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Original Article

Cost-effectiveness of olaparib versus routine surveillance in the maintenance setting for patients with *BRCA*-mutated advanced ovarian cancer after response to first-line platinum-based chemotherapy in Singapore

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ABSTRACT

Objective: To evaluate the cost-effectiveness of olaparib as a maintenance treatment versus routine surveillance (RS) in patients with *BRCA* mutated (*BRCA*m) advanced ovarian cancer (OC) following response to first-line platinum-based chemotherapy in Singapore.
Methods: A 4-health state partitioned survival model was developed to simulate the lifetime (50 years) incremental cost-effectiveness ratio (ICER) of olaparib versus RS from a healthcare payer perspective. Progression-free survival, time to second disease progression, and overall survival were estimated using SOLO-1 data and extrapolated beyond the trial period using parametric survival models. Any patient who remained progression-free at year 7 was assumed to be no longer at risk of progression. Mortality rates were based on all-cause mortality, adjusted based on *BRCA1/2* mutation. Health state utilities and adverse event frequencies were from SOLO-1. Drug costs were from local public healthcare institutions. Healthcare resource usage and costs were from local clinician input and publications. A 3% discount rate was applied to costs and outcomes. Deterministic and probabilistic sensitivity analyses (PSA) were performed to assess the robustness of results.
Results: The base-case analysis of olaparib maintenance therapy versus RS resulted in an ICER of Singapore dollar (SGD) 19,822 per quality-adjusted life-year (QALY) gained. The ICER was most sensitive to variations in the discount rate. PSA demonstrated that olaparib had an 87% probability of being cost-effective versus RS at a willingness-to-pay of SGD 60,000 per QALY gained.
Conclusion: Olaparib has a high potential of being a cost-effective maintenance treatment versus RS for patients with *BRCA1/2*m advanced OC after response to first-line chemotherapy in Singapore.

Keywords: Cost-Benefit Analysis; Ovarian Neoplasms; Quality-Adjusted Life Years; Poly(ADP-ribose) Polymerase Inhibitors; Singapore; Biomedical Technology Assessment

Presentation
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Conflict of Interest
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Conceptualization: T.D.S., C.J.J., H.R., G.W., V.A., Y.C.C.; Data curation: T.D.S., C.J.J., H.R., G.W., V.A., Y.C.C.; Formal analysis: T.D.S., C.J.J., H.R., G.W., V.A., Y.C.C.; Investigation: T.D.S., C.J.J., H.R., G.W., V.A., Y.C.C.; Methodology: T.D.S., C.J.J., H.R., G.W., V.A., Y.C.C.; Project administration: G.W., V.A., Y.C.C.; Resources: T.D.S., C.J.J., H.R., Y.C.C.; Supervision: Y.C.C.; Validation: T.D.S., C.J.J., H.R., G.W., V.A., Y.C.C.; Writing - original draft: T.D.S., C.J.J., H.R., G.W., V.A., Y.C.C.; Writing - review & editing: T.D.S., C.J.J., H.R., G.W., V.A., Y.C.C.

INTRODUCTION

Ovarian cancer (OC) is the fifth most common cancer and the seventh most common cause of cancer mortality among women in Singapore [1]. The rate of newly diagnosed patients has increased steadily over the last 40 years, from 7.3 per 100,000 (1975–1979) to 12.8 per 100,000 (2010–2014) [1]. Approximately 51% of women with OC in Singapore are diagnosed at advanced stage (International Federation of Gynecology and Obstetrics [FIGO] III/IV), with a 5-year survival rate of 14%–31% versus 58%–79% for patients diagnosed at early stage (FIGO I/II) [1].

Several clinical practice guidelines, including the National Comprehensive Cancer Network, the American Society of Clinical Oncology, and the Society of Gynecologic Oncology, recommend *BRCA* testing for all women with OC at the time of diagnosis as it informs the most appropriate course of maintenance treatment, and helps identify increased cancer risk in other organs and in family members [2-4]. In Singapore, 25.6% of OC patients tested have *BRCA1/2* mutations [5].

