CADTH | pCODR PAN-CANADIAN ONCOLOGY DRUG REVIEW

pan-Canadian Oncology Drug Review
Final Economic Guidance Report

Olaparib (Lynparza) for Newly Diagnosed Ovarian Cancer

December 5, 2019

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1 ECONOMIC GUIDANCE IN BRIEF

1.1 Submitted Economic Evaluation

The economic analysis **submitted to pCODR by AstraZeneca Canada Inc.** compared olaparib to routine surveillance for patients with advanced BRCA-mutated ovarian cancer in complete or partial response to platinum-based chemotherapy.

Table [1]. Submitted Economic Model

Funding Request/Patient Population Modelled	Aligns with the patient population (advanced ovarian cancer (FIGO Stage III-IV))
Type of Analysis	*CEA and CUA*
Type of Model	*Partitioned-survival model*
Comparator	*Routine surveillance (no active pharmacological treatments)*
Year of costs	*2018*
Time Horizon	*30 years*
Perspective	*Government*
Cost of olaparib	• $131.78 per dose (2 x 150 mg tablet) • $263.57 per day (two 150 mg tablet, taken twice daily) • $7,188.08 per month (30.44 days, assumed a relative dose intensity of 89.6%)
Cost of routine surveillance	• $0 (assumed no active pharmacological treatments)
Model Structure	The partitioned survival model was comprised of three health states: progression-free survival, post-progression, and death. (Refer to Figure 2 in Section 2.1 of the Technical Report).
Key Data Sources	• *SOLO-1 trial (Data cut-off: 17 May 2018) for PFS, PFS2, and OS data* • *A population-based, retrospective cohort study using data available at ICES for health care utilization data among patients with advanced ovarian cancer* • *SOLO-2 trial for treatment duration for subsequent PARP inhibitors*

1.2 Clinical Considerations

According to the pCODR Clinical Guidance Panel (CGP), this comparison is appropriate. Patients with known BRCA status were indicated to be put under observation. Although registered clinicians suggested that observation and maintenance with bevacizumab are standard of care for adult patients with newly diagnosed advanced BRCA-mutated high-grade epithelial ovarian, fallopian tube or primary peritoneal cancer who are in response to first-line platinum-based chemotherapy, the submitter did not include bevacizumab in the economic analysis due to the absence of published head-to-head studies between olaparib and bevacizumab. An indirect comparison of olaparib vs. bevacizumab was deemed infeasible by the submitter due to differences in clinical trial design, study population, and subsequent treatment patterns between trials focusing on olaparib and bevacizumab.

- Relevant issues identified included:
    - Overall survival (OS) was yet immature in the SOLO1 trial and it is unclear if an OS advantage is to be gained with the use of maintenance olaparib.

- It is unclear whether the results from the SOLO-1 trial can be generalizable to patients with ECOG >1, patients with non-serious histology type, patients who are not surgical candidates, patients who received non-platinum-based chemotherapy. The submitted economic evaluation did not address these populations due to limited evidence regarding the efficacy and safety of olaparib in these patients.
- The availability of companion germline and somatic BRCA tests are highly variable across Canadian provinces. The submitter addressed this concern by adding the cost of BRCA test in modifications to the main analysis for economic evaluation and budget impact analysis.
- There is uncertainty whether olaparib would be used beyond two years. The submitted economic evaluation addressed this issue by deriving treatment duration from time to discontinuation data observed in the SOLO-1 trial. On average, patients received olaparib for 20.6 months.
- The SOLO-1 trial reported that 1% and 1.9% of patients who received olaparib experienced acute myeloid leukaemia (AML) and pneumonitis, respectively. The submitter however did not consider these AEs in the submitted model.

Summary of registered clinician input relevant to the economic analysis
Registered clinicians considered olaparib as a new treatment option that would replace observation for most patients with known BRCA status. Several clinicians indicated that BRCA testing was available in their centre, or it was funded by a provincial health plan in their province. Clinicians who are members of the Cancer Care Ontario Gynecologic Cancers Drug Advisory Committee suggested all patients be referred to genetics for assessment in addition to BRCA testing; this would incur additional costs to the health care system. There is variation among registered clinicians' opinions on the frequency of disease monitoring. Furthermore, disease should be assessed as per current clinical practice. Two clinicians suggested patients be assessed monthly while on treatment, whereas another clinician suggested to reassess every three months and stop with clinical evidence of progression. All these factors were not considered in the submitted economic analysis. The EGP assessed the effect of these issues by including the cost of BRCA test and monitoring/follow-up visits observed in the SOLO-1 trial in the reanalysis.

