NEWS RELEASE

IMFINZI® (durvalumab)plus LYNPARZA® (olaparib)and IMFINZIalone both significantly improved progression-free survival in advanced endometrial cancer when added to chemotherapy

5/26/2023

DUO-E is the first global Phase III trial of immunotherapy plus PARP inhibition to demonstrate clinical benefit in this setting

WILMINGTON, Del.--(BUSINESS WIRE)-- Positive high-level results from the DUO-E Phase III trial showed IMFINZI® (durvalumab) in combination with platinum-based chemotherapy followed by either IMFINZI plus LYNPARZA®(olaparib)orIMFINZIalone as maintenance therapy both demonstrated a statistically significant and clinically meaningful improvement in progression-free survival (PFS) compared to standard-of-care chemotherapy alone in patients with newly diagnosed advanced or recurrent endometrial cancer. There was a greater clinical benefit observed with the combination of IMFINZIand LYNPARZAas maintenance treatment.

Overall survival (OS) data were immature at the time of this analysis however, a favorable trend was observed for both treatment regimens.

Endometrial cancer is the 6th most common cancer in women worldwide, with over 417,000 patients diagnosed and over 97,000 deaths in 2020.1 Diagnoses are expected to rise by almost 40% by 2040.2 The current standard of care for advanced endometrial cancer is chemotherapy.3,4 However, long-term outcomes in 1st-line endometrial cancer remain poor and novel treatment options are needed.5,6

Shannon N. Westin, Professor of Gynecologic Oncology and Reproductive Medicine at the University of Texas MD Anderson Cancer Center, and principal investigator of the DUO-E trial, said: “These exciting data demonstrate durvalumab immunotherapy can significantly delay disease progression for patients with endometrial cancer and the addition of the PARP inhibitor olaparib can improve the benefit further. These combinations could provide physicians with new treatment approaches to improve outcomes for patients.”

Susan Galbraith, Executive Vice President, Oncology R&D, AstraZeneca, said: “These DUO-E data demonstrate for the first time the power of combining immunotherapy and a PARP inhibitor to provide meaningful clinical improvements for patients with endometrial cancer. These results underscore our ambition to redefine cancer care and we hope to bring this innovative IMFINZIand LYNPARZAcombination to endometrial cancer patients as soon as possible.”

The safety and tolerability profile of IMFINZI plus chemotherapy and of IMFINZI in combination with LYNPARZA was broadly consistent with that observed in prior clinical trials and the known profiles of the individual medicines.7,8

These data will be presented at a forthcoming medical meeting, and we look forward to discussing them with health authorities.

IMPORTANT SAFETY INFORMATION FOR IMFINZI ® (durvalumab) and IMJUDO ® (tremelimumab-actl)

There are no contraindications for IMFINZI® (durvalumab) or IMJUDO® (tremelimumab-actl).

Severe and Fatal Immune-Mediated Adverse Reactions

Important immune-mediated adverse reactions listed under Warnings and Precautions may not include all possible severe and fatal immune-mediated reactions. Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue. Immune-mediated adverse reactions can occur at any time after starting treatment or after discontinuation. Monitor patients closely for symptoms and signs that may be clinical manifestations of underlying immune-mediated adverse reactions. Evaluate clinical chemistries including liver enzymes, creatinine, adrenocorticotropic hormone (ACTH) level, and thyroid function at baseline and before each dose. In cases of suspected immune-mediated adverse reactions, initiate appropriate workup to exclude alternative etiologies, including infection. Institute medical management promptly, including specialty consultation as appropriate. Withhold or permanently discontinue IMFINZI and IMJUDO depending on severity. See USPI Dosing and Administration for specific details. In general, if IMFINZI and IMJUDO requires interruption or discontinuation, administer systemic corticosteroid therapy (1 mg to 2 mg/kg/day prednisone or equivalent) until improvement to Grade 1 or less. Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Consider administration of other systemic immunosuppressants in patients whose immune-

mediated adverse reactions are not controlled with corticosteroid therapy.

Immune-Mediated Pneumonitis

IMFINZI and IMJUDO can cause immune-mediated pneumonitis, which may be fatal. The incidence of pneumonitis is higher in patients who have received prior thoracic radiation.