The current standard of care for newly diagnosed advanced OC patients in Singapore is debulking surgery followed by adjuvant platinum-based chemotherapy, which is administered with curative intent. Bevacizumab, a humanized anti-vascular endothelial growth factor monoclonal antibody, may also be used alongside platinum-based chemotherapy and continued as a maintenance treatment in high-risk patients [6]. Following response to platinum-based chemotherapy, patients who were not treated with bevacizumab undergo routine surveillance (RS), comprising follow-up, and general supportive or symptomatic care. Despite the initial treatment effectiveness, approximately 70% of patients with advanced OC relapse within 3 years [7]. Patients who remain platinum-sensitive after relapse may undergo multiple lines of retreatment with platinum-based chemotherapy. However, progression-free intervals shorten with each successive line of treatment, eventually leading to drug resistance and tolerability issues, limiting the long-term continuation in responders [8]. Recurrent OC is thus incurable and ultimately fatal for a substantial number of patients.

Olaparib is a poly (ADP-ribose) polymerase (PARP) inhibitor that exploits synthetic lethality by binding to PARP on DNA at sites of single-strand breaks, resulting in double strand breaks that are irreparable in tumor cells with *BRCA* mutations, and subsequent cell death [9]. SOLO-1 is a Phase 3 multicenter trial that assessed the efficacy and safety of olaparib as switch maintenance therapy versus placebo in patients with *BRCA*-mutated (*BRCA*m) advanced OC after complete or partial response to first-line platinum-based chemotherapy [9]. After a median follow-up of 41 months, patients treated with olaparib had a 70% lower risk of disease progression or death compared to those treated with placebo, and adverse events (AEs) were consistent with olaparib's known safety profile.

In October 2019, olaparib was approved in Singapore as a maintenance treatment for adult patients with germline or somatic *BRCA1/2* mutation after response to first-line platinum-based chemotherapy based on results from SOLO-1 [10]. This approval is in addition to olaparib's previous approved indications: maintenance treatment for adult patients with platinum-sensitive relapsed OC based on results from SOLO-2 and Study 19; monotherapy for adult patients with germline *BRCA*m HER2-negative metastatic breast cancer who have previously been treated with chemotherapy based on results from OlympiAD. [11] Olaparib is the only PARP inhibitor that has received regulatory approval in Singapore. Niraparib and rucaparib are other Food and Drug Administration-approved PARP inhibitors indicated for

patients with relapsed ovarian cancer who have homologous recombinant deficiency (HRD) or *BRCA* mutations respectively [12,13]. However, neither have been approved as a first-line maintenance treatment.

Olaparib received a positive recommendation from the UK National Institute of Health and Care Excellence (NICE) for use within the Cancer Drugs Fund in 2019, as a first-line maintenance treatment following response to first-line platinum-based chemotherapy in patients with *BRCA*m advanced OC [14].

This study aimed to evaluate the cost-effectiveness of olaparib as a maintenance treatment in Singapore compared to RS in patients with *BRCA*m advanced OC following response to first-line platinum-based chemotherapy.

MATERIALS AND METHODS

1. SOLO-1 trial

SOLO-1 is a randomized, double-blind, placebo-controlled trial conducted in 15 countries, including China, Japan and South Korea [9]. Patients (≥18 years, with *BRCA*m advanced OC) were assigned to receive olaparib tablets (300 mg, twice daily) or placebo after completing platinum-based chemotherapy.

SOLO-1 demonstrated a substantial improvement in progression-free survival (PFS) for patients receiving olaparib compared with those receiving placebo as shown by the hazard ratio (HR) 0.30 (95% confidence interval [CI]=0.23–0.41; p<0.001). The median PFS was not reached in the olaparib arm versus 13.8 months in the placebo arm. The estimated difference in median PFS between the treatment arms is approximately 3 years. Furthermore, 52.6% of patients receiving olaparib remained progression-free (as assessed by investigator) at 4 years versus 11.4% of those receiving placebo.

Significant clinical benefit in multiple secondary endpoints was reported in patients in the olaparib arm versus the placebo arm, including a significant improvement in second PFS (PFS2) (HR=0.50; 95% CI=0.35–0.72; p<0.001). Median PFS2 was not reached for patients in the olaparib arm versus 41.9 months for patients in the placebo arm. At data cut-off, the interim overall survival (OS) data were immature (21% maturity) and showed no significant difference between the groups (HR=0.95; 95% CI=0.60–1.53; p=0.890). Median OS was not reached in either group.