Summary of patient input relevant to the economic analysis
Patients indicated that ovarian cancer affected their quality of life substantially. Most patients had concerns regarding work life, physical activity, and the level of well-being. They also identified the following areas as negative or extremely negative: fatigue, hair loss, neuropathy, ascites, and blood problems. Patients expected olaparib to prolong their survival and time until recurrent, improve their quality of life, and reduce visits to the cancer centre. A BRCA mutation test was covered by a provincial health care plan for most patients. The effects of ovarian cancer on patient quality of life were considered in the submitted economic evaluation. However, the health utility values used in the submitted model did not align with patient experience because the values were high and comparable to the age-sex Canadian utility norms, suggesting that ovarian cancer did not decrease patient quality of life. The submitted economic evaluation addressed patient concerns on life expectancy but not health care utilization. The submitter assumed patients receiving olaparib and routine surveillance to have comparable costs associated with health care utilization.

Summary of Provincial Advisory Group (PAG) input relevant to the economic analysis
PAG considered the following factors (enablers or barriers) important to consider if implementing a funding recommendation for olaparib, which is relevant to the economic analysis:

- A tablet formulation is considered as an enabling factor; however, the oral route of administration may limit access to treatment for patients in jurisdictions where oral medications are not funded in the same mechanisms as intravenous cancer medications.
- As olaparib is expected to replace routine surveillance, it would add extra pharmacy, laboratory, and nursing resources for dispensing and monitoring that would otherwise not require if patients are put on observation.
- Grade 3 or 4 anemia could affect patient quality of life and would be required significant resources to manage. Moreover, the additional resource would be needed to monitor the risks of developing myelodysplastic syndrome/acute myeloid leukemia and pneumonitis.
- Although BRCA testing is readily available in some provinces, the test may not be available at the time of diagnosis. Hence there will be an additional cost associated with a BRCA test. PAG is also concerned about the potential additional demand for constrained genetic testing resources as there will be many patients requiring BRCA testing to identify patients who would be eligible for olaparib.

1.3 Submitted and EGP Reanalysis Estimates

Table [2]. Submitted and EGP Estimates

Estimates (range/point)	Submitted	EGP Reanalysis
ΔE (LY)	4.31	1.88
Progression-free	6.24	3.37
Post-progression	-1.93	-1.48
ΔE (QALY)	3.731	1.203
Progression-free	5.299	1.836
Post-progression	-1.568	-0.632
Adverse event	-0.0005	-0.001
ΔC ($)	$80,276	$69,501
ICUR estimate ($/QALY)	$21,517	$57,784

The main assumptions and limitations with the submitted economic evaluation were:

- The use of a three-health state partition survival model: Although this modeling technique is commonly used in previous pCODR submissions, the EGP is concerned that using three health states may not accurately represent a treatment pathway as a patient can experience multiple progressions after the first-line treatment. The three-health state model did not allow the submitter to account for health outcomes (life years, quality-adjusted-life years, and potential health utility decrements) associated with subsequent therapies.

- High uncertainty in the comparative effect of olaparib on overall survival compared to routine surveillance: The submitter derived OS for olaparib from the SOLO-1 trial using standard model fit procedures. For routine surveillance, the submitter derived OS by applying a treatment effect of olaparib relative to routine surveillance based on PFS2 data to the olaparib OS curve. This approach was used to address the unreliable OS curve for routine surveillance that may be confounded by a large proportion of patients in the placebo arm of the SOLO-1 trial received subsequent PARP inhibitors.

  The EGP has several concerns regarding the submitter's approach of extrapolating OS. First, it is inappropriate to apply a treatment effect of routine surveillance to the OS curve of olaparib. Based on the OS curves reported in the SOLO-1 trial, it is unlikely that proportional hazard assumptions would hold for OS data given the cross of the survival curves for olaparib and routine surveillance. Second, the predicted OS curve for routine surveillance lacks face validity as it departs from the OS curve shown in the SOLO-1 trial.

As the survival curves crossed, it is possible that the QALYs gained from olaparib was a result of improved quality of life as opposed to increased survival.

