



IMPORTANT PRESCRIBING INFORMATION

Important Information for Lynparza (olaparib) for treatment of adult patients with deleterious or suspected deleterious germline *BRCA*-mutated (g*BRCA*m) advanced ovarian cancer who have been treated with three or more prior lines of chemotherapy

August 2022

Dear Healthcare Professional,

This letter is to inform you of a potential detrimental effect on overall survival (OS) for Lynparza, a poly (ADP-ribose) polymerase (PARP) inhibitor compared to the chemotherapy control arm when it is used for the treatment of adult patients with deleterious or suspected deleterious germline *BRCA*-mutated (g*BRCA*m) advanced ovarian cancer who have been treated with three or more prior lines of chemotherapy.

A recent subgroup analysis indicated a potential detrimental effect on overall survival (OS) for Lynparza compared to the chemotherapy control arm in the subgroup of patients who had received three or more prior lines of chemotherapy **corresponding to the current scope of the treatment indication for Lynparza** in the randomized Phase III study, SOLO3 (NCT02282020).

AstraZeneca is planning to voluntarily withdraw this indication. The Food and Drug Administration (FDA) and AstraZeneca are in active discussions about revisions to the Lynparza Prescribing Information related to this indication **ONLY**.

Prescriber Action

Physicians should not initiate new treatment with Lynparza in the treatment indication of adult patients with deleterious or suspected deleterious germline *BRCA*-mutated advanced ovarian cancer who have been treated with three or more prior lines of chemotherapy. Physicians who are treating patients with Lynparza in this indication should share this information with those patients so that they can make an informed decision regarding their ongoing care.

*Note: this recommendation **does not** apply to any other Lynparza indications including the following ovarian cancer **maintenance indications**: first-line maintenance treatment of *BRCA*-mutated advanced ovarian cancer; first-line maintenance treatment of HRD-positive advanced ovarian cancer in combination with bevacizumab; maintenance treatment of recurrent ovarian cancer.*

Background and Data Summary

The approval for Lynparza for the indication 'treatment of adult patients with deleterious or suspected deleterious germline *BRCA*-mutated (g*BRCA*m) advanced ovarian cancer who have been treated with three or more prior lines of chemotherapy' was based on objective response rate (ORR) and duration of response (DoR) observed in the single-arm Study 42 (NCT01078662).

SOLO3 was requested by the FDA to confirm the clinical benefit of Lynparza in the above indication. SOLO3 is a Phase III, open-label, randomized, controlled, multi-center study to assess the efficacy and safety of single agent Lynparza vs standard of care, based on physician's choice of single agent chemotherapy (i.e., weekly paclitaxel, topotecan, pegylated liposomal doxorubicin [PLD], or gemcitabine) in patients with platinum-sensitive relapsed (PSR) ovarian cancer who had received at

least 2 prior lines of platinum-based chemotherapy, and who carried a germline deleterious or suspected deleterious breast cancer susceptibility gene (*BRCA1/2*) mutation.

SOLO3 met its primary endpoint of ORR and the key secondary endpoint of progression-free survival (PFS). These data have been previously analyzed in 2018 (Penson et al)¹.

The final OS analysis subsequently occurred in 2021. In a recent OS subgroup analysis, a potential survival detriment was observed in the subgroup of patients treated with 3 or more prior lines of chemotherapy corresponding to the current scope of the indication for Lynparza.

Table 1. SOLO3 Final OS, 60.9% maturity (data cut-off 16 Apr 2021): OS for Full Analysis Set and OS subgroup analysis in patients who had received 3 or more prior lines of chemotherapy

	Full Analysis Set 2 or more prior lines of chemotherapy		3 or more prior lines of chemotherapy (Indicated population)	
	Olaparib 300 mg bd (N=178)	Chemo (N=88)	Olaparib 300 mg bd (N=90)	Chemo (N=42)
Deaths, n (%)	116 (65.2)	46 (52.3)	63 (70.0)	23 (54.8)
Median (months)	34.9	32.9	29.9	39.4
	OS HR = 1.07 95% CI = 0.76, 1.49		OS HR = 1.33 95% CI = 0.84, 2.18	

Safety of Lynparza

Safety data, other than OS, reported for Lynparza in the SOLO3 study were consistent with those reported in other clinical trials with Lynparza.

This letter is not intended as a complete description of the benefits and risks related to the use of Lynparza.

Please visit the www.LynparzaHCP.com website or see enclosure for full prescribing information.

Reporting Adverse Events

Health care providers and patients are encouraged to report adverse events in patients taking Lynparza (Olaparib) to AstraZeneca at 1-800-236-9933 (US toll free). You are also encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

You may also contact our medical information department at 1-800-236-9933 or visit www.AZMedical.com if you have any questions about the information contained in this letter for the safe and effective use of Lynparza (Olaparib).

Sincerely,

Cristian Massacesi

Cristian Massacesi, MD

Chief Medical Officer (CMO) and Oncology Chief Development Officer (CDO)

¹ Penson RT, Valencia RV, Cibula D, Colombo N, Leath CA, Bidzinski M, et al. Olaparib Versus Nonplatinum Chemotherapy in Patients With Platinum-Sensitive Relapsed Ovarian Cancer and a Germline BRCA1/2 Mutation (SOLO3): A Randomized Phase III Trial. *J Clin Oncol.* 2020;38(11):1164-74.