2. Model structure

A four-health state partitioned survival model was developed in Microsoft Excel to assess the cost-effectiveness of olaparib tablets versus RS (**Fig. 1**). This modeling approach aligns with the approach taken in NICE appraisals of maintenance treatment in OC and for other advanced cancers [14-16].

The current model assumed that all patients enter the model in the progression-free state and could either stay within that health state, or transition to the progressed disease 1 (after first progression [PD1]) or death state. Patients who progressed to the PD1 state could stay within that health state, or transition to the progressed disease 2 (after second progression [PD2]) or death state.

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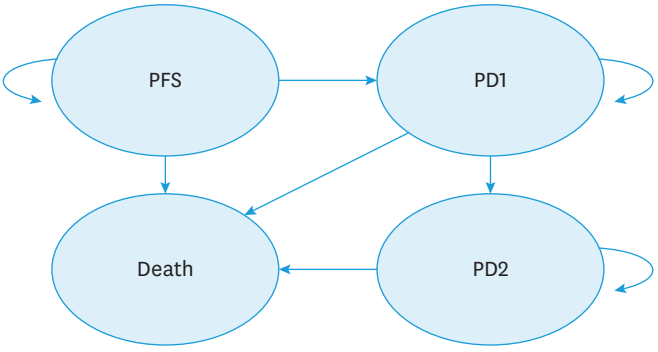

Fig. 1. Partitioned survival model with four health states.
PD1, first progressed disease; PD2, second progressed disease; PFS, progression-free survival.

In line with the Agency for Care Effectiveness (ACE), Singapore and NICE reference cases, a lifetime horizon (50 years) and a cycle length of 1 month (including half cycle correction) were used.

3. Treatment pathway

In line with the SOLO-1 trial, patients were assumed to receive either olaparib (300 mg tablets, twice daily) or RS in the maintenance setting after response to first-line platinum-based chemotherapy. Olaparib was the only PARP inhibitor included as it is the only PARP inhibitor approved in Singapore.

Upon progression, all patients were assumed to receive three subsequent lines of chemotherapy before moving to best supportive care (BSC).

The model assumed that 80.6% of patients would receive a platinum-based chemotherapy regimen while 19.4% would receive a non-platinum-based chemotherapy regimen for all three subsequent lines of treatment [17]. This was based on the percentage of patients who remain progression-free 6 months after first-line chemotherapy in SOLO-1, as this is the widely accepted definition of platinum sensitivity in OC [17]. The percentages of patients receiving each chemotherapy drug were based on local clinician input (**Supplementary Table 1**). Additionally, 20% of patients receiving platinum-based or non-platinum-based chemotherapy regimens were assumed to receive bevacizumab.

Following subsequent lines of chemotherapy, 7.7% of patients in the olaparib arm and 37.4% of patients in the RS arm were assumed to receive olaparib, based on the SOLO-1 trial. This was to ensure the treatment usage (and cost applied) matches the SOLO-1 trial, from which clinical data were obtained.

The treatment algorithm was reviewed and validated by T.D.S. and C.J.J. to ensure the analysis reflected the routine clinical management of *BRCA*m advanced OC in Singapore.

4. Outcomes

The analyses were conducted from the Singapore healthcare payer's perspective, with a discount rate of 3% applied to both costs and outcomes [18]. Clinical outcomes of interest were progression-free life-years (LYs), overall LYs, quality-adjusted life-years (QALYs); economic outcome of interest was the incremental cost-effectiveness ratio (ICER).

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5. Model parameters

Clinical efficacy data

Clinical data, which informed PFS and OS in the model, were obtained from the SOLO-1 trial as it is the only Phase 3 double-blind, randomized, placebo-controlled trial that evaluated the efficacy of olaparib in the population of interest. The baseline characteristics were balanced across treatment arms in the SOLO-1 trial population (**Supplementary Table 2**) and local clinicians validated that these were comparable to the Singapore patient population [9]. PFS, PFS2 and OS data were extrapolated beyond the trial period using parametric survival curves. The PD1 and PD2 states were modeled on the endpoints of PFS and PFS2 from SOLO-1. The death state captured deaths from cancer- and non-cancer-related causes. The process of survival model fitting followed the approaches recommended by the NICE Decision Support Unit [15]. A 'piecewise' method, where Kaplan-Meier data were used up to month 24 with a parametric model thereafter, was explored, as use of a single survival curve to the entire data may not yield plausible estimates of long-term survival. For PFS, a 'piecewise' method with log-normal survival from month 24 onwards for both olaparib and RS was used (**Supplementary Fig. 1** and **Supplementary Table 3**). For PFS2, a 'piecewise' method with exponential model from month 24 onwards for both olaparib and RS was used (**Supplementary Fig. 2** and **Supplementary Table 4**).