- Time horizon: The submitter used 24-month trial data to predict PFS and OS for over 30 years. The 24-month data cut was used because they had a better model fit than the entire data set that covering 52 months. This resulted in 99% of the difference in QALY and 20% in costs between olaparib and routine surveillance coming from extrapolated data. Thus, the submitted ICUR should be interpreted cautiously. Using a long-time horizon can lead to erroneous predictions of long-term survival based on extrapolation of trial data with limited follow-up. While the CADTH Economic Evaluation guideline recommends that "*the time horizon of the analysis should be conceptually driven, based on the natural history of the condition or anticipated impact of the intervention*", the guideline also states that, "*in cases where that extrapolation is required to estimate long-term effect, external data sources, biology or clinical expert judgment may be used to justify the plausibility of extrapolation*."

  The CGP suggested that a 30-year time horizon was not reflective of the clinical course of the disease and that using a 20-year time horizon would be more clinically plausible for this patient population.

- Uncertainty analysis for PFS data: The submitter did not perform uncertainty analyses on parametric survival models used to predict PFS data for olaparib and routine surveillance. This may underestimate the uncertainty in the ICUR estimates.

- Optimistic health state utility values: The EGP has concerns regarding the face validity of health utility values used in the submitted model. Specifically, a health utility value for the PFS health state was higher than the health utility of the Canadian general population aged 50-59 years (0.86 vs. 0.83).[1] A US study[2] reported that health utility values for newly diagnosed advanced ovarian cancer were 0.55 (SD=0.29). For those with recurrent/progressive ovarian cancer, the mean health utility value was 0.43 (SD=0.33). Consistently, a Canadian study[3] has shown that health utility values for Canadians with ovarian cancer stage 3 and 4 were 0.77 (0.02) and 0.77 (0.04), respectively.

  Moreover, the submitted model could not account for health utility decrements due to subsequent progressions. Consequently, health utility values used in the model might overestimate the true health states of patients with advanced ovarian cancer.

- Re-treatment with PARP inhibitors: The submitted model allowed patients to receive subsequent PARP inhibitors. The CGP suggested that re-treatment of patients with PARP inhibitors was unlikely in current practice due to the absence of supporting evidence.

- Underestimated health care costs: The submitted model applied the same health system costs for patients who received olaparib and routine surveillance (except in Year 2). The CGP and EGP believe this assumption is not reasonable as patients who receive olaparib are expected to have more frequent follow-up laboratory tests, such as complete blood count, due to the possible increased risk of myelodysplastic syndrome.

  The EGP is also concerned about the submitter's assumption that a constant health care cost is to be expected from Year 5 onwards. This assumption was not realistic, given that olaparib is expected to prolong life, and health care costs generally increase with older age.[4,5]

- Exclusion of important cost components from the submitted model: The submitter did not consider the cost of BRCA mutation test and mark-up/dispensing fees in the main analysis. The CADTH economic guideline states that "*Researchers must consider all resources that occur along the pathway and that are attributable to the interventions of interest.*"

Because the BRCA testing and mark-up/dispensing fees are considered part of the care pathway for ovarian cancer, their costs should be considered in the main analysis as opposed to modifications to the main analysis.

- Inappropriate real-world evidence used for the validation of predicted OS data: The submitter compared the predicted OS data with OS shown in a Canadian study[6] that determined factors associated with 10-year survival in ovarian cancer patients with BRCAm and those with BRCA wild-type. The study included Ontario patients who were diagnosed with ovarian cancer from 1995-1999 and 2002-2004. The EGP was concerned that OS data shown in this study are not comparable to the SOLO-1 trial as the study defined OS from BRCA status confirmation to death. More importantly, the reported OS may not reflect patient survival observed in current practice because the study was published before olaparib was approved for maintenance treatment of adult patients with platinum-sensitive relapsed BRCA mutation on September 1, 2018.[7]

1.4 Detailed Highlights of the EGP Reanalysis

The EGP made the following changes to the submitted economic model:

- Lack of comparative effectiveness of olaparib on overall survival compared to routine surveillance: The submitted model derived OS for patients on routine surveillance from PFS2 data because there was concern that the treatment switching might confound OS data for patients under routine surveillance given that 37.4% of patients in the placebo arm of the SOLO-1 trial received subsequent PARP inhibitors after progression. OS for patients on routine surveillance was derived from PFS2 by applying a treatment effect of olaparib relative to routine surveillance (based on PFS2 data obtained from the SOLO-1 trial) to the olaparib OS curve. The EGP has several concerns regarding the submitter's approach. First, as shown in Figure 1, the OS curves for olaparib and placebo crossed, suggesting that proportional hazard assumptions might be violated. It is therefore inappropriate to derive OS for routine surveillance by applying a treatment effect of routine surveillance to the OS olaparib curve. Second, derived OS data for routine surveillance did not reflect the OS curve for placebo shown in the SOLO-1 trial, which converged to the OS curve of olaparib after 40 months of follow-up. Thirdly, the EGP was unable to apply any statistical approaches to adjust for treatment switching due to the absence of individual-level data. The EGP assessed the impact of this OS assumptions by conducting the following exploratory analyses: 1) assuming patients on routine surveillance to have the same OS as those receiving olaparib, and 2) using parametric survival models to fit the OS data obtained from the SOLO-1 trial for both olaparib and routine surveillance groups instead of deriving OS data for routine surveillance from PFS2 data.

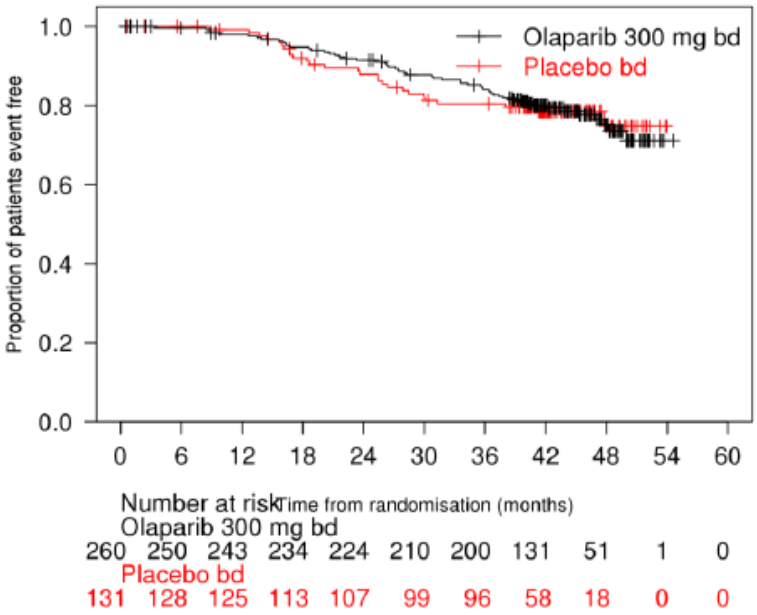

Figure 1. Overall survival data from the SOLO-1 trial

- Long-term data extrapolation and time horizon: Due to the high uncertainty in the long-term PFS and OS data and input from the CGP on the disease course of patients with ovarian cancer, the EGP shortened the time horizon from 30 years to 20, 15, and 10 years. Moreover, the EGP assumed no long-term cure and used extrapolated long-term data obtained from the SOLO-1 trial. The EGP assessed the assumptions on the waning effect, the time at which hazard rates for olaparib were equal to placebo, by varying the waning timepoint between 5 and 15 years. As an exploratory analysis, the EGP shortened the time horizon to the trial data cut off date (~4.17 years).
- Sensitivity analyses of parametric survival models used to predict PFS data: The submitter did not assess the structural uncertainty in the choice of parametric survival models used to extrapolate PFS data for olaparib and routine surveillance beyond the trial. The EGP assessed this uncertainty by using Weibull and log-logistic survival models as opposed to a lognormal distribution used in the main analysis.
- Health utility values: The EGP is concerned that health utility values used in the submitted model were too optimistic. Alternative and lower health utility values obtained from a published US study were therefore used for PFS and PD health states.
- BRCA mutation test cost and mark-up/dispensing fees: As recommended by the CADTH economic evaluation guideline, the EGP included the cost of BRCA mutation test and mark-up/dispensing fees in the EGP reanalysis. Consistent with the submitted model, the EGP assumed that 4.55 patients are required to be tested to identify one individual with BRCA mutation.
- Monitoring and follow-up costs: The EGP addressed the concerns raised by the CGP that patients receiving olaparib are likely to have more frequent monitoring visits by adding the follow-up and monitoring costs estimated from the SOLO-1 trial to health care costs.
- Subsequent use of PARP inhibitor: Due to the absence of evidence supporting re-treatment with a PARP inhibitor and input from the CGP, the EGP assumed that none of the patients in the olaparib arm would receive subsequent PARP inhibitors.

