CADTH

pan-Canadian Oncology Drug Review Stakeholder Feedback on a pCODR Expert Review Committee Initial Recommendation (Sponsor)

Olaparib (Lynparza) for metastatic Castration-Resistant Prostate Cancer

April 21, 2021

Sponsor Feedback on pERC Initial Recommendation

Name of the Drug and Indication(s):	Olaparib (Lynparza) for HRRm (BRCA or ATM) mCRPC
Eligible Stakeholder Role	Sponsor/Manufacturer
Organization Providing Feedback	AstraZeneca

3.1 Comments on the Initial Recommendation

a) Please indicate if the stakeholder agrees, agrees in part, or disagrees with the initial recommendation:

☒ Agrees ☐ Agrees in part ☐ Disagrees

AstraZeneca (AZ) agrees with pERC's Initial Recommendation to reimburse olaparib for metastatic castration-resistant prostate cancer (mCRPC) based on statistically significant and clinically meaningful improvements in radiographic progression-free survival (rPFS) and overall survival (OS), a manageable toxicity profile, and no detrimental impact on quality of life (QoL), as demonstrated in the PROfound trial. AZ also agrees with pERC's assessment that there is an unmet need for effective new therapies with manageable toxicity profile in the mCRPC setting, as well as for treatments with new mechanisms of action and biomarker-directed regimens specific for patients with mCRPC who harbour germline and/or somatic HRR gene BRCA or ATM mutations.

Cost-effectiveness analysis

pERC concluded that olaparib was not cost-effective at the submitted price versus available comparators in Canada. However, only the sequential incremental cost effectiveness ratio (ICER) for olaparib versus docetaxel was reported. As pERC noted, standard of care options for patients with mCRPC include taxanes (docetaxel and cabazitaxel), ARATs (abiraterone or enzalutamide), and radium-223 (for patients with symptomatic bone metastases only and no visceral metastases). Without pairwise ICERs, cost-effectiveness of olaparib is not informed in the following populations:

a) Patients ineligible for or previously progressed on docetaxel, as cabazitaxel is only approved and reimbursed after docetaxel
b) Patients undergoing ARAT rechallenge, as seen in the submitted RWE from IC/ES
c) Patients who are not eligible for taxanes, as pERC highlighted
d) Patients with symptomatic bone metastases only and no visceral metastases who are treated with radium-223

Of the past 14 pCODR reviews, 7 had multiple comparators and all reported pairwise ICERs. Therefore, AZ is requesting that CADTH also present pairwise ICERs between olaparib and all relevant comparators (see details of first editorial feedback below).

b) Please provide editorial feedback on the initial recommendation to aid in clarity. Is the initial recommendation or are the components of the recommendation (e.g., clinical and economic evidence) clearly worded? Is the intent clear? Are the reasons clear?

Page No.	Section Title	Para, Line Number	Comments and Suggested Changes to Improve Clarity
Initial Reco	Economic Evaluation;	Economic Evaluation:	The summary of pERC deliberations confirmed that many patients are not eligible to receive taxane-based

Page No.	Section Title	Para, Line Number	Comments and Suggested Changes to Improve Clarity
Pg. 11 Initial EGR Pg. 7-8	Table 2; Conclusion	Para 5 Table 2: Submitted results for base case; CADTH reanalysis results Concl: Para 2	chemotherapy and olaparib should not be reserved for patients who have progressed on all ARATs and taxane-based therapies. Sequential analysis assumes that all comparators can be chosen equally and does not give consideration to: a) Patients that are ineligible for or refuse taxanes b) Patients that have progressed on docetaxel and docetaxel rechallenge is not recommended c) Patients with symptomatic bone metastases only and no visceral metastases Presenting the sequential ICER alone oversimplifies these clinical considerations and conceals the cost-effectiveness of olaparib vs. ARAT, cabazitazel and radium-223. RWE demonstrate that ARATs comprise the most commonly used therapies for the treatment of first, second and third line mCRPC, highlighting the relevance of ARAT rechallenge. Additionally, in the IC/ES study, radium-223 was the single largest cost driver to the Ontario system. **AZ proposed changes to improve clarity:** Present sequential ICER with all pairwise ICERs OR present two sequential ICERs, one with and one without docetaxel. *"The submitted deterministic pairwise ICERs were:* • *Olaparib vs. docetaxel: $155,874* • *Olaparib vs. cabazitaxel: $71,796* • *Olaparib vs. ARATs: $116,812* • *Olaparib vs. radium-223: dominant"* Based upon the changes implemented by CADTH to create the CADTH base case, AZ estimated that: *"The deterministic pairwise reanalysis ICERs would be as follows for each combination of therapies:* • *Olaparib vs. docetaxel: $459,527/QALYs* • *Olaparib vs. cabazitaxel: $162,333/QALYs* • *Olaparib vs. ARATs: $165,163/QALYs* • *Olaparib vs. radium-223: dominant"*

3.2 Comments Related to Eligible Stakeholder Provided Information

Notwithstanding the feedback provided in part a) above, please indicate if the stakeholder would support this initial recommendation proceeding to final recommendation ("early conversion"), which would occur two business days after the end of the feedback deadline date.

☒ Support conversion to final recommendation.

Recommendation does not require reconsideration by pERC.

☐ Do not support conversion to final recommendation.

Recommendation should be reconsidered by pERC.