For consistency with the PFS analysis, the 'piecewise' method was used for modeling of OS for the olaparib arm, with the log-logistic model selected for the post-24-month period based on goodness of fit, and conservative and plausible median OS estimate for olaparib (**Supplementary Fig. 3** and **Supplementary Table 5**). The survival models fitted to the olaparib arm were used to predict OS for the RS arm with the use of a constant treatment effect to account for the expected longer-term difference in OS between RS and olaparib. This treatment effect was estimated using PFS2, with a predicted gain in median OS of 24 months.

Survival curves for PFS and PFS2 were extrapolated up to a landmark of 7 years, after which point patients who remained progression-free would assume an all-cause mortality rate, based on the age and gender-adjusted Singapore life tables, but adjusted based on the presence of a *BRCA1/2* mutation (excess mortality risk) [19,20]. This was based on clinician advice that patients who remain progression-free at year 7 are expected to be 'exceptional' responders and can be assumed to be long-term survivors. The excess mortality risk was based on the hazard ratio for mortality from Mai et al. [20], which was applied throughout the lifetime of the cohort as a simplifying assumption. For OS, the extrapolated OS curve was used until it crossed the PFS curve. From this point on, the OS followed the trajectory of the PFS curves. The proportion of patients occupying each state over time was estimated based on the PFS, PFS2, and OS curves.

The model independently simulates treatment duration using Kaplan-Meier data from the time of randomization to discontinuation of study drug in SOLO-1. This ensures that modeled drug costs for olaparib reflect drug usage in SOLO-1, including the time on treatment for those who discontinued treatment before 2 years due to unacceptable toxicity.

SOLO-1 data were used to estimate the proportion of patients starting subsequent therapy in each model cycle. The duration of subsequent PARP inhibitor use was simulated based on data from SOLO-2, a phase 3, double-blind, multicenter, randomized controlled trial to evaluate the efficacy, safety and tolerability of olaparib tablets as a maintenance monotherapy in patients who had relapsed OC, and who were in objective response following platinum-based chemotherapy [21]. Due to its second-line setting, SOLO-2 was a suitable data source for simulating the duration of subsequent therapy utilization.

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AEs

Only grade ≥3 treatment-related AEs from SOLO-1 were included in the model as they were more likely to be associated with significant costs and a transient impact on patients' quality-of-life. These included anemia, neutropenia and diarrhea. The model assumed that AEs were mutually exclusive and the incidence was informed by SOLO-1 (**Supplementary Table 6**) [9].

Health-state utility values (HSUV)

In the absence of local data, HSUV were obtained from SOLO-1 which elicited these from patients using the EuroQol-5-dimensions-5-level (EQ-5D-5L) instrument. All completed EQ-5D-5L questionnaires that contained responses to five health domains were then mapped to EQ-5D-3L utilities using the crosswalk method recommended by NICE [22].

The HSUV for progression-free, PD1 and PD2 were 0.819 (standard error [SE]=0.003; 95% CI=0.814–0.824), 0.771 (SE=0.007; 95% CI=0.757–0.785) and 0.680 (SE and 95% CI not reported), respectively. There was no evidence of a meaningful difference in mean HSUV across treatment groups or by study visit; therefore, HSUV data were pooled across treatment groups to increase sample size in the analysis. HSUVs were adjusted over the lifetime time horizon by age-related decrements to reflect aging of the cohort [23].

A one-off QALY adjustment for an AE was modeled based on its disutility multiplied by its assumed duration. In the absence of local data, the duration and the disutility applied were obtained from Swinburn et al., Nafees et al. and a previous NICE technology assessment [14,19,24].