- IMFINZI as a Single Agent
  - In patients who did not receive recent prior radiation, the incidence of immune-mediated pneumonitis was 2.4% (34/1414), including fatal (<0.1%), and Grade 3-4 (0.4%) adverse reactions. In patients who received recent prior radiation, the incidence of pneumonitis (including radiation pneumonitis) in patients with unresectable Stage III NSCLC following definitive chemoradiation within 42 days prior to initiation of IMFINZI in PACIFIC was 18.3% (87/475) in patients receiving IMFINZI and 12.8% (30/234) in patients receiving placebo. Of the patients who received IMFINZI (475), 1.1% were fatal and 2.7% were Grade 3 adverse reactions.
  - The frequency and severity of immune-mediated pneumonitis in patients who did not receive definitive chemoradiation prior to IMFINZI were similar in patients who received IMFINZI as a single agent or with ES-SCLC or BTC when in combination with chemotherapy.
- IMFINZI with IMJUDO
  - Immune-mediated pneumonitis occurred in 1.3% (5/388) of patients receiving IMFINZI and IMJUDO, including fatal (0.3%) and Grade 3 (0.2%) adverse reactions.
- IMFINZI with IMJUDO and Platinum-Based Chemotherapy
  - Immune-mediated pneumonitis occurred in 3.5% (21/596) of patients receiving IMFINZI in combination with IMJUDO and platinum-based chemotherapy, including fatal (0.5%), and Grade 3 (1%) adverse reactions.

Immune-Mediated Colitis

IMFINZI and IMJUDO can cause immune-mediated colitis that is frequently associated with diarrhea. Cytomegalovirus (CMV) infection/reactivation has been reported in patients with corticosteroid-refractory immune-mediated colitis. In cases of corticosteroid-refractory colitis, consider repeating infectious workup to exclude alternative etiologies.

- IMFINZI as a Single Agent
  - Immune-mediated colitis occurred in 2% (37/1889) of patients receiving IMFINZI, including Grade 4 (<0.1%) and Grade 3 (0.4%) adverse reactions.
- IMFINZI with IMJUDO

    - Immune-mediated colitis or diarrhea occurred in 6% (23/388) of patients receiving IMFINZI and IMJUDO, including Grade 3 (3.6%) adverse reactions. Intestinal perforation has been observed in other studies of IMFINZI and IMJUDO.

- IMFINZI with IMJUDO and Platinum-Based Chemotherapy
    - Immune-mediated colitis occurred in 6.5% (39/596) of patients receiving IMFINZI in combination with IMJUDO and platinum-based chemotherapy including fatal (0.2%) and Grade 3 (2.5%) adverse reactions. Intestinal perforation and large intestine perforation were reported in 0.1% of patients.

Immune-Mediated Hepatitis

IMFINZI and IMJUDO can cause immune-mediated hepatitis, which may be fatal.

- IMFINZI as a Single Agent
    - Immune-mediated hepatitis occurred in 2.8% (52/1889) of patients receiving IMFINZI, including fatal (0.2%), Grade 4 (0.3%) and Grade 3 (1.4%) adverse reactions.

- IMFINZI with IMJUDO
    - Immune-mediated hepatitis occurred in 7.5% (29/388) of patients receiving IMFINZI and IMJUDO, including fatal (0.8%), Grade 4 (0.3%) and Grade 3 (4.1%) adverse reactions.

- IMFINZI with IMJUDO and Platinum-Based Chemotherapy
    - Immune-mediated hepatitis occurred in 3.9% (23/596) of patients receiving IMFINZI in combination with IMJUDO and platinum-based chemotherapy, including fatal (0.3%), Grade 4 (0.5%), and Grade 3 (2%) adverse reactions.

Immune-Mediated Endocrinopathies

- Adrenal Insufficiency :IMFINZI and IMJUDO can cause primary or secondary adrenal insufficiency. For Grade 2 or higher adrenal insufficiency, initiate symptomatic treatment, including hormone replacement as clinically indicated.
    - IMFINZI as a Single Agent
        - Immune-mediated adrenal insufficiency occurred in 0.5% (9/1889) of patients receiving IMFINZI, including Grade 3 (<0.1%) adverse reactions.
    - IMFINZI with IMJUDO
        - Immune-mediated adrenal insufficiency occurred in 1.5% (6/388) of patients receiving IMFINZI and IMJUDO, including Grade 3 (0.3%) adverse reactions.
    - IMFINZI with IMJUDO and Platinum-Based Chemotherapy
        - Immune-mediated adrenal insufficiency occurred in 2.2% (13/596) of patients receiving IMFINZI in

combination with IMJUDO and platinum-based chemotherapy, including Grade 3 (0.8%) adverse reactions.