- Cost of olaparib: The submitter calculated the cost of olaparib using the mean dose of olaparib received by patients in the SOLO-1 trial. The EGP had concerns that this approach would underestimate the cost of olaparib in routine practice because the cost per tablet would remain unchanged regardless of dosage. The EGP used the full dose of olaparib with 100% relative dose intensity (600 mg) in the reanalysis.
- Using partial trial data to extrapolate long-term PFS and OS: Instead of using the entire trial data set, the submitter fitted survival models to 24-month trial data. Although the submitter claimed that the survival models with 24-month data had a better model fit than those based on the entire trial data, the submitter did not justify the reason why 24 months were used as a point to start a piecewise modeling approach, the EGP extended the time point when the extrapolated data were used in the model from 24 months to 48 months. Additionally, the EGP used the entire SOLO-1 trial data, i.e. from randomization to the data cut-off date, to predict long-term PFS and OS data.
- The EGP performed a probabilistic analysis using 5,000 Monte Carlo simulations to calculate the best estimate. Furthermore, the EGP's best case used the time horizon to 20 years, considered the entire PFS and OS data observed in the SOLO-1 trial as opposed to 24-month data, added the cost of BRCA mutation test, added the mark-up/dispensing fees, added follow-up costs obtained from the SOLO-1 trial to health services costs derived from ICES, assumed no subsequent PARP inhibitors for patients receiving olaparib, and assumed a full dose of olaparib (600 mg). This best estimate was conducted to address the high uncertainty in the long-term PFS and OS data as well as the proportion of patients who may be re-treated with olaparib and the underestimation of the costs associated with olaparib.

After the posting of the Initial EGR and pERC Initial Recommendation, the EGP considered feedback received from stakeholders on the EGP's reanalysis estimates.

The EGP clarified that the pessimistic scenario where the time horizon was shortened to reflect only the trial data is not part of the EGP's reanalysis of the best case estimate but represents a sensitivity analysis. The EGP reiterated that the best estimate is the point estimate presented in Table 2. The Conclusions of the Final EGR has been revised as follows "Based on the sensitivity analyses conducted by the EGP, ICURs of olaparib compared with routine surveillance may range from $15,721/QALY to $648,080/QALY". The EGP further clarified that the reanalysis did account for a number of inputs including time horizon (see Table 3 or 14). Based on the direction of the CGP, the time horizon was reduced from 30 to 20 years to reflect the clinical course of the disease. Furthermore, other sensitivity analyses were conducted for greater clarity but these were not considered to be clinically realistic and were therefore not included in the EGP's best estimate. In summary, the EGP's best-case estimate was $57,784/QALY gained, with a range as represented in Table 3 or 14.

The EGP also provided clarity on the sponsor's feedback speaking to pERC's interpretation of the uncertainty in long term OS. The EGP agrees with many of the concerns raised by pERC regarding the long-term extrapolation of OS. The uncertainty associated with the long-term benefit of olaparib was due to the EGP's concerns regarding the sponsor's approach used to extrapolate OS beyond the trial. The OS curves for the olaparib and placebo groups crossed, suggesting that proportional hazard assumptions might be violated. It is therefore inappropriate to derive OS for placebo (routine surveillance) by applying a treatment effect of routine surveillance to the olaparib OS curve. In addition, the EGP noted that OS data for routine surveillance incorporated into the economic model by the sponsor did not reflect the OS curve for placebo shown in the SOLO-1 trial, which converged to the OS curve of olaparib after 40 months of follow-up. As approximately 99% of the QALY gained with olaparib was based on extrapolated data, it is important to properly address the methodological

uncertainty associated with the true long-term OS benefit. The better approach to addressing uncertainty could be the use of statistical approaches to adjust for treatment switching and the use of non-proportional hazard models to predict long-term OS data. However, the EGP could not address such methodological uncertainty due to the lack of access to individual level data from SOLO-1. Finally, the EGP noted that the largest ICUR included in the sensitivity analysis table and mentioned in the pERC Initial Recommendation, is $648,000/QALY gained. This number is however not driven by changes in assumptions about OS but rather a reduction of the time horizon to 4.17 years (reflecting only trial data).