Cost

Only direct costs were incorporated into the model, including costs of somatic *BRCA* testing, drug acquisition, consultations, monitoring, and AE management (**Table 1** and **Supplementary Table 7**). The incidence of *BRCA1/2* mutation used to inform the cost of *BRCA* testing was 27%, which was also validated by local clinicians for the local setting [5]. The cost of olaparib was based on the average selling price across 3 public healthcare institutions in Singapore – National Cancer Center Singapore (NCCS), National University Hospital (NUH) and Tan Tock Seng Hospital. Chemotherapy acquisition costs were based on the average selling price in NCCS and NUH. For each chemotherapy cycle, facility fee (chemotherapy chair time of 2–4 hours) and chemotherapy preparation costs were included. There was no vial sharing in the analysis. The cost of consultations and monitoring were obtained from published local cost-effectiveness studies or directly from public healthcare institutions [26,27]. Costs of managing grade ≥3 AEs were obtained from local publications [26,28].

Table 1. Summary of chemotherapy drug costs

Drug	Cost, SGD (USD*)
Bevacizumab (100 mg/4mL)	762.00 (USD556.26)
Carboplatin (450 mg)	24.47 (USD17.86)
Cisplatin (50 mg)	10.00 (USD7.30)
Docetaxel (80 mg)	280.00 (USD204.40)
Gemcitabine (200 mg)	19.86 (USD14.50)
Paclitaxel (150 mg)	8.26 (USD6.03)
Pegylated doxorubicin (20 mg)	933.37 (USD681.36)

Data sourced from National Cancer Center and National University Hospital, Singapore.
SGD, Singapore dollar; USD, United States dollar.
*Based on an exchange rate of 1SGD=0.73USD [25].

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All costs obtained from literature were inflated to 2018 as appropriate, based on the most recent Monetary Authority of Singapore Health Consumer Price Index [29].

Healthcare resource use

T.D.S. and C.J.J. gave inputs for the frequency and types of relevant outpatient consultation visits and disease monitoring tests used in the olaparib and RS arms (**Supplementary Table 8**). They estimated that 30% of patients with terminal OC received BSC at a hospice while 70% received BSC from home.

6. Sensitivity analyses

One-way deterministic sensitivity analyses (DSA) were conducted to evaluate the impact of individual model parameters on the ICER. Key model parameters were varied independently by the upper and lower range of the 95% CIs, or by ±20% if CIs were not available.

A probabilistic sensitivity analysis (PSA) was also conducted to explore the uncertainty around key model inputs by varying them simultaneously using assigned distributions (**Supplementary Table 9**). Parameters for the models selected for PFS, PFS2 and OS were sampled from multivariate normal distributions. Monte-Carlo simulations were repeated for 1,000 iterations to generate a distribution of ICER outcomes.

As there is no set willingness-to-pay (WTP) threshold in Singapore, a WTP of Singapore dollar (SGD) 60,000 per QALY was used as this was the median of the only ICER range published by ACE for a cost-effective oncology treatment [30].

RESULTS

1. Base-case analysis

The base case analysis of olaparib versus RS resulted in an ICER of SGD 19,822 (USD 14,470) per QALY gained and SGD 16,402 (USD 11,973) per LY gained, with SGD 56,416 (USD 41,184) incremental costs, 2.85 incremental QALYs and 3.44 incremental LYs (**Table 2**).

2. Sensitivity analyses

The 10 factors that affected ICER the most in the DSA are shown in **Fig. 2**. The results were most sensitive to variations in the discount rate and excess mortality rate for the *BRCA*m population. However, the variation of these factors still resulted in ICERs below SGD 60,000 per QALY gained. Varying the costs associated with the health states had less impact on the ICER.

The results of the PSA were also consistent with the base-case analysis. Most ICERs obtained from the simulation fell below SGD 60,000 per QALY (**Supplementary Fig. 4**). Specifically, olaparib was associated with an 87% probability of being cost-effective versus RS at a WTP of SGD 60,000 per QALY (**Fig. 3**).