- Hypophysitis :IMFINZI and IMJUDO can cause immune-mediated hypophysitis. Hypophysitis can present with acute symptoms associated with mass effect such as headache, photophobia, or visual field cuts. Hypophysitis can cause hypopituitarism. Initiate symptomatic treatment including hormone replacement as clinically indicated.
    - IMFINZI as a Single Agent
        - Grade 3 hypophysitis/hypopituitarism occurred in <0.1% (1/1889) of patients who received IMFINZI.
    - IMFINZI with IMJUDO
        - Immune-mediated hypophysitis/hypopituitarism occurred in 1% (4/388) of patients receiving IMFINZI and IMJUDO.
    - IMFINZI with IMJUDO and Platinum-Based Chemotherapy
        - Immune-mediated hypophysitis occurred in 1.3% (8/596) of patients receiving IMFINZI in combination with IMJUDO and platinum-based chemotherapy, including Grade 3 (0.5%) adverse reactions.
- Thyroid Disorders (Thyroiditis, Hyperthyroidism, and Hypothyroidism) :IMFINZI and IMJUDO can cause immune-mediated thyroid disorders. Thyroiditis can present with or without endocrinopathy. Hypothyroidism can follow hyperthyroidism. Initiate hormone replacement therapy for hypothyroidism or institute medical management of hyperthyroidism as clinically indicated.
    - IMFINZI as a Single Agent
        - Immune-mediated thyroiditis occurred in 0.5% (9/1889) of patients receiving IMFINZI, including Grade 3 (<0.1%) adverse reactions.
        - Immune-mediated hyperthyroidism occurred in 2.1% (39/1889) of patients receiving IMFINZI.
        - Immune-mediated hypothyroidism occurred in 8.3% (156/1889) of patients receiving IMFINZI, including Grade 3 (<0.1%) adverse reactions.
    - IMFINZI with IMJUDO
        - Immune-mediated thyroiditis occurred in 1.5% (6/388) of patients receiving IMFINZI and IMJUDO.
        - Immune-mediated hyperthyroidism occurred in 4.6% (18/388) of patients receiving IMFINZI and IMJUDO, including Grade 3 (0.3%) adverse reactions.
        - Immune-mediated hypothyroidism occurred in 11% (42/388) of patients receiving IMFINZI and IMJUDO.
    - IMFINZI with IMJUDO and Platinum-Based Chemotherapy

        - Immune-mediated thyroiditis occurred in 1.2% (7/596) of patients receiving IMFINZI in combination with IMJUDO and platinum-based chemotherapy.
        - Immune-mediated hyperthyroidism occurred in 5% (30/596) of patients receiving IMFINZI in combination with IMJUDO and platinum-based chemotherapy, including Grade 3 (0.2%) adverse reactions.
        - Immune-mediated hypothyroidism occurred in 8.6% (51/596) of patients receiving IMFINZI in combination with IMJUDO and platinum-based chemotherapy, including Grade 3 (0.5%) adverse reactions.

- Type 1 Diabetes Mellitus, which can present with diabetic ketoacidosis : Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Initiate treatment with insulin as clinically indicated.
    - IMFINZI as a Single Agent
        - Grade 3 immune-mediated Type 1 diabetes mellitus occurred in <0.1% (1/1889) of patients receiving IMFINZI.
    - IMFINZI with IMJUDO
        - Two patients (0.5%, 2/388) had events of hyperglycemia requiring insulin therapy that had not resolved at last follow-up.
    - IMFINZI with IMJUDO and Platinum-Based Chemotherapy
        - Immune-mediated Type 1 diabetes mellitus occurred in 0.5% (3/596) of patients receiving IMFINZI in combination with IMJUDO and platinum-based chemotherapy including Grade 3 (0.3%) adverse reactions.

Immune-Mediated Nephritis with Renal Dysfunction

IMFINZI and IMJUDO can cause immune-mediated nephritis.

- IMFINZI as a Single Agent
    - Immune-mediated nephritis occurred in 0.5% (10/1889) of patients receiving IMFINZI, including Grade 3 (<0.1%) adverse reactions.
- IMFINZI with IMJUDO
    - Immune-mediated nephritis occurred in 1% (4/388) of patients receiving IMFINZI and IMJUDO, including Grade 3 (0.5%) adverse reactions.
- IMFINZI with IMJUDO and Platinum-Based Chemotherapy
    - Immune-mediated nephritis occurred in 0.7% (4/596) of patients receiving IMFINZI in combination with IMJUDO and platinum-based chemotherapy, including Grade 3 (0.2%) adverse reactions.

