8 May 2018 11:00 BST

LYNPARZA TABLETS RECEIVE EU APPROVAL FOR THE TREATMENT OF PLATINUM-SENSITIVE RELAPSED OVARIAN CANCER

Women with platinum-sensitive ovarian cancer now have access to maintenance therapy with AstraZeneca and MSD's Lynparza, regardless of BRCA status

Lynparza has over five years' efficacy and safety follow-up data

New formulation reduces dosing to two tablets twice daily

AstraZeneca and Merck & Co., Inc., Kenilworth, NJ, US (known as MSD outside the US and Canada) today announced that the European Medicines Agency (EMA) has approved *Lynparza* (olaparib) tablets (300mg twice daily) for use as a maintenance therapy for patients with platinum-sensitive relapsed high-grade, epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in complete response or partial response to platinum-based chemotherapy, regardless of *BRCA* status.

Dave Fredrickson, Executive Vice President, Head of the Oncology Business Unit at AstraZeneca, said: "With this new approval for *Lynparza*, we will now be able to offer more women with platinum-sensitive ovarian cancer, regardless of their *BRCA* status, a chance to achieve long-term disease control with an oral medicine that has a well-characterised safety and tolerability profile."

Roy Baynes, Senior Vice President and Head of Global Clinical Development, Chief Medical Officer, MSD Research Laboratories, said: "This is an important development for the thousands of women in Europe living with advanced ovarian cancer, historically a difficult-to-treat disease. Working with AstraZeneca, we are able to bring this innovative, targeted treatment that helps delay progression of the disease to a broader group of women."

The EU approval was based on two randomised trials, SOLO-2 and Study 19, which showed that *Lynparza* reduced the risk of disease progression or death for platinum-sensitive relapsed ovarian cancer patients compared to placebo.

Table 1. Summary of key efficacy results from randomised trials:

Analysis	SOLO-2 (germline *BRCA*-mutated platinum-sensitive relapsed) n=295		Study 19 (platinum-sensitive relapsed) n=265	
	Lynparza	Placebo	*Lynparza*	Placebo
Reduction in the risk of disease progression or death (PFS)	70% (HR 0.30 [95% CI, 0.22-0.41], p<0.0001; median 19.1 vs 5.5 months)*		65% (HR 0.35 [95% CI, 0.25-0.49], p<0.00001; median 8.4 vs 4.8 months)*	

* By investigator-assessed analysis

In SOLO-2, the investigator-assessed analysis of PFS was supported with a blinded, independent, central radiological review of PFS, which showed a two-year difference in median PFS between *Lynparza* and placebo (HR 0.25 [95% CI, 0.18-0.35], p<0.0001; median 30.2 months vs 5.5 months). Overall survival (OS) data from SOLO-2 is currently immature.

In the final analysis of Study 19, with greater than five years of follow-up, the significant improvement in PFS translated into improvements in other key efficacy endpoints, regardless of *BRCA* status (Table 2). Additionally, the analysis showed 13% of patients treated with *Lynparza* remained progression-free and on therapy for five years or more years.

Table 2. Summary of other key efficacy endpoints from Study 19:

Analysis	Study 19 (platinum-sensitive relapsed) n=265	
	Lynparza	Placebo
Time to first subsequent therapy or death*	HR 0.39 (95% CI, 0.30-0.52), p<0.00001; median 13.3 months vs. 6.7 months	
OS	HR 0.73 (95% CI, 0.55-0.95), p=0.02138**; median 29.8 vs. 27.8 months***	

* statistical tests not adjusted for multiplicity
** P-value considered nominal as criterion for statistical significance (P<0.0095) not met
*** not adjusted for treatment crossover

The most frequently observed adverse reactions across clinical trials in patients receiving *Lynparza* monotherapy (≥ 10%) were nausea, vomiting, diarrhoea, dyspepsia, fatigue, headache, dysgeusia, decreased appetite, dizziness and anaemia. The majority of patients on *Lynparza* remained on the starting dose and only 6-11% of patients discontinued treatment due to an adverse event.

Approximately half of women with high grade epithelial ovarian cancer are expected to have deficiencies in homologous recombination repair (HRR), an important DNA damage response (DDR) pathway. Mutations most often occur within one of the *BRCA* genes, however other gene mutations can also impact the HRR pathway. While there are currently no routine tests to identify patients with these deficiencies beyond *BRCA* mutations, responsiveness to platinum-based chemotherapy can predict sensitivity to PARP inhibition.

Lynparza, the first PARP inhibitor approved*,* was initially licensed in Europe as a capsule formulation for women with *BRCA*-mutated platinum-sensitive relapsed ovarian cancer. The new tablet formulation, which reduces dosing from eight capsules twice daily to two tablets twice daily, will now be available for a broader group of women with platinum-sensitive relapsed ovarian cancer.

Lynparza tablets were also recently submitted to the EMA for approval in patients with *BRCA*-mutated, HER2-negative metastatic breast cancer based upon the successful Phase III OlympiAD trial.