DISCUSSION

This is the first economic analysis conducted to evaluate the cost-effectiveness of olaparib versus RS in the maintenance setting after response to first-line platinum-based chemotherapy in patients with *BRCA*m advanced OC in Singapore. Our analysis showed

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Table 2. Costs and outcomes of olaparib versus RS

Variables	Olaparib	RS	Incremental difference
Total costs	332,634 (USD242,823)	276,217 (USD201,63)	56,416 (USD41,184)
Total cost of first-line maintenance treatment and subsequent therapies	261,492 (USD190,889)	210,404 (USD153,595)	51,088 (USD37,294)
Cost of PFS state (first 2 years)	14,083 (USD10,281)	3,233 (USD2,360)	10,850 (USD7,921)
Cost of PFS state (subsequent years)	16,245 (USD11,859)	2,489 (USD1,817)	13,756 (USD10,042)
Cost of PD1 state	4,255 (USD3,106)	12,098 (USD8,832)	−7,843 (USD-5,725)
Cost of PD2 state	4,829 (USD3,525)	15,915 (USD11,618)	−11,087 (USD-8,094)
Cost of terminal disease	5,167 (USD3,772)	5,961 (USD4,352)	−794 (USD-580)
Cost of AEs	638 (USD466)	192 (USD140)	446 (USD326)
Cost of *BRCA* testing	25,926 (USD 18,926)	25,926 (USD 18,926)	0
Total benefits (QALYs)	8.53	5.68	2.85
PFS	7.70	3.16	4.54
PD1	0.42	1.19	−0.77
PD2	0.41	1.34	−0.92
AEs	−0.0006	−0.0001	−0.0005
Total benefits (LYs)	11.26	7.82	3.44
PFS	10.08	4.08	6.01
PD1	0.55	1.68	−1.13
PD2	0.63	2.06	−1.44
ICER: Costs/QALY gained	-	-	19,822 (USD14,470)
ICER: Costs/LY gained	-	-	16,402 (USD11,973)

Cost values are presented as SGD (USD*).
AE, adverse event; ICER, incremental cost-effectiveness ratio; LY, life-year; PFS, progression-free survival; PD1, first progressed disease; PD2, second progressed disease; QALY, quality-adjusted life-year; RS, routine surveillance; SGD, Singapore dollar; USD, United States dollar.
*Based on an exchange rate of 1SGD=0.73USD [25].