Immune-Mediated Dermatology Reactions

IMFINZI and IMJUDO can cause immune-mediated rash or dermatitis. Exfoliative dermatitis, including Stevens-Johnson Syndrome (SJS), drug rash with eosinophilia and systemic symptoms (DRESS), and toxic epidermal necrolysis (TEN), have occurred with PD-1/L-1 and CTLA-4 blocking antibodies. Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate non-exfoliative rashes.

- IMFINZI as a Single Agent
  - Immune-mediated rash or dermatitis occurred in 1.8% (34/1889) of patients receiving IMFINZI, including Grade 3 (0.4%) adverse reactions.
- IMFINZI with IMJUDO
  - Immune-mediated rash or dermatitis occurred in 4.9% (19/388) of patients receiving IMFINZI and IMJUDO, including Grade 4 (0.3%) and Grade 3 (1.5%) adverse reactions.
- IMFINZI with IMJUDO and Platinum-Based Chemotherapy
  - Immune-mediated rash or dermatitis occurred in 7.2% (43/596) of patients receiving IMFINZI in combination with IMJUDO in combination with platinum-based chemotherapy, including Grade 3 (0.3%) adverse reactions.

Immune-Mediated Pancreatitis

IMFINZI in combination with IMJUDO can cause immune-mediated pancreatitis. Immune-mediated pancreatitis occurred in 2.3% (9/388) of patients receiving IMFINZI and IMJUDO, including Grade 4 (0.3%) and Grade 3 (1.5%) adverse reactions.

Other Immune-Mediated Adverse Reactions

The following clinically significant, immune-mediated adverse reactions occurred at an incidence of less than 1% each in patients who received IMFINZI and IMJUDO or were reported with the use of other immune-checkpoint inhibitors.

- Cardiac/vascular : Myocarditis, pericarditis, vasculitis.
- Nervous system : Meningitis, encephalitis, myelitis and demyelination, myasthenic syndrome/myasthenia gravis (including exacerbation), Guillain-Barré syndrome, nerve paresis, autoimmune neuropathy.
- Ocular : Uveitis, iritis, and other ocular inflammatory toxicities can occur. Some cases can be associated with retinal detachment. Various grades of visual impairment to include blindness can occur. If uveitis occurs in combination with other immune-mediated adverse reactions, consider a Vogt-Koyanagi-Harada-like syndrome, as this may require treatment with systemic steroids to reduce the risk of permanent vision loss.
- Gastrointestinal : Pancreatitis including increases in serum amylase and lipase levels, gastritis, duodenitis.
- Musculoskeletal and connective tissue disorders : Myositis/polymyositis, rhabdomyolysis and associated sequelae including renal failure, arthritis, polymyalgia rheumatic.

- Endocrine : Hypoparathyroidism.
- Other (hematologic/immune) : Hemolytic anemia, aplastic anemia, hemophagocytic lymphohistiocytosis, systemic inflammatory response syndrome, histiocytic necrotizing lymphadenitis (Kikuchi lymphadenitis), sarcoidosis, immune thrombocytopenia, solid organ transplant rejection.

Infusion-Related Reactions

IMFINZI and IMJUDO can cause severe or life-threatening infusion-related reactions. Monitor for signs and symptoms of infusion-related reactions. Interrupt, slow the rate of, or permanently discontinue IMFINZI and IMJUDO based on the severity. See USPI Dosing and Administration for specific details. For Grade 1 or 2 infusion-related reactions, consider using pre-medications with subsequent doses.

- IMFINZI as a Single Agent
    - Infusion-related reactions occurred in 2.2% (42/1889) of patients receiving IMFINZI, including Grade 3 (0.3%) adverse reactions.
- IMFINZI with IMJUDO
    - Infusion-related reactions occurred in 10 (2.6%) patients receiving IMFINZI and IMJUDO.
- IMFINZI with IMJUDO and Platinum-Based Chemotherapy
    - Infusion-related reactions occurred in 2.9% (17/596) of patients receiving IMFINZI in combination with IMJUDO and platinum-based chemotherapy, including Grade 3 (0.3%) adverse reactions.

