18 June 2019 07:00 BST

***Lynparza* approved in the EU for 1st-line maintenance
treatment of BRCA-mutated advanced ovarian cancer**

***60% of patients receiving Lynparza remained free of disease progression
after three years vs. 27% on placebo in pivotal Phase III SOLO-1 trial***

***AstraZeneca and MSD’s Lynparza is the only PARP
inhibitor approved in the EU for this indication***

AstraZeneca and MSD Inc., Kenilworth, N.J., US (MSD: known as Merck & Co., Inc. inside the US and Canada) today announced that the European Commission (EC) has approved *Lynparza* (olaparib) as a 1st-line maintenance treatment for women with BRCA-mutated advanced ovarian cancer.

The licensed indication is as a maintenance treatment of adult patients with advanced (FIGO stages III and IV) BRCA1/2-mutated (germline and/or somatic) high-grade epithelial ovarian, fallopian tube or primary peritoneal cancer who are in response (complete or partial) following completion of 1st-line platinum-based chemotherapy.

Dave Fredrickson, Executive Vice President, Oncology Business Unit, said: “This approval sets the stage for a new standard of care in the EU for women with ovarian cancer and a BRCA mutation. The goals of front-line therapy have always been long-term remission and even cure, yet currently 70% of patients relapse within three years of initial treatment. The progression-free survival benefit of *Lynparza* observed in SOLO-1 represents a major step forward in our ambition to help transform patient outcomes.”

Roy Baynes, Senior Vice President and Head of Global Clinical Development, Chief Medical Officer, MSD Research Laboratories, said: “In SOLO-1, *Lynparza* demonstrated clinically-meaningful results with a 70% reduction in the risk of disease progression or death in the first-line maintenance treatment of patients with BRCAm advanced ovarian cancer. Merck and AstraZeneca are committed to improving outcomes for people with cancer and we will work to bring this new option to women in the EU, many of whom have historically poor outcomes, as quickly as possible.”

The EC approval was based on data from the pivotal Phase III SOLO-1 trial which tested *Lynparza* as maintenance monotherapy compared with placebo in patients with BRCAm advanced ovarian cancer following 1st-line platinum-based chemotherapy. Results [announced](https://www.nejm.org/doi/full/10.1056/NEJMoa1810858) in October 2018 at 40.7 months of follow-up showed the median time of progression for patients treated with *Lynparza* had not yet been reached vs. 13.8 months for those on placebo (HR 0.30 [95% CI, 0.23-0.41], p<0.001).

This is the third indication for *Lynparza* in the EU. AstraZeneca and MSD are exploring additional trials in ovarian cancer, including the ongoing Phase III PAOLA-1 trial, which is testing *Lynparza* in combination with bevacizumab as a 1st-line maintenance treatment for women with newly-diagnosed, advanced, stage IIIB-IV high grade serous or endometrioid ovarian cancer, regardless of BRCA status.

Elisabeth Åvall Lundqvist, Professor in clinical oncology at the Department of Oncology and Department of Clinical and Experimental Medicine at Linköping University, Linköping, Sweden comments on the SOLO 1 results: The results from SOLO-1 will change standard of care for women with newly diagnosed advanced ovarian cancer with BRCA mutation. The effect of maintenance treatment with Lynparza has sustained after cessation, the median progression-free survival has not yet been reached for those treated with Lynparza, after a median follow-up time of 41 months. The SOLO-1 results are important and positive for women who in general have a very high risk of recurrence within the first 3 years. The results also underscore the need to determine BRCA status at diagnosis.

**About SOLO-1**

SOLO-1 was a Phase III, randomised, double-blinded, placebo-controlled, multi-centre trial to evaluate the efficacy and safety of *Lynparza* tablets (300mg twice daily) as a maintenance monotherapy compared with placebo in patients with BRCAm advanced ovarian cancer following first-line platinum-based chemotherapy. The trial randomised 391 patients with a deleterious or suspected deleterious germline or somatic BRCA1 or BRCA2 mutation who were in clinical complete or partial response following platinum-based chemotherapy.