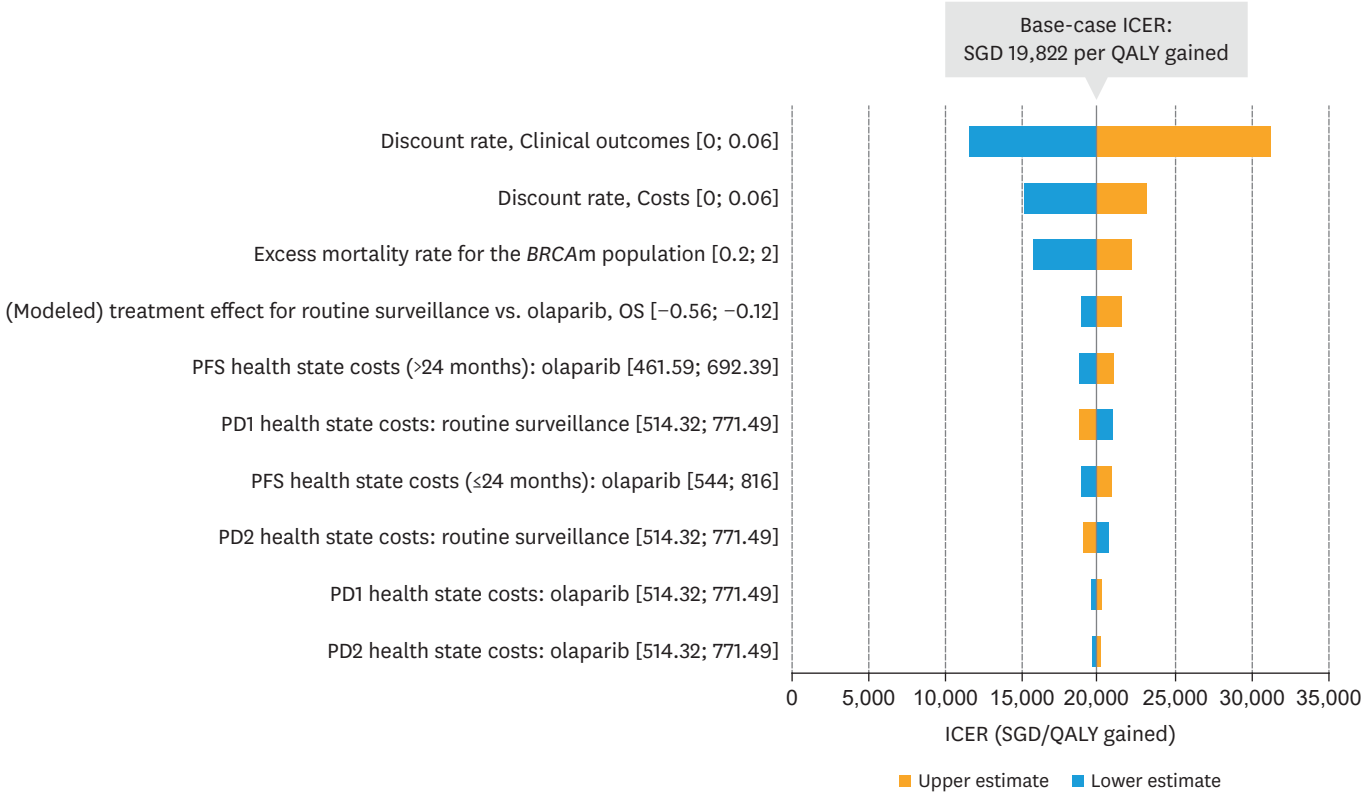

Fig. 2. One-way deterministic sensitivity analysis.
*BRCA*m, *BRCA*-mutated; ICER, incremental cost-effectiveness ratio; OS, overall survival; PD1, first progressed disease; PD2, second progressed disease; PFS, progression-free survival; QALY, quality-adjusted life-year; SGD, Singapore dollar.

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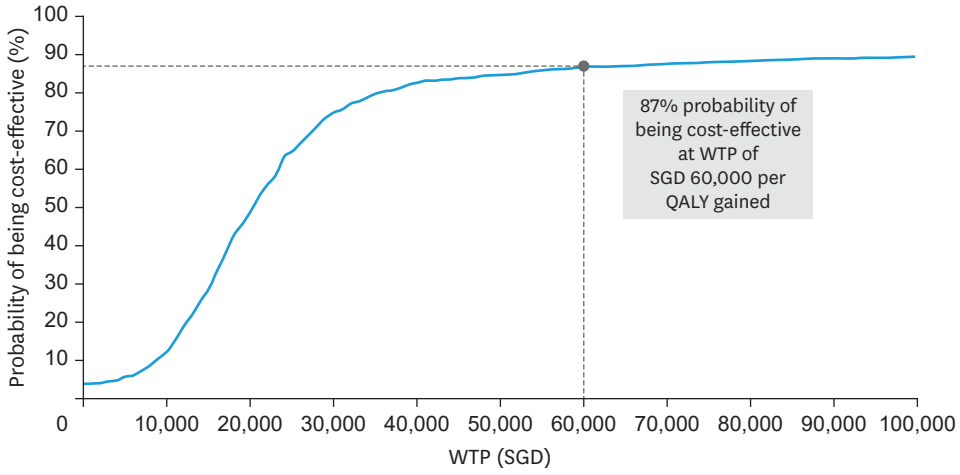

Fig. 3. Probabilistic sensitivity analysis: cost-effectiveness acceptability curve.
QALY, quality-adjusted life-year; SGD, Singapore dollar; WTP, willingness-to-pay.

that olaparib has high potential of being cost-effective versus RS as the resultant base-case ICER of SGD 19,822 (USD 14,470) per QALY gained was much lower than the ICER range of trastuzumab for metastatic breast cancer (SGD 45,000–75,000), which was considered cost-effective in Singapore [30]. These results were generally robust across the sensitivity analyses as variations in model estimates by ±20% consistently resulted in an ICER below the WTP of SGD 60,000 per QALY gained. Moreover, the PSA showed that olaparib had an 87% probability of being cost-effective at the aforementioned WTP.

Our results were comparable to the ICER of the UK-based model that similarly evaluated the cost-effectiveness of olaparib versus RS as a first-line maintenance treatment based on SOLO-1, using the same four health-state model structure. In the base-case analysis, the ICER was £17,480 (USD 22,549) per QALY gained [14], which is below the WTP threshold in the UK (£30,000 per QALY gained) [31]. Moreover, the PFS benefits projected by the model for olaparib vs RS at 5 years were similar to those observed in the 5-year follow-up SOLO-1 data, which supports the credibility of the survival extrapolation (projected: 48.5% vs 17.8%; observed: 48.3% vs 20.5%) [32].