Complications of Allogeneic HSCT after IMFINZI

Fatal and other serious complications can occur in patients who receive allogeneic hematopoietic stem cell transplantation (HSCT) before or after being treated with a PD-1/L-1 blocking antibody. Transplant-related complications include hyperacute graft-versus-host-disease (GVHD), acute GVHD, chronic GVHD, hepatic veno-occlusive disease (VOD) after reduced intensity conditioning, and steroid-requiring febrile syndrome (without an identified infectious cause). These complications may occur despite intervening therapy between PD-1/L-1 blockade and allogeneic HSCT. Follow patients closely for evidence of transplant-related complications and intervene promptly. Consider the benefit versus risks of treatment with a PD-1/L-1 blocking antibody prior to or after an allogeneic HSCT.

Embryo-Fetal Toxicity

Based on their mechanism of action and data from animal studies, IMFINZI and IMJUDO can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. In females of reproductive potential, verify pregnancy status prior to initiating IMFINZI and IMJUDO and advise them to use effective contraception during treatment with IMFINZI and IMJUDO and for 3 months after the last dose of IMFINZI and IMJUDO.

Lactation

There is no information regarding the presence of IMFINZI and IMJUDO in human milk; however, because of the potential for serious adverse reactions in breastfed infants from IMFINZI and IMJUDO, advise women not to breastfeed during treatment and for 3 months after the last dose.

- Adverse Reactions
- In patients with Stage III NSCLC in the PACIFIC study receiving IMFINZI (n=475), the most common adverse reactions (≥20%) were cough (40%), fatigue (34%), pneumonitis or radiation pneumonitis (34%), upper respiratory tract infections (26%), dyspnea (25%), and rash (23%). The most common Grade 3 or 4 adverse reactions (≥3%) were pneumonia (7%) and pneumonitis/radiation pneumonitis (3.4%)
- In patients with Stage III NSCLC in the PACIFIC study receiving IMFINZI (n=475), discontinuation due to adverse reactions occurred in 15% of patients in the IMFINZI arm. Serious adverse reactions occurred in 29% of patients receiving IMFINZI. The most frequent serious adverse reactions (≥2%) were pneumonitis or radiation pneumonitis (7%) and pneumonia (6%). Fatal pneumonitis or radiation pneumonitis and fatal pneumonia occurred in <2% of patients and were similar across arms
- In patients with mNSCLC in the POSEIDON study receiving IMFINZI and IMJUDO plus platinum-based chemotherapy (n=330), the most common adverse reactions (occurring in ≥20% of patients) were nausea (42%), fatigue (36%), musculoskeletal pain (29%), decreased appetite (28%), rash (27%), and diarrhea (22%).
- In patients with mNSCLC in the POSEIDON study receiving IMFINZI in combination with IMJUDO and platinum-based chemotherapy (n=330), permanent discontinuation of IMFINZI or IMJUDO due to an adverse reaction occurred in 17% of patients. Serious adverse reactions occurred in 44% of patients, with the most frequent serious adverse reactions reported in at least 2% of patients being pneumonia (11%), anemia (5%), diarrhea (2.4%), thrombocytopenia (2.4%), pyrexia (2.4%), and febrile neutropenia (2.1%). Fatal adverse reactions occurred in a total of 4.2% of patients.
- In patients with extensive-stage SCLC in the CASPIAN study receiving IMFINZI plus chemotherapy (n=265), the most common adverse reactions (≥20%) were nausea (34%), fatigue/asthenia (32%), and alopecia (31%). The most common Grade 3 or 4 adverse reaction (≥3%) was fatigue/asthenia (3.4%)
- In patients with extensive-stage SCLC in the CASPIAN study receiving IMFINZI plus chemotherapy (n=265), IMFINZI was discontinued due to adverse reactions in 7% of the patients receiving IMFINZI plus chemotherapy. Serious adverse reactions occurred in 31% of patients receiving IMFINZI plus chemotherapy. The most frequent serious adverse reactions reported in at least 1% of patients were febrile neutropenia (4.5%), pneumonia (2.3%), anemia (1.9%), pancytopenia (1.5%), pneumonitis (1.1%), and COPD (1.1%). Fatal adverse reactions occurred in 4.9% of patients receiving IMFINZI plus chemotherapy
- In patients with locally advanced or metastatic BTC in the TOPAZ-1 study receiving IMFINZI (n=338), the most common adverse reactions (occurring in ≥20% of patients) were fatigue, nausea, constipation, decreased appetite, abdominal pain, rash, and pyrexia