Table [3]: Detailed Description of EGP Reanalysis

One-way and multi-way sensitivity analyses					
Description of Reanalysis	ΔC	ΔE QALYs	ΔE LYs	ICUR (QALY)	Δ from baseline submitted ICER
1. *Using OS data obtained from the SOLO-1 trial for both olaparib and routine surveillance*	$19,975	0.469	0.27	$42,614	$21,097
2. *Assuming the same OS after the data cut off (4.17 years)*	$19,337	0.373	0.17	$51,829	$30,312
3. *Assuming the same OS before the cross of olaparib and routine surveillance curves (i.e. at month 36)*	$17,649	0.302	0.15	$58,425	$36,908
4. *Shorten the time horizon from 30 to 20 years*	$73,041	2.514	2.87	$29,049	$7,532
5. *Shorten the time horizon from 30 to 15 years*	$72,910	1.701	1.91	$42,875	$21,358
6. *Shorten the time horizon from 30 to 10 years*	$78,187	0.837	0.90	$93,465	$71,948
7. *Shorten the time horizon from 30 to the data cut off (4.17 years)*	$113,135	0.175	0.16	$648,080	$626,563
8. *Using log-logistic model to predict PFS data for olaparib and routine surveillance*	$75,251	3.146	3.61	$23,917	$2,400
9. *Using Weibull model to predict PFS data for olaparib and routine surveillance*	$66,344	2.245	2.53	$29,551	$8,034
10. *Using predicted PFS data from month 48 onwards instead of month 24 onwards*	$78,245	4.112	4.74	$19,028	-$2,489
11. *Using predicted OS data from month 48 onwards instead of month 24 onwards*	$73,948	3.406	3.91	$21,711	$194
12. *Using the entire trial data to predict PFS and OS data*	$80,297	2.546	2.95	$31,536	$10,019
13. *Using predicted PFS data from the SOLO-1 trial without a waning effect*	$79,060	3.612	4.17	$21,888	$371
14. *Using predicted PFS data from the SOLO-1 trial and applying a waning effect at the data cut off date*	$65,483	1.545	1.73	$42,371	$20,854
15. *Using predicted PFS data from the SOLO-1 trial and applying a waning*	$73,471	2.715	3.11	$27,064	$5,547

effect from year 10					
16. Using alternative health utility values for PFS and PD health states (reducing baseline utilities)	$80,276	2.574	4.31	$31,191	$9,674
17. Including the cost of BRCA mutation test	$88,912	3.731	4.31	$23,831	$2,314
18. Including mark-up/dispensing fees	$81,082	3.731	4.31	$21,733	$216
19. Adding follow-up costs obtained from the SOLO-1 trial to health services costs derived from ICES	$86,797	3.731	4.31	$23,264	$1,747
20. Assuming no re-treatment with PARP inhibitor for patient receiving olaparib	$58,652	3.731	4.31	$15,721	-$5,796
21. Assuming a full dose of olaparib (600 mg)	$97,336	3.731	4.31	$26,089	$4,572
EGP's Reanalysis for the Best Case Estimate					
Description of Reanalysis	ΔC	ΔE QALY	ΔE LY	ICUR	Δ from baseline submitted ICER
Baseline (Submitter's best case)	$80,276	3.731	4.31	$21,517	--
Best case estimate of above parameters					
Combining EGP reanalysis No. 4, 12, 16, 17, 18, 19, 20, 21	$69,501	1.203	1.88	$57,784	$36,267

1.5 Evaluation of Submitted Budget Impact Analysis

The factors that most influence the budget impact analysis include the market share of olaparib, the extent to which the use of olaparib in the front-line setting can replace the second-line olaparib or bevacizumab, the inclusion of drug wastage, and the inclusion of mark-up/dispensing fees. The budgetary impact increased with the greater market share of olaparib and when drug wastage, mark-up, and dispensing fees and the cost of BRCA test were considered. However, the budgetary impact of olaparib decreased if the use of olaparib in the front-line setting displaced the use of bevacizumab in the front-line setting or olaparib in the platinum-sensitive relapsed setting.

