Direct Healthcare Professional Communication

December 2022

Olaparib - For Treatment of Adult Patients with Deleterious or Suspected Deleterious Germline BRCA-mutated (gBRCAm) Advanced Ovarian Cancer who have been Treated with Three or More Prior Lines of Chemotherapy

Dear Healthcare Professional,

The General Administration for Pharmaceutical Vigilance of the Central Administration for Pharmaceutical Care at The Egyptian Drug Authority would like to inform you of the following:

Summary:

- MAH of Olaparib is voluntarily withdrawing 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. MAH is in active discussions with agencies about revisions to the Olaparib Prescribing Innnformation related to this indication **ONLY**.
- This decision is made after a recent subgroup analysis indicated a potential detrimental effect on overall survival (OS) for Olaparib, a poly (ADP-ribose) polymerase (PARP) inhibitor 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 Olaparib in the randomized Phase III study, SOLO3 (NCT02282020).
- **Prescriber Action**: Physicians should not initiate new treatment with Olaparib 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 Olaparib 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 Olaparib 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 on the Safety Concern

The approval for Olaparib for the indication 'treatment of adult patients with deleterious or suspected deleterious germline BRCA-mutated (gBRCAm) advanced ovarian cancer who have been treated with

21st Abdel-Aziz Al-Saud, Manial Al-Roda,Cairo
pv.head@edaegypt.gov.eg; pv.safety@edaegypt.gov.eg;
Tel.: 237484988 Ext.:1470

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 Olaparib 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 Olaparib 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 Olaparib.

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 Olaparib

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

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

21st Abdel-Aziz Al-Saud, Manial Al-Roda,Cairo
pv.head@edaegypt.gov.eg; pv.safety@edaegypt.gov.eg;
Tel.: 237484988 Ext.:1470

References

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.
2. https://www.lynparzahcp.com/content/dam/physician-services/us/590-lynparza-hcp-branded/hcp-global/pdf/solo3-dhcp-final-signed.pdf

Call for reporting

Healthcare professionals are asked to report any suspected adverse reactions via the Egyptian reporting system:

Name: General Administration for Pharmaceutical Vigilance

Email: pv.followup@edaegypt.gov.eg

Online reporting: https://primaryreporting.who-umc.org/EG
QR Code:

Hotline: 15301

21st Abdel-Aziz Al-Saud, Manial Al-Roda,Cairo
pv.head@edaegypt.gov.eg; pv.safety@edaegypt.gov.eg;
Tel.: 237484988 Ext.:1470