- In patients with locally advanced or metastatic BTC in the TOPAZ-1 study receiving IMFINZI (n=338), discontinuation due to adverse reactions occurred in 6% of the patients receiving IMFINZI plus chemotherapy. Serious adverse reactions occurred in 47% of patients receiving IMFINZI plus chemotherapy. The most frequent serious adverse reactions reported in at least 2% of patients were cholangitis (7%), pyrexia (3.8%), anemia (3.6%), sepsis (3.3%) and acute kidney injury (2.4%). Fatal adverse reactions occurred in 3.6% of patients receiving IMFINZI plus chemotherapy. These include ischemic or hemorrhagic stroke (4 patients), sepsis (2 patients), and upper gastrointestinal hemorrhage (2 patients)
- In patients with unresectable HCC in the HIMALAYA study receiving IMFINZI and IMJUDO, the most common adverse reactions (occurring in ≥20% of patients) were rash, diarrhea, fatigue, pruritus, musculoskeletal pain, and abdominal pain
- In patients with unresectable HCC in the HIMALAYA study receiving IMFINZI and IMJUDO, serious adverse reactions occurred in 41% of patients. Serious adverse reactions in >1% of patients included hemorrhage (6%), diarrhea (4%), sepsis (2.1%), pneumonia (2.1%), rash (1.5%), vomiting (1.3%), acute kidney injury (1.3%), and anemia (1.3%). Fatal adverse reactions occurred in 8% of patients who received IMJUDO in combination with durvalumab, including death (1%), hemorrhage intracranial (0.5%), cardiac arrest (0.5%), pneumonitis (0.5%), hepatic failure (0.5%), and immune-mediated hepatitis (0.5%). Permanent discontinuation of treatment regimen due to an adverse reaction occurred in 14% of patients

The safety and effectiveness of IMFINZI and IMJUDO have not been established in pediatric patients.

Indications:

IMFINZI is indicated for the treatment of adult patients with unresectable Stage III non-small cell lung cancer (NSCLC) whose disease has not progressed following concurrent platinum-based chemotherapy and radiation therapy.

IMFINZI, in combination with IMJUDO and platinum-based chemotherapy, is indicated for the treatment of adult patients with metastatic NSCLC with no sensitizing epidermal growth factor receptor (EGFR) mutations or anaplastic lymphoma kinase (ALK) genomic tumor aberrations.

IMFINZI, in combination with etoposide and either carboplatin or cisplatin, is indicated for the first-line treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC).

IMFINZI, in combination with gemcitabine and cisplatin, is indicated for the treatment of adult patients with locally advanced or metastatic biliary tract cancer (BTC).

IMFINZI in combination with IMJUDO is indicated for the treatment of adult patients with unresectable

hepatocellular carcinoma (uHCC).

Please see Full Prescribing Information for **IMFINZI** and **IMJUDO** , including Medication Guide.

IMPORTANT SAFETY INFORMATION FOR LYNPARZA® (olaparib)

CONTRAINDICATIONS

There are no contraindications for LYNPARZA.

WARNINGS AND PRECAUTIONS

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

Do not start LYNPARZA until patients have recovered from hematological toxicity caused by previous chemotherapy (≤Grade 1). Monitor complete blood count for cytopenia at baseline and monthly thereafter for clinically significant changes during treatment. For prolonged hematological toxicities, interrupt LYNPARZA and monitor blood count weekly until recovery.

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

Pneumonitis: Occurred in 0.8% of patients exposed to LYNPARZA monotherapy, and some cases were fatal. If patients present with new or worsening respiratory symptoms such as dyspnea, cough, and fever, or a radiological abnormality occurs, interrupt LYNPARZA treatment and initiate prompt investigation. Discontinue LYNPARZA if pneumonitis is confirmed and treat patient appropriately.

Venous Thromboembolic Events (VTE): Including severe or fatal pulmonary embolism (PE) occurred in patients treated with LYNPARZA. VTE occurred in 7% of patients with metastatic castration-resistant prostate cancer who received LYNPARZA plus androgen deprivation therapy (ADT) compared to 3.1% of patients receiving enzalutamide or abiraterone plus ADT in the PROfound study. Patients receiving LYNPARZA and ADT had a 6% incidence of pulmonary embolism compared to 0.8% of patients treated with ADT plus either enzalutamide or abiraterone. Monitor patients for signs and symptoms of venous thrombosis and pulmonary embolism, and treat

as medically appropriate, which may include long-term anticoagulation as clinically indicated.