The submitted BIA model was transparent, and the submitter conducted comprehensive sensitivity analyses. However, the EGP has concerns regarding the exclusion of mark-up/dispensing fees and drug wastage from the base case. According to the guideline published by the Patented Medicine Prices Review Board (PMPRB), *"drug costs affected by adding the new drug to a given drug plan should be included."*[8] It is, therefore, appropriate to include dispensing and mark-up fees in the BIA main analysis. In addition, the cost for olaparib does not change with dosage. Hence, listing olaparib would add the same budget impact to a drug plan regardless of drug wastage. The EGP explored these parameters by including mark-up/dispensing fees and considering a full dose of olaparib (600 mg) in the reanalysis. Results from the EGP reanalysis revealed that the 3-year budgetary impact increased to $14,702,335 for Ontario and $53,303,071 for Canada.

1.6 Conclusions

The EGP's best estimate of ΔC and ΔE for olaparib when compared to routine surveillance is: $57,784/QALY

- The extra cost of olaparib is $69,501. The *main factors that influence ΔC include the assumption on long-term OS data for patients receiving routine surveillance and a study time horizon.*

- The extra clinical effect of olaparib is 1.203 QALYs. The *main factors that influence ΔE include the assumption on long-term OS data for patients receiving routine surveillance and a study time horizon.*
- *A smaller difference in OS observed in patients receiving olaparib and routine surveillance and a shorter time horizon result in smaller incremental costs and QALYs but larger ICURs.*

Overall conclusions of the submitted model:

- *The submitted model is transparent. Assumptions made are well-described and adequate. However, there is the high uncertainty in the comparative effect of olaparib on overall survival compared to routine surveillance due to immature OS data observed in the SOLO-1 trial and a large proportion of patients on routine surveillance who were receiving subsequent PARP inhibitors. The cost-effectiveness of olaparib compared to routine surveillance is highly sensitive to the approach used to estimate the overall survival of patients on routine surveillance.*
- *Based on the sensitivity analyses conducted by the EGP, ICURs of olaparib* compared with routine surveillance *may range from $15,721/QALY to $648,080/QALY. The pessimistic and unlikely scenario with an ICUR of $648,080/QALY occurred when the time horizon was shortened to reflect only the trial data. In this scenario, olaparib would be associated with the extra cost of $113,135 and additional 0.175 QALYs compared to routine surveillance.*

2 DETAILED TECHNICAL REPORT

This section outlines the technical details of the pCODR Economic Guidance Panel's evaluation of the economic evidence that is summarized in Section 1. Pursuant to the *pCODR Disclosure of Information Guidelines*, this section is not eligible for disclosure. It was provided to the pCODR Expert Review Committee (pERC) for their deliberations.

3 ABOUT THIS DOCUMENT

This Economic Guidance Report was prepared by the pCODR Economic Guidance Panel and supported by the pCODR Genitourinary Clinical Guidance Panel and the pCODR Methods Team. This document is intended to advise the pCODR Expert Review Committee (pERC) regarding resource implications and the cost-effectiveness of olaparib (Lynparza) for ovarian cancer. A full assessment of the clinical evidence of olaparib (Lynparza) for ovarian cancer is beyond the scope of this report and is addressed by the relevant pCODR Clinical Guidance Report. Details of the pCODR review process can be found on the pCODR website (www.cadth.ca/pcodr).

pCODR considers it essential that pERC recommendations be based on information that can be publicly disclosed. Information included in the Economic Guidance Report was handled in accordance with the *pCODR Disclosure of Information Guidelines*. There was no non-disclosable information in the Economic Guidance Report provided to pERC for their deliberations.

This Final Economic Guidance Report is publicly posted at the same time that a pERC Final Recommendation is issued. The Final Economic Guidance Report supersedes the Initial Economic Guidance Report. Note that no revisions were made in between posting of the Initial and Final Guidance Reports.

The Economic Guidance Panel is comprised of economists selected from a pool of panel members established by the pCODR Secretariat. The panel members were selected by the pCODR secretariat, as outlined in the pCODR Nomination/Application Information Package and the Economic Guidance Panel Terms of Reference, which are available on the pCODR website (www.cadth.ca/pcodr). Final selection of the pool of Economic Guidance Panel members was made by the pERC Chair in consultation with the pCODR Executive Director. The Economic Guidance Panel is editorially independent of the provincial and territorial Ministries of Health and the provincial cancer agencies.

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