARP inhibitor first line maintenance therapy is associated with improved outcomes in certain patients with advanced ovarian cancer.[16,18,28] One such PARP inhibitor that is used is LYNPARZA, in combination with bevacizumab, and supported by the PAOLA-1 study - let's explore the clinical data behind this maintenance therapy.[16]

Dr Chase:
So, the PAOLA-1 trial was the first phase 3 clinical trial to investigate LYNPARZA as a first-line combination maintenance regimen with bevacizumab, against an active comparator, bevacizumab.[16] It's important to remember that the results we're going to discuss here were prespecified exploratory subgroup analyses.[25] In PAOLA-1, HRD-positive was defined as either a tumor *BRCA* mutation and/or HRD score of 42 or higher by Myriad MyChoice®CDx.[20,23]

Dr Lewin:
The primary endpoint of the PAOLA-1 trial was progression-free survival, or PFS. In a prespecified exploratory analysis of the HRD subgroup in PAOLA-1, a clinically meaningful improvement in PFS was reported, with a median of 3.1 years for LYNPARZA and bevacizumab versus 1.5 years with placebo and bevacizumab, with a hazard ratio of 0.33, corresponding to a 67% reduction in the risk of progression or death.[5,16,23]

This prespecified exploratory analysis was not controlled for Type 1 error, and no benefit was seen in the HRD-negative subgroup.[16]

Dr Chase:
And when we look at the secondary endpoint overall survival, or OS, a prespecified exploratory analysis of the OS in the HRD-positive subgroup showed a clinically meaningful survival benefit after response to first-line platinum-based chemotherapy.[5,16,23] Median OS was 6.3 years for bevacizumab plus LYNPARZA vs 4.8 years with bevacizumab plus placebo, with a hazard ratio of 0.62, corresponding to a 38% reduction in the risk of death.[16]

Again, these data were based on a pre-specified, exploratory subgroup analysis that was not controlled for type 1 error and HRD was not a stratification factor in PAOLA-1.[25]

These OS results are notable as LYNPARZA in combination with bevacizumab is the only maintenance combination therapy to demonstrate clinically meaningful OS results in patients with HRD-positive disease after response to first-line platinum-based chemotherapy although the study was not statistically powered for OS.[5,9,16,19,25]

Dr Lewin:
There is one more set of efficacy results from PAOLA-1 that I think we should cover. That is a post-hoc exploratory analysis of OS in patients with HRD-positive advanced ovarian cancer based on their clinical risk of relapse. Lower-risk patients were defined as those with stage III disease and no residual disease following primary debulking surgery, and higher-risk patients had stage IV disease, or stage III disease and either received interval surgery or had residual disease following primary surgery.[15]

The reduction in the risk of death was 30% in the higher-risk group and 69% in the lower-risk group.[15]

Note that there is no official clinical consensus on what is considered lower vs higher risk. Data are based on post hoc exploratory subgroup analyses in 2 clinical subgroups, lower risk and higher risk, including biomarker status. Neither HRD status nor risk factor was a stratification factor in PAOLA-1, and analysis was not controlled for Type 1 error.[15]

Based on my own clinical experience and observation, these results were really impactful and practice-changing for me. Bevacizumab is appropriate for patients with higher-risk features, such as stage IV disease or ascites.[3] Given my interpretation of the lower-risk data, I consider using the combination for lower-risk patients as well.[15] So, I'm using front-line bevacizumab with chemotherapy and maintenance therapy more than I used to.

Dr Chase:
I agree, and I believe it's very important to remember that these so-called lower-risk patients, those with stage III, optimally resected disease, are still at high risk of disease recurrence.[22] So, we don't necessarily need to restrict the PAOLA-1 regimen to higher-risk patients. It may be appropriate for all eligible women newly diagnosed with HRD-positive advanced ovarian cancer.[15,16]

Dr Lewin:
We cannot cover efficacy without talking about the safety results; Dr Chase, can you walk us through the PAOLA-1 trial safety results?