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

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

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

ADVERSE REACTIONS—First-Line Maintenance BRCAm Advanced Ovarian Cancer

Most common adverse reactions (Grades 1-4) 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 thromboembolic events occurred more commonly in patients receiving LYNPARZA/bevacizumab (5%) than in those receiving placebo/bevacizumab (1.9%).

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

ADVERSE REACTIONS—Maintenance Recurrent Ovarian Cancer

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

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

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

ADVERSE REACTIONS—Adjuvant Treatment of gBRCAm, 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—gBRCAm, 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%).

ADVERSE REACTIONS—First-Line Maintenance gBRCAm Metastatic Pancreatic Adenocarcinoma

Most common adverse reactions (Grades 1-4) 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%).

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).

INDICATIONS

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

First-Line Maintenance BRCAm Advanced Ovarian Cancer

For the maintenance treatment of adult patients with deleterious or suspected deleterious germline or somatic BRCA-mutated (gBRCAm or sBRCAm) 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 Recurrent Ovarian Cancer

For the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer, who are in complete or partial response to platinum-based chemotherapy.

Adjuvant Treatment of gBRCAm, HER2-Negative, High-Risk Early Breast Cancer

For the adjuvant treatment of adult patients with deleterious or suspected deleterious gBRCAm, 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.

gBRCAm, HER2-Negative Metastatic Breast Cancer

For the treatment of adult patients with deleterious or suspected deleterious gBRCAm, 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 gBRCAm Metastatic Pancreatic Cancer

For the maintenance treatment of adult patients with deleterious or suspected deleterious gBRCAm 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.

Please see complete **Prescribing Information** , including **Medication Guide** .

Notes

Endometrial cancer

Endometrial cancer is a highly heterogenous disease that originates in the tissue lining of the womb and is most common in women who have already been through the menopause, with the average age at diagnosis being over 60 years old.9-11 Both the incidence and mortality of endometrial cancer are expected to increase from 417,400 cases and 97,400 deaths in 2020 to 608,130 cases and 157,813 deaths in 2040.1,2

The majority of patients with endometrial cancer are diagnosed at an early stage of disease where the cancer is confined to the uterus. They are typically treated with surgery and/or radiation and the 5-year survival rate is high (approximately 95%). However, patients with advanced disease (Stage III-IV) are usually treated with chemotherapy and have a much poorer prognosis, with a 5-year survival rate falling to around 20-30%.4,5,11,12,13

For patients where the disease has already advanced or returned, treatment options are limited as the cancer is not considered likely to respond to hormonal therapy and will be treated with chemotherapy.5,6

DUO-E

The DUO-E trial (GOG 3041/ENGOT-EN10) is a three-arm, randomized, double-blind, placebo-controlled, multicenter Phase III trial of 1st-line IMFINZIin combination with platinum-based chemotherapy (carboplatin and paclitaxel)followed by IMFINZI with LYNPARZAor IMFINZI alone as maintenance therapy versus platinum-based chemotherapy alone as a treatment for patients with newly diagnosed advanced or recurrent endometrial cancer.

The DUO-E trial randomized 699 patients with newly diagnosed or recurrent Stage III or IV epithelial endometrial carcinoma (excluding sarcomas) to receive either 1120mg of IMFINZI or placebo, given every three weeks in combination with standard-of-care platinum-based chemotherapy. Following cessation of chemotherapy, patients were given either 1500mg of IMFINZI or placebo every four weeks as maintenance, either in combination with 300mg BID (2x150mg tablets, twice a day) of LYNPARZAor placebo until progressive disease for 24 months.

The dual primary endpoint was PFS. Mismatch repair (MMR) status was one of the stratification factors. Key secondary endpoints included OS, objective response rate (ORR), duration of response (DoR) and safety and tolerability. The trial was conducted in 253 study locations across 22 countries including the US, Europe, South America and Asia.

For more information about the trial please visit **ClinicalTrials.gov**.

IMFINZI

IMFINZI® (durvalumab) is a human monoclonal antibody that binds to the PD-L1 protein and blocks the interaction of PD-L1 with the PD-1 and CD80 proteins, countering the tumor's immune-evading tactics and releasing the inhibition of immune responses.