About Ovarian Cancer in Europe
Among women in Europe, ovarian cancer is the fifth most common cancer and the sixth leading cause of cancer death. The five-year survival rate for ovarian cancer in Europe is 38%. In 2012, there were nearly 65,000 new cases diagnosed and around 42,700 deaths. As there is no cure for relapsed ovarian cancer, the primary aim of treatment is to slow progression of the disease for as long as possible and improve or maintain the patient's quality of life.

About SOLO-2

SOLO-2 was a randomised, double-blinded, multicentre trial designed to determine the efficacy of *Lynparza* tablets compared to placebo as maintenance monotherapy in patients with platinum-sensitive relapsed or recurrent germline *BRCA*-mutated ovarian, fallopian tube and primary peritoneal cancer. The trial, conducted in collaboration with the European Network for Gynaecological Oncological Trial Groups and Groupe d'Investigateurs National pour l'Etude des Cancers de l'Ovaire et du sein, randomised 295 patients with documented germline *BRCA*1 or *BRCA*2 mutations who had received at least two prior lines of platinum-based chemotherapy and were in complete or partial response. Eligible patients were randomised to receive 300mg *Lynparza* tablets twice daily or placebo tablets twice daily.

About Study 19
Study 19 was a randomised, double-blinded, placebo-controlled, multi-centre trial, which evaluated the efficacy and safety of *Lynparza* compared with placebo in relapsed, high-grade serous ovarian cancer patients. The trial randomised 265 patients regardless of *BRCA* mutation status and who had completed at least two courses of platinum-based chemotherapy and their most recent treatment regimen. Eligible patients were randomised to receive *Lynparza* maintenance monotherapy at a dose of 400mg per day or matching placebo.

About *Lynparza* (olaparib)
Lynparza is a first-in-class poly ADP-ribose polymerase (PARP) inhibitor and the first targeted treatment to potentially exploit tumour DDR-pathway dependencies to preferentially kill cancer cells. Specifically, *in vitro* studies have shown that *Lynparza*-induced cytotoxicity may involve inhibition of PARP enzymatic activity and increased formation of PARP-DNA complexes, resulting in DNA damage and cancer-cell death.

Lynparza is being investigated in a range of DDR-dependent tumour types and is the foundation of AstraZeneca's industry-leading portfolio of compounds targeting DDR mechanisms in cancer cells.

About the AstraZeneca and MSD Strategic Oncology Collaboration
In July 2017, AstraZeneca and Merck & Co., Inc., Kenilworth, NJ, US, known as MSD outside the United States and Canada, announced a global strategic oncology collaboration to co-develop and co-commercialise *Lynparza*, the world's first PARP inhibitor, and potential new medicine selumetinib, a MEK inhibitor, for multiple cancer types. The collaboration is based on increasing evidence that PARP and MEK inhibitors can be combined with PD-L1/PD-1 inhibitors for a range of tumour types. Working together, the companies will develop *Lynparza* and selumetinib in combination with other potential new medicines and as monotherapies. Independently, the companies will develop *Lynparza* and selumetinib in combination with their respective PD-L1 and PD-1 medicines.

About AstraZeneca in Oncology
AstraZeneca has a deep-rooted heritage in Oncology and offers a quickly growing portfolio of new medicines that has the potential to transform patients' lives and the Company's future. With at least six new medicines to be launched between 2014 and 2020 and a broad pipeline of small molecules and biologics in development, we are committed to advance Oncology as a key growth driver focused on lung, ovarian, breast and blood cancers. In addition to our core capabilities, we actively pursue innovative partnerships and investments that accelerate the delivery of our strategy as illustrated by our investment in Acerta Pharma in haematology.

By harnessing the power of four scientific platforms - Immuno-Oncology, Tumour Drivers and Resistance, DNA Damage Response and Antibody Drug Conjugates - 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 commercialisation of prescription medicines, primarily for the treatment of diseases in three therapy areas - Oncology, Cardiovascular, Renal & Metabolism and Respiratory. The Company also is selectively active in the areas of autoimmunity, neuroscience and infection. AstraZeneca operates in over 100 countries and its innovative medicines are used by millions of patients worldwide. For more information, please visit www.astrazeneca.com and follow us on Twitter @AstraZeneca.

Media Relations

Karen Birmingham	UK/Global	+44 203 749 5634
Rob Skelding	UK/Global	+44 203 749 5821
Matt Kent	UK/Global	+44 203 749 5906
Gonzalo Viña	UK/Global	+44 203 749 5916
Jacob Lund	Sweden	+46 8 553 260 20
Michele Meixell	US	+1 302 885 2677

Investor Relations

Thomas Kudsk Larsen		+44 203 749 5712
Craig Marks	Finance; Fixed Income; M&A	+44 7881 615 764
Henry Wheeler	Oncology	+44 203 749 5797
Mitchell Chan	Oncology; Other	+1 240 477 3771
Christer Gruvris	*Brilinta*; Diabetes	+44 203 749 5711
Nick Stone	Respiratory; Renal	+44 203 749 5716
US toll free		+1 866 381 7277

Adrian Kemp
Company Secretary, AstraZeneca PLC