Patients were randomised (2:1) to receive *Lynparza* or placebo for up to two years or until disease progression. Patients who had a partial response at two years were permitted to stay on therapy at the investigator’s discretion. The primary endpoint was progression-free survival (PFS) and key secondary endpoints included time to second disease progression or death, time to first subsequent treatment and overall survival.

The data were presented on 21 October 2018, at the Presidential Symposium of the ESMO (European Society for Medical Oncology) 2018 Congress in Munich, Germany and published simultaneously online in [*The New England Journal of Medicine.*](https://www.nejm.org/doi/full/10.1056/NEJMoa1810858)

**Summary of PFS**i,ii

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|  | *Lynparza* (n=260) | Placebo (n=131) |
| Number of patients with event (%)**iii** | 102 (39) | 96 (73) |
| Median PFS (in months) | Not reached | 13.8 |
| Hazard ratio (95% CI) | 0.30 (0.23-0.41) |
| P-value | p<0.001 |

i Investigator-assessed.

ii Median (interquartile range) duration of follow-up 40.7 months (34.9–42.9) for*Lynparza*and 41.2 months (32.2–41.6) for placebo.

iii Analysis was done at 50.6% maturity.

The SOLO-1 safety profile was in line with that observed in prior clinical trials. The most common adverse events (AEs) ≥ 20% were nausea (77%), fatigue (63%), vomiting (40%), anaemia (39%) and diarrhoea (34%). The most common ≥ Grade 3 AEs were anaemia (22%) and neutropenia (9%). Some 71% of patients on *Lynparza* remained on the recommended starting dose. Additionally, 88% of patients on *Lynparza* continued treatment without an AE-related discontinuation.

**Financial considerations**

Under the oncology collaboration with MSD and following this new approval for *Lynparza*, AstraZeneca will receive $30m as Ongoing Collaboration Revenue, anticipated to be booked by the Company during the second quarter of 2019.

**About ovarian cancer**

Ovarian cancer is a leading cause of cancer deaths in women worldwide, with a five-year survival rate of 19%.1 In 2018, there were nearly 300,000 new cases diagnosed and around 185,000 deaths.2 For newly-diagnosed advanced ovarian cancer, the primary aim of treatment is to delay progression of the disease for as long as possible and maintain the patient’s quality of life with the intent of achieving complete remission or cure.3,4,5,6

**About BRCA mutations**

BRCA1 and BRCA2 are human genes that produce proteins responsible for repairing damaged DNA and play an important role in maintaining the genetic stability of cells. When either of these genes is mutated, or altered, such that its protein product either is not made or does not function correctly, DNA damage may not be repaired properly, and cells become unstable. As a result, cells are more likely to develop additional genetic alterations that can lead to cancer.

**About *Lynparza***

*Lynparza* (olaparib) is a first-in-class PARP inhibitor and the first targeted treatment to block DNA damage response (DDR) in cells/tumours harbouring a deficiency in homologous recombination repair (HRR), such as mutations in BRCA1 and/or BRCA2. 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 being tested in a range of PARP-dependent tumour types with defects and dependencies in the DDR.

*Lynparza* is currently approved in over 60 countries, including those in the EU, for the maintenance treatment of platinum-sensitive relapsed ovarian cancer regardless of BRCA status. It is approved in the US, Canada, Brazil and now the EU as 1st-line maintenance treatment of BRCAm advanced ovarian cancer following response to platinum-based chemotherapy. It is also approved in nearly 40 countries for germline BRCAm HER2-negative metastatic breast cancer previously treated with chemotherapy. Regulatory reviews are underway in other jurisdictions for both ovarian cancer and breast cancer.

*Lynparza* has the broadest and most advanced clinical trial development programme of any PARP inhibitor, and AstraZeneca and MSD are working together to understand how it may affect multiple PARP-dependent tumours as a monotherapy and in combination across multiple cancer types. *Lynparza* is the foundation of AstraZeneca’s industry-leading portfolio of potential new medicines 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. 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 one of AstraZeneca’s four Growth Platforms 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 personalised 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. AstraZeneca operates in over 100 countries and its innovative medicines are used by millions of patients worldwide. For more information, please visit [astrazeneca.com](http://www.astrazeneca.com/) and follow us on Twitter @AstraZeneca.

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