IMFINZI is the only approved immunotherapy and the global standard of care in the curative-intent setting of unresectable, Stage III non-small cell lung cancer (NSCLC) in patients whose disease has not progressed after chemoradiation therapy based on the PACIFIC Phase III trial. IMFINZI is also approved in the US, EU, Japan, China and many other countries around the world for the treatment of extensive-stage small cell lung cancer (SCLC) based on the CASPIAN Phase III trial. Additionally, IMFINZI is approved in combination with a short course of IMJUDO® (tremelimumab-actl) and chemotherapy for the treatment of metastatic NSCLC in the US, EU and Japan based on the POSEIDON Phase III trial.

In addition to its indications in lung cancer, IMFINZIis also approved in combination withchemotherapy in locally advanced or metastatic biliary tract cancer in the US, EU, Japan and several other countries; in combination with IMJUDOin unresectable hepatocellular carcinoma in the US, EU and Japan; and in previously treated patients with advanced bladder cancer in a small number of countries.

Since the first approval in May 2017, more than 150,000 patients have been treated with IMFINZI. As part of a broad development program, IMFINZI is being tested as a single treatment and in combinations with other anti-cancer treatments for patients with SCLC, NSCLC, bladder cancer, several gastrointestinal cancers and other solid tumors.

LYNPARZA

LYNPARZA®(olaparib) is a first-in-class PARP inhibitor and the first targeted treatment to block DNA damage response (DDR) in cells/tumors harboring a deficiency in homologous recombination-related (HRR) genes, such as those with mutations in BRCA1 and/or BRCA2, or those where deficiency is induced by other agents (such as new hormonal agents [NHAs]).

Inhibition of PARP with LYNPARZA leads to the trapping of PARP bound to DNA single-strand breaks, stalling of replication forks, their collapse and the generation of DNA double-strand breaks and cancer cell death.

LYNPARZA is currently approved in a number of countries across multiple tumor types including maintenance treatment of platinum-sensitive relapsed ovarian cancer and as both monotherapy and in combination with bevacizumab for the 1st-line maintenance treatment of BRCA-mutated (BRCAm) and homologous recombination

repair deficient (HRD)-positive advanced ovarian cancer, respectively; for germline BRCA mutation (gBRCAm), HER2-negative metastatic breast cancer (in the EU and Japan this includes locally advanced breast cancer); for gBRCAm, HER2-negative high-risk early breast cancer (in Japan this includes all BRCAm HER2-negative high-risk early breast cancer); for gBRCAm metastatic pancreatic cancer; in combination with abiraterone for the treatment of metastatic castration-resistant prostate cancer in whom chemotherapy is not clinically indicated (EU only) and as monotherapy for HRR gene-mutated metastatic castration-resistant prostate cancer in patients who have progressed on prior NHA treatment (BRCAm only in the EU and Japan). In China, LYNPARZA is approved for the treatment of BRCA-mutated metastatic castration-resistant prostate cancer as well as a 1st-line maintenance treatment with bevacizumab for HRD-positive advanced ovarian cancer.

LYNPARZA, which is being jointly developed and commercialized by AstraZeneca and Merck & Co., Inc., known as MSD outside the US and Canada, in combination, has been used to treat over 75,000 patients worldwide. The companies develop LYNPARZA in combination with their respective PD-L1 and PD-1 medicines independently. LYNPARZA is the foundation of AstraZeneca's industry-leading portfolio of potential new medicines targeting DDR mechanisms in cancer cells.

AstraZeneca in oncology

AstraZeneca is leading a revolution in oncology with the ambition to provide cures for cancer in every form, following the science to understand cancer and all its complexities to discover, develop and deliver life-changing medicines to patients.

The Company's focus is on some of the most challenging cancers. It is through persistent innovation that AstraZeneca has built one of the most diverse portfolios and pipelines in the industry, with the potential to catalyze changes in the practice of medicine and transform the patient experience.

By harnessing the power of six scientific platforms – Immuno-Oncology, Tumor Drivers and Resistance, DNA Damage Response, Antibody Drug Conjugates, Epigenetics and Cell Therapies – and by championing the development of personalized combinations, AstraZeneca has the vision to redefine cancer treatment and, one day, eliminate cancer as a cause of death.

About AstraZeneca

AstraZeneca is a global, science-led biopharmaceutical company that focuses on the discovery, development and commercialization of prescription medicines in Oncology, Rare Diseases and BioPharmaceuticals, including Cardiovascular, Renal & Metabolism, and Respiratory & Immunology. Based in Cambridge, UK, AstraZeneca operates in over 100 countries, and its innovative medicines are used by millions of patients worldwide. For more information, please visit **www.astrazeneca-us.com** and follow us on Twitter **@AstraZenecaUS**.

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