Dr Chase:
Of course. Adverse reactions and laboratory abnormalities from the primary analysis were mostly Grades 1 and 2.[16] The most common Grade 3 adverse reactions were anemia, lymphopenia, fatigue, and nausea, which we know are class effects for all PARP inhibitors.[13,16] Serious adverse reactions occurred in 31% of patients who received LYNPARZA plus bevacizumab. Serious adverse reactions in more than 5% of patients included hypertension, at 19%, and anemia, at 17%.[2,16]

Eight out of ten patients remained on LYNPARZA as prescribed, in combination with bevacizumab, without discontinuation due to ARs. Specific ARs that most frequently led to discontinuation in patients treated with LYNPARZA plus bevacizumab were anemia, at 4% and nausea, at 3%.[16]

Dr Lewin:
And we don't want to forget the importance of monitoring for ARs during therapy that includes bevacizumab. Hypertension and proteinuria are concerns, so checking blood pressure and testing for proteinuria should be conducted regularly during bevacizumab therapy.[2] Also, MDS/AML and drug-induced liver injury have occurred in patients treated with LYNPARZA. So, complete blood counts should be taken monthly to monitor for cytopenia, and bilirubin and transaminases should be evaluated throughout treatment to monitor for hepatic toxicity.[16]

Moving on to our final question, "who should be tested?". And the answer is straightforward. All women with advanced ovarian cancer should be tested for *BRCA* germline, tumor mutations and HRD. That is what guidelines say, and it is so critically important to allow us to plan a patient's care.[6,8,12]

Dr Chase:
And despite the clear clinical value, testing rates remain lower than optimal. A significant proportion of patients still do not undergo germline *BRCA* testing. In some studies, up to 49% of patients with advanced ovarian cancer remain untested. Rates for HRD testing are even lower, with reports indicating that only about half to three-quarters of patients complete HRD testing successfully in real-world settings, often due to logistical challenges or insufficient tumor samples.[4,11,17,27]

Dr Lewin:
It means that many patients aren't receiving the optimal treatment plan based on their characteristics and biomarker status.[16-17,27]

Dr Chase:
So, we can't emphasize enough, our advice is to test all patients. It is the standard of care as well as suggested by guidelines.[6,8,12] If you are part of a multidisciplinary treatment team, coordinate with your colleagues to ensure that testing is part of your treatment protocol.[1]

Dr Lewin:
So, now that we've covered who should be tested, we want to consider the question of "when should testing occur?". And again, the answer is pretty simple. Testing should occur at diagnosis or as soon as is feasible. We want to know a patient's *BRCA* and HRD status as early as possible, so we can plan their maintenance therapy.[6,8]

Dr Chase:
To accomplish that, treatment guidelines describe two ways to approach the sequencing of biomarker tests. One is to conduct tumor testing simultaneous with germline *BRCA* testing and the other is to conduct germline *BRCA* testing first, and if the results are negative, to reflex to tumor testing. In my practice, our preference is to order tests simultaneously to make sure nothing gets missed.

Dr Lewin:
In our practice, we typically begin with germline testing first, and then if the germline results are negative in women with ovarian cancer, we conduct HRD testing with MyChoice.

Dr Chase:
I see, and while each of us may have our own practice preference, the important thing is that both are guideline-recommended, so there's no right or wrong as long as the testing is being conducted.

Dr Lewin:
That concludes the topics we wanted to talk about today. Dr Chase, any final thoughts?

Dr Chase:
I think the take-home message is test all your patients with advanced ovarian cancer for *BRCA* mutations, and HRD.[6,8,12] Do this testing as early as possible so you know their eligibility for treatments like LYNPARZA plus bevacizumab, and can discuss and plan your patient's maintenance therapy options.[6,8] And, if your patient is going to undergo interval debulking surgery, make sure you have enough of a tumor biopsy sample to allow successful testing.[10,26]

Dr Lewin:
Yes, I agree. I will just end by noting that I feel hopeful for my newly diagnosed ovarian cancer patients with HRD-positive tumors. I know a cancer patient's journey is not easy and can be very stressful, but the availability of PARP inhibitor treatments provides a better outlook than we've had in the past.

Treatments in this class such as LYNPARZA plus bevacizumab, may provide improved outcomes for these patients.[16] Before PARP inhibitors became available, the prognosis for these women was grim.[3,14] But in my own clinical experience, I've observed patients who received the PAOLA-1 regimen, had no evidence of disease after primary treatment, and were still in response with no progression.[25] That is so satisfying.

Dr. Chase:
That's a wonderful way to wrap up our discussion today. Thank you all for listening.

Dr Lewin:
Thank you. Please continue watching for Important Safety Information about LYNPARZA.

Announcer:
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.

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. 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.

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%).

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.

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

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

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

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

Please see complete Prescribing Information, including Medication Guide.

You may report side effects related to AstraZeneca products (Opens new window).

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