The treatment benefit of olaparib in *BRCA1/2*m OC has augmented the role of *BRCA* testing to inform treatment decisions in mutation-positive patients. While the accessibility of clinical genetic testing in Singapore has improved, the rate of *BRCA* testing among high-risk individuals remains low [33,34]. The high cost of somatic *BRCA* testing has been cited as the main barrier to uptake as testing typically costs approximately SGD 2,000–7,000 which is fully self-paid by patients [33-35].

Our model is subject to limitations. Firstly, OS data from SOLO-1 were only 21% mature but showed no evidence that olaparib had a detrimental effect on survival [9]. The certainty will increase as OS data mature. The variation of OS inputs in the DSA had limited impact on the ICER. Final OS analysis will be conducted at approximately 60% maturity (approximately 206 events), which is expected by the end of 2023. Secondly, the costs of managing AEs (anemia, neutropenia and diarrhea) were largely based on the cost of grade ≥3 AEs associated with other indications such as non-small-cell lung and hematological diseases due to the absence of local data for OC. These costs may not be generalizable to patients with OC.

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However, since the proportion of AE cost in each treatment arm was minimal (0.2% in the olaparib arm versus 0.08% in the RS arm), it did not significantly impact the ICER. Thirdly, the utility inputs in the model were obtained from the SOLO-1 trial which was conducted predominantly in Western countries (81.8% of the study population were White and only 15.1% were Asian) [36]. However, the generalizability of the clinical characteristics of the SOLO-1 population to Singapore patient population was validated by local oncologists.

In conclusion, our results support the use of olaparib as a first-line maintenance treatment after response to first-line platinum-based chemotherapy for patients with *BRCA*m advanced OC as olaparib is not only highly efficacious but also has a strong potential of being a cost-effective treatment option versus RS in Singapore. This would potentially improve patient outcomes and decrease the cost of illness management in subsequent years. Recent preliminary results of ongoing clinical trials also support the extended therapeutic potential of PARP inhibitors in a wider population of patients with advanced OC: in the PAOLA-1 trial, olaparib in combination with bevacizumab in the first-line maintenance setting significantly improved PFS versus placebo plus bevacizumab in the intention-to-treat population, with the greatest benefit observed in the HRD-positive population, regardless of surgical outcome or *BRCA* mutations [37]; in the PRIMA trial, niraparib as a first-line maintenance monotherapy treatment following response to platinum-based chemotherapy also met its primary endpoint of significantly improved PFS versus placebo in women at high risk for relapse with HRD-positive disease and in the overall population [38]; in the VELIA trial, veliparib integrated with first-line chemotherapy and continued in the maintenance setting significantly improved PFS versus first-line chemotherapy alone in newly-diagnosed patients [39]. Further economic analyses should be conducted to evaluate the cost-effectiveness of PARP inhibitors in a wider population of patients with advanced OC.

SUPPLEMENTARY MATERIALS

Supplementary Table 1
Percentage of patients receiving each chemotherapy drug

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Supplementary Table 2
Patient characteristics at baseline in SOLO-1

Click here to view

Supplementary Table 3
Summary of separate AIC and BIC goodness of fit data for PFS

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Supplementary Table 4
AIC and BIC statistics for the models fitted to PFS2

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Supplementary Table 5
Summary of separate AIC and BIC goodness of fit data for OS

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Supplementary Table 6
Incidence, disutility values and duration of AEs

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Supplementary Table 7
Unit costs for healthcare resource and adverse events

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Supplementary Table 8
Monthly frequency of outpatient consultation visits and disease monitoring tests

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Supplementary Table 9
Distribution of model parameters

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Supplementary Fig. 1
Visual representation of fitted parametric models to PFS in the post-24-month period of SOLO-1.

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Supplementary Fig. 2
Plot comparing model fit to PFS2 in the post-24-month period of SOLO-1.

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Supplementary Fig. 3
Fit of independent models to the post-24-month Kaplan-Meier period for OS in SOLO-1.

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Supplementary Fig. 4
Probabilistic cost-effectiveness scatterplot.

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